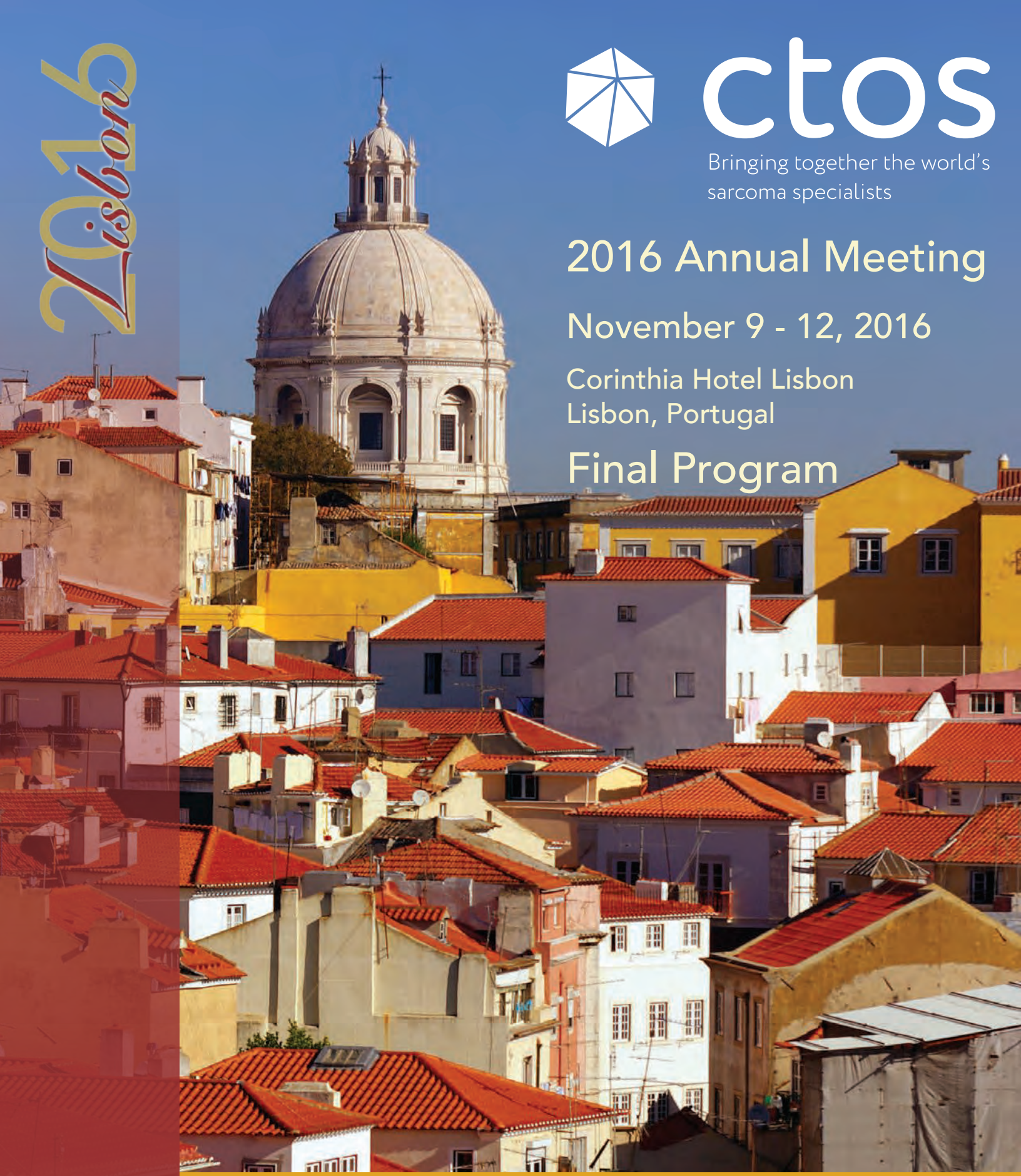


Lisbon 2016

ctos

Bringing together the world's sarcoma specialists

2016 Annual Meeting

November 9 - 12, 2016

Corinthia Hotel Lisbon
Lisbon, Portugal

Final Program

2016 CTOS President: Alessandro Gronchi, MD

Program Chair: Paolo G. Casali, MD

Thank You

The Connective Tissue Oncology Society
greatly appreciates your support of the 2016 Annual Meeting.
Your funding is vital and will advance the medical science
and care of patients with bone and soft tissue tumors.

Platinum Sponsor

Lilly | ONCOLOGY

Gold Sponsors

PharmaMar

janssen Oncology
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

NOVARTIS

Silver Sponsor

BAYER

Additional Sponsor

NANOBIOTIX

ctos

Connective Tissue Oncology Society

2016 Annual Meeting

November 9 - 12, 2016

Corinthia Hotel Lisbon, Lisbon, Portugal

Welcome to Lisbon and the 21st Annual Meeting of CTOS!

We have a wonderful program set for you in a city that is famous for its culture, climate, beauty and history among the few reasons to meet in Lisbon.

This year the programme is shaped around the main disease groups of:
1) Soft Tissue Sarcomas; 2) Osteosarcoma and Ewing Sarcoma; 3) Other Bone and Soft Tissue Neoplasms; 4) GIST.

As usual, new science results will be conveyed through the formal presentations of Abstracts, chosen amongst the many received. They have been grouped as consistently as possible and are followed in each session by either Commentaries or Reviews, in addition to some Round tables. These are aimed at critically putting into perspective the abstracts and/or to expand the scope of the session from the educational point of view. An impressive number of abstracts will be displayed as posters, in front of which vis-a-vis lively discussions are expected to occur throughout the meeting.

All sessions have a title, to make it easier for the audience to appreciate what abstracts and the rest are about. Topics were selected primarily following the abstracts which were received. However, an effort was made to try and cover the whole sarcoma spectrum as widely as possible, to represent the entire world of sarcomas. In the end, the program has been conceived both for the sarcoma experts, probably the main CTOS annual meeting attendees, and those who are starting right now their sarcoma professional journey. Looking at the needs of both was the challenge, clearly difficult to meet, however. A reasonable balance has been attempted and has been asked of the Faculty.

An “app” has been set up to better serve the aims of the program. We hope that it may make the program easier to access but also to exploit, primarily through tools by which attendees will have the opportunity to interact with the presenters even outside the meeting room. Indeed, especially within such a focussed society such as CTOS, the best of the annual meeting is that the sarcoma people have a unique opportunity to have breakfasts, lunches and dinners together for a few days. This creates and strengthens collaborations throughout the world. Our goal is that the “app” may also serve this aim beyond the end of the 2016 CTOS Congress in Lisbon, where we warmly welcome you!

Alessandro Gronchi, MD
2016 CTOS President

Paolo G. Casali, MD
2016 CTOS Program Chair

Welcome

ctos

2016 Lisbon

2016 Board of Directors

ctos

Connective Tissue Oncology Society

2016 Annual Meeting

November 9 - 12, 2016

Corinthia Hotel Lisbon, Lisbon, Portugal

– PROGRAM AT A GLANCE –

Wednesday, 9 November

12:00 pm – 7:00 pm	Poster Session 1 Set Up	*Foyer*
12:00 pm – 7:00 pm	Registration	*Foyer*
7:00 pm – 8:00 pm	Welcome Reception	*Foyer*

Thursday, 10 November

6:30 am – 6:00 pm	Registration	*Foyer*
7:00 am – 8:30 am	Coffee & Poster Viewing	*Foyer*
7:00 am – 6:00 pm	**POSTER SESSION 1: BONE SARCOMAS – GIST**	*Foyer*
8:30 am – 12:30 pm	**– SARC MEETING –**	*Floriana*
	(The SARC meeting is open to all attendees of CTOS)	
	8:30 am **Welcome**	
	8:40 am **Chawla/Rosenfeld Developmental Therapeutics Symposium "Sarcoma Survivorship: Exploring the Issues"**	
	10:15 am **Enhancing Collaboration**	
	10:45 am Break	
	11:00 am **SARC Career Development Awardees' Presentations**	
	Presenting: ***Masanori Hayashi, MD***	
	David Van Mater, MD, PhD	
	11:45 am **Immunotherapy Trials in Sarcoma**	
	12:30 pm **Closing Remarks/Adjourn**	
12:30 pm – 1:30 pm	Lunch	*Sete Colinas*
1:30 pm – 2:00 pm	**– WELCOME - OPENING REMARKS –**	*Floriana*
2:00 pm – 5:50 pm	**ORAL SESSION: SOFT TISSUE SARCOMAS 1**	*Floriana*
2:00 pm – 3:35 pm	**Adjuvant & Neoadjuvant Chemotherapy (including the EUROSARC Round Table)**	*Floriana*
3:35 pm – 4:05 pm	Refreshment Break / View Posters	*Foyer*
4:05 pm – 5:10 pm	**Radiation Therapy**	*Floriana*
5:10 pm – 5:50 pm	**Retroperitoneal STS**	*Floriana*
6:00 pm – 7:00 pm	**POSTER SESSION 1: BONE SARCOMAS – GIST**	*Foyer*

Friday, 11 November

6:30 am – 6:00 pm	Registration	*Foyer*
7:00 am – 8:00 am	Coffee & Networking	*Foyer*
7:00 am – 10:10 am	**POSTER SESSION 1: BONE SARCOMAS – GIST**	*Foyer*
7:00 am – 8:00 am	Executive Committee Meeting	*Ametista*
8:00 am – 11:30 am	**ORAL SESSION: OSTEOSARCOMA & EWING**	*Floriana*
8:00 am – 9:15 am	**Immune Therapy of Osteosarcoma**	*Floriana*
9:15 am – 10:10 am	**Amid Surgery and Dose Intensity: What Matters in Ewing Sarcoma?**	*Floriana*
10:10 am – 10:40 am	Refreshment Break / Poster I Dismantle & Poster 2 Set Up	*Foyer*
10:10 am – 7:00 pm	**POSTER SESSION 2: SOFT TISSUE SARCOMAS**	*Foyer*
10:40 am – 11:30 am	**The Spectrum of Ewing Sarcoma**	*Floriana*
11:30 am – 12:30 pm	**NINA AXELRAD LECTURE:**	*Floriana*
	Looking, Listening, Learning & Luck *(I. Judson)*	

PROGRAM AT A GLANCE, continued

Friday, 11 November, continued

12:30 pm – 1:30 pm	Lunch	*Sete Colinas*
12:30 pm – 1:30 pm	Board of Directors Meeting	*Ametista*
1:30 pm – 6:15 pm	**Oral Session: SOFT TISSUE SARCOMAS 2**	*Floriana*
1:30 pm – 2:25 pm	**WSN Sarcoma of the Year: Alveolar Soft Part Sarcoma**	*Floriana*
2:25 pm – 3:50 pm	**Immune Therapy of STS (including the Young Investigator Award)**	*Floriana*
3:50 pm – 4:20 pm	Refreshment Break / View Posters	*Foyer*
4:20 pm – 5:05 pm	**Uterine Sarcomas**	*Floriana*
5:05 pm – 6:15 pm	**Desmoplastic Small Round Cell Tumor**	*Floriana*
6:15 pm – 7:00 pm	**POSTER SESSION 2: SOFT TISSUE SARCOMAS**	*Foyer*
7:30 pm – 11:00 pm	Gala Reception and Dinner	*Kais Restaurant*

Saturday, 12 November

7:00 am – 5:00 pm	Registration	*Foyer*
7:00 am – 8:00 am	Coffee & Poster Viewing	*Foyer*
7:00 am – 4:00 pm	**POSTER SESSION 2: SOFT TISSUE SARCOMAS**	*Foyer*
8:00 am – 11:30 am	**ORAL SESSION: OTHER BONE & ST NPLS**	*Floriana*
8:00 am – 8:40 am	**Giant Cell Tumor of Bone**	*Floriana*
8:40 am – 9:20 am	**Pigmented Villonodular Synovitis**	*Floriana*
9:20 am – 10:25 am	**Desmoid Fibromatosis**	*Floriana*
10:25 am – 10:50 am	Refreshment Break / View Posters	*Foyer*
10:50 am – 11:30 am	**Extraskeletal Osteosarcoma**	*Floriana*
11:30 am – 12:30 pm	**HERMAN SUIT LECTURE: Advances in Sarcoma Genetics *(F. Mertens)***	*Floriana*
12:30 pm – 1:30 pm	Lunch	*Sete Colinas*
1:30 pm – 3:50 pm	**ORAL SESSION: GIST**	*Floriana*
1:30 pm – 2:05 pm	**Surgery of Residual Disease to TKIs**	*Floriana*
2:05 pm – 2:50 pm	**Long-term Survival of Metastatic GIST**	*Floriana*
2:50 pm – 3:50 pm	**"WT" Gastrointestinal Stromal Tumors**	*Floriana*
3:50 pm – 4:00 pm	**CLOSING REMARKS**	*Floriana*
4:00 pm	Poster 2 Dismantle	*Foyer*
4:00 pm – 5:00 pm	CTOS Members' Business Meeting	*Floriana*
5:00 pm	ADJOURN	

Meeting Registration

The CTOS Registration Desk is located in the *Foyer*.

Registration Hours

Wednesday, 9 November	12:00 pm – 7:00 pm
Thursday – Friday, 10-11 November	6:30 am – 6:00 pm
Saturday, 12 November	7:00 am – 5:00 pm

Onsite Registration Fees

Members	$625
Nonmembers	$900
Fellows / Residents	$425
Allied Healthcare Professionals	$425
Guest at Gala Dinner	$150

Registration fees include scientific program materials, receptions, breaks, lunches, and Friday Gala dinner.

*To receive discounted fees, a letter confirming residency, fellowship, or student status must be emailed to Barbara Rapp at ctos@ctos.org or provided onsite at the meeting. If no proof is received, the difference of the full non-member rate will be applied to the registration transaction.

In soft tissue sarcoma, where does the stroma end and the tumor begin?

The interplay between the microenvironment and tumor may contribute to poor survival outcomes in cancer.[1,2] In soft tissue sarcoma (STS), there is limited histological distinction between the stroma and tumor.[3]

Lilly Oncology is working to unravel the science of STS by improving our understanding of the relationship and shared signaling pathways between the stroma and tumor.[1,2]

For more information, visit global.lillyoncology.com/sts

Lilly | ONCOLOGY

References:
1. Quail DF, Joyce JA. Microenvironmental regulation of tumor progression and metastasis. *Nat Med.* 2013;19:1423-1437.
2. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell.* 2011;144:646-674.
3. Grisendi G, Bussolari R, Veronesi E, et al. Understanding tumor-stroma interplays for targeted therapies by armed mesenchymal stromal progenitors: the Mesenkillers. *Am J Cancer Res.* 2011;1:787-805.

ctos

Connective Tissue Oncology Society

2016 Annual Meeting

November 9 - 12, 2016

Corinthia Hotel Lisbon, Lisbon, Portugal

Wednesday, 9 November, 2016

12:00 pm – 7:00 pm	**Set Up – Poster Session 1: Bone Sarcomas & GIST**	*Foyer*
12:00 pm – 7:00 pm	**Registration**	*Foyer*
7:00 pm – 8:00 pm	**WELCOME RECEPTION**	*Foyer*

Thursday, 10 November, 2016

6:30 am – 6:00 pm	**Registration**	*Foyer*
7:00 am – 8:30 am	**Coffee & Poster Viewing**	*Foyer*
7:00 am – 6:00 pm	**Poster Session 1: Bone Sarcomas & GIST**	*Foyer*
8:30 am – 12:30 pm	**– SARC MEETING –** *(The SARC meeting is open to all attendees of CTOS)*	*Floriana*
12:30 pm – 1:30 pm	**Lunch**	*Sete Colinas*
1:30 pm – 2:00 pm	**– 2016 CTOS ANNUAL MEETING BEGINS –** **Welcome – Opening Remarks**	*Floriana*
1:30 pm	Message from the 2016 CTOS President **WELCOME** **A. Gronchi**	
1:40 pm	Message from Sarcoma PAGs **WELCOME FROM PATIENTS** **M. Wartenberg**	
1:50 pm	Message from the Programme Chair **HOW THIS MEETING WILL WORK** **P.G. Casali**	

2:00 pm – 3:35 pm — – SOFT TISSUE SARCOMAS – — *Floriana*

Adjuvant & Neoadjuvant Therapies

Moderators: **B. Kasper, R.G. Maki**

2:00 pm Paper 001 #2566582
RADIOMIC FEATURES EXTRACTED FROM T1-WEIGHTED MAGNETIC RESONANCE IMAGES PREDICT OUTCOMES IN SOFT TISSUE SARCOMA
***M. B. Spraker**; L. Wootton; W.A. Chaovalitwongse; M.W. Macomber; S.M. Pollack; E.Y. Kim; M. Nyflot*

2:10 pm *Review*
WHAT IS RADIOMICS ABOUT? AND WHAT IS IT FOR?
P. Lambin

2:25 pm *Discussion*

2:40 pm Paper 002 #2546312
HISTOLOGIC RESPONSE TO RADIATION IN SOFT TISSUE SARCOMA (STS): HYALINIZATION/FIBROSIS IS ASSOCIATED WITH FAVORABLE OUTCOME
***I.-M. Schaefer**; J. Hornick; C.M. Barysauskas; C. Raut; S.A. Patel; T.J. Royce; C.D. Fletcher; E.H. Baldini*

2:50 pm Paper 003 #2570259
EXTREMITY SOFT TISSUE SARCOMA: THE IMPACT OF ADJUVANT THERAPIES ACROSS THE MAJOR HISTOLOGICAL SUBTYPES. A RETROSPECTIVE ANALYSIS OF A LARGE MULTI-INSTITUTIONAL DATA BASE.
***D. Callegaro**; R. Miceli; S. Bonvalot; P. Ferguson; D.C. Strauss; A. Levy; A: Griffin; A.J. Hayes; C. Le Péchoux; M. Fiore; A.P. Dei Tos; C. Catton; P.G. Casali; J. Wunder; A. Gronchi*

3:00 pm *EUROSARC Round Table*
IS NEOADJUVANT CHEMOTHERAPY A NEW STANDARD FOR VERY HIGH-RISH STS?
A. Gronchi** and **R. Jones

3:20 pm *Discussion*

3:35 pm – 4:05 pm — Afternoon Break – Visit Posters — *Foyer*

4:05 pm – 5:10 pm

– SOFT TISSUE SARCOMAS –

Floriana

Radiation Therapy

Moderators: **R. Haas, E. Baldini**

4:05 pm Paper 004 #2542801
VORTEX TRIAL: A RANDOMISED CONTROLLED MULTI-CENTRE PHASE III TRIAL OF VOLUME OF POST-OPERATIVE RADIOTHERAPY GIVEN TO ADULT PATIENTS WITH EXTREMITY SOFT TISSUE SARCOMA (STS)
***M. Robinson**; P. Gaunt; R. Grimer; B. Seddon; J. Wylie; A. Davis; D. Hughes; D. Peake; A. Cassoni; D. Spooner; A. Miah; A. Hughes; C. West; K. Venables; L. Billingham*

4:15 pm Paper 005 #2570451
PREOPERATIVE HYPOFRACTIONATED RADIATION THERAPY +/- INTRAOPERATIVE RADIATION THERAPY FOR SOFT TISSUE SARCOMAS OF EXTREMITIES AND SUPERFICIAL TRUNK: AN INSTITUTIONAL EXPERIENCE
***A. De Paoli**; F. Navarria; G. Boz; R. Innocente; V. Canzonieri; A. Buonadonna; M. Forlin; F. Gherlinzoni; G. Bertola*

4:25 pm Paper 006 #2546357
BENEFIT OF ADJUVANT RADIOTHERAPY FOR LOCAL CONTROL, DISTANT METASTASIS, AND SURVIVAL OUTCOMES IN PATIENTS WITH LOCALIZED SOFT TISSUE SARCOMA: COMPARATIVE EFFECTIVENESS ANALYSIS OF AN OBSERVATIONAL COHORT STUDY
***F. Posch**; L. Leitner; B. Liegl-Antzager; A. Wink; M. Stotz; A. Bezan; M. Pichler; A. Gerger; M. Bergovec; H. Stoeger; A. Leithner; J. Szkandera*

4:35 pm Paper 007 #2570207
META-ANALYSIS OF THE EFFECT OF RADIATION THERAPY ON LOCAL RECURRENCE AND OVERALL SURVIVAL IN SOFT TISSUE SARCOMA
***M. Albertsmeier**; F. Roeder; A. Gronchi; A. Rauch; M.K. Angele*

4:45 pm *Commentary*
SHOULD WE USE RADIATION THERAPY IN ALL PATIENTS WITH HIGH-GRADE, >5 CM, DEEP STS?
C. Catton

4:55 pm *Discussion*

5:10 pm – 5:50 pm | – SOFT TISSUE SARCOMAS – | *Floriana*

Retroperitoneal STS

Moderators: **F. Eilber, D. Strauss**

5:10 pm Paper 008 #2565241

SECOND SAFETY ANALYSIS OF A PHASE III RANDOMIZED STUDY OF PRE OPERATIVE RADIOTHERAPY (RT) PLUS SURGERY VERSUS SURGERY ALONE FOR PATIENTS WITH RETRO PERITONEAL SARCOMA (RPS) - EORTC 62092-22092- STRASS-

***S. Bonvalot**; R. Haas; S. Litiere; C. Le Péchoux; D.C. Strauss; C. Swallow; P. Rutkowski; C. Raut; P. Meeus; E. Stoekle; S. Marreaud; A. Gronchi*

5:20 pm Paper 009 #2555264

POST-RELAPSE OUTCOMES AFTER PRIMARY EXTENDED RESECTION OF RETROPERITONEAL SARCOMA: A REPORT FROM THE TRANS-ATLANTIC RPS WORKING GROUP (TARPSWG)

***A.J. MacNeill**; R. Miceli; D.C. Strauss; S. Bonvalot; P. Hohenberger; F. van Coevorden; P. Rutkowski; D. Callegaro; R. Haas; M. Fiore; P.G. Casali; R. Pollock; C. Raut; A. Gronchi; C. Swallow*

5:30 pm *Commentary*

THE CONSENSUS DEVELOPMENT PROCESS OVER SURGERY OF RETROPERITONEAL SARCOMAS

R.E. Pollock

5:40 pm *Discussion*

6:00 pm – 7:00 pm | – BONE SARCOMAS - GIST – | *Foyer*

Poster Session 1

Friday, 11 November, 2016

6:30 am – 6:00 pm	**Registration**	*Foyer*
7:00 am – 8:00 am	**Coffee & Networking**	*Foyer*
7:00 am – 10:10 am	**Poster Session 1: Bone Sarcomas & GIST**	*Foyer*
7:00 am – 8:00 am	**Executive Committee Meeting**	*Ametista*

8:00 am – 9:15 am — – OSTEOSARCOMA & EWING SARCOMA – — *Floriana*

Immune Therapy of Osteosarcoma

Moderators: **A. Kawai, S.P. D'Angelo**

8:00 am — Paper 010 — #2565919
PD-1, PD-L1 AND CD8 EXPRESSION IN HUMAN EWING SARCOMA AND OSTEOSARCOMA PATIENT TUMOR SAMPLES SUGGESTS PUTATIVE ROLE FOR TARGETED CHECKPOINT INHIBITION
***N. Federman**; R. Akiyama; A.S. Singh; S.M. Dry; N. Bernthal; F.C. Eilber; S. Bukata; C. Denny*

8:10 am — Paper 011 — #2570021
TARGETING THE PD-1/PDL-1 SIGNALING PATHWAY FOR THE TREATMENT OF OSTEOSARCOMA LUNG METASTASIS
***P. Dhupkar**; E.S. Kleinerman; N. Gordon*

8:20 am — Paper 012 — #2569674
TUMOR ASSOCIATED MACROPHAGES BUT NOT PD1/PDL1 CHECKPOINTS ARE CRUCIAL EVENTS IN THE INHIBITION OF OSTEOSARCOMA PROGRESSION
***C. Illac**; C. Bouvier; S. Piperno-Neumann; S. Aubert; M.-F. Heymann; J.-M. Guinebretiere; B. Marie; F. Larousserie; G. de Pinieux; E. Mascard; F. Gouin; D. Heymann; L. Brugieres; F. Redini; A. Gomez-Brouchet*

8:30 am — Paper 013 — #2569712
COMBINED TARGETING OF IL6 AND IL8 AXES PREVENTS OSTEOSARCOMA LUNG METASTASIS
***R.D. Roberts**; A. Gross; H. Cam; M.F. Wedekind; S. Winget; P. Houghton*

8:40 am — Paper 014 — #2564941
CHANGES IN HLA CLASS I EXPRESSION, PD-L1 AND T-CELLS DURING OSTEOSARCOMA PROGRESSION: A RETROSPECTIVE STUDY USING IMMUNOHISTOCHEMISTRY
***Y.T. Sundara**; M. Kostine; M.W. Schilham; J.V. Bovée; A.-M. Cleton-Jansen*

8:50 am — *Commentary*
WHERE DO WE GO FROM HERE WITH IMMUNE THERAPY IN OSTEOSARCOMA?
R. Gorlick

9:00 am — *Discussion*

9:15 am – 10:10 am | – OSTEOSARCOMA & EWING SARCOMA – | *Floriana*

Amid Surgery and Dose Intensity: What Matters in Ewing Sarcoma?

Moderators: **P. Picci, J. Wunder**

9:15 am | Paper 015 | #2570256
FACTORS INFLUENCING LOCAL CONTROL IN EWING SARCOMA (EWS) PATIENTS: AN ANALYSIS OF THE DATA OF THE EURO-EWING99 TRIAL
***D. Andreou**; A. Ranft; S. Dijkstra; H. Gelderblom; G. Gosheger; J. Hardes; R. Ladenstein; A. Leithner; M. Paulussen; A. Streitbuerger; B. Timmermann; P.-U. Tunn; E. Wardelmann; H. Juergens; U.T. Dirksen*

9:25 am | Paper 016 | #2570181
DO TREATMENT DELAYS IMPACT PROGNOSIS IN PATIENTS WITH EWING SARCOMA (EWS)? AN ANALYSIS OF THE DATA OF THE EURO-EWING99 TRIAL AND REGISTRY
***U.T. Dirksen**; A. Ranft; D. Baumhoer; B. Timmermann; G. Gosheger; J. Hardes; W. Hartmann; R. Ladenstein; A. Leithner; H.R. Dürr; A. Streitbuerger; P.-U. Tunn; H. Eich; H. Juergens; D. Andreou*

9:35 am | *Round Table*
HIGH-DOSE THERAPY AS A STANDARD IN HIGH-RISK EWING SARCOMA?
J. Whelan** and **N. Marina

9:55 am | *Discussion*

10:10 am – 10:40 am | Morning Break | *Foyer*

10:10 am – 10:40 am | Dismantle – Poster Session 1: Bone Sarcomas & GIST | *Foyer*

10:10 am – 10:40 am | Set Up – Poster Session 2: Soft Tissue Sarcomas | *Foyer*

10:40 am – 7:00 pm | **Poster Session 2: Soft Tissue Sarcomas** | *Foyer*

10:40 am – 11:30 am — – OSTEOSARCOMA & EWING SARCOMA – — *Floriana*

The Spectrum of Ewing Sarcoma

Moderators: **L.J. Helman**, **S.L. Lessnick**

10:40 am Paper 017 #2570427
FREQUENT INACTIVATING GERMLINE MUTATIONS IN DNA REPAIR GENES IN PATIENTsS WITH EWING SARCOMA
***A.S. Brohl**; R. Patidar; C. Turner; X. Wen; B. Gryder; J. Wei; K. Calzone; J. Khan*

10:50 am Paper 018 #2570156
EWSR1-CREB FUSIONS IN SARCOMAS
***S. Z. Millis**; V. Subbiah; O. Holmes; A. Schrock; D. Stockman; J. Elvin; P. Stephens; V. Miller; J. Ross; S. Ali*

11:00 am *Review*
THE SPECTRUM OF EWING SARCOMA AND EWING-LIKE SMALL ROUND CELL SARCOMAS
J. Bovée

11:15 am *Discussion*

11:30 am – 12:30 pm — – NINA AXELRAD LECTURE – — *Floriana*

Moderators: **P.G. Casali, A. Gronchi**

11:30 am *Career Award Lecture*
LOOKING, LISTENING, LEARNING & LUCK
I. Judson

12:30 pm – 1:30 pm Lunch *Sete Colinas*

12:30 pm – 1:30 pm **Board of Directors Meeting** *Ametista*

1:30 pm – 2:25 pm

– SOFT TISSUE SARCOMAS –

Floriana

WSN "Sarcoma of the Year"

Alveolar Soft Part Sarcoma

Moderators: **J.Y. Blay, P. Schoffski**

1:30 pm Paper 019 #2548431
LONG-TERM RESULTS OF THERAPY WITH SUNITINIB IN METASTATIC ALVEOLAR SOFT PART SARCOMA (ASPS) PATIENTS
***P. Rutkowski**; K. Kozak; A. Klimczak; H. Kosela-Paterczyk; S. Falkowski; T. Switaj*

1:40 pm Paper 020 #2569540
PAZOPANIB (P) AND TRABECTEDIN (T) IN ALVEOLAR SOFT PART SARCOMA (ASPS)
***S. Stacchiotti**; O. Mir; B. Vincenzi; A. Fedenko; R.G. Maki; N. Somaiah; M. Brahmi; K. Boye; N. Hindi; H.K. Paterczyk; A. Italiano; E. Kobayashi; S. Provenzano; A. Kawai*

1:50 pm Paper 021 #2570689
EXPLORATORY ANALYSIS OF IMMUNOMODULATION AND APOPTOSIS FACTORS IN ALVEOLAR SOFT-PART SARCOMA: A RETROSPECTIVE STUDY FROM THE SPANISH GROUP FOR RESEARCH ON SARCOMA (GEIS)
***N. Hindi**; J. Martinez-Trufero; A. Carranza; A. Lopez-Pousa; R. Alvarez; J.L. Arranz; J. Martinez; C. Valverde; J.M. Cano; C. Tous; R. Ribas; R. Gonzalez-Campora; J. Martin-Broto*

2:00 pm *Commentary*
DO WE HAVE A STANDARD MEDICAL THERAPY FOR ASPS?
S. Patel

2:10 pm *Discussion*

2:25 pm – 3:50 pm — – SOFT TISSUE SARCOMAS – — *Floriana*

Immune Therapy of STS

Moderators: **S. Bauer, S. Schuetze**

2:25 pm Paper 022 #2566350
OPEN LABEL NON-RANDOMIZED MULTI-COHORT PILOT STUDY OF GENETICALLY ENGINEERED NY-ESO-1 SPECIFIC NY- ESO-1^{C259} SPEAR T-CELLS^{TM} IN HLA-A*02^{+} PATIENTS WITH SYNOVIAL SARCOMA (NCT01343043)
***C. Mackall**; S. D'Angelo; S. Grupp; J. Glod; M. Druta; W. Chow; K. Chagin; M. Mehler; G. Kari; T. Trivedi; T. Holdich; L. Pandite; R. Amado*

2:35 pm *Poster View*
M. Burgess

#2570708
Poster View 1 **PEMBROLIZUMAB (P) IN PATIENTS WITH ADVANCED SOFT TISSUE (STS) AND BONE SARCOMAS (BS): UPDATED EFFICACY RESULTS OF MULTICENTER PHASE II STUDY SARC028 AND CORRELATES OF RESPONSE**
***M. Burgess, MD**; J. Crowley; B. Van Tine; J. Hu; S. Schuetze; S. D'Angelo; S. Attia; D. Priebat; S. Okuno; R. Riedel; L. Davis; S. Movva; D. Reed; D.K. Reinke; H. Tawbi*

Poster View 2 #2562782
ANTI-PD1 THERAPY WITH NIVOLUMAB IN SARCOMA
***L. Paoluzzi**; A. Cacavio; M. Ghesani; A. Karambelkar; A. Rapkiewicz; G. Rosen*

Poster View 3 #2570703
PD-1 AND CTLA-4 INHIBITORS IN UNSELECTED METASTATIC SARCOMA PATIENTS
***E.T. Loggers**; S.M. Pollack; K. Hammer; C. Lee; L.D. Cranmer*

Poster View 4 #2570261
COMBINATION OF PEMBROLIZUMAB AND METRONOMIC CYCLOPHOSPHAMIDE IN PATIENTS WITH ADVANCED SARCOMAS: A FRENCH SARCOMA GROUP STUDY
***A. Italiano**; N. Penel; C. Chevreau; J.-Y. Blay; A. Le Cesne; E. Bompas; S. Piperno- Neumann; S. Cousin; T. Ryckewaert; M. Pulido; A. Bessede; F. Ghiringhelli; M. Toulmonde*

Young Investigator Award Winners

3:05 pm Paper 023

#2570351
INCREASED INFILTRATION OF M2-MACROPHAGES, T-CELLS AND PD-L1 EXPRESSION IN HIGH GRADE LEIOMYOSARCOMAS SUPPORTS IMMUNOTHERAPEUTIC STRATEGIES
***M. Kostine**; A.H. Cleven; C. Vervat; W.E. Corver; M.W. Schilham; A.-M. Cleton-Jansen; J.V. Bovée*

3:15 pm Paper 024

#2556786
INCREASE IN PD-L1 EXPRESSION AFTER PRE-OPERATIVE RADIATION THERAPY FOR SOFT TISSUE SARCOMA
***K.R. Patel**; A. Martinez; S.B. Huff; M. Ford; K. Delman; D. Monson; S. Oskouei; N. Reimer; K. Cardona; M. Yushak; E. Fortune; R. Cassidy; M. Edgar; J. Landry; K. Godette*

3:25 pm

Commentary
WHERE DO WE GO FROM HERE WITH IMMUNE THERAPY IN STS?
W. Tap

3:35 pm

Discussion

3:50 pm – 4:20 pm

Afternoon Break – View Posters *Foyer*

4:20 pm – 5:05 pm

– SOFT TISSUE SARCOMAS –

Floriana

Uterine Sarcomas

Moderators: **P. Dileo, K. Sundby-Hall**

4:20 pm Paper 025 #2570383
A PHASE II RANDOMIZED – NON COMPARATIVE – STUDY ON THE ACTIVITY OF TRABECTEDIN OR GEMCITABINE + DOCETAXEL IN METASTATIC OR LOCALLY RELAPSED UTERINE LEIOMYOSARCOMA (MLRUL) PRETREATED WITH CONVENTIONAL CHEMOTHERAPY
***F. Grosso**; G. Scambia; F. Raspagliesi; N. Colombo; G. Grignani; P.G. Casali; A. Buonadonna; A. Santoro; D. Lorusso; E. Negri; M. D'Incalci; I. Pacchetti; E. Biagioli; R. Fossati; A. Gadducci*

4:30 pm Paper 026 #2544038
PROGNOSTIC FACTORS FOR ADENOSARCOMA OF THE UTERUS
***M.J. Nathenson**; A.P. Conley; H.Y. Lin; W.-L. Wang; A. Lazar; D. Araujo; N. Somaiah; M.A. Zarzour; R. Ratan; S.R. Patel; R.S. Benjamin; V. Ravi*

4:40 pm *Commentary*
RECOGNIZING THE HISTOLOGICAL VARIETY OF UTERINE SMOOTH MUSCLE TUMORS (FROM STUMP ON)?
A.P. Dei Tos

4:50 pm *Discussion*

5:05 pm – 6:15 pm — – SOFT TISSUE SARCOMAS – — *Floriana*

Desmoplastic Small Round Cell Tumor (DSCRT)

Moderators: **C.J. Swallow, W. Van der Graaf**

5:05 pm Paper 027 #2565759
THERAPEUTIC TRIAL FOR PATIENTS WITH DESMOPLASTIC SMALL ROUND CELL TUMORS
***S.M. Federico**; M.E. McCarville; M. Doubrovin; M. Krasin; M.W. Bishop; C. Lam; W. Furman; F. Navid; A. Pappo*

5:15 pm Paper 028 #2570178
RELAPSE OR DISEASE PROGRESSION IN 45 DESMOPLASTIC SMALL ROUND CELL TUMOR PATIENTS FOLLOWING CYTOREDUCTION AND HYPERTHERMIC INTRAPERITONEAL PERFUSION OF CISPLATIN (HIPEC)
***L. Salvador**; W. Huh; J.A. Ludwig; M. McAleer; A. Morani; L. Xiao; A. Hayes-Jordan*

5:25 pm Paper 029 #2543656
ABDOMINAL DESMOPLASTIC SMALL ROUND CELL TUMOR WITHOUT EXTRAPERITONEAL METASTASES: IS THERE A BENEFIT OF HIPEC AFTER MACROSCOPICALLY COMPLETE SURGERY?
***C. Honoré**; V. Atallah; O. Mir; D. Orbach; G. Ferron; C. Le Péchoux; P. Terrier; O. Glehen; V. Minard-Colin; F. Bertucci; J.-Y. Blay; S. Bonvalot; A. Le Cesne; P. Sargos*

5:35 pm Paper 030 #2554404
INTRAPERITONEAL RADIOIMMUNOTHERAPY FOR DESMOPLASTIC SMALL ROUND CELL TUMOR: PRELIMINARY RESULTS OF A PHASE I STUDY (CLINICALTRIALS.GOV NCT01099644)
***S. Modak**; M. LaQuaglia; N. Pandit-Taskar; P. Zanzonico; T. Heaton; J. Lewis; N.-K. V. Cheung; J. Carrasquillo*

5:45 pm *Review*
WHAT WAS TRIED IN DSCRT?
A.M. Frezza

6:00 pm *Discussion*

6:15 pm – 7:00 pm — – SOFT TISSUE SARCOMAS – Poster Session 2

7:30 pm – 11:00 pm — **Gala Reception and Dinner** — *Kais Restaurant*

Saturday, 12 November, 2016

7:00 am – 5:00 pm	**Registration**	*Foyer*
7:00 am – 8:00 am	**Coffee & Poster Viewing**	*Foyer*
7:00 am – 4:00 pm	**Poster Session 2: Soft Tissue Sarcomas**	*Foyer*

8:00 am – 8:40 am — *Floriana*

– OTHER BONE & ST NEOPLASMS –

Giant Cell Tumor of Bone

Moderator: **K. Weiss**

8:00 am — Paper 031 — #2563920

DENOSUMAB TREATMENT OF INOPERABLE OR LOCALLY ADVANCED GIANT CELL TUMOR OF BONE (GCTB) - MULTICENTER RETROSPECTIVE ANALYSIS OUTSIDE CLINICAL TRIAL

***P. Rutkowski**; L. Gaston; A. Borkowska; S. Stacchiotti; G.G. Baldi; E. Palmerini; P.G. Casali; A. Gronchi; M. Parry; H. Gelderblom; S. Ferrari; A. Pienkowski; R. Grimer*

8:10 am — *Review*

STATE-OF-THE-ART APPROACH TO PROBLEMATIC GCT OF BONE

D. Thomas

8:25 am — *Discussion*

8:40 am – 9:20 am — *Floriana*

– OTHER BONE & ST NEOPLASMS –

Pigmented Villonodular Synovitis (PVNS)

Moderators: **A. Fedenko, M. van de Sande**

8:40 am — Paper 032 — #2570093

PRELIMINARY RESULTS ON THE INTERNATIONAL MULTICENTER RETROSPECTIVE TENOSYNOVIAL GIANT CELL TUMOUR DATABASE

***E. Palmerini**; M. Mastboom; F. Verspoor; H. Gelderblom; S. Stacchiotti; P. Daolio; E. Staals; R.G. Maki; M. Fiocco; A. Gronchi; S. Ferrari; P. Picci; B. Schreuder; M. van de Sande*

8:50 am — *Review*

STATE-OF-THE-ART APPROACH TO NODULAR- AND DIFFUSE-TYPE PVNS

L. Randall

9:05 am — *Discussion*

9:20 am – 10:25 am — – OTHER BONE & ST NEOPLASMS – — *Floriana*

Desmoid Fibromatosis

Moderators: **M. Erikson, M. Ghert**

9:20 am Paper 033 #2549467
AGGRESSIVE FIBROMATOSIS RESPONSE TO TAMOXIFEN: MRI FEATURES WITH SYMPTOMATIC CORRELATION - THE ROYAL MARSDEN EXPERIENCE.
***I. Mitra**; Z. Szucs; M. Libertini; C. Fisher; K. Thway; I. Judson; A. Miah; W. Van der Graaf; E. Moskovic; C. Messiou; C. Benson; R. Jones*

9:30 am Paper 034 #2544509
IMATINIB INDUCES SUSTAINED PROGRESSION ARREST IN RECIST PROGRESSIVE DESMOID TUMORS - FINAL RESULTS OF A PHASE II STUDY OF THE GERMAN INTERDISCIPLINARY SARCOMA GROUP (GISG)
***B. Kasper**; V. Gruenwald; P. Reichardt; S. Bauer; M. Sommer; G. Rauch; F. Haller; P. Hohenberger*

9:40 am Paper 035 #2566869
LONG TERM FOLLOW UP OF DESMOID FIBROMATOSIS TREATED WITH PF-03084014, A GAMMA SECRETASE INHIBITOR
***V.M. Villalobos**; A. Jimeno; Lia Gore; A. Elias; B. Hoffner; W. Messersmith*

9:50 am Paper 036 #2562590
SORAFENIB TARGETS THE MAPK/ERK PATHWAY AND RECEPTOR TYROSINE KINASES AND INHIBITS TUMOR GROWTH BY INDUCING TWO DIFFERENT DEATH PATHWAYS IN DESMOID TUMOR CELLS
***D. De Almeida Braggio**; A. Zewdu; G. Lopez; K. Batte; L. Casadei; N. Siva; O.H. Iwenofu; Am Strohecker; D. Lev; R. Pollock*

10:00 am *Commentary*
THE STEPWISE MEDICAL THERAPY OF DESMOIDS
M.M. Gounder

10:10 am *Discussion*

10:25 am – 10:50 am Morning Break – View Posters — *Foyer*

10:50 am – 11:30 am — – OTHER BONE & ST NEOPLASMS – — *Floriana*

Extraskeletal Osteosarcoma

Moderators: **S. Ferrari, D. Priebat**

10:50 am *Poster View*
M. Heng

#2565699
Poster View 5 **THE ROLE OF CHEMOTHERAPY AND RADIATION IN SOFT TISSUE OSTEOSARCOMA**
M. Heng*; T. Ueda; J. Healey; P. Rose; P. Ferguson; A. Gupta; A.A. Raza; G. Holt; D. Blau; X. Niu; N. Bernthal; S. Mottard; D. Davidson; R. Turcotte; J. Wunder*

Poster View 6 #2554781
EXTRASKELETAL OSTEOSARCOMA: A RETROSPECTIVE ANALYSIS OF 28 PATIENTS TREATED AT A SINGLE INSTITUTION
H. Wang*; R. Miao; A. Jacobson; S. Goldberg; D. Harmon; E. Choy; G. Cote; F. Hornicek; P. Nielsen; J. Schwab; K. Raskin; T.F. DeLaney; Y.-L. Chen*

Poster View 7 #2555544
ADJUVANT CHEMOTHERAPY FOR PATIENTS WITH EXTRASKELETAL OSTEOSARCOMA
S. Kakunaga*; T. Wakamatsu; H. Otani; K. Hamada; N. Naka; N. Araki; I. Kudawara; T. Ueda; Y. Aoki; H. Yoshikawa*

11:05 am *Commentary*
SHOULD WE TREAT EXTRASKELETAL OSTEOSARCOMA AS A STS?
R. Benjamin

11:15 am *Discussion*

11:30 am – 12:30 pm — – HERMAN SUIT LECTURE – — *Floriana*

Moderators: **P.G. Casali, A. Gronchi**

11:30 am *Career Award Lecture*
ADVANCES IN SARCOMA GENETICS: IMPLICATIONS FOR CLINICAL DIAGNOSIS
F. Mertens

12:30 pm – 1:30 pm Lunch *Sete Colinas*

1:30 pm – 2:05 pm — – GASTROINTESTINAL STROMAL TUMORS (GIST) – — *Floriana*

Surgery of Residual Disease to TKIs

Moderators: **P. Rutkowski, C. Raut**

1:30 pm Paper 037 #2567795
SURGICAL COMPLEXITY SCORE PREDICTS MORBIDITY FOLLOWING SURGERY FOR METASTATIC GASTROINTESTINAL STROMAL TUMOR (GIST) ON TYROSINE KINASE INHIBITOR (TKI) THERAPY
***M. Fairweather**; G. Li; M. Bertagnolli; C. Raut*

1:40 pm *Commentary*
THE EVOLVING USE OF SURGERY OF RESIDUAL DISEASE IN GIST: FROM PROPGRESSING TO RESPONDING TO FOCALLY PROGRESSING PATIENTS?
P. Hohenberger

1:50 pm *Discussion*

2:05 pm – 2:50 pm — – GASTROINTESTINAL STROMAL TUMORS (GIST) – — *Floriana*

Long-term Survival of Metastatic GIST

Moderators: **M. Montemurro, J. Trent**

2:05 pm Paper 038 #2556232
PREDICTION OF LONG-TERM SURVIVAL IN METASTATIC GASTROINTESTINAL STROMAL TUMOUR: ANALYSIS FROM A LARGE, SINGLE-INSTITUTION PATIENT COHORT
***I. Hompland**; O.S. Bruland; J.P. Poulsen; S. Stoldt; T. Hølmebakk; K. Sundby Hall; K. Boye*

2:15 pm Paper 039 #2556314
THE DANA-FARBER CANCER INSTITUTE (DFCI) EXPERIENCE OF EXTREME LONG-TERM RESPONDERS TO IMATINIB: 16 YEARS OF FOLLOW-UP FROM THE B-2222 TRIAL OF EFFICACY AND SAFETY OF IMATININB MESYLATE IN PATIENTS WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR (GIST)
***E. Ben-Ami**; K. Thornton; P. Merriam; J. Morgan; A. Wagner; S. George; G.D. Demetri*

2:25 pm *Commentary*
HOW WILL WE IMPROVE THE LONG-TERM SURVIVAL OF METASTATIC GIST?
M. Von Mehren

2:35 pm *Discussion*

2:50 pm – 3:50 pm — – GASTROINTESTINAL STROMAL TUMORS (GIST) – — *Floriana*

"Wild-Type" GIST

Moderators: **M.A. Pantaleo, A.J. Wagner**

2:50 pm Paper 040 #2561543
QUADRUPLE NEGATIVE GIST IS A SENTINEL FOR UNRECOGNIZED NEUROFIBROMATOSIS TYPE 1 SYNDROME
***R. Maestro**; D. Gasparotto; S. Rossi; M. Polano; E. Tamborini; M. Sbaraglia; A. Mondello; S. Lamon; R. Bracci; A. Mandolesi; F. Stanzial; G. Mazzoleni; S. Pilotti; A. Gronchi; A.P. Dei Tos*

3:00 pm Paper 041 #2557891
NF1 IS FREQUENTLY MUTATED IN GASTROINTESTINAL STROMAL TUMORS AT THE DUODENAL-JEJUNAL FLEXURE
***M. De Siena**; A. Burgoynge; C.-M. Tang; J. Thorson; K. Jones; P. Fanta; G. Lin; D. Stupack; M. Belinsky; M. von Mehren; O. Harismendy; J. K. Sicklick*

3:10 pm Paper 042 #2570353
PROGNOSTIC SIGNIFICANCE OF WNT SIGNALING PATHWAY MOLECULES IN NON-GASTRIC LOCALIZED GIST PATIENTS. A TISSUE MICROARRAY-BASED (TMA) ANALYSIS. A SPANISH GROUP FOR RESEARCH ON SARCOMA (GEIS) STUDY.
***J. Martin-Broto**; M. Mendiola; L. Guerra; A. Gutierrez; I. Felipe; J. Martinez-Trufero; L.M. de Sande Gonzalez; N. Hindi; C. Tous; C. Valverde; A. Casado; R. Ramos; V. Martinez-Marin*

3:20 pm *Review*
A "CLASSIFICATION" OF "WILD-TYPE" GIST FOR MULTIDISCIPLINARY CLINICAL DECISION-MAKING
K. Janeway

3:35 pm *Discussion*

3:50 pm – 4:00 pm — **Closing Remarks** — *Floriana*

3:50 pm Message from the 2016 CTOS President
GOODBYE FROM LISBON!
A. Gronchi

3:55 pm Message from the 2017 CTOS President
SEE YOU IN MAUI, HAWAII!
S.L. Lessnick

4:00 pm Dismantle – Poster Session 2: Soft Tissue Sarcomas — *Foyer*

4:00 pm – 5:00 pm — **CTOS Members' Business Meeting** — *Floriana*

Rising options in advanced STS: present and future treatment sequences

Symposium within the frame of CTOS 2016

Thursday, November 10th, 2016
19:00 hrs - 20:30 hrs
Plenary room
Corinthia Lisbon Hotel

Rising options in advanced STS: present and future treatment sequences

19.00 - 19.05 **Welcome**
Chair: José Casanova, Portugal

19.05 - 19.20 **The intensity of recent years: recap quiz**
Jean-Yves Blay, France

Sharing Today to draw the close future

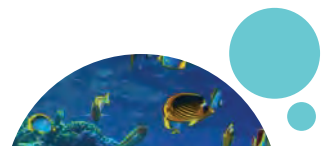
19.20 - 19.35 **Case 1**
Javier Martín-Broto, Spain

19.35 - 19.50 **Case 2**
Peter Reichardt, Germany

19.50 - 20.05 **Case 3**
Silvia Stacchiotti, Italy

20.05 - 20.20 **Anticipating the future: cases wrap-up**
Jean-Yves Blay, France

20.20 - 20.30 **Questions and closing**
José Casanova, Portugal



Pharma Mar

POSTER SESSION 1
– Bone Sarcomas - GIST –

Foyer

Set Up:	*9 November*	*12:00 pm – 7:00 pm*
Poster Exhibition:	*10 November*	*7:00 am – 6:00 pm*
	11 November	*7:00 am – 10:10 am*
Poster Session:	*10 November*	*6:00 pm – 7:00 pm*
Dismantle:	*11 November*	*10:10am – 10:40 am*

P1 - Poster 001 2565304

MOLECULAR EVOLUTION DURING TUMOR PROGRESSION IN GASTROINTESTINAL STROMAL TUMORS (GIST)

Milena Urbini[1]; Manuela Ianni[2]; Annalisa Astolfi[2]; Valentina Indio[1]; Margherita Nannini[1]; Maristella Saponara[1]; Lidia Gatto[1]; Guido Biasco[2]; Maria A. Pantaleo[1]

[1]Department of Specialized, Experimental and Diagnostic Medicine, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; [2]"Giorgio Prodi" Cancer Research Center, University of Bologna, Bologna, Italy

P1 - Poster 002 2558139

A PILOT STUDY ON INTRA-TUMORAL HETEROGENEITY IN GASTROINTESTINAL STROMAL TUMORS

Herbert H. Loong, MBBS, MRCP, FHKCP, FHKAM[1]; Chit Chow[2]; Enders K. Ng[3]; Stephen L. Chan[1]; Anthony W. Chan[2]

[1]Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong, Hong Kong; [2]Department of Anatomical & Cellular Pathology, The Chinese University of Hong Kong, Hong Kong, Hong Kong; [3]Department of Surgery, The Chinese University of Hong Kong, Hong Kong, Hong Kong

P1 - Poster 003 2570784

ABL1 IS AN ANTITARGET IN THE THERAPEUTIC RESPONSE OF GIST CELLS TO IMATINIB MESYLATE THAT ACTS THROUGH INCREASED CDK2/AKT SIGNALING

Jessica L. Rausch[1]; Sergei Boichuk[1]; Areej Ali[1]; Donna M. Lee[1]; Sneha Patil[1]; Matthew F. Brown[1]; Kathleen R. Makielski[1]; Ying Liu[1]; Takahiro Taguchi[1]; Shih-Fan Kuan[2]; Anette Duensing, MD[1]

[1]University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA; [2]University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

P1 - Poster 004 2570730

THE PROTEIN TRANSLATION INHIBITOR HOMOHARRINGTONINE IS A PROMISING NEW AGENT FOR THE TREATMENT OF GASTROINTESTINAL STROMAL TUMORS (GISTS)

Sneha Patil[1]; Parker Trent[1]; Donna M. Lee[1]; Areej Ali[1]; Jessica L. Rausch[1]; Takahiro Taguchi[2]; Anette Duensing, MD[1]

[1]University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA; [2]Kochi Medical School, Kochi, Japan

P1 - Poster 005 2562622

THE HEDGEHOG PATHWAY REGULATES KIT EXPRESSION AND CELL VIABILITY IN HUMAN GASTROINTESTINAL STROMAL TUMORS

Chih-Min Tang[4]; Sabriya A. Syed[1]; Tracy Lee[4]; Eileen Shi[4]; Juliann Chmielecki[2]; Deborah Morosini[2]; Kai Wang[2]; Jeffrey Ross[2]; Michael Kendrick[5]; Michael Bardsley[1]; Martina De Siena[4]; Junhao Mao[3]; Olivier Harismendy[6]; Tamas Ordog[1]; Jason K. Sicklick, MD[4]

[1]Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN, USA; [2]Foundation Medicine, Inc., Cambridge, MA, USA; [3]Department of Molecular, Cell and Cancer Biology, University of Massachusetts, Worchester, Worcester, MA, USA; [4]Division of Surgical Oncology, Department of Surgery, University of California, San Diego, La Jolla, CA, USA; [5]Department of Surgery, Mayo Clinic, Rochester, MN, USA; [6]Division of Biomedical Informatics, University of California, San Diego, La Jolla, CA, USA

P1 - Poster 006 2563845

BRAIN METASTASIS FROM GASTROINTESTINAL STROMAL TUMOR: A CASE REPORT

Ana M. Simas; Jose Dinis; Ana M. Ferreira; Mariana Afonso; Marta Soares

Medical Oncology, IPO-Porto, Porto, Porto, Portugal

P1 - Poster 007 2533131

THE TOXICITY AND EFFICACY PROFILE OF REGORAFENIB (RG) IN GASTROINTESTINAL TUMOR (GIST) PATIENTS (PTS) USING AN ALTERNATE DOSING REGIMEN

Gustavo Schvartsman, MD[1]; Michael J. Wagner[1]; Andrea G. Barbo[6]; Heather Y. Lin[6]; Behrang Amini[2]; Van A. Trinh[3]; Wei-Lien Wang[4]; SR Patel[5]; Robert S. Benjamin[5]; Neeta Somaiah[5]

[1]Department of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Department of Radiology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Department of Pharmacy Clinical Programs, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]Department of Sarcoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [6]Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

P1 - Poster 008 2562704

SURGICAL RESECTION IMPROVES THE SURVIVAL OF ADOLESCENTS AND YOUNG ADULTS WITH METASTATIC GASTROINTESTINAL STROMAL TUMORS: A POPULATION-BASED ANALYSIS IN THE UNITED STATES

Katherine Fero[1]; Taylor Coe[1]; Paul Fanta[3]; James Murphy[2]; Jason K. Sicklick, MD[1]

[1]Division of Surgical Oncology, Department of Surgery, University of California, San Diego, La Jolla, CA, USA; [2]Department of Radiation Oncology, University of California, San Diego, La Jolla, CA, USA; [3]Division of Hematology and Oncology, Department of Medicine, University of California, San Diego, La Jolla, CA, USA

P1 - Poster 009 2565842

QUANTITATING CIRCULATING TUMOR DNA IN PEDIATRIC SARCOMA PATIENTS USING CAPP-SEQ

Avanthi T. Shah[1]; Jake Chabon[2]; Tej Azad[2]; Marcus Breese[1]; Aviv Spillinger[1]; Stanley Leung[1]; Maximilian Diehn[2]; Ash Alizadeh[2]; Alejandro Sweet-Cordero[1]

[1]Pediatrics, Stanford University, Belmont, CA, USA; [2]Stanford University, Stanford, CA, USA

P1 - Poster 010 2570517

ERBB4 PROMOTES CELL SURVIVAL IN OSTEOSARCOMA LUNG METASTASIS THROUGH REGULATION OF NDRG1

Hongsheng Wang; Zhengdong Cai; Yingqi Hua, MD, PhD

Orthopedics, Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai, China

P1 - Poster 011 2547973

TARGETING STRESS GRANULES AS A NOVEL THERAPEUTIC APPROACH FOR HIGH-RISK CHILDHOOD SARCOMAS

Amal M. EL Naggar, PhD[1]; Hongwei Cheng[2]; Syam Prakash Somasekharan[3]; Yemin Wang[4]; Bo Rafn[1]; Poul H. Sorensen[1]

[1]Pathology and Laboratory Medicine, The University of British Columbia, Vancouver, BC, Canada; [2]Vancouver Prostate Centre, University of British Columbia, Vancouver, BC, Canada; [3]BC Cancer Research Center, University of British Columbia, Vancouver, BC, Canada

P1 - Poster 012 2565739

GENOME-WIDE MISTARGETING OF ONCOGENIC SWI/SNF(BAF) COMPLEXES IN SMARCB1(BAF47)-DEFICIENT SARCOMAS

Robert Nakayama, MD, PhD[1]; John Pulice[2]; Robert T. Williams[2]; Alfredo M. Valencia[2]; GD Demetri[3]; Cigall Kadoch[2]

[1]Orthopaedic Surgery, Keio University Hospital, Tokyo, Japan; [2]Pediatric Oncology, Dana Farber Cancer Institute, Boston, MA, USA; [3]Medical Oncology, Dana Farber Cancer Institute, Boston, MA, USA

P1 - Poster 013 2544143

THE EFFECTIVENESS OF ZOLEDRONIC ACID AS A RADIOSENSITIZER FOR RADIOTHERAPY AGAINST OSTEOSARCOMA

Chang-Bae Kong; Kyung-Hee Lee; Eun Ho Kim

KCCH, Seoul, Korea (the Republic of)

P1 - Poster 014 2555397

NON-INVASIVE BIOLUMINESCENCE IMAGING OF ENGINEERED SARCOMA TUMORS IN THE LIVING CHICKEN EMBRYO

Benedict Jefferies[1]; Florian Lenze[1]; Anuja Sathe[2]; Rüdiger von Eisenhart-Rothe[1]; Roman Nawroth[1]; Philipp Mayer-Kuckuk[2]
[1]Orthopedics, Technical University Munich, Munich, Germany; [2]Urology, Technical University Munich, Munich, Germany

P1 - Poster 015 2559102

CONCOMITANT REPROGRAMMING OF TUMOR CELL DIFFERENTIATION AND IMMUNE ENVIRONMENT INHIBITS OSTEOSARCOMA METASTATIC POTENTIAL

Claudia Chiodoni, PhD[1]; Ilaria Torselli[1]; Claudio Tripodo[2]; Chiara Ratti[1]; Cecilia Garofalo[3]; Silvia Galvan[1]; Maria Cristina Manara[3]; Katia Scotlandi[3]; Mario Paolo Colombo[1]
[1]Department of Experimental Oncology and Molecular Medicine, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [2]Department of Health Science, Human Pathology Section, University of Palermo, Palermo, Italy; [3]Experimental Oncology Lab, Istituto Ortopedico Rizzoli, Bologna, Italy

P1 - Poster 016 2562030

EFFECT OF BONE MICROENVIRONMENT IN JAW OSTEOSARCOMA DEVELOPMENT

Hélios Bertin[1]; Romain Guiho[2]; Benoit Piot[1]; Pierre Corre[1]; Anne Brouchet-Gomez[3]; Françoise Redini[2]
[1]Oral and Maxillo-facial Surgery, CHU de Nantes, Nantes, France; [2]UMR957, Laboratoire de Physiopathologie de la Résorption Osseuse, Nantes, France; [3]Laboratoire d'Anatomie et Cytologie Pathologiques, Oncopôle - CHU de Toulouse, Toulouse, France

P1 - Poster 017 2566098

RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS INDUCED OSTEOSARCOMA CANCER STEM-LIKE CELLS WITH CO-EXPRESSION OF CD133

Akihiko Takeuchi, MD, PhD[1]; Yasuhiko Yamamoto[2]; Seiichi Munesue[2]; Norio Yamamoto[1]; Katsuhiro Hayashi[1]; Takashi Higuchi[1]; Kensaku Abe[1]; Yuta Taniguchi[1]; Hisaki Aiba[1]; Hiroyuki Tsuchiya[1]
[1]Orthopaedic Surgery, Kanazawa University Graduate School of Medical Science, Kanazawa, Japan; [2]Biochemistry and Molecular Vascular Biology, Kanazawa University Graduate School of Medical Sciences, Kanazawa, Japan

P1 - Poster 018 2565773

TRENDS IN INCIDENCE AND OUTCOME OF GASTROINTESTINAL STROMAL TUMORS IN THE NETHERLANDS IN THE IMATINIB ERA

Ronald Tielen; Rob Verhoeven; Johannes Bonenkamp; Valery Lemmens; Winette van der Graaf; Johannes de Wilt
Radboudumc, Nijmegen, Netherlands

P1 - Poster 019 2553097

THE ANDROGEN RECEPTOR (AR) IS A POTENTIAL NOVEL PROGNOSTIC MARKER AND ONCOGENIC TARGET IN OSTEOSARCOMA WITH DEPENDENCE ON CDK11

Yunfei Liao; Slim Sassi; Stefan Halvorsen; Yong Feng; Edwin Choy; Gregory Cote; Francis Hornicek; Zhenfeng Duan
Massachusetts General Hospital, Boston, MA, USA

P1 - Poster 020 2566414

THE CDK4 & 6 INHIBITOR ABEMACICLIB BLOCKS TUMOR GROWTH IN PRECLINICAL MODELS OF PEDIATRIC EWING'S SARCOMA

Michele Dowless, BS; Caitlin May; Timothy Holzer; Wayne Blosser; Sean Buchanan; Gerard Oakley; Richard Beckmann; Louis F. Stancato
Eli Lilly and Company, Indianapolis, IN, USA

P1 - Poster 021 2570258

TARGETING THE EIF4E-MEDIATED TRANSLATIONAL MACHINERY OF EWING SARCOMA: THERAPEUTIC CONVERGENCE OF THE MTOR AND MNK PATHWAYS

Joseph A. Ludwig, MD[1]; Brian A. Menegaz[1]; Salah Lamhamedi-Cherradi[1]; Najat Daw[2]; Ravin Ratan[1]; Vivek Subbiah[3]; Hesham Amin[4]; Alexander Lazar[4]; Robert S. Benjamin[1]

[1]Sarcoma Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA; [2]Pediatrics, MD Anderson Cancer Center, Houston, TX, USA; [3]Investigational Cancer Therapeutics, MD Anderson Cancer Center, Houston, TX, USA; [4]Pathology, MD Anderson Cancer Center, Houston, TX, USA

P1 - Poster 022 2566290

HIGH-THROUGHPUT CHEMICAL SCREENING IDENTIFIES FOCAL ADHESION KINASE (FAK) AND AURORA KINASE B INHIBITION AS A SYNERGISTIC TREATMENT COMBINATION IN EWING SARCOMA

Brian Crompton, MD[1]; Sarah Wang[1]; Elizabeth Hwang[1]; Rajarshi Guha[2]; Matthew Boxer[2]; Crystal McKnight[2]; Min Shen[2]; Nicole Melong[3]; Chansey Veinotte[3]; Jason Berman[3]; Matthew Hall[2]; Mindy Davis[2]; Kimberly Stegmaier[1]

[1]Pediatric Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [2]National Center for Advancing Translational Sciences, Rockville, MD, USA; [3]Dalhousie University, Halifax, NS, Canada

P1 - Poster 023 2566408

AN EWS-FLI1-SYNTHETIC LETHAL SHRNA SCREEN IDENTIFIES CANDIDATE TUMOR-CELL SPECIFIC THERAPEUTIC TARGETS IN EWING SARCOMA

Christiane Schaefer, PhD Student[1]; Nikhil Mallela[2]; Philipp Berning[1]; Jochen Seggewiß[3]; Eberhard Korsching[2]; Uta T. Dirksen[1]; Jenny C. Potratz[1]

[1]University Children's Hospital Münster, Münster, Germany; [2]Institute of Bioinformatics, Westfälische Wilhelms-Universität Münster, Münster, Germany; [3]Institute of Human Genetics, University Hospital Münster, Münster, Germany

P1 - Poster 024 2564896

COMBINATION OF EPIGENETIC DRUGS (SAHA-HCI2509) SYNERGISTICALLY AFFECTS PROLIFERATION IN EWING SARCOMA

Lourdes Hontecillas-Prieto[1]; Daniel J. Garcia-Dominguez[1]; Pablo Rodríguez-Núñez[1]; Rosa García-Mejías[1]; Guillem Pascual- Pastó[2]; Angel Montero Carcaboso[2]; Laura Romero-Pérez[1]; Juan Diaz-Martin[1]; Enrique De Álava *Casado[1]*

[1]Molecular Pathology, Instituto de Biomedicina de Sevilla (IBiS)/Hospital Virgen del Rocio/CSIC/Universidad de Sevilla, Seville, Spain; [2]Developmental Tumor Biology Laboratory, Fundacio Sant Joan de Deu, Department of Pediatric Hematology and Oncology, Hospital Sant Joan de Deu, Barcelona, Spain

P1 - Poster 025 2556655

MOLECULAR TARGETING OF CDK4/6 AND IGF-1R IN A *FUS-ERG* FUSION DOXORUBICIN-RESISTANT EWING SARCOMA/PNET PATIENT-DERIVED ORTHOTOPIC XENOGRAFT (PDOX) MODEL

Takashi Murakami, MD[1]; Arun S. Singh[2]; Tasuku Kiyuna[1]; Sarah M. Dry[3]; Yunfeng Li[3]; Kentaro Igarashi[1]; Kei Kawaguchi[1]; Yong Zhang[1]; Tara A. Russell[4]; Mark A. Eckardt[4]; Jane Yanagawa[4]; Noah Federman[5]; Itaru Endo[6]; Frederick C. Eilber[4]; Robert M. Hoffman[1]

[1]AntiCancer, Inc., San Diego, CA, USA; [2]Division of Hematology-Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [3]Department of Pathology, University of California Los Angeles, Los Angeles, CA, USA; [4]Division of Surgical Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [5]Department of Pediatrics and Department of Orthopaedics, University of California, Los Angeles, Los Angeles, CA, USA; [6]Department of Gastroenterological Surgery, Yokohama City University, Graduate School of Medicine, Yokohama, Japan

P1 - Poster 026 2553440

DEPENDENCE RECEPTORS INTERFERENCE TO PREVENT OSTEOSARCOMA PROGRESSION AND METASTATIC DISSEMINATION

Morgane Monchanin[1]; Jean Baptiste Langlois[2]; François Leloarer[1]; Clementine Favrot[3]; Perrine Marec-Bérard[1]; Agnes Bernet[3]; Jean-Yves Blay[1]; Aurelie Dutour, PhD[1]

[1]Centre Léon Berard, Lyon, Rhone Alpes, France; [2]CERMEP, Lyon, France; [3]CRCL, Lyon, France

P1 - Poster 027 2554630

INHIBITION OF BET BROMODOMAIN PROTEINS IN EWING SARCOMA DOWN REGULATES THEIR TRANSCRIPTIONAL PROGRAM AND BLOCKS TUMORIGENICITY AND INVASIVENESS

Fiona A. Becker-Dettling[1]; Tim Hensel[1]; Chiara Giorgi[3]; Oxana Schmidt[1]; Julia Calzada-Wack[2]; Frauke Neff[2]; Beat W. Schäfer[3]; Stefan Burdach[1]; Günther Richter[1]

[1]Klinikum Rechts der Isar, Technische Universität München and Comprehensive Cancer Center Munich (CCCM), Children's Cancer Research Centre and Department of Pediatrics, München, Germany; [2]Helmholtz-Zentrum München, Institute of Pathology, Munich, Germany; [3]University Children's Hospital, Department of Oncology and Children's Research Center, Zurich, Switzerland

P1 - Poster 028 2537429

OVEREXPRESSION OF C/EBPβ-1 IN EWING SARCOMA CELLS INCREASES TRANSFORMATION AND ENRICHES CHEMOTHERAPY-RESISTANT CANCER STEM CELLS

Jamie Gardiner[1]; Lisa M. Abegglen[1]; Xiaomeng Huang[1]; Bryce Carter[2]; Elizabeth Schackmann[2]; Marcus Stucki[1]; Christian Paxton[3]; Lor Randall[4]; James Amatruda[5]; Angelica Putnam[6]; Heinrich Kovar[7]; Stephen L. Lessnick[8]; Joshua Schiffman[1]

[1]Departments of Pediatrics and Oncological Sciences, Huntsman Cancer Institute, University of Utah, Salt Lake CIty, UT, USA; [2]School of Medicine, University of Utah, Salt Lake City, UT, USA; [3]ARUP Institute for Clinical and Experimental Pathology, Salt Lake City, UT, USA; [4]Sarcoma Services, Department of Orthopaedic Surgery, University of Utah, Salt Lake City, UT, USA; [5]Departments of Pediatrics, Internal Medicine, and Molecular Biology, University of Texas Southwestern, Dallas, TX, USA; [6]Department of Pathology, University of Utah, Salt Lake City, UT, USA; [7]Children's Cancer Research Institute, Vienna, Austria; [8]Center for Childhood Cancer and Blood Disorders, Nationwide Children's Hospital, and the Division of Pediatric Heme/Onc/BMT, The Ohio State University, Columbus, OH, USA

P1 - Poster 029 2569795

D-3-PHOSPHOGLYCERATE DEHYDROGENASE (PHGDH) INHIBITION TARGETS SERINE BIOSYNTHESIS IN OSTEOSARCOMA

Richa Rathore; Bethany Prudner; Jeff Kremer; Abigail V. Giles; Brian Van Tine

Medical Oncology, Washington University in St. Louis, University City, MO, USA

P1 - Poster 030 2533471

PROTEOMIC APPROACHES REVEAL THE INHIBITATION OF THE IRE1/XPB1 PATHWAY REDUCES TUMOR GROWTH IN EWING'S SARCOMAS

Yu Tanabe[1]; Yoshiyuki Suehara[1]; Shinji Kohsaka[2]; Kenta Mukaihara[1]; Daisuke Kubota[1]; Keisuke Akaike[1]; Midori Ishii[1]; Saiko Kazuno[3]; Reiko Mineki[3]; Kazuo Kaneko[1]; Marc Ladanyi[2]; Tsuyoshi Saito[4]

[1]Department of Orthopedics, Juntendo University, Tokyo, Japan; [2]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [3]Laboratory of Biochemical Analysis, Central Laboratory of Medical Sciences, Juntendo University, Tokyo, Japan; [4]Department of Human Pathology, Juntendo University, Tokyo, Japan

Poster 031 2570670

INDOCYANINE GREEN ANGIOGRAPHY QUANTIFIES PRIMARY AND METASTATIC OSTEOSARCOMA TUMOR BURDEN IN AN IMMUNOCOMPETENT MOUSE MODEL

Mitchell S. Fourman, MD, M.Phil[2]; Adel Mahjoub[1]; Jonathan Mandell[2]; Jared Crasto[2]; Shibing Yu[2]; Jessica Tebbets[2]; Kurt Weiss[2]

[1]School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA; [2]Orthopaedic Surgery, University of Pittsburgh, Pittsburgh, PA, USA

P1 - Poster 032 2570663

FUNCTIONAL AND MOLECULAR CHARACTERIZATION OF B CELLS AND PLASMOCYTES IN OSTEOSSARCOMA

Sandra Santos, Resident; Ruben Fonseca; João Freitas; Paulo F. Tavares; Jose M. Casanova

Ortopedia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

P1 - Poster 033 2570483

EXPRESSION OF PRAME IN OSTEOSARCOMA TUMOR SPECIMENS

J. Andrew Livingston, MD[1]; Jen-Wei Tsai[2]; Shailesh Advani[3]; Alexander Lazar[4]; Anthony P. Conley[1]; Najat Daw[3]; Wei-Lien Wang[4]

[1]Sarcoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Department of Anatomic Pathology, E-Da Hospital, Kaohsiung City, Taiwan; [3]Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

P1 - Poster 034 2569655

TARGETING EWING SARCOMA CELLS AND THE TUMOR MICROENVIRONMENT WITH OMTX003 ANTI-ENDOGLIN MONOCLONAL ANTIBODIES

Pilar Puerto-Camacho, Biochemist[1]; Brian A. Menegaz[2]; Ana Teresa Amaral[1]; José Luis Ordóñez[4]; Saioa Domínguez[3]; Carmen Jordán-Pérez[1]; Michele Biscuola[1]; María José Robles[1]; María López-Álvarez[1]; Juan Diaz-Martin[1]; Salah Lamhamedi-Cherradi[2]; Keri Schadler[5]; Myriam Fabre[3]; Joseph A. Ludwig[2]; Enrique de Alava[1]

[1]Department of Molecular Pathology, Institute of Biomedicine of Seville (IBiS), Seville, Spain; [2]Department of Sarcoma Medical Oncology, University of Texas MD Anderson Cancer Center (MDACC), Houston, TX, USA; [3]Oncomatryx Biopharma SL, Derio, Bizkaia, Spain; [4]Cancer Research Center (University of Salamanca-CSIC), Salamanca, Spain; [5]Department of Pediatrics Research, MD Anderson Cancer Center, Houston, TX, USA

P1 - Poster 035 2569816

INTERFERON CONSENSUS SEQUENCE-BINDING PROTEIN (ICSBP) REGULATES THE TRANSFORMING GROWTH FACTOR- BETA TYPE I RECEPTOR EXPRESSION IN OSTEOSARCOMA CELLS

Byung-Kiu Park; Jee Young Sung; Kyung-Sil Yoon; Seog Yun Park; June Hyuk Kim; Hyun Guy Kang; Yong-Nyun Kim
National Cancer Center, Goyang, Gyeonggi-do, Korea (the Republic of)

P1 - Poster 036 2565736

EGFR-UPAR BISPECIFIC IMMUNOTOXIN SUCCESSFULLY TARGETS PEDIATRIC SARCOMA

Kristy Pilbeam, Doctor of Osteopathy[1]; Rachel Bergerson[2]; Elizabeth Taras[3]; Daniel Vallera[3]; Michael Verneris[4]

[1]Pediatric Hematology Oncology, University of Minnesota, Minneapolis, MN, USA; [2]Pediatrics, University of Minnesota, Minneapolis, MN, USA; [3]Radiation Oncology, University of Minnesota, Minneapolis, MN, USA; [4]Pediatric Bone Marrow Transplant, University of Minnesota, Minneapolis, MN, USA

P1 - Poster 037 2570090

NDRG1 INHIBITION SENSITIZES OSTEOSARCOMA CELLS TO COMBRETASTATIN A-4 BY SUPPRESSION OF AUTOPHAGOSOME-LYSOSOME FUSION

Hongsheng Wang; Zhengdong Cai; Yingqi Hua, MD PhD
Orthopedics, Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai, China

P1 - Poster 038 2566836

ATRX MUTATION IN CANINE AND HUMAN OSTEOSARCOMA: IN VITRO EXPLORATION OF A NOVEL THERAPEUTIC APPROACH

Suzanne Bartholf DeWitt, DVM[1]; Jason Somarelli[2]; Terese Camp[2]; Peng Zhang[1]; Warren Floyd[2]; Samantha Shetler[2]; Rachael Thomas[3]; Matthew Breen[3]; Brian Brigman[1]; Ben Alman[1]; William Eward[1]

[1]Orthopaedic Surgery, Duke University, Durham, NC, USA; [2]Duke University, Durham, NC, USA; [3]College of Veterinary Medicine, NC State University, Raleigh, NC, USA

P1 - Poster 039 2556924

THE EXTRACELLULAR MATRIX INDUCES EXPRESSION OF INTERLEUKIN 23 P19 IN SARCOMA

Magdalena Jegen; Florian Lenze; Rüdiger von Eisenhart-Rothe; Philipp Mayer-Kuckuk
Orthopedics, Technical University Munich, Munich, Germany

P1 - Poster 040 2541232

DEFINING THE MECHANISMS OF SENSITIVITY TO HCI-2509: A NOVEL LSD1 INHIBITOR FOR THE TREATMENT OF EWING SARCOMA

Kathleen I. Pishas, PhD[1]; Sunil Sharma[2]; Stephen L. Lessnick[1]

[1]Center for Childhood Cancer and Blood Disorders, Nationwide Children's Hospital, Columbus, OH, USA; [2]Center for Investigational Therapeutics, Huntsman Cancer Institute, Salt Lake City, UT, USA

P1 - Poster 041 2565165

IN VITRO EVALUATION OF CB-839 IN COMBINATION WITH METFORMIN IN OSTEOSARCOMA CELL LINES

Ling Ren, PhD; Christine Tran Hoang; Amy K. LeBlanc

Comparative Oncology Program, NIH, Bethesda, MD, USA

P1 - Poster 042 2570409

EVALUATION OF ALTERNATIVE IN VIVO SCREENING METHODOLOGY TO IDENTIFY NEW DRUGS FOR TREATING PEDIATRIC CANCER

Peter Houghton, PhD; Raushan T. Kurmasheva

Greehey Children's Cancer Research Institute, University of Texas Health Science Center, San Antonio, TX, USA

P1 - Poster 043 2567025

CLINICAL RELEVANCE AND PROGNOSTIC SIGNIFICANCE OF CELLULAR/TISSUE AND CIRCULATING MICRORNA DYSREGULATIONS IN PATIENTS WITH OSTEOSARCOMA

Tomohiro Fujiwara[3]; Toshiyuki Kunisada[3]; Koji Uotani[3]; Aki Yoshida[3]; Takuya Morita[3]; Masaharu Kiyono[3]; Joe Hasei[3]; Yutaka Nezu[2]; Akihiko Yoshida[1]; Eisuke Kobayashi[1]; Takahiro Ochiya[2]; Akira Kawai[1]; Toshifumi Ozaki[3]

[1]National Cancer Center Hospital, Japan, Tokyo, Tokyo, Japan; [2]National Cancer Center Research Institute, Tokyo, Japan; [3]Okayama University Hospital, Okayama, Japan

P1 - Poster 044 2568419

IDENTIFICATION OF PHARMACOLOGICALLY TRACTABLE KINASE TARGETS IN OSTEOSARCOMA

Harriet Holme[3]; Rachel Brough[1]; Helen Pemberton[1]; James Campbell[1]; Colm Ryan[2]; Adrienne Flanagan[3]; Alan Ashworth[4]; Chris Lord[1]; Sandra Strauss[3]

[1]CRUK Gene Function Laboratory and Breast Cancer Now Research Centre, The Institute of Cancer Research, London, United Kingdom; [2]System Biology Ireland, University College Dublin, Dublin, Ireland; [3]UCL Cancer Institute, London, United Kingdom; [4]Helen Diller Family Comprehensive Cancer Centre, San Francisco, CA, USA

P1 - Poster 045 2556367

EWS/FLI HIJACKS CHROMATIN REGULATORY COMPLEXES TO MAINTAIN MALIGNANCY IN EWING SARCOMA CELLS

Emily Theisen, PhD; Stephen L. Lessnick

Childhood Cancer and Blood Disorders, Nationwide Children's Hospital, Columbus, OH, USA

P1 - Poster 046 2556450

EWS/FLI REGULATES TRANSCRIPTIONAL ACTIVATION IN EWING SARCOMA VIA LENGTH DEPENDENT GGAA MICROSATELLITES

Kirsten Johnson, BS; Stephen L. Lessnick

Center for Childhood Cancer & Blood Disorders, The Research Institute at Nationwide Children's Hospital, Columbus, OH, USA

P1 - Poster 047 2566620

IDENTIFICATION OF A LONG-NON CODING RNA SIGNATURE ASSOCIATED WITH EWING SARCOMA RESPONSIVENESS TO CHEMOTHERAPY

Katia Scotlandi; Andrea Grilli; Alessandro Parra; Cristina Baricordi; Stefano Ferrari; Piero Picci

Rizzoli Institute, Bologna, Italy

P1 - Poster 048 2563240

MONOCYTE PHENOTYPE ALTERATIONS ACROSS SPECIES IN OSTEOSARCOMA (OS): A COMPARATIVE ANALYSIS IN MICE, DOGS, AND HUMANS

Joanne Tuohy, DVM[1]; Suzanne Bartholf DeWitt[2]; Brian Brigman[2]; Jason Somarelli[2]; Peng Zhang[2]; Duncan Lascelles[1]; William Eward[2]; Jonathan Fogle[1]

[1]North Carolina State University, Raleigh, NC, USA; [2]Duke University, Durham, NC, USA

P1 - Poster 049 2570311

INTERLEUKIN-23 LINKS GLUTAMATE METABOTROPIC RECEPTOR-4 TO OSTEOSARCOMA DEVELOPMENT AND PROGRESSION - IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS FOR OSTEOSARCOMA

Maya Kansara, PhD[1]; Puiyi Pang[2]; Nina Sulkowski[1]; Michele Teng[3]; Mark Smyth[3]; David Thomas[1]

[1]Cancer, Garvan Institute of Medical Research, Sydney, New South Wales, Australia; [2]Sarcoma Genomics and Genetics, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [3]Immunology in Cancer and Infection Laboratory and Cancer Immunoregulation and Immunotherapy Laboratory, QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia

P1 - Poster 050 2568493

MICROENVIRONMENT INFLUENCE ON OSTEOSARCOMA'S HISTOLOGICAL RESPONSE TO CHEMOTHERAPY: PRECLINICAL MODELING AND RETROSPECTIVE ANALYSIS

Vincent Crenn[2]; Kevin Biteau[1]; Jérôme Amiaud[1]; Clotilde Dumars[3]; Romain Guiho[1]; Dominique Heymann[1]; Anne Moreau[3]; François Gouin[2]; Françoise Redini[1]

[1]Inserm UMR 957, Nantes, France; [2]Orthopedic Department, Nantes, France; [3]Pathology Department, Nantes, France

P1 - Poster 051 2556933

DEREGULATION OF HIPPO TUMOR SUPRESSOR PATHWAY IN EWING SARCOMA

Pablo Rodríguez-Núñez, PhD Student; Laura Romero-Pérez; Rosa García-Mejías; Daniel J. Garcia-Dominguez; Ana Amaral; Lourdes Hontecillas-Prieto; Juan Diaz-Martin; Enrique De Álava *Casado*

Molecular Pathology, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocio/CSIC/Universidad de Sevilla, Seville, Seville, Spain

P1 - Poster 052 2544006

HYPOXIA AND RADIATION INDUCE THE TRANSDIFFERENTIATION OF EWING'S SARCOMA CELLS INTO EWS-FLI-1+ VASCULARE PERCITYES THAT CONTRIBUTE TO TUMOR VASCULARE EXPANSION

Eugenie S. Kleinerman, MD; Zhichao Zhou

Pediatrics, M.D. Anderson Cancer Center, Bellaire, TX, USA

P1 - Poster 053 2557963

TRITHORAX-DEPENDENT REGULATION OF HOXD13 REPRESENTS A THERAPEUTIC VULNERABILITY IN EWING SARCOMA

Laurie Svoboda; Jolanta Grembecka; Tomasz Cierpicki; Rajiv M. Patel; Dafydd G. Thomas; Elizabeth Lawlor

University of Michigan, Ann Arbor, MI, USA

P1 - Poster 054 2570456

LIMITED DIAGNOSTIC VALUE OF DMP1 AND SATB2 IMMUNOHISTOCHEMISTRY IN OSTEOSARCOMA

Arjen H. Cleven, MD, PhD[1]; Georgios Agrogiannis[2]; Olaejirinde Olaofe[3]; Inge Briaire-de Bruijn[1]; Judith V. Bovée[1]

[1]Pathology, Leiden University Medical Center, Leiden, Netherlands; [2]Pathology, School of Medicine National and Kapodistrian University of Athens, Athens, Greece; [3]Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University, Ile-Ife, Nigeria

P1 - Poster 055 2570718

ALPHA PARTICLE RADIUM-223 DICHLORIDE (223RACL2) THERAPY AND PERSONALIZED MOLECULAR IMAGING WITH BONE SCINTIGRAPHY, NAF-PET, AND FDG-PET IN HIGH RISK OSTEOSARCOMA

Vivek Subbiah[1]; Pete Anderson[2]; Kalevi Kairemo[3]; Winston Huh[4]; Vinod Ravi[4]; Najat Daw[4]; Neeta Somaiah[4]; Robert S. Benjamin[4]; David S. Hong[1]; Homer Macapinlac[4]; Gregory Ravizzini[4]; Eric Rohren[5]

[1]Investigational Cancer Therapeutics, UT MD Anderson Cancer Center, Houston, TX, USA; [2]Cleveland Clinic, Cleveland, OH, USA; [3]Docrates Cancer Center, Helsinki, Finland; [4]MD Anderson Cancer Center, Houston, TX, USA; [5]Baylor College of Medicine, Houston, TX, USA

P1 - Poster 056 2570092

DO WE NEED BONE SCANS FOR CARTILAGE TUMOURS?

Carola I. Brückmann[1]; Magdalena M. Gilg[1]; Lukas Holzer[1]; Franz Quehenberger[2]; Thomas Schwarz[3]; Andreas Leithner[1]

[1]Orthopedic Surgery, Medical University of Graz, Graz, Styria, Austria; [2]Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz, Graz, Styria, Austria; [3]Department of Radiology, Division of Nuclear Medicine Radiology, Medical University of Graz, Graz, Styria, Austria

P1 - Poster 057 2556460

OSTEOSARCOMA OF THE SPINE AND PELVIS: 115 PATIENTS OF A SINGLE INSTITUTION

Haotong Wang, MD[1]; Alex Jacobson[1]; Saveli Goldberg[1]; David Harmon[2]; Edwin Choy[2]; Gregory M. Cote[2]; Francis Hornicek[2]; Kevin Raskin[2]; Pateur Nielson[2]; Thomas F. DeLaney[1]; Yen-Lin Chen[1]

[1]Radiation Oncology, MGH, Burlington, MA, USA; [2]MGH, Boston, MA, USA

P1 - Poster 058 2565988

CARBON ION RADIOTHERAPY FOR UNRESECTABLE AXIAL OSTEOSARCOMA

Reiko Imai; Tadashi Kamada

National Institute of Radiological Sciences, Chiba, Japan

P1 - Poster 059 2570184

PROTON BEAM RADIOTHERAPY FOR INOPERABLE BONE AND SOFT TISSUE SARCOMA

Hirohisa Katagiri, PhD[1]; Shigeyuki Murayama[2]; Tetsuo Nishiumura[2]; Mitsuru Takahashi[1]; Hideki Murata[1]; Junji Wasa[1]; Seiichi Hosaka[1]; Yousuke Honda[1]

[1]Orthopedic Oncology, Shizuoka Cancer Center, Shizuoka, Japan; [2]Radiation and Proton Therapy Center, Shizuoka Cancer Center, Shizuoka, Japan

P1 - Poster 060 2560531

TWO CASES OF PELVIC SARCOMA ORIGINATING IN THE ACETABULUM WITH MORE THAN 10 YEARS OF FOLLOW-UP AFTER CARBON ION RADIOTHERAPY

Katsuhisa Kawanami; Toshihiro Matsuo; Keiji Sato; Masataka Deie

Aichi Medical University, Nagakute City, Japan

P1 - Poster 061 2565856

LIMB-SALVAGE RECONSTRUCTION AFTER ACETABULAR RESSECTION: CLINICAL OUTCOMES

Marta S. Silva; Pedro M. Serrano; Luis Barros; João Esteves; Pedro Neves; Vânia Oliveira; Pedro F. Cardoso

Centro Hospitalar do Porto, Porto, Portugal

P1 - Poster 062 2570532

FUNCTIONAL AND ONCOLOGICAL OUTCOME FOLLOWING RESECTION OF MALIGNANT BONE TUMORS OF THE PELVIS AND HIP TRANSPOSITION

Per-Ulf Tunn; Maya Niethard; Carmen Tiedke; Matthias Werner; Peter Reichardt; Jan Mettelsiefen

Sarcomacenter Berlin-Brandenburg, HELIOS Klinikum Berlin, Berlin, Berlin, Germany

P1 - Poster 063 2570403

ONCOLOGICAL AND FUNCTIONAL RESULTS OF SPINOPELVIC RECONSTRUCTION FOLLOWING THE RESECTION OF MALIGNANT BONE TUMORS INVOLVING IPSILATERAL SACROILIAC JOINT

Takeshi Okamoto[1]; Junya Toguchida[2]

[1]Orthopedic Surgery, Kyoto University, Kyoto, Japan; [2]Tissue Regeneration, Frontier Medical Sciences, Kyoto University, Kyoto City, Japan

P1 - Poster 064 2548727

RESULTS OF THE EN-BLOC VERTEBRECTOMY FOR PRIMITIVE SPINE TUMORS

Alessandro Luzzati, Chief[1]; Giuseppe Perrucchini[1]; Gennaro Scotto[1]; Marco Alloisio[2]; Alessandro Gronchi[3]; Roberto Biagini[4]; Carmine Zoccali[4]

[1]Oncological Orthopaedic Department, Istituto Ortopedico Galeazzi Milan, Milan, Italy; [2]Toracic Surgery, Humanitas, Milano, Italy; [3]Chirurgia dei Sarcomi, Istituto Nazionale dei Tumori, Milano, Italy; [4]Oncological Orthopaedics, Regina Elena National Cancer Institute, Rome, Italy

P1 - Poster 065 2565418

PELVIC RING TUMORS: RESECTION AND RECONSTRUCTION

João Esteves; Luis Barros; Marta S. Silva; Pedro Neves; Vânia Oliveira; Pedro F. Cardoso

Orthopaedics, Centro Hospitalar do Porto, Porto, Portugal

P1 - Poster 066 2557898

INTERCALARY ALLOGRAFT AUGMENTED WITH INTRAMEDULLARY CEMENT AND PLATE FIXATION: A RELIABLE SOLUTION AFTER TUMOUR RESECTION

Sanjay Gupta; Lisa Kafchinski; Kenneth R. Gundle; Anthony Griffin; Jay Wunder; Peter Ferguson

Mount Sinai Hospital, Glasgow, United Kingdom

P1 - Poster 067 2570591

LOWER EXTREMITY LIMB SALVAGE IN PEDIATRIC ONCOLOGY PATIENTS: A RETROSPECTIVE CASE SERIES EXAMINING COMPLICATION RATE AND FUNCTIONAL OUTCOMES AFTER NON-INVASIVE EXTENDIBLE ENDOPROSTHESIS RECONSTRUCTION

Andrea Gale[1]; Wendy Allen-Rhoades, MD[3]; Shiley Aguilar[3]; Hari Sankaran[3]; Lauren Nicholls [2]; Nino Rainusso[3]; Lisa L. Wang[3]; Rex A. Marco[1]

[1]Orthopedics & Sports Medicine, Houston Methodist Hospital, Houston, TX, USA; [2]Pediatrics, University of Arizona, Phoenix, AZ, USA; [3]Pediatrics, Baylor College of Medicine, Houston, TX, USA

P1 - Poster 068 2570269

EXTRAARTICULAR KNEE AND SHOULDER RESECTION FOR SARCOMAS: CLINICAL AND FUNCTIONAL OUTCOME

Eduardo J. Ortiz Cruz, MD, PhD[1]; Manuel Peleteiro-Pensado[2]; Irene Barrientos-Ruiz[2]; Daniel Bernabeu-Taboada[3]; Jose J. Pozo-Kreilinger[4]; Carmen Iglesias[5]

[1]Orthopaedic Oncology, Hospital Universitario La Paz, Hospital Ruber Internacional, Madrid, Madrid, Spain; [2]Orthopaedic Oncology, Hospital Universitario La Paz, Madrid, Madrid, Spain; [3]Musculoskeletal Radiology Department, Hospital Universitario La Paz, Madrid, Madrid, Spain; [4]Pathology Department. Musculoskeletal Pathology, Hospital Universitario La Paz, Madrid, Madrid, Spain; [5]Plastic Surgeon Department, Hospital Universitario La Paz, Madrid, Madrid, Spain

P1 - Poster 069 2565954

BIOLOGICAL DIAPHYSEAL RECONSTRUCTION AFTER EXCISION OF MALIGNANT BONE TUMORS USING A VSCULARISED FIBULAR GRAFT

Yoshikazu Tanzawa, PhD; Eisuke Kobayashi; Makoto Endo; Fumihiko Nakatani; Akira Kawai; Hirokazu Chuman

Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan

P1 - Poster 070 2570417

CUSTOM-MADE CERAMIC SPACER FOR CHILDREN WITH OSTEOSARCOMA OF LOWER EXTRIMITIES: A LONG FOLLOW- UP

Fumihiko Nakatani; Takeshi Hirose; Shunichi Toki; Tomoaki Mori; Yoshihiro Araki; Takenori Uehara; Koki Shimizu; Masato Sugawara; Eisuke Kobayashi; Makoto Endo; Yoshikazu Tanzawa; Akira Kawai; Hirokazu Chuman
National Cancer Center Hospital, Tokyo, Japan

P1 - Poster 071 2570493

TECHNIQUE AND RESULTS IN RETRANSPLANTATION OF RADIOSTERILIZED BONE TUMOURS WITH AND WITHOUT FIBULAR AUGMENTATION

Alexander Klein[1]; Yasmin Bakhshai[1]; Falk Roeder[2]; Andrea Baur-Melnyk[3]; Thomas Knösel[4]; Lars Lindner[5]; Volkmar Jansson[1]; Hans R. Dürr[1]
[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany; [2]Department of Radiotherapy, LMU Munich, Munich, Germany; [3]Institute of Radiology, LMU Munich, Munich, Germany; [4]Institute of Pathology, LMU Munich, Munich, Germany; [5]Medical Clinic III, LMU Munich, Munich, Germany

P1 - Poster 072 2544310

THE PROPHYLACTIC ANTIBIOTIC REGIMENS IN TUMOR SURGERY (PARITY) MULTICENTER RANDOMIZED CONTROLLED TRIAL: INTERNATIONAL EXPANSION OF THE COLLABORATIVE NETWORK

Michelle Ghert, MD, FRCSC; The PARITY Investigators
Surgery, McMaster University, Hamilton, ON, Canada

P1 - Poster 073 2570235

LIGASURE™ SYSTEM IN SARCOMA SURGERY CAN DECREASE INTRAOPERATIVE BLOOD LOSS AND POSTOPERATIVE HOSPITAL LENGTH OF STAY

Yidan H. Zhang[1]; Mikhail Bekarev[1]; Zach H. Jurkowski[1]; David Geller[1]; Hoang H. Bang[1]; Rui Yang[1]; Richard Gorlick[2]; Michael E. Roth[2]; Jonathan B. Gill[2]
[1]Orthopaedic Surgery, Montefiore Medical Center, New York, NY, USA; [2]Pediatrics, Children's Hospital at Montefiore, Bronx, NY, USA

P1 - Poster 074 2565814

SIMULTANEOUS BILATERAL OPEN THORACOTOMIES FOR PULMONARY METASTASES IN OSTEOSARCOMA TO REDUCE DELAY IN SYSTEMIC THERAPY

Caroline Kelmis; Antonio Logan; Caleb Oh; Graham A. Zolkowski; Michelle March; Paul Kent
Rush University Medical Center, Vernon Hills, IL, USA

P1 - Poster 075 2529558

THREE-DIMENSIONAL FLUOROSCOPIC NAVIGATION-ASSISTED SURGERY FOR TUMORS IN PATIENTS WITH TUMOR- INDUCED OSTEOMALACIA

Hiroshi Kobayashi[1]; Toru Akiyama[3]; Tomotake Okuma[1]; Yusuke Shinoda[1]; Nobuaki Ito[1]; Seiji Fukumoto[1]; Hirotaka Kawano[2]; Sakae Tanaka[1]
[1]The University of Tokyo Hospital, Tokyo, Japan; [2]University of Teikyo, Tokyo, Japan; [3]Saitama Medical Center, Jichi Medical University, Saitama, Japan

P1 - Poster 076 2562584

LONG-TERM (> 15 YEAR) OUTCOMES OF CEMENT IN CEMENT TECHNIQUE FOR REVISION ENDOPROSTHESIS SURGERY

Nicholas Bernthal[1]; Stephen Zoller[1]; Vishal Hegde[1]; Howard Park[1]; Daniel Johansen[1]; Frederick R. Eilber[2]; Frederick C. Eilber[2]; Chandhanarat Chandhanayingyong[2]; Jeffrey Eckardt[1]
[1]Orthopaedics, UCLA, Santa Monica, CA, USA; [2]UCLA, Los Angeles, CA, USA

P1 - Poster 077 2543749

AUTOREGISTRATION IN NAVIGATED BONE TUMOR SURGERY

Prakash R. Nayak, MD[1]; Michelle Arkhangorodsky[2]; Jimmy Qiu[2]; Michael Daly[2]; Harley Chan[2]; Robert Weersink[2]; David Jaffray[2]; Jonathan Irish[2]; Peter Ferguson[1]; Jay Wunder[1]

[1]Musculoskeletal Oncology, Mount Sinai Hospital and Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Guided Therapeutics (GTx) Program, Princess Margaret Cancer Centre, Toronto, ON, Canada

P1 - Poster 078 2571290

RECONSTRUCTION USING STERILISED TUMOUR BONE FOR PRIMARY MALIGNANT TUMOURS OF UPPER LIMB

Bhaskar S. Sugath, Fellowship Orthopaedic Oncology

Orthopaedics, Aster Medcity, Kochi, India, Trivandrum, Kerala, India

P1 - Poster 079 2556321

CORE NEEDLE BIOPSY IS A SAFE AND EFFECTIVE MODALITY FOR DIAGNOSIS OF ANEURYSMAL BONE CYST

Zachary Burke, MD[1]; Vishal Hegde[1]; Stephen Zoller[1]; Daniel Johansen[2]; Benjamin Kelley[2]; Noah Federman[3]; Leanne Seeger[4]; Scott Nelson[5]; Nicholas Bernthal[1]

[1]Orthopedics, UCLA, Santa Monica, CA, USA; [2]David Geffen School of Medicine, Los Angeles, CA, USA; [3]Mattel Children's Hospital at UCLA, Los Angeles, CA, USA; [4]Radiology, UCLA, Los Angeles, CA, USA; [5]Pathology, UCLA, Los Angeles, CA, USA

P1 - Poster 080 2543237

PRELIMINARY VALIDATION OF SKIN FIDUCIALS FOR NAVIGATION-ASSISTED MUSCULOSKELETAL TUMOR RESECTIONS: A CADAVER STUDY

Rodolfo Zamora Rendich, MD; Claudia Christman-Skieller; Cegniz Yildirim; John Shapton; Jedediah White; Stephanie Punt; Ernest U. Conrad

Orthopaedics and Sports Medicine, University of Washington, Seattle, WA, USA

P1 - Poster 081 2566216

INDOCYANINE GREEN DYE ANGIOGRAPHY PREDICTS RESIDUAL TUMOR GROWTH IN A POST-AMPUTATED IMMUNOCOMPETENT ORTHOTOPIC MOUSE MODEL

Adel Mahjoub, BS; Mitchell S. Fourman; Jonathan Mandell; Shibing Yu; Jessica Tebbets; David Hirsch; Kurt Weiss

Orthopedic Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

P1 - Poster 082 2570227

PRECLINICAL STUDY OF THE COMBINATION OF PEVONEDISTAT WITH DOXORUBICIN, GEMBITABINE OR BMN673 IN EWING SARCOMA

Daniel J. Garcia-Dominguez[1]; Lourdes Hontecillas-Prieto[1]; Pablo Rodríguez-Núñez[1]; Rosa García-Mejías[1]; Angel Montero Carcaboso[2]; Guillem Pascual-Pastó[2]; Juan Diaz-Martin[1]; Laura Romero-Pérez[1]; Enrique De Álava *Casado[1]*

[1]Molecular Pathology, Instituto de Biomedicina de Sevilla (IBiS)/Hospital Virgen del Rocio/CSIC/Universidad de Sevilla, Seville, Spain; [2]Developmental Tumor Biology Laboratory, Fundacio Sant Joan de Deu, Department of Pediatric Hematology and Oncology, Hospital Sant Joan de Deu, Barcelona, Spain

P1 - Poster 083 2570372

RESULTS OF METHOTREXATE-ETOPOSIDE-IFOSFAMIDE BASED REGIMEN IN OSTEOSARCOMA PATIENTS INCLUDED IN THE FRENCH OS/SARCOME-09 STUDY

Laurence Brugieres[1]; Bob Valery Occean[2]; Hélène Pacquement[3]; Cyril Lervat[4]; Perrine Marec-Bérard[5]; Jean Claude Gentet[6]; Nadège Corradini[7]; Natacha Entz Werle[8]; Marie Dominique Tabone[9]; Laure Saumet[7]; Nathalie Gaspar[1]; Emmanuelle Bompas[10]; Marta Jimenez[10]; Sophie Piperno-Neumann[3]; Marie-Cecile De Leley[2]

[1]Children and Adolescent Oncology, Gustave Roussy, Villejuif, France; [2]Gustave Roussy, Villejuif, France; [3]Institut Curie, Paris, France; [4]Centre Oscar Lambret, Lille, France; [5]CHU, Lyon, France; [6]AP-HM, Marseille, France; [7]CHU, Nantes, France; [8]CHU Hautes Pierres, Starsbourg, France; [9]APHP Trousseau, Paris, France; [10]Unicancer, Paris, France

P1 - Poster 084 2566193

COMPARISON OF METHOTREXATE-ETOPOSIDE-IFOSFAMIDE AND API-AI BASED REGIMEN IN 18-25 YR OSTEOSARCOMA PATIENTS INCLUDED IN THE FRENCH OS2006/SARCOME-09 STUDY

Valerie Laurence[1]; Laurence Brugieres[2]; Bob-Valery Occean[3]; Nathalie Gaspar[2]; Emmanuelle Bompas[4]; Jean Yves Blay[5]; Didier Cupissol[6]; Nicolas Penel[7]; Cyril Lervat[8]; Patrice Kerbrat[9]; Antoine Italiano[10]; Celine Mahier[11]; Marie-Cecile Le Deley[3]; Sophie Piperno-Neumann[1]; Perrine Marec-Berard[12]

[1]Institut Curie, Paris, France; [2]Children and Adolescent Oncology, Gustave Roussy, Villejuif, France; [3]Biostatistics, Gustave Roussy, Villejuif, France; [4]Medical Oncology, Centre René Gauducheau, Nantes, France; [5]Medical Oncology, Centre Leon Berard, Lyon, France; [6]Centre Val Aurelle, France, France; [7]Medical Oncology, Centre Oscar Lambret, Lille, France; [8]Pediatric Oncology, Centre Oscar Lambret, Lille, France; [9]Medical Oncology, Centre Eugene Marquis, Rennes, France; [10]Medical Oncology, Institut Bergonie, Bordeaux, France; [11]Unicancer, Paris, France; [12]Pediatric Oncology Department, Centre Leon Berard, Lyon, France

P1 - Poster 085 2523557

DOSE-INTENSITY RELATION TO EVENT-FREE SURVIVAL IN OSTEOSARCOMA PATIENTS: A NEW ANALYTIC APPROACH

Jakob Anninga[1]; Carlo Lancia, PhD[2]; Cristian Spitoni[3]; Jeremy Whelan[4]; Matthew Sydes[5]; Gordana Jovic[5]; Hans Gelderblom[6]; Pancras Hogendoorn[7]; Henk van den Berg[8]; Marta Fiocco[2]

[1]Oncology, Radboud University Medical Center, Nijmegen, Netherlands; [2]Medical Statistics and Bioinformatics, Leiden University Medical Center, Leiden, Netherlands; [3]Epidemiology, University Medical Center Utrecht, Utrecht, Netherlands; [4]Oncology, University College London Hospital, London, United Kingdom; [5]Clinical Trials Unit, Medical Research Council, London, United Kingdom; [6]Oncology, Leiden University Medical Center, Leiden, Netherlands; [7]Pathology, Leiden University Medical Center, Leiden, Netherlands; [8]Oncology, Emma Children Hospital, Academic Medical Centre, Amsterdam, Netherlands

P1 - Poster 086 2554306

PHASE 1 STUDY OF SIROLIMUS IN COMBINATION WITH ORAL CYCLOPHOSPHAMIDE AND TOPOTECAN IN CHILDREN AND YOUNG ADULTS WITH RELAPSED AND REFRACTORY SARCOMA AND OTHER SOLID TUMORS

Kieuhoa T. Vo, MD, MAS[1]; Erin E. Karski[1]; Nicole M. Nasholm[1]; Shelly Allen[1]; Fabienne Hollinger[1]; W. Clay Gustafson[1]; Janel R. Long-Boyle[2]; Stephen Shiboski[3]; Katherine K. Matthay[1]; Steven G. DuBois[1]

[1]Pediatric Hematology/Oncology, UCSF Benioff Children's Hospital, University of California, San Francisco School of Medicine, San Francisco, CA, USA; [2]Clinical Pharmacy, University of California, San Francisco School of Medicine, San Francisco, CA, USA; [3]Epidemiology and Biostatistics, University of California, San Francisco School of Medicine, San Francisco, CA, USA

P1 - Poster 087 2544843

AEROSOL GEMCITIBINE ADMINISTRATION FOLLOWING AMPUTATION ERADICATES OSTEOSARCOMA LUNG METASTASES WITHOUT INTERFERING WITH WOUND HEALING IN THE BONE OR SKIN

Eugenie S. Kleinerman, MD[1]; Ling Yu[1]; Andrea Hayes-Jordan[2]; Nancy Gordon[1]

[1]Pediatrics, M.D. Anderson Cancer Center, Houston, TX, USA; [2]Surgical Oncology, M.D. Anderson Cancer Center, Houston, TX, USA

P1 - Poster 088 2569866

RESULS OF API-AI BASED REGIMEN IN OSTEOSARCOMA PATIENTS (PTS) INCLUDED IN THE FRENCH OS2006/SARCOMA-09 STUDY

Sophie Piperno-Neumann, MD[1]; Bob-Valery Occean[2]; Jean-Yves Blay[3]; Didier Cupissol[4]; Nicolas Penel[5]; Perrine Marec-Berard[6]; Antoine Italiano[7]; Emmanuelle Bompas[8]; Olivier Collard[9]; Axel Le Cesne[10]; Maria Rios[11]; Patrice Kerbrat[12]; Marta Jimenez[13]; Laurence Brugieres[14]; Marie-Cecile Le Deley[2]

[1]Medical Oncology, Institut Curie, Paris, France; [2]Biostatistics, Gustave Roussy, Villejuif, France; [3]Medical Oncology, Centre Léon- Bérard, Lyon, France; [4]Medical Oncology, Institut de Cancérologie, Montpellier, France; [5]Medical Oncology, Centre Oscar-Lambret, Lille, France; [6]Pediatric Oncology Department, Centre Léon- Bérard, Lyon, France; [7]Medical Oncology, Institut Bergonié, Bordeaux, France; [8]Medical Oncology, ICO, Nantes, France; [9]Medical Oncology, ICL, Saint-Priest, France; [10]Medical Oncology, Gustave Roussy, Villejuif, France; [11]Medical Oncology, Institut de Cancérologie de Lorraine, Nancy, France; [12]Medical Oncology, Centre Eugène Marquis, Rennes, France; [13]Unicancer, Paris, France; [14]Children and Adolescent Oncology Department, Gustave Roussy, Villejuif, France

P1 - Poster 089 2570644

TEN-YEAR SURVIVAL OF PATIENTS WITH LOCALIZED RESECTABLE OSTEOSARCOMA TREATED WITHOUT METHOTREXATE

Michael W. Bishop[1]; Milena Villarroel[2]; Mariela Fuenzalida[2]; Juan Quintana[2]; Shenghua Mao[1]; Jianrong Wu[1]; Valerie McPherson[1]; Jesse Jenkins[1]; Bhaskar Rao[1]; Michael Neel[1]; Victor Santana[1]; Fariba Navid[1]; Najat Daw[3]
[1]St. Jude Children's Research Hospital, Memphis, TN, USA; [2]Hospital Luis Calvo Mackenna, Santiago, Chile; [3]University of Texas MD Anderson Cancer Center, Houston, TX, USA

P1 - Poster 090 2570633

NEW USES FOR OLD DRUGS: ARSENIC TRIOXIDE AS TREATMENT OPTION FOR PEDIATRIC SMALL ROUND BLUE CELL TUMORS

Frank Traub, MD, PhD[1]; Sabine Schleicher[2]; Rosa Riester[1]; Rupert Handgretinger[2]; Karen Boehme[1]
[1]Department of Orthopaedic Surgery, University Hospital Tuebingen, Tuebingen, Germany; [2]Department of Paediatric Hematology and Oncology, Children's Hospital of the University of Tuebingen, Tuebingen, Germany

P1 - Poster 091 2569609

REDUCING TOXICITY OF HIGH DOSE METHOTREXATE (MTX) IN OSTEOSARCOMA WITH GLUCARPIDASE (GLU) – RESULTS OF A RANDOMISED CROSSOVER STUDY, GLU-1 (EUDRACT 2006-003203-40)

Rachael Windsor; Martha Perisoglou; Menelaos Pavlou; Beatrice Seddon; Sandra Strauss; Maria Michelagnoli; Palma Dileo; Julie Barber; Jeremy Whelan
The London Sarcoma Service, University College Hospitals NHS Foundation Trust, London, United Kingdom

P1 - Poster 092 2571005

OUTCOMES IN NON-METASTATIC OSTEOSARCOMA PATIENTS WITH PLATINUM-BASED COMBINATION CHEMOTHERAPY WITHOUT HIGH-DOSE METHOTREXATE

Vikas T. Talreja, MBBS, MD (Medicine), DM (Medical Oncology 1st Year); Jyoti Bajpai; Arun Chandrasekharan
Medical Oncology, Tata Memorial Hospital, Mumbai, Maharashtra, India

P1 - Poster 093 2544677

THE RESPONSE EVALUATION CRITERIA IN SOLID TUMORS (RECIST) IS A POOR SURROGATE ENDPOINT FOR SURVIVAL IN OSTEOSARCOMA

Lillian M. Guenther, MD[1]; R. Grant Rowe[1]; Patricia Chang[2]; David W. Swenson[2]; Stephanie C. Meyer[1]; Catherine Clinton[1]; Dongjing Guo[1]; Madhumitha Sridharan[1]; Wendy B. London[1]; Holcombe E. Grier[1]; Kirsten Ecklund[2]; Katherine A. Janeway[1]
[1]Pediatric Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [2]Radiology, Boston Children's Hospital, Boston, MA, USA

P1 - Poster 094 2570615

COPPER IMPROVES TUMORICIAL EFFECTS OF DISULFIRAM IN BOTH MURINE AND HUMAN SARCOMA CELLS

Jonathan Mandell; Mitchell S. Fourman; Adel Mahjoub; Jessica Tebbets; Shibing Yu; Kurt Weiss
University of Pittsburgh, Gibsonia, PA, USA

P1 - Poster 095 2536216

A COMPARATIVE ONCOLOGY STUDY OF THE IMPACT OF SIROLIMUS ON METASTATIC PROGRESSION IN CANINE OSTEOSARCOMA AS A MODEL FOR THE PEDIATRIC DISEASE

Amy K. LeBlanc, DVM[1]; Christina Mazcko[1]; Laura E. Selmic[2]; Timothy M. Fan[2]
[1]Comparative Oncology Program, NIH/National Cancer Institute, Bethesda, MD, USA; [2]Department of Veterinary Clinical Medicine, University of Illinois at Urbana-Champaign, Urbana, IL, USA

P1 - Poster 096 2557811

A PHASE II STUDY OF HUMANIZED MONOCLONCAL ANTIBODY 3F8 (HU3F8) WITH GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR (GM-CSF) IN THE TREATMENT OF RECURRENT OSTEOSARCOMA

Alexander Chou, MD; Stephen Roberts; Heather Magnan; Srikanth Ambati; Emily Slotkin; Leonard Wexler; Paul Meyers; Yi Feng; Hoa Tran; Dara Schwam; Elizabeth Chamberlain; Irene Cheung; Nai-Kong V. Cheung
Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY, USA

P1 - Poster 097 2565832

OFF-LABEL USE OF PAZOPANIB FOR METASTATIC BONE SARCOMAS

Ninna Aggerholm-Pedersen, MSc, MD, PhD; Philip Rossen; Hanne Rose; Akmal Safwat
Aarhus University Hospital, Aarhus, Denmark

P1 - Poster 098 2566916

A CASE REPORT OF STABLE DISEASE WITH PAZOPANIB AND EVEROLIMUS IN A PATIENT WITH EWING'S VARIANT SARCOMA

James Chen
Department of Biomedical Informatics and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA

P1 - Poster 099 2526097

IMMUNE CHECKPOINT INHIBITOR EXPRESSION OF HUMAN AND CANINE OSTEOSARCOMA

Matthew Cascio, DO[1]; Rowan Milner[2]; Lung-Ji Chang[3]
[1]Pediatric Hematology/Oncology, University of Florida, Gainesville, FL, USA; [2]Veterinarian Medicine, University of Florida, Gainesville, FL, USA; [3]Molecular Genetics and Microbiology, University of Florida, Gainesville, FL, USA

P1 - Poster 100 2561834

INVESTIGATING THE IMMUNE MICROENVIRONMENT IN BONE AND SOFT-TISSUE SARCOMA

Nalan Gokgoz, PhD[1]; Junghyun Nam[1]; Beatrice Lau[2]; Brendan C. Dickson[2]; Jay Wunder[1]; Irene L. Andrulis[1]
[1]Lunenfeld-Tanenbaum Research Institute, Sinai Health System, Toronto, ON, Canada; [2]Department of Pathology and Laboratory Medicine, Sinai Health System, Toronto, ON, Canada

P1 - Poster 101 2567963

RETROPERITONEAL EWING SARCOMA (ES): AN ITALIAN SARCOMA GROUP (ISG) AND ROYAL MARSDEN HOSPITAL (RMH) JOINT STUDY

Emanuela Palmerini[1]; Robin Jones[2]; Dario Callegaro[3]; Giovanni Grignani[4]; Piero Picci[1]; Luca Cevolani[1]; Davide Donati[1]; Michela Libertini[1]; Emanuela Marchesi[1]; Martina Piccioni Leopardi[1]; Michela Pierini[1]; Lorenzo D'Ambrosio[4]; Charlotte Benson[2]; Alessandro Gronchi[3]; Stefano Ferrari[1]
[1]Istituto Ortopedico Rizzoli, Bologna, BO, Italy; [2]Royal Marsden Hospital, London, United Kingdom; [3]Istituto Nazionale Tumori, Milan, Italy; [4]IRCC Candiolo, Torino, Italy

P1 - Poster 102 2562359

EXTRASKELETAL EWING SARCOMA: A RETROSPECTIVE ANALYSIS FROM A SINGLE INSTITUTION SERIES OF PEDIATRIC AND ADULT PATIENTS

Michela Libertini[3]; Robin Jones[1]; Edward Armstrong[1]; Cyril Fisher[1]; Khin Twhay[1]; Aisha Miah[1]; Ian Judson[1]; Winette Van der Graaf[1]; Julia Chisholm[2]; Shane Zaidi[1]; Charlotte Benson[1]
[1]Sarcoma Unit, Royal Marsden Hospital, London, United Kingdom; [2]Children and Young People's Unit, Royal Marsden Hospital, Sutton, London, United Kingdom; [3]ESO Clinical Training Centres Fellow 2016, Sarcoma Unit, Royal Marsden Hospital, London, United Kingdom

P1 - Poster 103 2569888

EWING SARCOMA OF THE HEAD AND NECK (HN ES): LOCAL TREATMENT EVALUATION OF THE FRENCH POPULATION

Jebrane Bouaoud[2]; Stéphanie Bolle[1]; Stéphane Temam[1]; Kahina Belhous[2]; Louise Galmiche[2]; Frédéric Kolb[1]; Quentin Quassemyar[1]; François Bidault[1]; Vincent Couloigner[2]; Nathalie Cozic[1]; Marie-Cecile De Leley[1]; Natacha Kadlub[2]; Nathalie Gaspar[1]
[1]Gustave Roussy, Villejuif, France; [2]APHP Necker, Paris, France

P1 - Poster 104 2529965

CIC-REARRANGED SARCOMAS: CLINICAL FEATURES AND TREATMENT OUTCOME

Makoto Endo, MD, PhD; Akihiko Yoshida; Eisuke Kobayashi; Shunichi Toki; Takeshi Hirose; Takenori Uehara; Masato Sugawara; Tomoaki Mori; Koki Shimizu; Yoshikazu Tanzawa; Fumihiko Nakatani; Hirokazu Chuman; Akira Kawai
National Cancer Center, Tokyo, Japan

P1 - Poster 105 2526665

CLINICOPATHOLOGICAL FINDINGS AND TREATMENT RESULTS OF BCOR-CCNB3 SARCOMA

Masato Sugawara, MD, PhD[1]; Makoto Endo[2]; Akihiko Yoshida[3]; Eisuke Kobayashi[2]; Yoshikazu Tanzawa[2]; Fumihiko Nakatani[2]; Michiaki Takagi[1]; Hirokazu Chuman[2]; Akira Kawai[2]

[1]Orthopaedic Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan; [2]Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [3]Pathology, National Cancer Center Hospital, Tokyo, Japan

P1 - Poster 106 2556527

CUMULATIVE BURDEN OF CHRONIC HEALTH CONDITIONS IN ADULT SURVIVORS OF CHILDHOOD BONE SARCOMAS: A REPORT FROM THE ST. JUDE LIFETIME (SJLIFE) COHORT STUDY

Michael W. Bishop; Kiri Ness; Chenghong Li; Wei Liu; Kumar Srivastava; Nickhill Bhakta; Yutaka Yasui; Alberto Pappo; Les Robison; Melissa Hudson; Daniel Mulrooney

St. Jude Children's Research Hospital, Memphis, TN, USA

P1 - Poster 107 2570711

PROGNOSTIC NOMOGRAMS FOR PREDICTING THE 10-YEAR PROBABILITY OF LOCAL-CONTROL FAILURE, RECURRENCE, AND DEATH IN BONE OSTEOSARCOMA

Ruoyu Miao, MD; Haotong Wang; Alex Jacobson; Saveli Goldberg; Yen-Lin Chen

Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA

P1 - Poster 108 2570656

BONE LESIONS AT DIAGNOSIS: EXPERIENCE OF THE OS2006 STUDY

Cyril Lervat[1]; Laurence Brugieres[3]; Bob-Valery Occean[3]; Perrine Marec-Bérard[5]; Nadege Corradini[5]; Natacha Entz Werle[4]; Jean- Claude Gentet[7]; Ludovic Mansuy[8]; Hélène Pacquement[6]; Marie-Dominique Tabone[2]; Sophie Piperno-Neumann[6]; Marie-Cécile Le Deley[3]

[1]Pediatrics, Centre Oscar Lambret, Lille, France; [2]Trousseau, Paris, France; [3]Gustave Roussy, Villejuif, France; [4]Hôpital Hautepierre, Strasbourg, France; [5]Ihope, Lyon, France; [6]Curie, Paris, France; [7]La Timone, Marseille, France; [8]CHU Nancy, Nancy, France

P1 - Poster 109 2559702

PRIMARY OSTEOSARCOMA OF THE BONE WITH RHABDOID FEATURES: A RARE, PREVIOUSLY UNDESCRIBED PRIMARY MALIGNANT TUMOR OF BONE

Max Seiter, MD[1]; Motasem Al Maaieh[1]; Rosenberg Andrew[2]; Sheila Conway[1]

[1]Orthopaedic Surgery, University of Miami/Jackson Memorial Hospital, Miami, FL, USA; [2]Pathology, University of Miami Hospital, Miami, FL, USA

P1 - Poster 110 2554640

IDENTIFICATION OF PATIENTS WITH LOCALIZED EWING SARCOMA AT HIGHER RISK FOR LOCAL FAILURE: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP

Safia K. Ahmed, MD[1]; William Harmsen[2]; Steven G. DuBois[4]; Mark Krailo[3]; Karen Marcus[7]; Katherine A. Janeway[4]; David Geller[10]; Joel Sorger[5]; Richard B. Womer[8]; Linda Granowetter[11]; Holcombe E. Grier[4]; Lor Randall[9]; Richard Gorlick[6]; Nadia N. Laack[1]

[1]Radiation Oncology, Mayo Clinic, Rochester, MN, USA; [2]Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA; [3]Preventative Medicine, University Of Southern California, Los Angeles, CA, USA; [4]Pediatrics, Dana-Farber/Boston Children's Cancer and Blood Disorders Center and Harvard Medical School, Boston, MA, USA; [5]Pediatrics, Cincinnati Children's Hospital, Cincinnati, OH, USA; [6]Pediatric Hematology and Oncology, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, USA; [7]Radiation Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center and Harvard Medical School, Boston, MA, USA; [8]Pediatrics, University of Pennsylvania Perelman School of Medicine and Children's Hospital of Philadelphia, Philadelphia, PA, USA; [9]Orthopedics, Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA; [10]Pediatrics and Orthopedic Surgery, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, USA; [11]Pediatrics, New York University (NYU) Medical School and NYU Langone Medical Center, New York, NY, USA

P1 - Poster 111 2554555

OUTCOME OF 114 OSTEOSARCOMA PATIENTS OLDER THAN 50 YEARS: A RETROSPECTIVE STUDY FROM THE FRENCH GROUP SARCOMA (GSF-GETO)

Pascaline Boudou-Rouquette[1]; David Blau[2]; Jean-Yves Blay[3]; Antoine Italiano[4]; François Gouin[5]; Olivier Mir[6]; Nicolas Penel[7]; Florence Duffaud[8]; Nelly Firmin[11]; Christine Chevreau[12]; Jean-Emmanuel Kurtz[13]; Sophie Piperno-Neumann[10]; François Goldwasser[1]; Frédérique Larousserie[9]; Philippe Anract[2]

[1]Medical Oncology, Cochin Hospital, Assistance Publique-Hôpitaux de Paris, Université Paris Descartes, Sorbonne Paris Cité, Paris, France; [2]Orthopedic surgery, Cochin Hospital, Assistance Publique-Hôpitaux de Paris, Université Paris Descartes, Sorbonne Paris Cité, Paris, France; [3]Medical Oncology, Centre Leon Bérard, Lyon, France; [4]Early Phase Trials and Sarcoma Units, Institut Bergonié, Bordeaux, France; [5]Orthopedic surgery, CHU Nantes, Nantes, France; [6]Medical Oncology, Gustave Roussy Institute, Paris, France; [7]Medical Oncology, Centre Oscar Lambret, Paris, France; [8]Medical Oncology, Hopital Universitaire La Timone, Aix Marseille University, Paris, France; [9]Pathology, Cochin Hospital, Assistance Publique-Hôpitaux de Paris, Université Paris Descartes, Sorbonne Paris Cité, Paris, France; [10]Medical Oncology, Curie Institute, Paris, France; [11]Medical Oncology, Institut du Cancer, Montpellier, France; [12]Medical Oncology, Institut Universitaire du Cancer Toulouse - Oncopole, Paris, France; [13]Medical Oncology, CHRU Strasbourg, Paris, France

P1 - Poster 112 2565259

INITIAL REPORTS OF EURO EWING 2012 AND REECUR - INTERNATIONAL RANDOMISED CONTROLLED TRIALS OF CHEMOTHERAPY FOR NEWLY DIAGNOSED AND RECURRENT/REFRACTORY EWING SARCOMAS (ES)

Bernadette Brennan, MBChB MD[1]; Martin Mccabe[2]; Veronica Moroz[3]; Uta T. Dirksen[4]; Nathalie Gaspar[5]; Perrine Marec-Bérard[6]; Javier Martín[7]; Kirsten Sundby Hall[8]; Jukka Jukka Kanerva[9]; Hans Gelderblom[10]; Stefano Ferrari[11]; Sandra Strauss[12]; Jeremy Whelan[12]; Keith Wheatley[3]

[1]Paediatric Oncology, Royal Manchester Children's Hospital, Manchester, United Kingdom; [2]University of Manchester, Manchester, United Kingdom; [3]Cancer Research UK Clinical Trials Unit, Birmingham, United Kingdom; [4]Gesellschaft für Pädiatrische Onkologie und Hämatologie, Muenster, Germany; [5]Société Française de Lutte contre les Cancers et Leucémies de l'Enfant et de l'Adolescent, Paris, France; [6]Centre Léon Bérard, Lyon, France; [7]Grupo Español de Investigación en Sarcomas, Madrid, Spain; [8]Scandinavian Sarcoma Group, Oslo, Norway; [9]Helsinki University Central Hospital and University of Helsinki, Helsiniki, Finland; [10]European Organisation for Research and Treatment of Cancer, Brussels, Luxembourg; [11]Italian Sarcoma Group, Bologna, Italy; [12]University College Hospital london, London, United Kingdom

P1 - Poster 113 2561930

TIMELINES ASSOCIATED WITH OPENING TWO CLINICAL TRIALS (EURO EWING 2012 AND REECUR) FOR EWING SARCOMA (ES) PATIENTS ACROSS EUROPE

Bernadette Brennan, MBChB MD[1]; Martin Mccabe[2]; Jennifer Anderton[3]; Perrine Marec-Bérard[4]; Uta T. Dirksen[5]; Javier Martín[6]; Kirsten Sundby Hall[7]; Jukka Jukka Kanerva[8]; Stefano Ferrari[9]; Hans Gelderblom[10]; Veronica Moroz[3]; Nicola Fenwick[3]; Sandra Strauss[11]; Jeremy Whelan[11]; Keith Wheatley[3]

[1]Paediatric Oncology, Royal Manchester Children's Hospital, Manchester, United Kingdom; [2]University of Manchester, Manchester, United Kingdom; [3]Cancer Research UK Clinical Trials Unit, Birmingham, United Kingdom; [4]Centre Léon Bérard, Lyon, France; [5]Gesellschaft für Pädiatrische Onkologie und Hämatologie, Muenster, Germany; [6]Grupo Español de Investigación en Sarcomas, Madrid, Spain; [7]Oslo University Hospital, Oslo, Norway; [8]Helsinki University Central Hospital and University of Helsinki, Helsiniki, Finland; [9]Italian Sarcoma Group, Bologna, Italy; [10]European Organisation for Research and Treatment of Cancer, Brussels, Luxembourg; [11]University Hospital College London, London, United Kingdom

P1 - Poster 114 2567959

CAN DENOSUMAB CHANGE THE TREATMENT PARADIGM FOR ANEURYSMAL BONE CYSTS (ABC)?

Emanuela Palmerini[1]; Stefano Boriani[1]; Pietro Ruggieri[2]; Domenico Campanacci[3]; Giuseppe M. Milano[4]; Marilena Cesari[1]; Anna Paioli[1]; Alessandra Longhi[1]; Massimo E. Abate[1]; Guido Scoccianti[3]; Silvia Terzi[1]; Giulia Trovarelli[1]; Piero Picci[1]; Stefano Ferrari[1]

[1]Istituto Ortopedico Rizzoli, Bologna, BO, Italy; [2]Università di Padova, Padova, Italy; [3]Florence University, Florence, Italy; [4]Ospedale Pediatrico Bambin Gesù, Rome, Italy

P1 - Poster 115 2559023

DENOSUMAB-INDUCED RANK-RANKL PATHWAY CHANGES IN RESECTABLE GCT

Maria Serena Benassi, PhD; Irene Quattrini; Laura Pazzaglia; Laura Campanacci; Piero Picci; Stefano Ferrari; Emanuela Palmerini

Oncology, Istituto Ortopedico Rizzoli, Bologna, Italy

P1 - Poster 116 2569562

PROTEIN EXPRESSION PROFILES CORRESPONDING TO HISTOLOGICAL CHANGES WITH DENOSUMAB TREATMENT IN GIANT CELL TUMORS OF BONE

Yoshiyuki Suehara[1]; Kenta Mukaihara[1]; Yu Tanabe[1]; Shinji Kohsaka[2]; Saiko Kazuno[3]; Midori Ishii[1]; Keisuke Akaike[1]; Daisuke Kubota[1]; Kazuo Kaneko[1]; Tsuyoshi Saito[4]

[1]Department of Orthopedic Surgery, Juntendo University School of Medicine, Tokyo, Japan; [2]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [3]Laboratory of Biochemical Analysis, Central Laboratory of Medical Sciences, Juntendo University School of Medicine, Tokyo, Japan; [4]Department of Human Pathology, Juntendo University School of Medicine, Tokyo, Japan

P1 - Poster 117 2562256

GIANT CELL TUMOR OF THE PROXIMAL FEMUR HAS A HIGHER LOCAL RECURRENCE RATE COMPARED TO OTHER SITES AFTER CURETTAGE AND PACKING THE BONE CAVITY WITH CEMENT OR BONE ALLOGRAFTS

Costantino Errani, MD, PhD; Giulio Leone; Luca Cevolani; Alberto Righi; Marco Gambarotti; Davide Donati
Musculoskeletal Oncology, Istituto Ortopedico Rizzoli, Bologna, Italy

P1 - Poster 118 2570264

DENOSUMAB AS STAND-ALONE TREATMENT IN GIANT CELL TUMOR OF BONE

Sandra Santos, Resident; Ruben Fonseca; João Freitas; Paulo F. Tavares; Jose M. Casanova
Ortopedia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

P1 - Poster 119 2567761

BONE TURNOVER MARKERS IN A PHASE II STUDY OF DENOSUMAB IN GIANT CELL TUMORS OF BONE (GCTB): CAN WE USE IT BETTER?

Emanuela Palmerini; Loredana Pratelli; Maria Serena Benassi; Annalisa Nobile; Emanuela Marchesi; Laura Campanacci; Eric Staals; Davide Donati; Piero Picci; Stefano Ferrari
Istituto Ortopedico Rizzoli, Bologna, BO, Italy

P1 - Poster 120 2570499

PIGMENTED VILLONODULAR SYNOVITIS (GIANT-CELL TUMOR OF TENDON SHEATH) RESULTS OF SURGICAL AND ADJUVANT THERAPY

Carl F. Capellen[1]; Reinhold Tiling[2]; Alexander Klein[1]; Andrea Baur-Melnyk[3]; Thomas Knösel[4]; Volkmar Jansson[1]; Hans R. Dürr[1]

[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany; [2]Department of Nuclear Medicine, LMU Munich, Munich, Germany; [3]Institute of Radiology, LMU Munich, Munich, Germany; [4]Institute of Pathology, LMU Munich, Munich, Macao

P1 - Poster 121 2544543

THE SURGICAL COMPLICATIONS OF THE TENOSYNOVIAL GIANT CELL TUMOUR OF THE FINGER

Michihito Miyagi, MD, PhD[2]; Yoji Shido[2]; Kaori Sugiura[1]; Ryosuke Furuhashi[1]; Takao Omura[2]; Hiroaki Ogihara[1]

[1]Orthopedics Surgery, Hamamatsu Red Cross Hospital, Hamamatsu, Shizuoka, Japan; [2]Orthopaedics Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan

P1 - Poster 122 2570766

CLINICAL AND HISTOLOGIC RISK FACTORS FOR LOCAL RECURRENCE AND SURVIVAL IN CHORDOMA

Kamil M. Amer, BS (MD in progress)[1]; Bryan Hozack[4]; Stacey Mardekian[2]; Atrayee BasuMallick[3]; Mitchell Maltenfort[4]; Wei Jiang[2]; John A. Abraham[4]

[1]Temple University Lewis Katz School of Medicine, Philadelphia, PA, USA; [2]Pathology, Thomas Jefferson University Hospital, Philadelphia, PA, USA; [3]Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, PA, USA; [4]Orthopedic Surgery, Thomas Jefferson University Hospital, Philadelphia, PA, USA

P1 - Poster 123 2555566

RESPONSE TO CHECKPOINT INHIBITION IN A PEDIATRIC PATIENT WITH METASTATIC REFRACTORY CHORDOMA

Steven J. Jonas, MD, PhD[1]; Caroline J. Gross[1]; Mitchell Kamrava[2]; Arun S. Singh[3]; Jeffrey Goldstein[4]; Nicholas Bernthal[5]; Frederick C. Eilber[6]; Erlinda M. Gordon[7]; Sant P. Chawla[7]; Noah Federman[1]

[1]Pediatric Hematology/Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [2]Radiation Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [3]Medicine, Hematology & Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [4]Pathology and Laboratory Medicine, University of California, Los Angeles, Los Angeles, CA, USA; [5]Orthopaedic Surgery, University of California, Los Angeles, Los Angeles, CA, USA; [6]Surgical Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [7]Sarcoma Oncology, Cancer Center of Southern California, Santa Monica, CA, USA

P1 - Poster 124 2569944

TRENTO PROTON THERAPY CENTRE INITIAL EXPERIENCE FOR SPINE CHORDOMA, CHONDROSARCOMA AND OTHER SARCOMAS

Irene Giacomelli; Daniele Scartone; Marco Cianchetti; Francesco Dionisi; Dante Amelio; Barbara Rombi; Sabina Vennarini; Francesco Fracchiolla; Marco Schwarz; Maurizio Amichetti

Centro Protonterapia Trento, Trento, Italy

P1 - Poster 125 2570211

POSTOPERATIVE OUTCOME AND PATHOLOGICAL INFILTRATIVE FEATURE OF SACRAL CHORDOMAS: A RETROSPECTIVE ANALYSIS OF 46 CASES

Toru Akiyama, MD, PhD[1]; Koichi Ogura[2]; Tabu Gokita[3]; Satoshi Tsukushi[4]; Shintaro Iwata[5]; Tomoki Nakamura[6]; Akihiko Matsumine[6]; Tsukasa Yonemoto[5]; Yoshihiro Nishida[7]; Kazuo Saita[1]; Akira Kawai[2]; Seiichi Matsumoto[3]; Takehiko Yamaguchi[8]

[1]Departments of Orthopaedic Surgery, Saitama Medical Center, Jichi Medical University, Saitama, Japan; [2]Department of Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [3]Department of Orthopedic Surgery, Cancer Institute Hospital, Tokyo, Japan; [4]Department of Orthopedic Surgery, Aichi Cancer Center Hospital, Nagoya, Japan; [5]Division of Orthopaedic Surgery, Chiba Cancer Center, Chiba, Japan; [6]Department of Orthopaedic Surgery, Mie University Hospital, Tsu, Japan; [7]Nagoya University Graduate School and School of Medicine, Nagoya, Japan; [8]Department of Pathology, Dokkyo Medical University Koshigaya Hospital, Koshigaya, Japan

P1 - Poster 126 2570749

TREATMENT OUTCOMES OF PATIENTS WITH PRIMARY CHORDOMAS TREATED WITH PREOPERATIVE RADIATION (ALONE) FOLLOWED BY SURGERY

Karen De Amorim Bernstein, MD[1]; Saveli Goldberg[1]; Norbert Liebsch[1]; Joseph Schwab[2]; Francis Hornicek[2]; Gregory M. Cote[3]; Edwin Choy[3]; Alex Haynes[4]; John T. Mullen[4]; Yen-Lin Chen[1]; Thomas F. DeLaney[1]

[1]Radiation Oncology, MassachusettGeneral Hospital, Boston, MA, USA; [2]Orthopedic Surgery, Massachusetts General Hospital, Boston, MA, USA; [3]Hematology/Oncology, Massachusetts General Hospital, Boston, MA, USA; [4]General Surgery, Massachusetts General Hospital, Boston, MA, USA

P1 - Poster 127 2553038

MULTIDISCIPLINARY APROACH TO SACRAL CHORDOMA

José Manuel Asencio[2]; Maitane Orue-Echebarria González[2]; Pablo Lozano[2]; Julien Ariel[2]; Felipe Calvo[1]; Javier Serrano[1]; José Antonio Calvo Haro[3]; Ana Alvarez[1]; Miguel Cuervo[3]

[1]Radiotherapy, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [2]General Surgery, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [3]Orthopaedic Surgery, Hospital General Universitario Gregorio Marañón, Madrid, Spain

P1 - Poster 128 2570460

THERAPY AND PROGNOSIS IN CHONDROSARCOMA

Julian Fromm[1]; Alexander Klein[1]; Andrea Baur-Melnyk[2]; Thomas Knösel[3]; Volkmar Jansson[1]; Hans R. Dürr[1]

[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany; [2]Institute of Radiology, LMU Munich, Munich, Germany; [3]Institute of Pathology, LMU Munich, Munich, Germany

P1 - Poster 129 2563640
CLEAR CELL CHONDROSARCOMA MIMICKING BENIGN BONE TUMORS
Chang-Bae Kong; Seung Yong Lee; Won Seok Song; Wan Hyeong Cho; Jae Soo Koh; Dae-Geun Jeon
KCCH, Seoul, Korea (the Republic of)

P1 - Poster 130 2565811
EFFICIENCY OF TC-99 M MDP AND THALLIUM-201 SCINTIGRAPHY IN THE DIFFERENTIAL DIAGNOSIS OF CHONDROSARCOMA AND CHONDROBLASTIC OSTEOSARCOMA
Yuta Taniguchi; Norio Yamamoto; Katsuhiro Hayashi; Akihiko Takeuchi; Takashi Kato; Takashi Higuchi; Kensaku Abe; Hisaki Aiba; Hiroyuki Tsuchiya
Orthopeadics, Kanazawa University Hospital, Kanazawa, Ishikawa, Japan

P1 - Poster 131 2530300
EFFECT OF CYTOSTATIC PRP-1 ON TUMOR SUPPRESSORS OF INFLAMMATORY PATHWAY AND IL6 MEDIATED SIGNALING IN CHONDROSARCOMA
Karina Galoian, PhD[1]; Shihua Luo[1]; Amir Qureshi[1]; Parthik Patel[1]; Rachel Price[1]; Ashlyn Morse[1]; H.T. Temple[2]
[1]Orthopaedic Surgery, University of Miami, Miller School of Medicine, Miami, FL, USA; [2]Translational Research and Economic Development, Nova Southeastern University, Davie, FL, USA

P1 - Poster 132 2570109
EPIDEMIOLOGICAL AND SURVIVAL ANALYSIS OF DEDIFFERENTIATED CHONDROSARCOMA: RESULTS FROM EVALUATION OF SEER DATABASE
Kamil M. Amer, BS (MD in progress)[1]; John A. Abraham[2]; Barry Kenneally[2]; Mitchell Maltenfort[2]; Atrayee BasuMallick[3]
[1]Temple University Lewis Katz School of Medicine, Philadelphia, PA, USA; [2]Orthopedic Surgery, Thomas Jefferson University Hospital, Philadelphia, PA, USA; [3]Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, PA, USA

P1 - Poster 133 2570625
CHOLESTEROL ACTS DOWNSTREAM OF HEDGEHOG (HH) SIGNALING IN CHONDROSARCOMA: IMPLICATION FOR THERAPY
Qingxia Wei[1]; Eyal Ramu[1]; Robert Turcotte[2]; Ben Alman[1]; Jay Wunder[3]
[1]The Hospital for Sick Children, Toronto, ON, Canada; [2]McGill University, Montreal, QC, Canada; [3]University of Toronto, Toronto, ON, Canada

P1 - Poster 134 2566497
ROLE OF MIRNA-143/5 CLUSTER IN CHONDROSARCOMA PROGRESSION
Joaquin Urdinez, MS; Aleksandar Boro; Ana Gvozdenovic; Bruno Fuchs Orthopedics, Balgrist, Zurich, Zurich, Switzerland

P1 - Poster 135 2555190
EPIDEMIOLOGICAL AND SURVIVAL ANALYSIS OF MESENCHYMAL CHONDROSARCOMA: RESULTS FROM EVALUATION OF SEER DATABASE
Kamil M. Amer, BS (MD in progress)[1]; Atrayee BasuMallick[3]; Mitchell Maltenfort[2]; Barry Kenneally[2]; John A. Abraham[2]
[1]Temple University Lewis Katz School of Medicine, Philadelphia, PA, USA; [2]Orthopedic Surgery, Thomas Jefferson University Hospital, Philadelphia, PA, USA; [3]Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, PA, USA

P1 - Poster 136 2564876
EXPLORATION OF CANDIDATE GENES TO INDUCE CARTILAGE TUMORS WITH MUTANT IDH1 GENE USING IPSC
Takeshi Kamakura[1]; Yonghui Jin[1]; Kazuhito Matsunaga[3]; Makoto Watanabe[4]; Sakura Tamaki[1]; Takeshi Okamoto[2]; Hiroyuki Yoshitomi[1]; Junya Toguchida[1]
[1]Tissue Regeneration, Institute for Frontier Medical Sciences, Kyoto University, Kyoto, Kyoto, Japan; [2]Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan; [3]Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine, Yamaguchi University, Ube, Yamaguchi, Japan; [4]Cell Growth and Differentiation, Center for iPS Cell Research and Application, Kyoto University, Kyoto, Kyoto, Japan

P1 - Poster 137 2564829

MUTANT IDH1 DYSREGULATES THE DIFFERENTIATION OF MESENCHYMAL STEM CELLS IN ASSOCIATION WITH GENE- SPECIFIC HISTONE MODIFICATIONS TO CARTILAGE - AND BONE-RELATED GENES

Yonghui Jin, PhD[1]; Makoto Watanabe[2]; Sakura Tamaki[1]; Takeshi Okamoto[3]; Junya Toguchida[1]

[1]Institute for Frontier Medical Sciences, Kyoto University, Kyoto, Japan; [2]Department of Cell Growth and Differentiation, Center for IPS Cell Research and Application, Kyoto University, Kyoto, Japan; [3]Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

P1 - Poster 138 2568392

A PHASE 1 STUDY OF AG-120, AN IDH1 MUTANT ENZYME INHIBITOR: RESULTS FROM THE CHONDROSARCOMA DOSE ESCALATION AND EXPANSION COHORTS

William Tap[2]; Victor M. Villalobos[3]; Gregory M. Cote[4]; Howard Burris[5]; Filip Janku[6]; Olivier Mir[7]; Murali Beeram[8]; Andrew Wagner[9]; Julia Auer[1]; Hua Liu[1]; Bin Wu[1]; Katharine Yen[1]; Sam Agresta[1]; Shuchi S. Pandya[1]; Jonathan Trent[10]

[1]Agios Pharmaceuticals, Cambridge, MA, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]University of Colorado, Denver, CO, USA; [4]Massachusetts General Hospital, Boston, MA, USA; [5]Sarah Cannon Research Institute, Nashville, TN, USA; [6]MD Anderson Cancer Center, Houston, TX, USA; [7]Gustave Roussy Cancer Institute, Paris, France; [8]The START Center for Cancer Care, San Antonio, TX, USA; [9]Dana-Farber Cancer Center, Boston, MA, USA; [10]University of Miami, Miami, FL, USA

P1 - Poster 139 2541711

IDENTIFICATION OF A POSSIBLE THERAPEUTIC CANDIDATE FOR ADVANCED CHONDROSARCOMA WITH AN IDH1 MUTANT INHIBITOR

Makoto Nakagawa[1]; Fumihiko Nakatani[2]; Makoto Endo[2]; Eisuke Kobayashi[2]; Yoshikazu Tanzawa[2]; Akira Kawai[2]; Hirokazu Chuman[2]; Akihiko Yoshida[3]; Takehiko Seki[4]; Kazushi Araki[4]; Yukihide Iwamoto[5]; Issay Kitabayashi[1]

[1]Hematological Malignancy, National Cancer Center Research Institute, Tokyo, Japan; [2]Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [3]Pathology and Clinical Laboratories, National Cancer Center Hospital, Tokyo, Japan; [4]R&D Division, Daiichi-Sankyo, Tokyo, Japan; [5]Orthopaedic Surgery, Kyushu University, Fukuoka, Japan

P1 - Poster 140 2570238

D-2HG LEVELS AND IDH MUTATION TYPE CORRELATE WITH DISEASE FREE SURVIVAL IN CHONDROSARCOMA

Makoto Hirata[1]; Nalan Gokgoz[2]; Qingxia Wei[1]; Shingo Sato[1]; Yuning J. Tang[1]; Irene L. Andrulis[2]; Benjamin Alman[3]; Jay Wunder[4]

[1]Developmental and Stem Cell Biology, Hospital for Sick Children, Toronto, ON, Canada; [2]Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, ON, Canada; [3]Department of Orthopaedic Surgery, Duke University, Durham, NC, USA; [4]University of Toronto Musculoskeletal Oncology Unit, Mount Sinai Hospital, Toronto, ON, Canada

P1 - Poster 141 2552801

FORTY-EIGHT CASES OF LEIOMYOSARCOMA OF BONE: A MULTICENTER STUDY IN JAPAN

Tomoaki Mori[1]; Robert Nakayama[2]; Makoto Endo[1]; Eisuke Kobayashi[1]; Akira Kawai[1]; Takafumi Ueda[3]; Hideo Morioka[2]

[1]Division of Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [2]School of Medicine, Keio University, Tokyo, Japan; [3]National Hospital Organization Osaka National Hospital, Osaka, Japan

P1 - Poster 142 2554149

DIFFERENTIAL MIRNA EXPRESSION PROFILING OF PDGFRA-MUTATED GASTROINTESTINAL STROMAL TUMORS (GIST)

Margherita Nannini, MD[1]; Gloria Ravegnini[2]; Milena Urbini[1]; Sabrina Angelini[2]; Annalisa Astolfi[3]; Valentina Indio[1]; Maristella Saponara[1]; Lidia Gatto[1]; Guido Biasco[3]; Maria A. Pantaleo[1]

[1]Department of Specialized, Experimental and Diagnostic Medicine, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; [2]Department of Pharmacy and Biotechnology, University of Bologna, Bologna, Italy; [3]"Giorgio Prodi" Cancer Research Center, University of Bologna, Bologna, Italy

P1 - Poster 143 2571368

EVALUATION OF DMD DELETIONS IN NON-METASTATIC GIST PATIENTS TREATED WITH ADJUVANT IMATINIB

Ana Sebio, MD, PhD[1]; Pia Gallano[2]; Maria Jose Rodriguez[2]; Silvia Bague[3]; Juliana Salazar[2]; Lidia Gonzalez[2]; Vicenç Artigas[4]; Ana Virgili[1]; Oscar Gallego[1]; Agusti Barnadas[1]; Antonio Lopez-Pousa[1]

[1]Medical Oncology, Santa Creu I Sant Pau Hospital, Barcelona, Spain; [2]Genetics, Santa Creu I Sant Pau Hospital, Barcelona, Spain; [3]Pathology, Santa Creu I Sant Pau Hospital, Barcelona, Spain; [4]Surgery, Santa Creu I Sant Pau Hospital, Barcelona, Spain

P1 - Poster 144 2559490

BUSULFAN-MELPHALAN WITH BLOOD STEM CELL RESCUE (BUMEL) FOR HIGH RISK LOCALISED EWING SARCOMA (ES): RESULTS OF R2LOC RANDOMISED STUDY

Jeremy Whelan, MD MBBS FRCP[1]; Marie-Cecile De Leley[2]; Uta T. Dirksen[3]; Nathalie Gaspar[2]; Ian Judson[4]; Bernadette brennan[5]; Andreas Ranft[3]; Jendrik Hardes[3]; Perrine Marec-Bérard[6]; Michael Paulussen[7]; Gwenael Le Teuff[2]; Ian Lewis[8]; Alan Craft[9]; Heribert Juergens[3]; Odile Oberlin[2]

[1]Oncology, University College Hospital London, London, United Kingdom; [2]Gustave Roussy, Villejuif, France; [3]University Hospital Muenster, Muenster, Germany; [4]Royal Marsden Hospital, London, United Kingdom; [5]Royal Manchester Childrens Hospital, Manchester, United Kingdom; [6]Centre Léon Bérard, Lyon, France; [7]Witten/Herdecke University, Datteln, Germany; [8]University of Leeds, Leeds, United Kingdom; [9]Newcastle University, Newcastle, United Kingdom

P1 - Poster 145 2550561

EFFICACY OF BUSULFAN-MELPHALAN HIGH DOSE CHEMOTHERAPY CONSOLIDATION (BUMEL) COMPARED TO CONVENTIONAL CHEMOTHERAPY COMBINED WITH LUNG IRRADIATION IN EWING SARCOMA (ES) WITH PRIMARY LUNG METASTASES: RESULTS OF EURO-EWING 99-R2PULM RANDOMIZED TRIAL (EE99R2PUL)

Douglas S. Hawkins, MD[1]; Marie-Cecile Le Deley[2]; Bernadette Brennan[3]; Ian Judson[4]; Richard Gorlick[5]; Richard B. Womer[6]; Nathalie Gaspar[2]; Gwenael Le Teuff[2]; Perrine Marec-Berard[7]; Andreas Faldum[8]; Michael Paulussen[9]; Heribert Juergens[8]; Keith Wheatley[10]; Mark Krailo[11]; Uta T. Dirksen[8]

[1]Pediatrics, Seattle Children's Hospital, Seattle, WA, USA; [2]Institute Gustave Roussy, Villejuif, France; [3]Royal Manchester Children's Hospital, Manchester, United Kingdom; [4]The Royal Marsden Hospital, Sutton, United Kingdom; [5]The Children's Hospital, Bronx, NY, USA; [6]Children's Hospital of Philadelphia, Philadelphia, PA, USA; [7]Institut d'Hématologie et d'Oncologie Pédiatrie, Lyon, France; [8]Westfälische Wilhelm's-Universität Münster, Muenster, Germany; [9]Witten-Herdecke University, Datteln, Germany; [10]University of Birmingham, Birmingham, United Kingdom; [11]Department of Preventive Medicine, University of Southern California, Los Angeles, CA, USA

P1 - Poster 146 2566848

INSTITUTIONALLY-REPORTED HISTOLOGIC RESPONSE (HR) AND OUTCOME IN EWING SARCOMA: A REPORT FROM CHILDREN'S ONCOLOGY GROUP STUDY AEWS0031

Richard B. Womer, MD[1]; Mark Krailo[2]; Daniel C. West[9]; Bruce R. Pawel[3]; Paul Dickman[4]; John Healey[10]; John P. Dormans[11]; Karen Marcus[5]; Neyssa Marina[6]; Holcombe E. Grier[7]; Aaron Weiss[12]; Richard Gorlick[8]

[1]Pediatrics / Oncology, Children's Hosp of Phila / Univ of Penn, Philadelphia, PA, USA; [2]Children's Oncology Group, Monrovia, CA, USA; [3]Pathology, Children's Hosp of Phila / Univ of Penn, Philadelphia, PA, USA; [4]Pathology, Phoenix Children's Hospital, Phoenix, AZ, USA; [5]Radiation Oncology, Dana-Farber Cancer Center, Boston, MA, USA; [6]Pediatrics, Lucille Packard Children's Hospital, Palo Alto, CA, USA; [7]Pediatrics, Dana-Farber Cancer Institute, Boston, MA, USA; [8]Pediatrics, Montefiore Medical Center, New York, NY, USA; [9]Pediatrics, University of California, San Francisco, San Francisco, CA, USA; [10]Orthopedics, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [11]Orthopedics, Texas Children's Hospital, Houston, TX, USA; [12]Pediatrics, Maine Medical Center, Portland, ME, USA

P1 - Poster 147 2559012

GEIS-21: A MULTICENTRIC PHASE II STUDY OF INTENSIVE CHEMOTHERAPY INCLUDING GEMCITABINE/ DOCETAXEL FOR THE TREATMENT OF EWING SARCOMA OF CHILDREN AND ADULTS: A REPORT FROM THE SPANISH GROUP OF SARCOMA INVESTIGATION (GEIS)

Jaume Mora, MD, PhD[1]; Alicia Castañeda[1]; Antonio Lopez-Pousa[4]; Claudia Valverde[3]; Javier Martin-Broto[2]; Xavier Garcia del Muro[5]; Enrique de Alava[2]; Carmen de Torres[1]

[1]Pediatric Oncology, Hospital Sant Joan de Déu, Barcelona, Spain; [2]Hopsital Virgen del Rocio, Sevilla, Spain; [3]Hospital Vall de Hebron, Barcelona, Spain; [4]Hospital de Sant Pau, Barcelona, Spain; [5]Institut Català d'Oncologia, Barcelona, Spain

P1 - Poster 148 2571077

PEDIATRIC PATIENT WITH SIADH RELATED TO HIGH DOSE METHOTREXATE REGIMEN

Jennifer A. Misasi, Masters[1]; Anil P. George[2]; Paul Kent[1]

[1]Pediatrics-Oncology, Rush University Medical Center, Chicago, IL, USA; [2]Pediatrics-Oncology, University of Illinois, Chicago, IL, USA

P1 - Poster 149 2570646

OUTCOMES IN PATIENTS WITH RECURRENT DESMOID TUMOR MANAGED WITH SURGERY ALONE, COMBINED SURGERY AND RADIATION THERAPY OR RADIATION THERAPY ALONE

Michelle S. Gentile, MD, PhD[1]; Alex Jacobson[1]; Haotong Wang[1]; Saveli Goldberg[1]; Edwin Choy[3]; John T. Mullen[2]; Kevin Raskin[4]; Nielsen Petur[5]; Francis Hornicek[4]; Thomas F. DeLaney[1]; Yen-Lin Chen[1]

[1]Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [2]General Surgery, Massachusetts General Hospital, Boston, MA, USA; [3]Medical Oncology, Massachusetts General Hospital, Boston, MA, USA; [4]Orthopedic Oncology, Massachusetts General Hospital, Boston, MA, USA; [5]Pathology, Massachusetts General Hospital, Boston, MA, USA

P1 - Poster 150 2565620

THE SAFETY AND RESULTS OF INTRATUMORAL STERIOD INJECTION FOR PROGRESSIVE FIBROMATOSIS: PHASE-I CLINICAL TRIAL STUDY

Dumnoensun Pruksakorn, MD, PhD[1]; Areerak Phanphaisarn[1]; Saratwadee Lorsomradee[2]; Natthapong Kosachumhanun[3]; Pimpis Piyakasem[1]; Jongkolnee Settakorn[4]

[1]Department of Orthopedics, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [2]Department of Anesthesiology, Chiang Mai University, Chiang Mai, Thailand; [3]Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [4]Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

P1 - Poster 151 2555901

CLINICAL FEATURES AND TREATMENT OUTCOME OF DESMOID-TYPE FIBROMATOSIS BASED ON DATA OF THE BONE AND SOFT TISSUE TUMOR REGISTRY IN JAPAN

Yoshihiro Nishida, MD, PhD[1]; Akira Kawai[2]; Junya Toguchida[3]; Akira Ogose[4]; Keisuke Ae[5]; Toshiyuki Kunisada[6]; Tomoya Matsunobu[7]; Shunsuke Hamada[1]; Tomohisa Sakai[1]

[1]Orthopaedic Surgery, Nagoya University Graduate School and School of Medicine, Nagoya, Aichi, Japan; [2]National Cancer Center, Tokyo, Japan; [3]Kyoto University, Kyoto, Japan; [4]Uonuka Kikan Hospital, Niigata University, MInami Uonuma, Japan; [5]Cancer Institute Hospital, Tokyo, Japan; [6]Okayama University, Okayama, Japan; [7]Kyusyu Rosai Hospital, Kitakyusyu, Japan

P1 - Poster 152 2531917

IS SYMPTOM WORSENING (SW) ASSOCIATED WITH RECIST RESPONSE IN DESMOID TUMORS (DT) PATIENTS (PTS)?

Nuria Kotecki[1]; Armelle Renaud[2]; Meriem Ben Haj Amor[2]; Desfachelles Anne-Sophie[3]; Thomas Ryckewaert[1]; Vincent Gamblin[4]; Yves-Marie Robin[5]; Sophie Taieb[2]; Nicolas Penel[1]

[1]Medical Oncology, Centre Oscar Lambret, Lille, France; [2]Imaging Department, Centre Oscar Lambret, Lille, France; [3]Pediatric Oncology Unit, Centre Oscar Lambret, Lille, France; [4]Palliative Care Unit, Centre Oscar Lambret, Lille, France; [5]Pathology Unit, Centre Oscar Lambret, Lille, France

P1 - Poster 153 2558252

A REFRACTORY DESMOID-TYPE FIBROMATOSIS WITH A REMARKABLE RESPONSE TO PAZOPANIB TREATMENT

Eisuke Kobayashi, MD, PhD; Makoto Endo; Yoshikazu Tanzawa; Fumihiko Nakatani; Hirokazu Chuman; Akira Kawai Orthopaedic, National Cancer Research Center Hospital, Tokyo, Japan

P1 - Poster 154 2570475

THERAPY AND PROGNOSIS IN DESMOID TUMOR

Laura Wirth[1]; Falk Roeder[2]; Andrea Baur-Melnyk[3]; Thomas Knösel[4]; Lars Lindner[5]; Alexander Klein[1]; Volkmar Jansson[1]; Hans R. Dürr[1]

[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany; [2]Institute of Radiotherapy, LMU Munich, Munich, Germany; [3]Institute of Radiology, LMU Munich, Munich, Germany; [4]Institute of Pathology, LMU Munich, Munich, Germany; [5]Medical Clinic III, LMU Munich, Munich, Germany

P1 - Poster 155 2553792

USE OF HYDROXYUREA IN CHILDREN, ADOLESCENTS AND ADULTS WITH RECURRENT AND/OR REFRACTORY AGGRESSIVE FIBROMATOSES

Caroline J. Gross, BS[1]; Arun S. Singh[2]; Bartosz Chmielowski[2]; Frederick C. Eilber[3]; Nicholas Bernthal[4]; Susan Bukata[4]; Leanne Seeger[5]; Scott Nelson[6]; Mitchell Kamrava[7]; Noah Federman[8]

[1]UCLA David Geffen School of Medicine, Los Angeles, CA, USA; [2]Medicine, Hematology & Oncology, UCLA, Los Angeles, CA, USA;

[3]Surgical Oncology, UCLA, Los Angeles, CA, USA; [4]Orthopaedic Surgery, UCLA, Los Angeles, CA, USA; [5]Radiological Sciences, UCLA, Los Angeles, CA, USA; [6]Pathology, UCLA, Los Angeles, CA, USA; [7]Radiation Oncology, UCLA, Los Angeles, CA, USA; [8]Pediatrics, Hematology & Oncology, UCLA, Los Angeles, CA, USA

P1 - Poster 156 2561516

DESMOID PATIENTS AND THE RISK OF FAMILIAL ADENOMATOUS POLYPOSIS: WHO SHOULD HAVE A COLONOSCOPY?

Winan van Houdt, MD, PhD[1]; Deborah Kuk[3]; Li-Xuan Qin[3]; Anthony Villano[2]; Meera Hameed[4]; Frits van Coevorden[5]; Samuel Singer[2]; Aimee M. Crago[2]

[1]Department of Surgery, Royal Marsden Hospital, London, United Kingdom; [2]Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Department of Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [5]Surgery, Netherlands Cancer Institute, Amsterdam, Netherlands

P1 - Poster 157 2570645

CONSERVATIVE MANAGEMENT OF DESMOID TUMORS IS SAFE AND EFFECTIVE

Jiwon S. Park[1]; Robert D. Boutin[2]; Arta M. Monjazeb[3]; Robert J. Canter[1]

[1]Surgery, UC Davis, Sacramento, CA, USA; [2]Radiology, UC Davis, Sacramento, CA, USA; [3]Radiation Oncology, UC Davis, Sacramento, CA, USA

P1 - Poster 158 2543288

EXOSOME DERIVED FROM OSTEOSARCOMA CELL LINE WITH HIGHLY PULMONARY METASTATIC POTENTIAL PROMOTE CELL PROLIFERATION AND MOVEMENT OF OSTEOSARCOMA CELLS

***Takuya Kakimoto**[2]; Akihiko Matsumine[1]; Kunihiro Asanuma[1]; Takao Matsubara[1]; Tomoki Nakamura[1]; Yuki Yada[1]; Tomohito Hagi[1]; Takahiro Iino[1]; Atsushi Kitao[2]; Akihiro Sudo[1]*

POSTER SESSION 2
– Soft Tissue Sarcomas –

Foyer

Set Up:	*11 November*	*10:10 am – 10:40 am*
Poster Exhibition:	*11 November* *12 November*	*10:40 am – 7:00 pm* *7:00 am – 4:00 pm*
Poster Session:	*11 November*	*6:15 pm – 7:00 pm*
Dismantle:	*12 November*	*4:00 pm*

P2–Poster 001 2557776

ACTIVATION OF THE PI3K/MTOR PATHWAY PROVIDES A THERAPEUTIC TARGET FOR FGFR4-DRIVEN RHABDOMYOSARCOMAS

Timothy McKinnon[1]; Rosemarie E. Venier[1]; Marielle Yohe[2]; Berkley Gryder[2]; Brendan C. Dickson[4]; Krista Schleicher[1]; Abha Gupta[3]; Javed Khan[2]; Rebecca Gladdy[1]

[1]Lunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada; [2]Oncogenomics, National Cancer Institute, Gaithersburg, MD, USA; [3]Hematology/Oncology, The Hospital for Sick Children, Toronto, ON, Canada; [4]Pathology, Mount Sinai Hospital, Toronto, ON, Canada

P2–Poster 002 2556403

OPPORTUNITIES FOR NOVEL MOLECULAR THERAPEUTIC INTERVENTION TARGETING THE EPIGENETIC/ MIRNA SIGNATURE OF CLEAR CELL SARCOMA OF THE SOFT TISSUES (CCSST)

Peter W. Halcrow, PhD Candidate[1]; Christopher D. Walden[1]; Joyce E. Ohm[2]

[1]Biomedical Sciences, University of North Dakota, Grand Forks, ND, USA; [2]Cancer Genetics, Roswell Park Cancer Institute, Buffalo, NY, USA

P2–Poster 003 2565140

CIRCSARC - DISEASE MONITORING BY LIQUID BIOPSIES IN SARCOMAS

Heidi M. Namløs, PhD[1]; Olga Zaikova[1]; Bodil Bjerkehagen[1]; Anders Ståhlberg[2]; Synnøve Granlien[1]; Stefan Filges[2]; Daniel Vodák[1]; Lars B. Aasheim[1]; Stine Næss[1]; Eivind Hovig[1]; Ola Myklebost[1]; Kjetil Boye[1]; Kirsten S. Hall[1]; Leonardo A. Meza-Zepeda[1]

[1]Norwegian Radium Hospital, Oslo University Hospital, OSLO, Norway; [2]Sahlgrenska Cancer Center, University of Gothenburg, Gothenburg, Sweden

P2–Poster 004 2555233

TERTIARY LYMPHOID STRUCTURES IN WELL DIFFERENTIATED / DEDIFFERENTIATED LIPOSARCOMA: POTENTIAL IMPLICATIONS IN DISEASE BIOLOGY?

William W. Tseng, MD[1]; Shefali Chopra[2]; Susan Groshen[3]; Sophia Hernandez[1]; Eric E. Jung[1]

[1]Surgery, Section of Surgical Oncology, University of Southern California, Keck School of Medicine, Los Angeles, CA, USA; [2]Pathology, University of Southern California, Keck School of Medicine, Los Angeles, CA, USA; [3]Biostatistics, University of Southern California, Keck School of Medicine, Los Angeles, CA, USA

P2–Poster 005 2535507

THE EFFECT OF SS18-SSX ON TUMOR-GROWTH AND INITIATION OF SYNOVIAL SARCOMA

Hidetatsu Otani[2]; Takaaki Tanaka[2]; Yoshinori Imura[2]; Kazuya Oshima[2]; Nobuhito Araki[2]; Takaaki Nakai[1]; Kenichiro Hamada[1]; Takafumi Ueda[3]; Hideki Yoshikawa[1]; Norifumi Naka[1]

[1]Orthopaedic Surgery, Osaka University Graduate School of Medicine, Osaka, Osaka, Japan; [2]Musculoskeletal Oncology Service, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Osaka, Japan; [3]Orthopaedic Surgery, Osaka National Hospital, Osaka, Japan

P2–Poster 006 2570166

MESENCHYMAL TUMORS CAN DERIVE FROM NG2-EXPRESSING PERICYTES WITH β-CATENIN MODULATING THE NEOPLASTIC PHENOTYPE

Shingo Sato, MD, PhD[1]; Yuning J. Tang[2]; Qingxia Wei[3]; Makoto Hirata[4]; Ilkyu Han[5]; Shu Takeda[1]; David Kirsch[6]; Jay Wunder[7]; Benjamin Alman[2]

[1]Department of Physiology and Cell Biology, Tokyo Medical and Dental University Graduate School and Faculty of Medicine, Tokyo, Japan; [2]Department of Orthopaedic Surgery, Duke University, Durham, NC, USA; [3]Developmental and Stem Cell Biology, The Hospital for Sick Children, Toronto, ON, Canada; [4]The Institute of Medical Science, The University of Tokyo, Tokyo, Japan; [5]Department of Orthopaedic Surgery, Seoul National University Hospital, Seoul, Korea (the Republic of); [6]Department of Pharmacology & Cancer Biology, Duke University, Durham, NC, USA; [7]Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, ON, Canada

P2–Poster 007 2565770

SS18-SSX, THE ONCOGENIC FUSION PROTEIN IN SYNOVIAL SARCOMA, IS A CELLULAR CONTEXT-DEPENDENT EPIGENETIC MODIFIER

Sakura Tamaki[1]; Makoto Fukuta[2]; Kazuya Sekiguchi[3]; Kazuo Hayakawa[2]; Yonghui Jin[1]; Takeshi Okamoto[4]; Knut Woltjen[5]; Hiroyuki Yoshitomi[1]; Junya Toguchida[1]

[1]Department of Tissue Regeneration, Institute for Frontier Medical Sciences, Kyoto University, Kyoto, Japan; [2]Department of Orthopaedic Surgery, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan; [3]Department of Cell Growth and Differentiation, Center for iPS Cell Research and Application, Kyoto University, Kyoto, Japan; [4]Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan; [5]Department of Life Science Frontiers, Department of Reprogramming Sciences, Kyoto University, Kyoto, Japan

P2–Poster 008 2557497

MONITORING RESPONSE TO TREATMENT IN LEIOMYOSARCOMA PATIENTS USING CIRCULATING TUMOR DNA

Joanna Przybyl, PhD[1]; Jacob J. Chabon[2]; Lien Spans[3]; Kristen Ganjoo[4]; Sujay Vennam[1]; Aaron M. Newman[2]; Erna Forgó[1]; Agnieszka Wozniak[5]; Raf Sciot[6]; Patrick Schöffski[5]; Maria Debiec-Rychter[3]; Ash Alizadeh[2]; Maximilian Diehn[2]; Matt van de Rijn[1]

[1]Department of Pathology, Stanford University, Stanford, CA, USA; [2]Institute for Stem Cell Biology and Regenerative Medicine, Stanford University, Stanford, CA, USA; [3]Department of Human Genetics, KU Leuven and University Hospitals Leuven, Leuven, Belgium; [4]Medical Oncology, Stanford Medical Institute, Stanford, CA, USA; [5]Department of Oncology, KU Leuven and Department of General Medical Oncology, University Hospitals Leuven, Leuven Cancer Institute, Leuven, Belgium; [6]Department of Pathology, KU Leuven and University Hospital Leuven, Leuven, Belgium

P2–Poster 009 2568664

COMPREHENSIVE GENOMIC SEQUENCING OF LIPOSARCOMA PATIENTS IDENTIFIES A NOVEL NTRK2 SUBGROUP

Sherri Z. Millis, PhD[1]; Sujana Movva[2]; James Chen[3]; Gregory M. Cote[4]; Edwin Choy[5]; Julia Elvin[1]; Alexa Schrock[1]; Jeffrey Ross[1]; Philip Stephens[1]; Vincent Miller[1]; Arun S. Singh[6]; Siraj Ali[1]

[1]Medical Affairs, Foundation Medicine, Phoenix, AZ, USA; [2]Fox Chase Cancer Center, Philadelphia, PA, USA; [3]Ohio State University Medical Center, Columbus, OH, USA; [4]Massachusetts General Hospital, Boston, MA, USA; [5]Harvard University, Cambridge, MA, USA; [6]UCLA, Los Angeles, CA, USA

P2–Poster 010 2568085

ESTABLISHMENT OF JAPANESE SARCOMA GENOME CONSORTIUM (JSGC) FOR GENOMIC ANALYSIS

Makoto Hirata[1]; Koichi Matsuda[2]

[1]Institute of Medical Science, University of Tokyo, Tokyo, Japan; [2]Graduate School of Frontier Sciences, University of Tokyo, Tokyo, Japan

P2–Poster 011 2569560

PATIENT-DERIVED XENOGRAFTS (PDX) AS RELIABLE PRECLINICAL MODELS TO COMPARATIVELY ASSESS THE ACTIVITY OF NOVEL DRUGS IN SOLITARY FIBROUS TUMOR (SFT)

Denis Cominetti[1]; Silvia Stacchiotti[2]; Roberta Frapolli[5]; Monica Tortoreto[1]; Tiziana Negri[4]; Gian Paolo Dagrada[4]; Ezia Bello[5]; Maristella Saponara[2]; Alessandro Gronchi[3]; Chiara Colombo[3]; Paolo Casali[2]; Silvana Pilotti[4]; Maurizio D'Incalci[5]; Nadia Zaffaroni[1]

[1]Experimental Oncology and Molecular Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milan, Milan, Italy; [2]Cancer Medicine Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Italy; [3]Department of Surgery, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Italy; [4]Department of Diagnostic Pathology and Laboratory, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Italy; [5]Department of Oncology, IRCCS, Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy

P2–Poster 012 2560400

H3K27ME3 IMMUNOHISTOCHEMISTRY IN THE DIAGNOSIS OF MALIGNANT PERIPHERAL NERVE SHEATH TUMORS: INSIGHTS FROM A VALIDATION STUDY

Naofumi Asano[1]; Hitoshi Ichikawa[2]; Taisuke Mori[3]; Masaya Nakamura[4]; Nobuyoshi Hiraoka[3]; Akira Kawai[5]; Akihiko Yoshida[3]

[1]Rare Cancer Research, National Cancer Center, Tokyo, Japan, Tokyo, Japan; [2]Clinical Genomics, National Cancer Center, Tokyo, Japan, Tokyo, Japan; [3]Pathology and Clinical Laboratories, National Cancer Center, Tokyo, Japan, Tokyo, Japan; [4]Orthopaedic Surgery, Keio University School of Medicine, Tokyo, Japan; [5]Musculoskeletal Oncology, National Cancer Center, Tokyo, Japan, Tokyo, Japan

P2–Poster 013 2570712

ACTIVATION OF INHIBITED GSK3 MALIGNANT PERIPHERAL NERVE SHEATH TUMORS (MPNST) WITH AUL12 LEADS TO RAPID CELL DEATH

Bethany Prudner; Davinelle Daniels; Jeff Kremer; Richa Rathore; Brian Van Tine
Washington University in Saint Louis, St. Louis, MO, USA

P2–Poster 014 2570248

MALIC ENZYME 1 (ME1) EXPRESSION CORRELATES WITH ROS-MEDIATED CELL DEATH IN SYNOVIAL SARCOMA

Sara Lange; Jeff Kremer; Bethany Prudner; Richa Rathore; Brian Van Tine
Washington University in Saint Louis, St. Louis, MO, USA

P2–Poster 015 2543698

ATRX-ASSOCIATED ALTERNATIVE LENGTHENING OF TELOMERE (ALT) MAY BE CORRELATED WITH CHEMOTHERAPY RESPONSE IN LEIOMYOSARCOMA (LMS)

Brett Po-Hsiang Huang[1]; Jau-Yu Liau[2]; Yung-Ming Jeng[2]; Tom W. Chen[1]

[1]Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan; [2]Department of Pathology, National Taiwan University Hospital, Taipei, Taiwan

P2–Poster 016 2558429

REDUCED ARGINOSUCCINATE SYNTHETASE EXPRESSION IN REFRACTORY SARCOMAS: THE IMPACT ON THERAPEUTIC POTENTIAL AND DRUG RESISTANCE

Youngi Kim[1]; Eisuke Kobayashi[1]; Daisuke Kubota[2]; Yoshiyuki Suehara[2]; Kenta Mukaihara[2]; Keisuke Akaike[2]; Ayumu Ito[3]; Kazuo Kaneko[2]; Hirokazu Chuman[1]; Akira Kawai[1]; Shigehisa Kitano[4]

[1]Division of Musculoskeletal Oncology, National Cancer Center Hospital (Tokyo, Japan), Tokyo, Japan; [2]Department of Orthopaedic Surgery, Juntendo University School of Medicine, Tokyo, Japan; [3]Department of Hematopoietic Stem Cell Transplantation, National Cancer Center Hospital (Tokyo, Japan), Tokyo, Japan; [4]Department of Experimental Therapeutics, National Cancer Center Hospital (Tokyo, Japan), Tokyo, Japan

P2–Poster 017 2570609

MATRIGEL SUPPORTS FORMATION OF SARCOSPHEROIDS AND UPREGULATION OF CANCER STEM CELL MARKERS

Jonathan Mandell; Shibing Yu; Jessica Tebbets; Adel Mahjoub; Mitchell S. Fourman; David Hirsch; Kurt Weiss
University of Pittsburgh, Gibsonia, PA, USA

P2–Poster 018 2561311

CIRCULATING TUMOR CELLS USING TELOMERASE-SPECIFIC REPLICATION-SELECTIVE ADENOVIRUS AS A PROGNOSTIC FACTOR IN SOFT TISSUE SARCOMA

Toshihiro Matsuo, MD, PhD[1]; Masataka Deie[1]; Shoji Shimose[2]; Yasuo Urata[3]; Katsuhisa Kawanami[1]; Keiji Sato[1]
[1]Orthopaedic Surgery, Aichi Medical University, Nagakute, Japan; [2]Kure Medical Center, Kure, Japan;
[3]Oncolys BioPharma, Tokyo, Japan

P2–Poster 019 2570249

ARGININE DEPRIVATION INDUCED AUTOPHAGY RENDERS ASS1 DEFICIENT SARCOMAS DEPENDENT ON SERINE METABOLISM AND SENSITIVE TO 3-PHOSPHOGLYCERATE DEHYDROGENASE (PHGDH) INHIBITION

Jeff Kremer[1]; Bethany Prudner[1]; Assama Ketegou[2]; Brian Van Tine[1]
[1]Oncology, Washington University In St. Louis, University City, MO, USA; [2]New York University, New York City, NY, USA

P2–Poster 020 2570660

COMPREHENSIVE GENOMIC SEQUENCING OF TUMORS OF PEDIATRIC PATIENTS WITH HEMANGIOMAS

Sherri Z. Millis, PhD[1]; Julie Blatt[2]; Alexa Schrock[1]; Julia Elvin[1]; Laurie Gay[1]; Jeffrey Ross[1]; Philip Stephens[1];
Vincent Miller[1]; Siraj Ali[1]
[1]Medical Affairs, Foundation Medicine, Phoenix, AZ, USA; [2]University of North Carolina, Research Triangle Park, NC, USA

P2–Poster 021 2570405

TRANSCRIPTOME ANALYSIS OF METASTATIC AND NON-METASTATIC PATIENT SARCOMA REVEALS DIFFERENCES IN ALDH ACTIVITY AND NOTCH SIGNALLING

Jonathan Mandell; Stuti Patel; Mitchell S. Fourman; David Hirsch; Adel Mahjoub; Jessica Tebbets; Shibing Yu; Kurt Weiss
University of Pittsburgh, Gibsonia, PA, USA

P2–Poster 022 2569798

FACTORS IMPACTING THE ESTABLISHMENT OF INDIVIDUAL SOFT TISSUE SARCOMA PATIENT-DERIVED ORTHOTOPIC XENOGRAFT (PDOX) MOUSE MODELS: A UCLA SARCOMA PROGRAM PROSPECTIVE CLINICAL TRIAL

Mark A. Eckardt[1]; Tara A. Russell, MD, MPH[2]; Takashi Murakami[3]; Arun S. Singh[4]; Tasuku Kiyuna[3]; Kentaro Igarashi[3];
Kei Kawaguchi[3]; Yunfeng Li[5]; Joseph G. Crompton[2]; Sarah M. Dry[5]; Noah Federman[6]; Bartosz Chmielowski[4];
Elizabeth Shurell[2]; Robert M. Hoffman[7]; Frederick C. Eilber[1]
[1]Department of Surgery, Yale University School of Medicine, New Haven, CT, USA; [2]Division of Surgical Oncology, Jonsson Comprehensive Cancer Center Sarcoma Program, University of California Los Angeles, Los Angeles, CA, USA; [3]Department of Surgery, University of California San Diego, San Diego, CA, USA; [4]Division of Hematology-Oncology, Jonsson Comprehensive Cancer Center Sarcoma Program, University of California Los Angeles, Los Angeles, CA, USA; [5]Department of Pathology, Jonsson Comprehensive Cancer Center Sarcoma Program, University of California Los Angeles, Los Angeles, CA, USA; [6]Department of Pediatrics, Jonsson Comprehensive Cancer Center Sarcoma Program, University of California Los Angeles, Los Angeles, CA, USA; [7]AntiCancer Inc., San Diego, CA, USA

P2–Poster 023 2566129

SIRT1 AND SIRT2 INHIBITION IMPAIRS PEDIATRIC SOFT TISSUE SARCOMA GROWTH

limin Ma; Bertha A. Brodin
Oncology&Pathology, Karolinska institutet, SOLNA, Stockholm, Sweden

P2–Poster 024 2563283

DECIPHERING THE GENE REGULATORY NETWORKS OF MESENCHYMAL-EPITHELIAL TRANSITIONS IN SARCOMAS

Jason Somarelli, PhD[1]; Samantha Shetler[1]; Mohit Jolly[2]; Sarah Wang[3]; Suzanne Bartholf DeWitt[4]; Alexander Hish[1]; Shivee Gilja[1]; William Eward[4]; Kathryn Ware[1]; Herbert Levine[2]; Andrew Armstrong[1]; Mariano Garcia-Blanco[5]

[1]Medicine, Duke University, Durham, NC, USA; [2]Rice University, Houston, NC, USA; [3]Johns Hopkins University, Baltimore, MD, USA; [4]Orthopaedics, Duke University, Durham, NC, USA; [5]Biochemistry, University of Texas Medical Branch, Galveston, TX, USA

P2–Poster 025 2562298

MIR-X AND MIR-Y ARE POTENTIAL BIOMARKERS IN LIPOSARCOMA AND AFFECT THE TUMOR MICROENVIRONMENT INDUCING INFLAMMATORY RESPONSE

Lucia Casadei, PhD; Federica Calore; Kara Batte; Abeba Zewdu; Danielle Braggio; Carlo Maria Croce; Raphael Pollock

CCC, Ohio State University, Columbus, OH, USA

P2–Poster 026 2558863

TARGETING FGFR1 FOR TREATMENT OF SOFT-TISSUE SARCOMA

Priya Chudasama, PhD[1]; Marcus Renner[2]; Melanie Straub[3]; Barbara Hutter[6]; Matthias Scheffler [4]; Simon Schimmack[5]; Christof von Kalle[1]; Jürgen Wolf[4]; Benedikt Brors[6]; Wilko Weichert[3]; Hanno Glimm[1]; Claudia Scholl[1]; Gunhild Mechtersheimer[2]; Katja Specht[3]; Stefan Fröhling[1]

[1]Translational Oncology, German Cancer Research Center and National Center for Tumor Diseases, Heideleberg, BW, BW, Germany; [2]Institute of Pathology, Heidelberg University Hospital, Heidelberg, Germany; [3]Institute of Pathology, Technische Universität München, Munich, Germany; [4]Department of Internal Medicine I, Center for Integrated Oncology, Cologne University Hospital, Cologne, Germany; [5]Heidelberg University Hospital, Heidelberg, Germany; [6]Division Applied Bioinformatics, German Cancer Research Center and National Center for Tumor Diseases, Heidelberg, Heidelberg, Germany

P2–Poster 027 2556643

ANTI-PHAGOCYTIC MARKER CD47 EXPRESSION IN SARCOMAS

Amanda R. Dancsok, MD, PhD Student[1]; David Thomas[3]; Jean Yves Blay[4]; Robert G. Maki[2]; Torsten Nielsen[1]; Elizabeth G. Demicco[2]

[1]University of British Columbia, Vancouver, BC, Canada; [2]Mount Sinai Hospital, New York, NY, USA; [3]Garvan Institute of Medical Research, Sydney, New South Wales, Australia; [4]Centre Léon Bérard, Lyon, France

P2–Poster 028 2556570

THE REGULATION OF MALIGNANT TRANSFORMATION BY PPP2R1A IN ALVEOLAR RHABDOMYOSARCOMA BASED ON A PROTEOMIC APPROACH CORRESPONDING TO THE PAX3-FOXO1 FUSION GENE

Keisuke Akaike[1]; Yoshiyuki Suehara[1]; Shinji Kohsaka[2]; Kenta Mukaihara[1]; Midori Ishii[1]; Daisuke Kubota[1]; Yu Tanabe[1]; Saiko Kazuno[3]; Reiko Mineki[3]; Tsutomu Fujimura[3]; Kazuo Kaneko[1]; Marc Ladanyi[2]; Tsuyoshi Saito[4]

[1]Orthopaedic Surgery, Juntendo University School of Medicine, Bunkyo-ku, Tokyo, Japan; [2]Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [3]Laboratory of Biochemical Analysis, Central Laboratory of Medical Sciences, Juntendo University School of Medicine, Tokyo, Japan; [4]Human Pathology, Juntendo University School of Medicine, Tokyo, Japan

P2–Poster 029 2553539

MUTATIONAL SPECTRUM OF UNDIFFERENTIATED PLEOMORPHIC SARCOMAS

Andrew Seto[1]; Nalan Gokgoz[1]; Yael Babichev[1]; Qingxia Wei[2]; Richard de Borja[3]; Brendan C. Dickson[4]; Adam Shlien[3]; Benjamin Alman[2]; Rebecca Gladdy[1]; Jay Wunder[1]; Irene L. Andrulis[1]

[1]Lunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada; [2]Developmental and Stem Cell Biology, Hospital for Sick Children, Toronto, ON, Canada; [3]Genetics & Genome Biology, Hospital for Sick Children, Toronto, ON, Canada; [4]Department of Laboratory Medicine and Pathobiology, Mount Sinai Hospital, Toronto, ON, Canada

P2–Poster 030 2551164

HDAC AND PROTEASOME INHIBITORS SYNERGIZE AGAINST SYNOVIAL SARCOMA

Aimee N. Laporte[1]; Robert Ren Jie Yao[1]; Jared J. Barrott[2]; Neal Poulin[1]; Kevin B. Jones[2]; T. Michael Underhill[1]; Torsten Nielsen[1]

[1]University of British Columbia, Vancouver, BC, Canada; [2]University of Utah, Salt Lake City, UT, USA

P2–Poster 031 2550053

IN VITRO SCREEN IDENTIFIES NOVEL DRUG TARGETS IN PRIMARY UNDIFFERENTIATED PLEOMORPHIC SARCOMA CELL LINES

Rosemarie E. Venier[1]; Yael Babichev[1]; Winan van Houdt[2]; Leah Kabaroff[1]; Alessandro Datti[1]; Adrian Pasculescu[1]; Richard Marcellus[3]; David Uehling[3]; Brendan C. Dickson[4]; Rima Al-awar[3]; Albiruni A. Razak[5]; Jay Wunder[1]; Irene L. Andrulis[1]; Rebecca Gladdy[1]

[1]Lunenfeld Tanenbaum Research Institute, Toronto, ON, Canada; [2]Department of Surgery, University of Toronto, Toronto, ON, Canada; [3]Drug Discovery Group, Ontario Institute for Cancer Research, Toronto, ON, Canada; [4]Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada; [5]Medical Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada

P2–Poster 032 2544296

MYXOID LIPOSARCOMA FUSION PROTEIN FUS-DDIT3 ASSOCIATES WITH PARP1, RNA PROCESSING AND DBHS FAMILY PROTEINS (SFPQ, NONO, PSPC1)

Jamie S. Yu[1]; Chia-Chin Wu[2]; Hannah C. Beird[2]; Judith V. Bovée[3]; Alexander Lazar[2]; Neeta Somaiah[2]; Torsten Nielsen[1]

[1]University of British Columbia, Vancouver, BC, Canada; [2]MD Anderson Cancer Center, Houston, TX, USA; [3]Leiden University Medical Center, Leiden, Netherlands

P2–Poster 033 2564681

IMMUNOHISTOCHEMISTRY SCREENING TO INCREASE THE EFFICIENCY OF NEXT GENERATION SEQUENCING FOR DETECTION OF RARE NTRK, ROS1, AND ALK GENE FUSIONS IN SARCOMA PATIENTS

K. Kumar Sankhala[2]; Steven J. Potts, PhD[1]; Jason Christiansen[1]; Patrick Foley[1]; Katherine Kim[2]; Suzan Arasheben[2]; Bryan Leong[2]; Shayan Senaati[2]; Pratik Multani[1]; Zach Hornby[1]; Danielle Murphy[1]; Jennifer Lamoureux[1]; Sant P. Chawla[2]

[1]Ignyta Pharmaceuticals, San Diego, CA, USA; [2]Sarcoma Oncology Center, Santa Monica, CA, USA

P2–Poster 034 2569357

VERSICAN AS A KEY DETERMINANT OF TUMOR GRADE IN SOFT TISSUE SARCOMAS

Paul Keire[2]; Prakash Vishnu[3]; Thomas Wight[2]; Kevin MacDonald[1]

[1]Department of Orthopedics, Virginia Mason Medical Center, Seattle, WA, USA; [2]Benaroya Research Institute, Virginia Mason Medical Center, Seattle, WA, USA; [3]Department of Medical Oncology, Virginia Mason Medical Center, Seattle, WA, USA

P2–Poster 035 2568571

A CRISPRI SCREEN REVEALS SYNTHETIC LETHALITY BETWEEN PAX3-FOXO1 AND GATOR2

Amit J. Sabnis, MD[1]; Jonathan Weissman[3]; Trever G. Bivona[2]

[1]Pediatric Hematology-Oncology, UCSF Benioff Children's Hospital, San Francisco, San Francisco, CA, USA; [2]Hematology-Oncology, University of California, San Francisco, San Francisco, CA, USA; [3]Howard Hughes Medical Institute/University of California, San Francisco, San Francisco, CA, USA

P2–Poster 036 2556322

ACTIVATION OF THE CANONICAL WNT/β-CATENIN SIGNALING PATHWAY IN SOFT TISSUE SARCOMA TUMORIGENESIS: A COMPARATIVE STUDY OF SYNOVIAL SARCOMAS AND LEIOMYOSARCOMAS

Laurence M. Briski, MD[1]; Dafydd G. Thomas[1]; Rajiv M. Patel[1]; Elizabeth R. Lawlor[2]; Rashmi Chugh[3]; Jonathan B. McHugh[1]; David R. Lucas[1]

[1]Department of Pathology, University of Michigan, Ann Arbor, MI, USA; [2]Department of Pediatrics, University of Michigan, Ann Arbor, MI, USA; [3]Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA

P2–Poster 037 2543033

GENERATING PRIMARY SOFT TISSUE SARCOMAS IN MICE BY CRISPR/CAS9 TECHNOLOGY

Jianguo Huang, PhD[1]; Melodi J. Whitley[1]; Mark Chen[1]; Hsuan-Cheng Kuo[1]; Yvonne Mowery[1]; David V. Mater[1]; Lixia Luo[1]; Yan Ma[1]; Jacqueline Robinson-Hamm[2]; Christopher Nelson[2]; Anupama Reddy[3]; Charles Gersbach[2]; Sandeep Dave[3]; Rebecca D. Dodd[1]; David Kirsch[1]

[1]Radiation Oncology, Duke University Medical Center, Durham, NC, USA; [2]Department of Biomedical Engineering, Duke University Medical Center, Durham, NC, USA; [3]Center for Genomic and Computational Biology, Duke University Medical Center, Durham, NC, USA

P2–Poster 038 2566226

PDGFRA PROTEIN EXPRESSION IN RHABDOMYOSARCOMA PATIENT SAMPLES

Yvonne M. Versleijen-Jonkers, PhD[1]; Melissa H. Hillebrandt-Roeffen[1]; Uta E. Flucke[2]; Erik Wiemer[3]; Stefan Sleijfer[3]; Winette Van der Graaf[4]

[1]Medical Oncology, Radboud University Medical Center, Nijmegen, Netherlands; [2]Pathology, Radboud University Medical Center, Nijmegen, Netherlands; [3]Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; [4]The Institute of Cancer Research and the Royal Marsden NHS Foundation Trust, London, United Kingdom

P2–Poster 039 2565149

HDAC8 INHIBITION FOR THE TREATMENT OF LEIOMYOSARCOMA

Gonzalo Lopez, PhD[1]; Wei-Jan Huang[2]; Abeba Zewdu[1]; Danielle Braggio[1]; Anne M. Strohecker[1]; Dina Lev[3]; Raphael Pollock[1]

[1]Comprehensive Cancer Center, The Ohio State University, Grandview Heights, OH, USA; [2]Taipei Medical University, Taipei, Taiwan; [3]Sheba Medical Center, Tel Aviv, Israel

P2–Poster 040 2562822

TAMOXIFEN INDUCES APOPTOSIS IN RHABDOMYOSARCOAM VIA ESTROGEN-RECEPTOR ACTIVATION OF STRESS-ACTIVATED PROTEIN KINASES

Zainab A. Motala, PhD Candidate[1]; Kevin Chen[2]; Adam D. Durbin[3]; Gino R. Somers[4]; David Malkin[1]

[1]Department of Pediatrics, The Hospital for Sick Children, Toronto, ON, Canada; [2]MD Program, University of Toronto, Toronto, ON, Canada; [3]Department of Pediatric Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [4]Department of Pediatric Laboratory Medicine, The Hospital for Sick Children, Toronto, ON, Canada

P2–Poster 041 2562413

IDENTIFICATION OF ESSENTIAL SIGNALING PATHWAYS IN SYNOVIAL SARCOMA AND MYXOID LIPOSARCOMA USING FUNCTIONAL GENOMICS

Ya-Yun Cheng[1]; Patrizia Jensen[1]; Priya Chudasama[1]; Sophie Rabe[1]; Thomas Kindler[2]; Claudia Scholl[1]; Stefan Fröhling[1]

[1]Department of Translational Oncology, National Center for Tumor Diseases and German Cancer Research Center, Heidelberg, Germany; [2]Department of Medicine III, Johannes Gutenberg University Mainz, Mainz, Germany

P2–Poster 042 2553268

A NOVEL SYNOVIAL SARCOMA MOUSE MODEL IDENTIFIES COOPERATIVE GENETIC PATHWAY WITH SS18-SSX1

Miwa Tanaka; Takuro Nakamura, MD, PhD

Division of Carcinogenesis, The Cancer Institute, Japanese Foundation for Cancer Research, Tokyo, Japan

P2–Poster 043 2570585

COMPARATIVE PROTEOMICS OF PRIMARY SARCOMA AND THEIR PAIRED METASTASES REVEALS HIGH EXPESSION OF PARP-1 IN SACROMA METASTASES

Winan van Houdt, MD, PhD[1]; Hester van Boven[3]; Tim Schelfhorst[2]; Linde Braaf[4]; Thang Pham[2]; Jaco Knol[2]; Sander Piersma[2]; Frits van Coevorden[1]; Connie Jimenez[2]

[1]Surgery, Netherlands Cancer Institute, Amsterdam, Netherlands; [2]OncoProteomics Laboratory, Department of Medical Oncology, VU University Medical Center, Amsterdam, Netherlands; [3]Pathology, Netherlands Cancer Institute, Amsterdam, Netherlands; [4]Division of Molecular Pathology, Netherlands Cancer Insitute, Amsterdam, Netherlands

P2–Poster 044 2570584
VERTICILLIN A INHIBITS LEIOMYOSARCOMA AND MALIGNANT NERVE SHEATH TUMOR GROWTH VIA INDUCTION OF APOPTOSIS
Abeba Zewdu, PhD[1]; Gonzalo Lopez[1]; Danielle De Almeida Braggio[1]; Hemant Bid[2]; Connor Kenney[1]; Kara Batte[1]; Kate Lynn Bill[1]; O. Hans Iwenofu[1]; Nicholas Oberlies[3]; Cedric Pearce[5]; Anne M. Strohecker[1]; Dina Lev[4]; Raphael Pollock[1]
[1]Surgical Oncology, The Ohio State University, Columbus, OH, USA; [2]Resonant Therapeutics, Ann Arbor, MI, USA; [3]University of North Carolina, Greensboro, NC, USA; [4]Sheba Medical Center, Tel Aviv, Israel; [5]Mycosynthetix, Hillsborough, NC, USA

P2–Poster 045 2569570
IDENTIFICATION OF NOVEL GENETIC DEPENDENCIES IN SYNOVIAL SARCOMA MODELS
Samuel E. Jones, BSc (PhD submitted by meeting)[1]; Christopher Williamson[1]; Emmy Fleuren[1]; Helen Pemberton[1]; Dragomir Krastev[1]; Rachel Brough[1]; Alan Ashworth[2]; Winette Van der Graaf[1]; Janet Shipley[1]; Christopher Lord[1]
[1]Breakthrough Breast Cancer/Cancer Therapeutics, Institute of Cancer Research, London, United Kingdom; [2]University College San Francisco, San Francisco, CA, USA

P2–Poster 046 2567792
A WHOLE-BODY IMAGEABLE PATIENT-DERIVED ORTHOTOPIC XENOGRAFT (PDOX) MOUSE MODEL OF UNDIFFERENTIATED PLEOMORPHIC SOFT-TISSUE SARCOMA FOR RAPID DRUG SCREENING OF INDIVIDUAL PATIENT TUMORS
Tasuku Kiyuna[1]; Takashi Murakami[1]; Yasunori Tome[3]; Kentaro Igarashi[1]; Kei Kawaguchi[1]; Tara A. Russell[4]; Mark A. Eckardt[5]; Joseph G. Crompton[4]; Arun S. Singh[6]; Nicholas Bernthal[7]; Susan Bukata[7]; Noah Federman[8]; Fuminori Kanaya[3]; Frederick C. Eilber[4]; Robert M. Hoffman, PhD[2]
[1]AntiCancer Inc., San Diego, CA, USA; [2]Department of Surgery, University of California San Diego, San Diego, CA, USA; [3]Department of Orthopedic Surgery, University of the Ryukyus, Okinawa, Japan; [4]Department of Surgery, University of California Los Angeles, Los Angeles, CA, USA; [5]Department of Surgery, Yale School of Medicine, New Haven, CT, USA; [6]Division of Hematology- Oncology, University of California Los Angeles, Los Angeles, CA, USA; [7]Department of Orthopedic Surgery, University of California Los Angeles, Los Angeles, CA, USA; [8]Department of Pediatrics, University of California Los Angeles, Los Angeles, CA, USA

P2–Poster 047 2567790
EFFICACY OF NOVEL ANIONIC AND CATIONIC PLATINUM COMPLEXES AGAINST UNDIFFERENTIATED PLEOMORPHIC SARCOMA IN A PATIENT-DERIVED ORTHOTOPIC XENOGRAFT (PDOX) MODEL
Kentaro Igarashi[1]; Takashi Murakami[1]; Tasuku Kiyuna[1]; Kei Kawaguchi[1]; Akira Odani[3]; Arun S. Singh[4]; Noah Federman[5]; Hiroyuki Tsuchiya[6]; Frederick C. Eilber[7]; Robert M. Hoffman, PhD[2]
[1]AntiCancer Inc., San Diego, CA, USA; [2]Department of Surgery, University of California San Diego, San Diego, CA, USA; [3]Division of Pharmaceutical Sciences, Kanazawa University, Kanazawa, Japan; [4]Division of Hematology-Oncology, University of California Los Angeles, Los Angeles, CA, USA; [5]Department of Pediatrics, University of California Los Angeles, Los Angeles, CA, USA; [6]Department of Orthopaedic Surgery, Kanazawa University, Kanazawa, Japan; [7]Division of Surgical Oncology, University of California Los Angeles, Los Angeles, CA, USA

P2–Poster 048 2562942
DISIALOGANGLIOSIDE GD2 EXPRESSION IN PEDIATRIC RHABDOMYOSARCOMA
Amanda Saraf[2]; Paul Dickman[1]; Pooja Hingorani[1]
[1]Center for Cancer and Blood Disorders, Phoenix Children's Hospital, Phoenix, AZ, USA; [2]Nationwide Children's Hospital, Columbus, OH, USA

P2–Poster 049 2562145
EFFICACY OF BORTEZOMIB IN SARCOMAS WITH HIGH LEVELS OF MAP17 (PDZK1IP1)
Amancio Carnero, PhD; Marco Perez; Javier Peinado-Serrano; Jose Manuel Garcia-Heredia; Irene Felipe-Abrio; Cristina Tous; Irene Ferrer; Javier Martin-Broto; Carmen Saez
Oncohematology and Genetics, IBIS/CSIC/HUVR, Sevilla, Spain

P2–Poster 050 2559109
INSERTIONAL MUTAGENESIS SCREEN FOR IDENTIFICATION OF DRUG RESISTANCE MECHANISMS IN SOFT-TISSUE SARCOMA
Tim Rath; Priya Chudasama; Martina Tedesco; Claudia Scholl; Manfred Schmidt; Stefan Fröhling
Translational Oncology, German Cancer Research Center and National Center for Tumor Diseases, Heidelberg, Germany

P2–Poster 051 2548496
NEXT GENERATION SEQUENCING WITH LINKED CASE REPORTS FOR GRANULAR CELL SARCOMAS
Elizabeth T. Loggers, MD, PhD[1]; Bradley J. Petek[2]; Julia Elvin[3]; Seth M. Pollack[1]; Edward Y. Kim[2]; Gabrielle M. Kane[2]; Darin Davidson[2]; Ernest U. Conrad[2]; Lee D. Cranmer[2]
[1]Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [2]University of Washington, Seattle, WA, USA; [3]Foundation Medicine, Boston, MA, USA

P2–Poster 052 2563399
ACIDIC MICROENVIRONMENTS CREATED BY VACUOLAR-ATPASE PROMOTES SARCOMA PROGRESSION
Toshihiko Nishisho; Ryo Miyagi; Shunichi Toki; Koichi Sairyo
Orthopedics, The University of Tokushima Graduate School, Tokushima, Japan

P2–Poster 053 2571158
DRUG SENSITIVITY TESTING ON PATIENT DERIVED SARCOMA CELLS: NEW POSSIBILITIES FOR PATIENT-TAILORED TREATMENT
Christina Linder Stragliotto[2]; Elisabet Lidbrink[2]; Swapnil Potdar[6]; Otte Brosjö[3]; Henrik Bauer[3]; Asle Hesla[3]; Iimin Ma[1]; Tani Edneia[4]; Johan Wejde[4]; Olli Kallioniemi[5]; Krister Wennerberg[6]; Bertha A. Brodin[1]
[1]Oncology and Pathology, Karolinska Institutet, Stockholm, Sweden; [2]Breast and Sarcoma, Oncology Clinic, Karolinska University Hospital, Stockholm, Sweden; [3]Tumor Orthopedic Surgery, Karolinska University Hospital, Stockholm, Sweden; [4]Pathology, Karolinska University Hospital, Stockholm, Sweden; [5]Karolinska Institutet, ScienceLifeLaboratory, Stockholm, Sweden; [6]FIMM, Institute for Molecular Medicine Finland, Helsinki, Finland

P2–Poster 054 2557744
DCE-MRI IN PATIENTS WITH EXTREMITY SOFT TISSUE SARCOMA TREATED WITH PRE-OP RADIOTHERAPY
Ying Hitchcock, MD[1]; Matthias Schabel[2]; Michael Mclaughlin[2]; Matthew Poppe[1]; Lor Randall[3]; Kevin B. Jones[3]; Dennis C. Shrieve[1]; Christopher Hanrahan[2]
[1]Radiation Oncology, Huntsman Cancer Hospital, University of Utah, Salt Lake City, UT, USA; [2]Radiology, University of Utah, Salt Lake City, UT, USA; [3]Huntsman Cancer Hospital, University of Utah, Salt Lake City, UT, USA

P2–Poster 055 2565637
NOVEL MR IMAGING METHOD -MAVRIC- FOR METAL ARTIFACT SUPPRESSION AFTER MUSCULOSKELETAL TUMOR SURGERY
Michiro Susa[1]; Sota Oguro[2]; Kazutaka Kikuta[2]; Kazumasa Nishimoto[2]; Keisuke Horiuchi[2]; Masahiro Jinzaki[2]; Kazuhiro Chiba[1]; Hideo Morioka[2]
[1]National Defense Medical College, Tokorozawa, Saitama, Japan; [2]Keio University, Tokyo, Japan

P2–Poster 056 2570172
FEASIBILITY OF VOLUMETRIC ADC MAPPING TO TUMOR HABITATS DERIVED FROM DYNAMIC CONTRAST ENHANCED MRI IN SOFT TISSUE SARCOMAS
Jared Mahan[1]; Ty K. Subhawong[1]; Breelyn A. Wilky, MD[3]; Yu-Cherng C. Chang[2]; Raphael Yechieli[2]; Radka Stoyanova[2]
[1]Radiology, University of Miami, Miami, FL, USA; [2]Radiation Oncology, University of Miami, Miami, FL, USA; [3]Department of Medicine, Division of Hematology/Oncology, University of Miami, Miami, FL, USA

P2–Poster 057 2543067
CONTRAST-ENHANCED ULTRASOUND (CEUS) IN DIAGNOSIS, EVALUATION, AND MANAGEMENT OF SOFT TISSUE SARCOMA (STS)
Mittul Gulati, MD[1]; William W. Tseng[2]; James Hu[3]; Sant P. Chawla[3]; Darryl Hwang[1]; Bhushan Desai[1]; Vinay Duddalwar[1]
[1]Radiology, Keck USC School of Medicine, La Canada Flintridge, CA, USA; [2]Surgery, Keck USC School of Medicine, Los Angeles, CA, USA; [3]Medicine, Keck School of Medicine of USC, Los Angeles, CA, USA

P2–Poster8 2544489
EFFECTIVENESS OF CONTRAST COLOR DOPPLER ULTRASONOGRAPHY IN PREOPERATIVE DIAGNOSIS BETWEEN MALIGNANT AND BENIGN OF SOFT TISSUE TUMORS
Naoto Oebisu; Manabu Hoshi; Yoshitaka Ban; Hiroaki Nakamura
Osaka City University, Osaka, Japan

P2–Poster 059 2566632
APPARENT DIFFUSION COEFFICIENT: A POTENTIAL IMAGING BIOMARKER FOR PREDICTION OF METASTATIC DEVELOPMENT IN SOFT TISSUE SARCOMAS?
Manpreet Bedi, MD[1]; David M. King[2]; Eric Paulson[1]; John Charlson[3]; Donald Hackbarth[2]; John Neilson[2]
[1]Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI, USA; [2]Orthopaedic Surgery, Medical College of Wisconsin, Milwaukee, WI, USA; [3]Medical Oncology, Medical College of Wisconsin, Milwaukee, WI, USA

P2–Poster 060 2566214
CLINICOPATHOLOGICAL INVESTIGATION OF LOW-GRADE FIBROMYXOID SARCOMA (EVANS TUMOR)
Naomasa Fukase, MD, PhD[3]; Ikuo Fujita[1]; Teruya Kawamoto[3]; Toshiko Sakuma[2]; Takanori Hirose[2]; Naoe Jimbo[4]; Tomoo Itoe[4]; Hitomi Hara[3]; Takuya Fujimoto[1]; Masayuki Morishita[3]; Etsuko Kamata[3]; Toshiyuki Takemori[3]; Ryosuke Kuroda[3]; Toshihiro Akisue[3]
[1]Orthopaedic Surgery, Hyogo Cancer Center, Akashi, Japan; [2]Diagnostic Pathology, Hyogo Cancer Center, Akashi, Japan; [3]Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan; [4]Diagnostic Pathology, Kobe University Graduate School of Medicine, Kobe, Japan

P2–Poster 061 2565681
ACCURACY OF IMAGE-GUIDED PERCUTANEOUS CORE NEEDLE BIOPSY OF PERIPHERAL NERVE SHEATH TUMORS
Tara A. Russell, MD, MPH[2]; Kambiz Motamedi[1]; Leanne Seeger[1]; Arun S. Singh[3]; Chmielowski Bartosz[3]; Nicholas Bernthal[4]; Susan Bukata[4]; Joseph G. Crompton[2]; Scott Nelson[5]; Sarah M. Dry[5]; Frederick R. Eilber[2]; Frederick C. Eilber[2]; Benjamin D. Levine[1]
[1]Department of Radiology, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [2]Division of Surgical Oncology, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [3]Department of Medicine, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [4]Department of Orthopedic Surgery, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [5]Department of Pathology and Laboratory Medicine, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA

P2–Poster 062 2565891
WHICH PERCUTANEOUS BIOPSY IN THE DIAGNOSIS OF BONE TUMOURS?
Pedro F. Cardoso[1]; João Esteves[1]; Vânia Oliveira[1]; André Coelho[2]; Tiago Couto[3]
[1]Orthopaedics, Centro Hospitalar do Porto, Porto, Portugal; [2]Pathology, Centro Hospitalar do Porto, Porto, Portugal; [3]Radiology, Centro Hospitalar do Porto, Porto, Portugal

P2–Poster 063 2570472
EXPRESSION OF PAX7 DISTINGUISHES RHABDOMYOSARCOMA FROM HISTOLOGIC MIMICS
Gregory Charville, MD, PhD[1]; Sushama Varma[1]; Erna Forgó[1]; Sarah Dumont[2]; Eduardo Zambrano[1]; Jonathan Trent II[3]; Alexander Lazar[4]; Matt van de Rijn[1]
[1]Department of Pathology, Stanford University School of Medicine, Stanford, CA, USA; [2]Department of Medical Oncology, Institut Gustave-Roussy, Villejuif, France; [3]Division of Hematology/Oncology, Department of Internal Medicine, University of Miami Miller School of Medicine, Miami, FL, USA; [4]Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

P2–Poster 064 2560449
TARGETED RNA-BASED NEXT-GENERATION SEQUENCING PANEL IN THE DIAGNOSIS OF SOFT TISSUE AND BONE TUMOURS
David Swanson; George S. Charames; Andrew Wong; Rita Kandel; Brendan C. Dickson, MD, MSc
Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada

P2–Poster 065 2570716

MAGEA3 EXPRESSION AND CLINICAL CORRELATION IN SARCOMA SUBTYPES

Anthony P. Conley, MD; Wei-Lien Wang; Vinod Ravi; Christina Roland; Neeta Somaiah; Patrick Hwu; Cassian Yee; Andrew Futreal; Alexander Lazar; Jason Roszik

Sarcoma Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA

P2–Poster 066 2570324

UNDIFFERENTIATED SARCOMA ACCOMPANIED BY INFLAMMATION: A CASE SERIES AND A COMPARISON WITH CONVENTIONAL UNDIFFERENTIATED SARCOMAS

Jun Sugaya[1]; Shintaro Iwata[2]; Yoko Hagiwara[1]; Tsukasa Yonemoto[2]; Hiroto Kamoda[2]; Yasuaki Murata[1]; Takeshi Ish[2]

[1]Orthopedics, Tokyo Women's Medical University, Tokyo, Japan; [2]Chiba Cancer Center, Chiba, Japan

P2–Poster 067 2566054

RETROSPECTIVE STUDY BETWEEN FNCLCC GRADE 2 AND GRADE 3 CASES IN RESECTABLE SYNOVIAL SARCOMAS

Yusuke Minami, Dr., PhD[2]; Seiichi Matsumoto[2]; Keisuke Ae[2]; Taisuke Tanizawa[2]; Tabu Gokita[2]; Keiko Hayakawa[2]; Yuki Funauchi[2]; Munehisa Kito[2]; Atsushi Okawa[1]

[1]Orthopedic Surgery, Tokyo Medical and Dental University, TOKYO, Japan; [2]Department of Orthopedic Surgery, The Cancer Institute Hospital of The Japanese Foundation for Cancer Research, Tokyo, Japan

P2–Poster 068 2570484

GRM1 EXPRESSION IN CHONDROMYXOID FIBROMAS AND OTHER BONE AND SOFT TISSUE TUMORS

Arjen H. Cleven, MD, PhD[1]; Olaejirinde Olaofe[2]; Georgios Agrogiannis[3]; Inge Briaire-de Bruijn[1]; Karolin Nord[4]; Pancras Hogendoorn[1]; Karoly Szuhai[1]; Judith V. Bovée[1]

[1]Pathology, Leiden University Medical Center, Leiden, Netherlands; [2]Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University, Ile-Ife, Nigeria; [3]Pathology, School of Medicine National and Kapodistrian University of Athens, Athens, Greece; [4]Department of Clinical Genetics, University and Regional Laboratories, Skåne University Hospital, Lund, Sweden

P2–Poster 069 2554214

INSTRUMENTS AND GLOVES AS A SOURCE OF WOUND SEEDING IN SOFT TISSUE SARCOMA SURGERY

David Berger-Richardson, MD; Aaron Pollett; Peter Ferguson; Jay Wunder; Anthony Griffin; Roland Xu; Carol Swallow

Mount Sinai Hospital, Toronto, ON, Canada

P2–Poster 070 2557681

ONCOLOGICAL OUTCOME AND QUALITY OF LIFE AFTER HINDQUARTER AMPUATION FOR SARCOMA: IS IT WORTH IT?

Winan van Houdt, MD, PhD[1]; Anthony Griffin[2]; Jay Wunder[2]; Peter Ferguson[2]

[1]Surgical Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; [2]Musculoskeletal Oncology Unit, Mount Sinai Hospital, Toronto, ON, Canada

P2–Poster 071 2525270

ASSOCIATION OF CORE NEEDLE BIOPSY TRACT RESECTION WITH LOCAL RECURRENCE IN EXTREMITY SOFT TISSUE SARCOMA

M. Ather Siddiqi[2]; Han-Soo Kim[1]; Jong Woong Park[1]; Ilkyu Han, MD, PhD[1]

[1]Orthopedic Surgery, Seoul National University Hospital, Seoul, Korea (the Republic of); [2]Department of Orthopaedic Surgery, Liaquat National Hospital and Medical College, Karachi, Pakistan

P2–Poster 072 2570188

BIOPSY TRACT SEEDING: HISTOPATHOLOGICAL CONFIRMATION AND RELEVANCE IN CLINICAL PRACTICE

Irene Barrientos-Ruiz, MD[1]; Eduardo J. Ortiz Cruz[1]; Jose Serrano-Montilla[2]; Daniel Bernabeu-Taboada[1]; Juan Jose Pozo- Kreilinger[1]

[1]Pathology Department, Musculoskeletal Oncology Unit, University Hospital La Paz, Madrid, Madrid, Spain; [2]Traumatology and Orthopedics Department, Musculoskeletal Oncology Unit, University Hospital Rey Juan Carlos, Mostoles, Madrid, Spain

P2–Poster 073 2541530
SURGICAL AND TUMOR-RELATED CONTRIBUTIONS TO INADVERTENT POSITIVE MARGINS AFTER SOFT TISSUE SARCOMA RESECTION
Kenneth R. Gundle, MD[1]; Sanjay Gupta[2]; Lisa Kafchinski[2]; Anthony Griffin[2]; Rita Kandel[3]; Brendan C. Dickson[3]; Peter Chung[4]; Charles Catton[4]; Brian O'Sullivan[4]; Peter Ferguson[2]; Jay Wunder[2]
[1]Orthopaedics & Rehabilitation, Oregon Health & Science University, Portland, OR, USA; [2]University of Toronto Dept of Surgery, Mount Sinai Hospital, Toronto, ON, Canada; [3]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada; [4]Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada

P2–Poster 074 2543689
FEASABILITY AND RESULTS OF SURGERY WITH FREE FLAP COVERAGE AFTER ISOLATED LIMB PERFUSION FOR SOFT TISSUE SARCOMA
Olivier Camuzart[1]; Andrea Cavalcanti[1]; Françoise Rimareix[1]; Olivier Mir[2]; Philippe Terrier[3]; Cecile Le Péchoux[4]; Axel Le Cesne[2]; Charles Honoré, MD, PhD[1]
[1]Surgical Oncology, Gustave Roussy Cancer Campus, Villejuif, France; [2]Medical Oncology, Gustave Roussy Cancer Campus, Villejuif, France; [3]Pathology, Gustave Roussy Cancer Campus, Villejuif, France; [4]Radiotherapy, Gustave Roussy Cancer Campus, Villejuif, France

P2–Poster 075 2570195
SURGICAL MANAGEMENT OF LOCALLY RECURRENT SOFT TISSUE SARCOMA: PREVIOUS SURGICAL SCAR RESECTIONS REDUCE THE RISK OF SUBSEQUENT LOCAL RECURRENCE
Tabu Gokita, MD; Seiichi Matsumoto; Keisuke Ae; Taisuke Tanizawa; Keiko Hayakawa; Yuki Funauchi; Munehisa Kito
Orthopedic Oncology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

P2–Poster 076 2563279
INTRAOPERATIVE OPTICAL COHERENCE TOMOGRAPHY FOR SOFT TISSUE SARCOMA SURGICAL MARGIN ASSESSMENT
Laura E. Selmic, BVetMed (Hons), MPH[1]; Kelly J. Mesa[3]; Elizabeth A. Driskell[2]; Jonathan Samuelson[2]; Jennifer Reagan[1]; Marina Marjanovic[3]; Stephen A. Boppart[3]
[1]Department of Veterinary Clinical Medicine, University of Illinois at Urbana-Champaign, Urbana, IL, USA; [2]Department of Pathobiology, University of Illinois at Urbana-Champaign Urbana-Champaign, Urbana, IL, USA; [3]Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign, Urbana-Champaign, IL, USA

P2–Poster 077 2553058
TARGET REGISTRATION ERROR COLORMAPS: GOING BEYOND THE SINGLE METRIC FOR SURGICAL NAVIGATION ACCURACY
Prakash R. Nayak, MD[1]; Michelle Arkhangorodsky[2]; Michael Daly[2]; Jimmy Qiu[2]; Harley Chan[2]; Robert Weersink[2]; David Jaffray[2]; Jonathan Irish[2]; Peter Ferguson[1]; Jay Wunder[1]
[1]Musculoskeletal Oncology, Mount Sinai Hospital and Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Guided Therapeutics (GTx) Program, Princess Margaret Cancer Centre, Toronto, ON, Canada

P2–Poster 078 2538198
SYMPTOMATIC SMALL SCHWANNOMA IS A RISK FACTOR FOR POSTOPERATIVE NEUROLOGICAL DEFICITS AND CORRELATES WITH DIFFICULTY OF ENUCLEATION
Kensaku Abe; Norio Yamamoto; Katsuhiro Hayashi; Akihiko Takeuchi; Takashi Higuchi; Yuta Taniguchi; Hisaki Aiba; Hiroyuki Tsuchiya
Orthopaedic Surgery, Kanazawa University, Kanazawa, Ishikawa, Japan

P2–Poster 079 2561413
NEW VESSEL SEALING SYSTEM CAN REDUCE POST-OPERATIVE COMPLICATION ON SURGERY FOR MALIGNANT SOFT TISSUE TUMORS IN THE THIGH
Yoshitaka Ban; Manabu Hoshi; Naoto Oebisu; Hiroaki Nakamura
Osaka City University, Osaka, Osaka, Japan

P2–Poster 080 2556005

MULTI-INSTITUTIONAL SOFT TISSUE SARCOMA REAL TIME PEER REVIEW RADIOTHERAPY QUALITY ASSURANCE ROUNDS

Charles Catton[1]; Colleen Dickie[1]; Simon Xie[1]; Anthony Griffin[3]; Peter Ferguson[3]; Jay Wunder[3]; Lyndon Morley[1]; Conrad Falkson[2]; Michael Sharpe[1]; Peter Chung[1]; David Shultz[1]; Ho Kit Tam[2]; Alex Hammond[4]; Samuel Appiah[1]; Brian O'Sullivan[1]

[1]Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Kingston General Hospital, Kingston, ON, Canada; [3]Mount Sinai Hospital, Toronto, ON, Canada; [4]London Health Sciences Centre, London, ON, Canada

P2–Poster 081 2565741

CLINICAL OUTCOMES OF LIMB SALVAGE SURGERY WITH POSTOPERATIVE INTENSITY-MODULATED RADIATION THERAPY FOR MALIGNANT TUMORS OF THE EXTREMITIES

Ryosuke Takahashi[1]; Toshihiro Matsuo[1]; Shintaro Yuki[3]; Shoji Shimose[3]; Katsuhisa Kawanami[1]; Masataka Deie[2]

[1]Orthopaedic Oncology, Aichi Medical University, Nagakute City, Japan; [2]Orthopaedic surgery, Aichi Medical University, Nagakute City, Japan; [3]Kure Medical Center, Kure City, Japan

P2–Poster 082 2566725

U.S. RACIAL/ETHNIC DISPARITIES WITHIN MODERN TRENDS OF RADIATION TREATMENT OF SOFT-TISSUE SARCOMAS

Felix Chinea; Vivek N. Patel, MD; Deukwoo Kwon; Jonathan Trent; Raphael Yechieli

Radiation Oncology, University of Miami, Parkland, FL, USA

P2–Poster 083 2567998

COMPLETE RESPONSE OF SOFT TISSUE SARCOMAS TO PREOPERATIVE RADIOTHERAPY

Jungo Imanishi, MD[1]; John Slavin[3]; Fiona Chan[3]; Lester W. Chan[2]; Samuel Y. Ngan[4]; Sarat Chander[4]; Stephen Sharp[5]; Peter F. Choong[2]

[1]Orthopaedic Oncology and Surgery, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [2]Orthopedics, St. Vincent's Hospital, Fitzroy, Victoria, Australia; [3]Pathology, St. Vincent's Hospital, Fitzroy, Victoria, Australia; [4]Radiation Oncology, Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia; [5]The University of Melbourne, Parkville, Victoria, Australia

P2–Poster 084 2570435

TRENDS IN UTILIZATION OF RADIOTHERAPY FOR TREATMENT OF SOFT TISSUE SARCOMAS: A POPULATION-BASED ASSESSMENT

Vivek N. Patel, MD; Felix M. Chinea; Deukwoo Kwon; Jonathan Trent; Raphael Yechieli

Radiation Oncology, University of Miami, Parkland, FL, USA

P2–Poster 085 2560692

COST EFFECTIVENESS ANALYSIS OF NEOADJUVANT VERSUS ADJUVANT RADIOTHERAPY TREATMENT FOR SOFT TISSUE SARCOMA OF THE LOWER EXTREMITIES

Megan Crosmer, Residency[1]; Richard Mather[1]; Perez Agaba[1]; Howard Levinson[2]; William Eward[1]

[1]Orthopaedic Surgery, Duke University, Durham, NC, USA; [2]Plastic Surgery, Duke University, Durham, NC, USA

P2–Poster 086 2565663

OVARIES ARE IMPORTANT ORGANS AT RISK (OAR) FOR RADIATION THERAPY (RT) TREATMENT PLANNING FOR SOFT TISSUE SARCOMA (STS) OF THE THIGH, GROIN AND BUTTOCK

Konstantin A. Kovtun, MD[1]; Wee-Pin Yeo[1]; Catherine Philips[2]; Akila Viswanathan[1]; Elizabeth H. Baldini[1]

[1]Radiation Oncology, Dana-Farber/Brigham and Women's Hospital, Boston, MA, USA; [2]Diagnostic Radiology Department, Brigham and Women's Hospital, Boston, MA, USA

P2–Poster 087 2570315

PREGNANCY OUTCOMES AFTER RADIATION THERAPY

Karen De Amorim Bernstein, MD[3]; Saveli Goldberg[1]; Torunn Yock[1]; Yen-Lin Chen[1]; Joseph Schwab[2]; Francis Hornicek[2]; Alex Haynes[4]; John T. Mullen[4]; Gregory M. Cote[5]; Edwin Choy[5]; Jennifer Wo[3]; Thomas F. DeLaney[3]
[1]Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [2]Orthopedic Surgery, Massachusetts General Hospital, Boston, MA, USA; [3]Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [4]Surgery, Massachusetts General Hospital, Boston, MA, USA; [5]Hematology/Oncology, Massachusetts General Hospital, Boston, MA, USA

P2–Poster 088 2562317

A LIMITED INDICATION FOR ADJUVANT RADIOTHERAPY FOR HIGH-GRADE SOFT TISSUE SARCOMA

Shintaro Iwata, MD[1]; Takeshi Ishii[1]; Akira Kawai[2]
[1]Div.Orthopaedic Surgery, Chiba Cancer Center, Chiba, Japan; [2]Div. Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan

P2–Poster 089 2570319

MINIMALLY-INVASIVE SURGERY USING INTRAOPERATIVE ELECTRON-BEAM RADIOTHERAPY FOR THE SOFT TISSUE SARCOMA WITH TENDON INVOLVEMENT

Akihiko Matsumine, MD, PhD[1]; Masaya Tsujii[1]; Tomoki Nakamura[1]; Kunihiro Asanuma[1]; Takao Matsubara[1]; Takuya Kakimoto[1]; Yuki Yada[1]; Tomohito Hagi[1]; Akinori Takada[2]; Noriko Ii[2]; Yoshihito Nomoto[2]; Akihiro Sudo[1]
[1]Department of Orthopedic Surgery, Mie University Graduate School of Medicine, Tsu City, Mie, Japan; [2]Department of Radiology, Mie University Graduate School of Medicine, Tsu City, Mie, Japan

P2–Poster 090 2567158

RESECTION OF SOFT TISSUE SARCOMA WITH ADEQUATE WIDE MARGIN CAN LEAD TO GOOD LOCAL CONTROL WITHOUT ADJUVANT RADIOTHERAPY

Toshiyuki Kunisada[1]; Tomohiro Fujiwara[1]; Joe Hasei[1]; Hiroyuki Yanai[2]; Toshifumi Ozaki[1]
[1]Orthopaedic Surgery, Okayama University Hospital, Okayama, Japan; [2]Pathology, Okayama University Hospital, Okayama, Japan

P2–Poster 091 2570753

SURGERY ALONE IS SUFFICIENT THERAPY FOR LOW-RISK SYNOVIAL SARCOMA PATIENTS

Andrea Ferrari[2]; Yueh-Yun Chi[4]; Gian Luca de Salvo[6]; R. L. Randall[5]; Douglas S. Hawkins[3]; Gianni Bisogno[7]; Sheri Spunt[1]
[1]Stanford University School of Medicine, Palo Alto, CA, USA; [2]Istituto Nazionale dei Tumori, Milano, Italy; [3]Seattle Children's Hospital, Seattle, WA, USA; [4]COG Data Center, Gainesville, FL, USA; [5]Huntsman Cancer Institute, Salt Lake City, UT, USA; [6]Istituto Oncologico Veneto, Padova, Italy; [7]Universita degli Studi di Padova, Padova, Italy

P2–Poster 092 2555378

MULTI-AGENT CHEMOTHERAPY IN ADVANCED SOFT TISSUE SARCOMA (STS): MORE IS NOT ALWAYS BETTER

Alona Zer, MD[2]; Rebecca Prince[1]; Eitan Amir[1]; Albiruni A. Razak[1]
[1]DMOH, Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Rabin Medical Center, Petach Tikva, Israel

P2–Poster 093 2565308

A PHASE 1/2 STUDY OF ALDOXORUBICIN AND 14 DAYS CONTINUOUS INFUSION OF IFOSFAMIDE/MESNA IN METASTATIC OR LOCALLY ADVANCED SARCOMAS

Sant P. Chawla, MD[1]; K. Kumar Sankhala[1]; Shanta Chawla[2]; Victoria Chua[1]; Erlinda M. Gordon[1]; Neal Chawla[1]; Kelli Sung[2]; Doris Quon[1]; Katherine Kim[1]; Lita Fernandez[1]; Bryan Leong[1]; Scott Wieland[2]; Daniel Levitt[2]
[1]Sarcoma Oncology Center, Santa Monica, CA, USA; [2]CytRx Corporation, Los Angeles, CA, USA

P2–Poster 094 2554705

RANDOMIZED PHASE 3, MULTICENTER, OPEN-LABEL STUDY COMPARING EVOFOSFAMIDE (EVO) IN COMBINATION WITH DOXORUBICIN (D) VS. D ALONE IN PATIENTS (PTS) WITH ADVANCED SOFT TISSUE SARCOMA (STS); STUDY TH-CR-406/SARC021

William Tap[1]; Zsuzsanna Papai[2]; Brian Van Tine[3]; Steven Attia[4]; Kristen Ganjoo[5]; Robin Jones[6]; Scott Schuetze[7]; Damon Reed[8]; Sant P. Chawla[9]; Richard Riedel[11]; Antoine Italiano[14]; Peter Hohenberger[10]; Thierry Alcindor[15]; Stewart Kroll[12]; Patrick Schöffski[13]

[1]Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [2]Allami Egeszsegugyi Kozpont, Budapest, Hungary; [3]Washington University St. Louis, St. Louis, MO, USA; [4]Mayo Clinic Florida, Jacksonville, FL, USA; [5]Stanford University, Stanford, CA, USA; [6]Royal Marsden, London, United Kingdom; [7]University of Michigan, Ann Arbor, MI, USA; [8]Moffitt Cancer Center, Tampa, FL, USA; [9]Sarcoma Oncology, Santa Monica, CA, USA; [10]Universitatsklinikum Mannheim, Mannheim, Germany; [11]Duke University, Durham, NC, USA; [12]Threshold Pharmaceuticals, South San Francisco, CA, USA; [13]Universitair Ziekenhuis Leuven - Gathuisberg, Leuven, Belgium; [14]Institut Bergonie, Bordeaux, France; [15]Canadian Clinical Trials Group, Kingston, ON, Canada

P2–Poster 095 2530606

PROGNOSIS OF PATIENTS RECEIVING FIRST LINE CHEMOTHERAPY FOR ADVANCED SOFT TISSUE SARCOMAS WITH LOCALLY ADVANCED VS DISTANT METASTASIS VS BOTH: AN EORTC-STBSG DATABASE ANALYSIS

Arjan Verschoor[1]; Saskia Litiere[2]; Sandrine Marreaud[2]; Ian Judson[3]; Maud Toulmonde[4]; Eva Wardelmann[5]; Winette Van der Graaf[3]; Axel Le Cesne[6]; Alessandro Gronchi[7]; Hans Gelderblom[1]

[1]Medical Oncology, Leiden University Medical Center, Leiden, Netherlands; [2]European Organisation for Research and Treatment of Cancer, Brussels, Belgium; [3]Royal Marsden Hospital, London, United Kingdom; [4]Institut Bergonié, Bordeaux, France; [5]Gerhard Domagk Institute of Pathology, University Hospital Muenster, Muenster, Germany; [6]Institut Gustave Roussy, Villejuif, France; [7]Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

P2–Poster 096 2570640

PROSPECTIVE VALIDATION OF A MOLECULAR SIGNATURE PREDICTIVE OF RESPONSE TO TRABECTEDIN IN SOFT- TISSUE SARCOMAS WITHIN EORTC 62091 TRIAL

Antoine Italiano[1]; Nathan Touati[2]; Saskia Litiere[2]; James Butrynski[11]; Nicolas Penel[3]; Jean Yves Blay[4]; Nicolas Isambert[5]; Mohammed Milhem[6]; Jan Kerst[7]; An Reyners[7]; Sandrine Marreaud[2]; Françoise Collin[5]; Winette Van der Graaf[8]; Hans Gelderblom[9]; Alessandro Gronchi[10]

[1]Institut Bergonie, Bordeaux, France; [2]EORTC, Bruxelles, Belgium; [3]Centre Oscar Lambret, Lille, France; [4]Centre Léon Bérard, Lyon, France; [5]Centre Georges François Leclerc, Dijon, France; [6]University of Iowa, Iowa, IA, USA; [7]Netherlands Cancer Institute, Groningen, Netherlands; [8]Royal Marsden Hospital, London, United Kingdom; [9]Leiden University, Leiden, Netherlands; [10]Istituto Nazionale dei Tumori, Milan, Italy; [11]Overlake Hospital, Bellevue, WA, USA

P2–Poster 097 2558960

PHASE II STUDY OF PM01183 AS A SINGLE AGENT OR IN COMBINATION WITH CONVENTIONAL CHEMOTHERAPY IN METASTATIC AND/OR UNRESECTABLE SOFT TISSUE SARCOMAS

Gregory M. Cote, MD, PhD[1]; Edwin Choy[1]; Jeffrey A. Morgan[2]; Priscilla Merriam[2]; Andrew Wagner[2]; Katherine Thornton[2]; GD Demetri[2]; Suzanne George[2]

[1]Hematology/Oncology, Massachusetts General Hospital, Boston, MA, USA; [2]Hematology/Oncology, Dana-Farber Cancer Institute, Boston, MA, USA

P2–Poster 098 2565673

PHASE 2 TRIAL OF 5-IMINO-13-DEOXYDOXORUBICIN (GPX-150) IN METASTATIC AND NON-RESECTABLE SOFT TISSUE SARCOMAS

Brian Van Tine[1]; Mark Agulnik[2]; Richard D. Olsen[4]; Gerald M. Walsh[4]; Arthur Klausner[4]; Mohammed Milhem[3]

[1]Washington University in Saint Louis, St. Louis, MO, USA; [2]Northwestern University, Chicago, IL, USA; [3]University of Iowa, Iowa City, IA, USA; [4]Gem Pharmaceuticals, Birmingham, AL, USA

P2–Poster 099 2565733

TRABECTEDIN WITH PROPHYLACTIC N-ACETYLCYSTEINE (NAC) CO-TREATMENT IN PATIENTS WITH RECURRENT SOFT TISSUE SARCOMA (STS) AND REDUCED LIVER AND RENAL FUNCTION

Salvatore Grisanti[1]; Vittorio D. Ferrari[1]; Susanna Bianchi[1]; Vincenza Azzara[2]; Barbara P. Lazzari[1]; Francesca Consoli[1]; Elisa Roca[1]; Paola Rehmann[2]; Salvatore Golemi[1]; Cristina Gurizzan[1]; Carla Galloni[2]; Alfredo Berruti[1]

[1]Medical Oncology, University of Brescia, Brescia, Italy; [2]Clinical Pharmacology, Spedali Civili of Brescia, Brescia, Italy

P2–Poster 100 2555443

PLATINUM-BASED REGIMENS IN ADVANCED PEDIATRIC TYPE RHABDOMYOSARCOMA IN ADULTS: EXPERIENCE OF TWO CENTERS

Nadia Hindi, MD[1]; Pablo Luna[2]; Jose Duran[2]; Pilar Sancho[1]; Roberto Lasso[1]; Alvaro Montaño[1]; Rafael Ramos[2]; Javier Martin- Broto[1]

[1]Medical Oncology, Virgen del Rocio University Hospital, Seville, Spain; [2]Medical Oncology, Son Espases University Hospital, Palma de Mallorca, Spain

P2–Poster 101 2569845

TRABECTEDIN IN WELL DIFFERENTIATED VERSUS DEDIFFERENTIATED LIPOSARCOMA

Roberta Sanfilippo[1]; Vittoria Colia[1]; Elena Fumagalli[1]; Rossella Bertulli[1]; Salvatore Provenzano[1]; Silvana Pilotti[1]; Angelo Paolo Dei Tos[2]; Carlo Morosi[1]; Alessandro Gronchi[1]; Paolo Casali[1]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [2]General Hospital of Treviso, Milan, Italy

P2–Poster 102 2534346

SAFETY PROFILE OF TRABECTEDIN THERAPY IN PATIENTS WITH ADVANCED SOFT TISSUE SARCOMAS (STS) FOLLOWING FAILURE OF PRIOR CHEMOTHERAPY: UPDATED RESULTS OF A GLOBAL EXPANDED ACCESS PROGRAM

R. Jones[1]; R.G. Maki[2]; S.R. Patel[3]; C.R. Shin[4]; T. McGowan[4]; L. Marquez[5]; T.V. Parekh[5]; M. von Mehren[6]; G.D. Demetri[7]

[1]Royal Marsden Hospital / Institute of Cancer Research, London, United Kingdom; [2]Mount Sinai Medical Center, New York, NY, USA; [3]The University of Texas, MD Anderson Cancer Center, Houston, TX, USA; [4]Janssen Scientific Affairs, LLC, Horsham, PA, USA; [5]Janssen Research & Development, LLC, Raritan, NJ, USA; [6]Fox Chase Cancer Center, Philadelphia, PA, USA; [7]Dana-Farber Cancer Institute and Ludwig Center at Harvard, Boston, MA, USA

P2–Poster 103 2554229

INCREMENTAL BENEFIT-COST RATIO OF TRABECTEDIN VS PAZOPANIB FOR THE TREATMENT OF ADVANCED, METASTATIC, SOFT TISSUE SARCOMA IN SPAIN

Jose Miguel Fernandez[1]; Roberto Diaz Beveridge[2]

[1]Health Economics, Pharmamar, Colmenar Viejo, Madrid, Spain; [2]Hospital Universitario La Fe, Valencia, Spain

P2–Poster 104 2570688

TRABECTEDIN THERAPY FOR HIGH-GRADE SARCOMAS: A SINGLE INSTITUTION'S EXPERIENCE

Sandra Santos, Resident; Ruben Fonseca; João Freitas; Paulo F. Tavares; Jose M. Casanova

Ortopedia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

P2–Poster 105 2566640

RELATIONSHIP BETWEEN MONOCYTE REDUCTION AND RADIOLOGICAL TISSUE MODIFICATION IN STS PATIENTS TREATED WITH TRABECTEDIN

Bruno Vincenzi; Marianna Silletta; Grazia Armento; Mariella Spalato Ceruso; Giovanna Catania; Daniele Santini; Giuseppe Tonini

Medical Oncology, University Campus Bio Medico of Rome, Rome, Italy

P2–Poster 106 2556970

ANTI-TUMOR EFFECTS OF TRABECTEDIN ON CLEAR CELL SARCOMA CELL LINES

Takaaki Nakai[1]; Yoshinori Imura[2]; Shutaro Yamada[1]; Sho Nakai[1]; Hidetatsu Otani[2]; Satoshi Takenaka[1]; Kenichiro Hamada[1]; Akira Myoui[1]; Nobuhito Araki[2]; Kazuyuki Itoh[3]; Hideki Yoshikawa[1]; Norifumi Naka[1]

[1]Orthopedic Surgery, Osaka University Graduate School of Medicine, Osaka, Osaka, Japan; [2]Musculoskeletal Oncology Service, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan; [3]Department of Biology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan

P2–Poster 107 2567652

TRABECTEDIN AS FIRST LINE IN ADVANCED SOFT TISSUE SARCOMA (STS) PATIENTS UNFIT TO RECEIVE STANDARD CHEMOTHERAPY: SAFETY AND EFFICACY FROM TR1US STUDY

Federica Grosso[1]; Lorenzo D'Ambrosio[2]; Toni Ibrahim[4]; Stefano Tamberi[5]; Emanuela Palmerini[6]; Danila Comandini[9]; Giacomo Giulio Baldi[7]; Marina Bergaglio[8]; Andrea De Censi[10]; Massimo Zucchetti[11]; Emanuela Marchesi[3]; Matteo Puntoni[12]; Domenico Marra[10]; Maurizio D'Incalci[11]; Giovanni Grignani[2]

[1]SC Oncologia, ASO SS Antonio e Biagio e C Arrigo, Alessandria, Italy; [2]Division of Medical Oncology, Candiolo Cancer Institute - FPO, IRCCS, Candiolo (TO), Italy; [3]Italian Sarcoma Group, Bologna, Italy; [4]Osteoncology and Rare Tumors Center, IRST Meldola, Meldola (FC), Italy; [5]Oncology Unit, Ospedale per gli Infermi, Faenza (RA), Italy; [6]Chemotherpy Unit, Istituto Ortopedico Rizzoli, Bologna, Italy; [7]Medical Oncology Unit, Hospital of Prato, Prato, Italy; [8]Oncology Unit, Villa Scassi Hospital, ASL3 Genovese, Genova, Italy; [9]Divisione di Oncologia Medica, Ospedale San Martino, Genova, Italy; [10]Division of Medical Oncology Unit, EO Ospedali Galliera, Genova, Italy; [11]IRCCS-Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy; [12]E.O. Ospedali Galliera, Biostatistic Unit, Genova, Italy

P2–Poster 108 2542257

OVERCOMING PRIMARY RESISTANCE TO VEGF TARGETED AGENTS IN ANGIOSARCOMA BY TARGETING THE MITOGEN- ACTIVATED PROTEIN KINASE PATHWAY

Michael J. Wagner, MD[1]; Vinod Ravi[2]; Wei-Lien Wang[3]; Jean M. Hanson[4]; Yasmin Lyons[4]; Rebecca A. Previs[4]; Archana Nagaraja[4]; Kyunghee Noh[4]; Monika Haemmerle[4]; Selanere Mangala[4]; Sunila Pradeep[4]; Prahlad Ram[5]; Alexander Lazar[3]; Anil Sood[4]

[1]Cancer Medicine, M.D. Anderson Cancer Center, Houston, TX, USA; [2]Sarcoma Medical Oncology, M.D. Anderson Cancer Center, Houston, TX, USA; [3]Pathology, M.D. Anderson Cancer Center, Houston, TX, USA; [4]Gynecologic Oncology and Reproductive Medicine, M.D. Anderson Cancer Center, Houston, TX, USA; [5]Systems Biology, M.D. Anderson Cancer Center, Houston, TX, USA

P2–Poster 109 2570651

A PHASE I / II STUDY OF THE SAFETY AND EFFICACY OF THE COMBINATION OF GEMCITABINE AND DOCETAXEL WTIH MORAB-004 IN METASTATIC SOFT TISSUE SARCOMA

Robin L. Jones[3]; Sant P. Chawla[2]; Steven Attia[6]; Patrick Schöffski[4]; Hans Gelderblom[5]; Bartosz Chmielowski[7]; Axel LeCesne[13]; Brian Van Tine[8]; Jonathan C. Trent[9]; Shreyaskumar Patel[10]; Andrew J. Wagner[11]; Rashmi Chugh[12]; John W. Heyburn[1]; Susan C. Weil[1]; Robert G. Maki[14]

[1]Clinical, Morphotek, Inc., Exton, PA, USA; [2]Sarcoma Oncology Research Center, Santa Monica, CA, USA; [3]Seattle Cancer Care Alliance, Seattle, WA, USA; [4]UZ Leuven Medical Hematology Oncology, Leuven, Belgium; [5]Leiden University Medical Center, Leiden, Netherlands; [6]Mayo Clinic – Jacksonville, Jacksonville, FL, USA; [7]Hematology/Oncology, UCLA Department of Medicine, Los Angeles, CA, USA; [8]Washington University School of Medicine, St. Louis, MO, USA; [9]University of Miami School of Medicine – Sylvester Comprehensive Cancer Center, Miami, FL, USA; [10]MD Anderson Cancer Center, Houston, TX, USA; [11]Dana-Farber Cancer Institute, Boston, MA, USA; [12]Division of Hematology / Oncology, University of Michigan, Ann Arbor, MI, USA; [13]Department of Medicine, Institut Gustave Roussy, Villejuif, France; [14]Mount Sinai School of Medicine, New York, NY, USA

P2–Poster 110 2569989

TRC105 (ENDOGLIN ANTIBODY) IN COMBINATION WITH PAZOPANIB (P) IN PATIENTS (PTS) WITH ADVANCED ANGIOSARCOMA (AS)

K. Kumar Sankhala[1]; Steven Attia[2]; Minal A. Barve[3]; Jennifer Wright[4]; Richard Riedel[5]; Steven I. Robinson[6]; Robert M. Conry[7]; Patrick M. Boland[8]; Ben K. Seon[8]; Delia Alvarez[9]; Bonne J. Adams[9]; Ronald L. Shazer[9]; Charles P. Theuer[9]; Robert G. Maki[10]

[1]Sarcoma Oncology Research Center, Santa Monica, CA, USA; [2]Mayo Clinic, Jacksonville, Jacksonville, FL, USA; [3]Mary Crowley Cancer Research, Dallas, TX, USA; [4]University of Utah, Salt Lake City, UT, USA; [5]Duke University, Durham, NC, USA; [6]Mayo Clinic, Rochester, Rochester, MN, USA; [7]University of Alabama at Birmingham, Birmingham, AL, USA; [8]Roswell Park Cancer Institute, Buffalo, NY, USA; [9]TRACON Pharmaceuticals, San Diego, CA, USA; [10]Icahn School of Medicine at Mount Sinai, New York, NY, USA

P2–Poster 111 2570725

SAFETY, TOXICITY, AND ACTIVITY OF MULTI-KINASE VEGFR TKI VANDETANIB COMBINED WITH MTOR INHIBITOR EVEROLIMUS IN AN ADVANCED SARCOMAS COHORT OF A PHASE I STUDY

Anthony P. Conley, MD; Vinod Ravi; Neeta Somaiah; SR Patel; Robert S. Benjamin; Maria A. Zarzour; Joseph A. Ludwig; Dejka Araujo; Winston Huh; Vivek Subbiah

Sarcoma Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA

P2–Poster 112 2541028

THE REAL-LIFE CLINICAL OUTCOME OF PAZOPANIB TREATMENT IN PATIENTS WITH SOFT TISSUE SARCOMA: A JAPANESE MUSCULOSKELETAL ONCOLOGY GROUP STUDY

Tomoki Nakamura, MD, PhD[1]; Akihiko Matsumine[1]; Eisuke Kobayashi[11]; Nobuhito Araki[2]; Takahiro Goto[3]; Tsukasa Yonemoto[4]; Hideshi Sugiura[5]; Yoshihiro Nishida[6]; Hiroaki Hiraga[12]; Kanya Honoki[7]; Taketoshi Yasuda[8]; Shogen Boku[9]; Akihiro Sudo[1]; Takafumi Ueda[10]

[1]Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Tsu, Mie, Japan; [2]Department of Orthopaedic Surgery, Osaka General Medical Center, Osaka, Japan; [3]of Orthopedic Surgery and Musculoskeletal Oncology, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan; [4]Division of Orthopedic Surgery, Chiba Cancer Center, Chiba, Japan; [5]Department of Orthopedic Surgery, Aichi Cancer Center, Nagoya, Japan; [6]Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan; [7]Department of Orthopaedic Surgery, Nara Medical University, Kashihara, Japan; [8]Departmemt of Orthopaedic Surgery, University of Toyama, Toyama, Japan; [9]Department of Medical Oncology, Hyogo Cancer Center, Akashi, Japan; [10]Department of Orthopaedic Surgery, Osaka National Hospital, Osaka, Japan; [11]Department of Orthopaedic Surgery, National Cancer Center Hospital, Tokyo, Japan; [12]Department of Orthopaedic Surgery, Hokkaido Cancer Center, Sapporo, Japan

P2–Poster 113 2562838

IMPACT ON OUTCOME OF CONCOMITANT ADMINISTRATION OF GASTRIC ACID SUPPRESSION (GAS) THERAPY AND PAZOPANIB IN SOFT TISSUE SARCOMA (STS) PATIENTS TREATED WITHIN EORTC 62043/62072 TRIALS

Olivier Mir, MD, PhD[1]; Nathan Touati[2]; Michela Lia[2]; Saskia Litiere[2]; Axel Le Cesne[1]; Stefan Sleijfer[3]; Michael Leahy[4]; Robin Young[5]; Jean-Yves Blay[6]; Zsuzsanna Papai[7]; Ron Mathijssen[3]; Nielka Van Erp[8]; Hans Gelderblom[9]; Winette Van der Graaf[10]; Alessandro Gronchi[11]

[1]Sarcoma Group, Gustave Roussy Cancer Campus, Villejuif, France; [2]European Organization for Research and Treatment of Cancer, Brussels, Belgium; [3]Erasmus MC - Cancer Institute, Rotterdam, Netherlands; [4]The Christie NHS Foundation Trust, Manchester, United Kingdom; [5]Weston Park Hospital, Sheffield, United Kingdom; [6]Centre Leon Berard, Lyon, France; [7]National Medical Canter, Budapest, Hungary; [8]Radboud University Medical Centre, Nijmegen, Netherlands; [9]Leiden University Medical Center, Leiden, Netherlands; [10]The Institute of Cancer Research and the Royal Marsden NHS Foundation Trust, London, United Kingdom; [11]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy

P2–Poster 114 2529585

MECHANISIM OF PAZOPANIB RESISTANCE IN SYNOVIAL SARCOMA

Yoshihiro Matsumoto, MD, PhD[1]; Nobuhiko Yokoyama[1]; Tomoya Matsunobu[2]; Makoto Endo[3]; Setsu Nokitaka[1]; Kiichiro Iida[1]; Fukushima Suguru[1]; Yukihide Iwamoto[2]

[1]Orhopaedic Surgery, Kyushu University School of Medicine, Fukuoka, Fukuoka, Japan; [2]Kyushu Rosai Hospital, Fukuoka, Japan; [3]National Cancer Center Hospital, Tokyo, Japan

P2–Poster 115 2531913

BODY COMPOSITION VARIATION IN DOXORUBICIN-REFRACTORY SOFT TISSUE SARCOMA (STS) PATIENTS (PTS) TREATED WITH REGORAFENIB VERSUS PLACEBO: AN ANCILLARY ANALYSIS OF REGOSARC TRIAL

Nicolas Penel, MD, PhD[1]; Aurélien Carnot[1]; Thomas Brodowicz[2]; Axel Le Cesne[3]; Blay Jean-Yves[4]; Sophie Taieb[5]; Emilie Decoupigny[6]; Jennifer Wallet[7]; Emmanuelle Tresch-Bruneel[7]; Stéphanie Clisant-Delaine[6]; Olivier Mir[3]

[1]Medical Oncology, Centre Oscar Lambret, Lille, France; [2]Medical Oncology, Wien University Hospital, Wien, Austria; [3]Medical Oncology, Gustave Roussy, Villejuif, France; [4]Medical Oncology, Centre Léon Bérard, Lyon, France; [5]Imaging Department, Centre Oscar Lambret, Lille, France; [6]Clinical Research Unit, Centre Oscar Lambret, Lille, France; [7]Biostatistics and Methodology Unit, Centre Oscar Lambret, Lille, France

P2–Poster 116 2531836

REGOSARC: REGORAFENIB VERSUS PLACEBO IN DOXORUBICIN-REFRACTORY SOFT TISSUE SARCOMA: A QUALITY- ADJUSTED TIME WITHOUT SYMPTOMS OF PROGRESSION OR TOXICTY (Q-TWIST)

Vincent Berry[1]; Laurent Basson[2]; Emilie Bogart[2]; Olivier Mir[3]; Blay Jean-Yves[4]; Antoine Italiano[5]; François Bertucci[6]; Christine Chevreau[10]; Bernadette Liegl-Antzager[7]; Stéphanie Clisant-Delaine[8]; Emmanuelle Tresch-Bruneel[2]; Emilie Decoupigny[8]; Axel Le Cesne[3]; Thomas Brodowicz[9]; Nicolas Penel[1]

[1]Medical Oncology, Centre Oscar Lambret, Lille, France; [2]Biostatistics and Methodology Unit, Centre Oscar Lambret, Lille, France; [3]Medical Oncology, Gustave Roussy, Villejuif, France; [4]Medical Oncology, Centre Leon Beard, Lyon, France; [5]Medical Oncology, Institut Bergonie, Bordeaux, France; [6]Medical Oncology, Institut Paoli Calmette, Marseille, France; [7]Pathology Department, Graz University Hospital, Graz, Austria; [8]Clinical Research Unit, Centre Oscar Lambret, Lille, France; [9]Medical Oncology, Wien University Hospital, Wien, Austria; [10]Medical Oncology, Institut Universitaire du Cancer Toulouse - Oncopole, Toulouse, France

P2–Poster 117 2570680

SYSTEMATIC REVIEW AND META-ANALYSIS OF PAZOPANIB (PZB) VERSUS OTHER ANTI-ANGIOGENIC, TYROSINE KINASE INHIBITORS (AATKI) IN ADVANCED SARCOMAS

Lee D. Cranmer, MD PhD FACP[1]; Elizabeth T. Loggers[2]; Seth M. Pollack[2]; Ivo Abraham[3]

[1]Division of Medical Oncology, University of Washington, Seattle, WA, USA; [2]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [3]Department of Pharmacy Practice and Science, University of Arizona, Tucson, AZ, USA

P2–Poster 118 2537944

THE ANTI-PLATELET-DERIVED GROWTH FACTOR RECEPTOR α ANTIBODY OLARATUMAB (LY3012207/IMC-3G3) DEMONSTRATES ANTI-TUMOR ACTIVITY IN MODELS OF PEDIATRIC BONE AND SOFT TISSUE SARCOMA

Caitlin May; Nick Loizos; Ruslan Novosiadly; Wayne Blosser; Michele Dowless; Gerard Oakley; Christophe Marchal; Amelie Forest; Robert Iliaria; Louis F. Stancato

Eli Lilly and Company, Indianapolis, IN, USA

P2–Poster 119 2550045

PHOSPHOPROTEOMIC PROFILING IN SARCOMAS REVEALS ALK AND MET AS NOVEL ACTIONABLE TARGETS IN SYNOVIAL SARCOMAS

Emmy Fleuren[1]; Myrella Vlenterie[2]; Winette Van der Graaf[1]; Melissa H. Hillebrandt-Roeffen[2]; Sabri Cebeci[2]; Amy van de Ven[2]; Uta E. Flucke[2]; Jianmin Wu[3]; Yvonne M. Versleijen-Jonkers[2]; Roger Daly[4]

[1]Institute of Cancer Research, London, United Kingdom; [2]Radboud UMC, Nijmegen, Netherlands; [3]Center for Cancer Bioinformatics, Being, China; [4]Monash University, Melbourne, Victoria, Australia

P2–Poster 120 2570512

REGORAFENIB IN PATIENTS WITH METASTATIC SOFT TISSUE SARCOMAS (STS): PRELIMINARY RESULTS FROM AN OPEN-LABEL PHASE II STUDY (RESOUND)

Rita De Sanctis, MD; Silvia Bozzarelli; Andrea Marrari; Lorenza Rimassa; Simona Sala; Vittorio Quagliuolo; Armando Santoro

Humanitas Cancer Center, Rozzano (Milan), Italy

P2–Poster 121 2565555

TEMOZOLOMIDE POST PAZOPANIB TREATMENT FAILURE MAY EXTENT PROGRESSION FREE SURVIVAL IN PATIENTS WITH ADVANCED SARCOMA: A CASE SERIES

Manojkumar Bupathi[2]; James Chen[1]

[1]Department of Biomedical Informatics and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA; [2]Department of Medical Oncology, The Ohio State University, Columbus, OH, USA

P2–Poster 122 2556482

SIROLIMUS AND ZOLEDRONIC ACID FOR MULTIOSTEOTIC PSEUDOMYOGENIC HEMANGIOENDOTHELIOMA OF THE BONE IN A CHILD: CASE REPORT AND REVIEW OF LITERATURE

Olivia M. Danforth, BS; Caleb Oh; Paul Kent

Rush Medical College, Chicago, IL, USA

P2–Poster 123 2536123

PAZOPANIB IN ADVANCED VASCULAR SARCOMAS: AN EORTC SOFT TISSUE AND BONE SARCOMA GROUP RETROSPECTIVE ANALYSIS

Attila Kollár[1]; R Jones[3]; Silvia Stacchiotti[4]; Hans Gelderblom[5]; Michele Guida[2]; Giovanni Grignani[6]; Neeltje Steeghs[7]; Akmal Safwat[8]; Daniela Katz[9]; Florence Duffaud[10]; Stefan Sleijfer[11]; Winette Van der Graaf[12]; Nathan Touati[13]; Saskia Litiere[13]; Bernd Kasper[14]

[1]Medical Oncology, University Hospital Bern, Inselspital, Bern, Switzerland; [2]National Cancer Institute "Giovanni Paolo II", Bari, Italy; [3]Royal Marsden Hospital, London, United Kingdom; [4]Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy; [5]University Medical Center, Leiden, Netherlands; [6]Institute of Cancer Research and Treatment, Torino, Italy; [7]The Netherlands Cancer Institute, Amsterdam, Netherlands; [8]Aarhus University Hospital, Aarhus, Denmark; [9]Hadassah-Hebrew University Medical Center, Jerusalem, Israel; [10]La Timone University Hospital & Aix-Marseille University, Marseille, France; [11]Erasmus MC - Cancer Institute, Rotterdam, Netherlands; [12]The Institute of Cancer Research and the Royal Marsden NHS Foundation Trust, London, United Kingdom; [13]European Organisation for Research and Treatment of Cancer (EORTC), Bruxelles, Belgium; [14]Mannheim University Medical Center, Mannheim, Germany

P2–Poster 124 2554618

AXI-STS: A UK NCRI SARCOMA CLINICAL STUDIES GROUP PHASE II TRIAL OF THE VEGFR INHIBITOR AXITINIB IN ADVANCED SOFT TISSUE SARCOMA (STS)

Penella Woll[2]; Piers Gaunt[1]; Ian Judson[3]; Sandra Strauss[4]; Jeremy Whelan[4]; Michael Leahy[5]; Ana Hughes[1]; Penny Goodby[1]; Christine Ingram[6]; David Hughes[6]; Lucinda Billingham[1]

[1]University of Birmingham, Birmingham, United Kingdom; [2]University of Sheffield, Sheffield, United Kingdom; [3]The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom; [4]University College Hospital, London, United Kingdom; [5]The Christie Hospital NHS Foundation Trust, Manchester, United Kingdom; [6]Royal Hallamshire Hospital, Sheffield, United Kingdom

P2–Poster 125 2566345

ASSESSMENT OF PATIENT-SPECIFIC T CELL RESPONSES AMONGTHE SARCOMA SPECTRUM

Jessica Thaxton, PhD, MsCR; Lee Leddy

Orthopaedics, Medical University of South Carolina, Charleston, SC, USA

P2–Poster 126 2537288

A PHASE I TRIAL OF DENDRITIC CELL VACCINATION WITH AND WITHOUT INHIBITION OF MYELOID DERIVED SUPPRESSOR CELLS BY GEMCITABINE PRE-TREATMENT FOR CHILDREN AND ADULTS WITH SARCOMA

Gabriel Tinoco, MD[2]; John M. Goldberg[1]; Edward Ziga[1]; Emil Kamar[2]; Georges Tahhan[2]; Eric Wieder[2]; Despina Kolonias[2]; Eli Gilboa[3]; Geoffrey Stone[3]; Jonathan Trent II[2]; Julio Barredo[1]; Krishna Komanduri [2]; Breelyn A. Wilky[2]

[1]Pediatric Hematology/Oncology, University of Miami, Miami, FL, USA; [2]University of Miami Miller School of Medicine and Sylvester Comprehensive Cancer Center, Miami, FL, USA; [3]Department of Immunology, University of Miami, Miami, FL, USA

P2–Poster 127 2563651

HIGH PDL1 EXPRESSION IN TREATED SARCOMAS MAY BE ALTERED BY NEOADJUVANT TREATMENT AND CORRELATE WITH DECREASED OVERALL SURVIVAL

Matthew J. Lasowski, MS; Matthew Stemm; Manpreet Bedi; John Charlson; Craig Mackinnon

Cancer Center, Medical College of Wisconsin, Milwaukee, WI, USA

P2–Poster 128 2555232

A PILOT FEASIBILITY STUDY OF IMMUNOTHERAPY WITH COMBINATION TRABECTEDIN AND NIVOLUMAB IN ADVANCED SOFT TISSUE SARCOMA

William W. Tseng, MD[2]; K. Kumar Sankhala[1]; Erlinda M. Gordon[1]; Suzan Arasheben[1]; Justin Daneshrad[1]; Sant P. Chawla[1]

[1]Sarcoma Oncology Center, Santa Monica, CA, USA; [2]Surgery, Section of Surgical Oncology, University of Southern California, Keck School of Medicine, Los Angeles, CA, USA

P2–Poster 129 2570652

RADIOTHERAPY ENHANCES NATURAL KILLER HOMING AND FUNCTION IN CANINE BONE AND SOFT TISSUE SARCOMAS

Jiwon S. Park[1]; Steven K. Grossenbacher[2]; Jaime F. Modiano[3]; Erik Ames[2]; Arta M. Monjazeb[4]; William T. Culp[5]; Mingyi Chen[6]; Michael S. Kent[5]; William J. Murphy[2]; Robert J. Canter[1]

[1]Surgery, UC Davis, Sacramento, CA, USA; [2]Dermatology, UC Davis, Sacramento, CA, USA; [3]Veterinary Clinical Sciences, University of Minnesota, Minneapolis, MN, USA; [4]Radiation Oncology, UC Davis, Sacramento, CA, USA; [5]School of Veterinary Medicine, UC Davis, Davis, CA, USA; [6]Pathology, UC Davis, Sacramento, CA, USA

P2–Poster 130 2561280

M1 MACROPHAGES AS PREDICTOR OF POOR RESPONSE TO TRABECTEDIN TREATMENT IN MYXOID LIPOSARCOMA

Marco Fioramonti; Michele Iuliani; Giulia Ribelli; Francesco Pantano; Daniele Santini; Giuseppe Tonini; Bruno Vincenzi
Campus Bio-Medico University of Rome, Rome, Italy

P2–Poster 131 2537146

NEOADJUVANT INTRALESIONAL INJECTION OF TALIMOGENE LAHERPAREPVEC WITH CONCURRENT PREOPERATIVE RADIATION IN PATIENTS WITH LOCALLY ADVANCED SOFT TISSUE SARCOMAS: PHASE 1B/2 TRIAL

Varun Monga, MBBS[1]; Benjamin Miller[2]; Carryn Anderson[6]; Bryan Allen[6]; Monzer Abu-Yousef[7]; Catherine Metz [7]; Maheen Rajput[7]; Eve Clark[7]; David Kuehn[7]; Munir Tanas[3]; Sarah Mott[4]; Zuhair Ballas[8]; Chinemerem Abanonu[5]; Sudershan Bhatia[6]; Mohammed Milhem[1]

[1]Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [2]Department of Orthopedics and Rehabilitation, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [3]Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [4]Biostatistics, Holden Comprehensive Cancer Center, Iowa City, IA, USA; [5]DaVita HealthCare Partners of Nevada, Las Vegas, NV, USA; [6]Radiation Oncology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [7]Radiology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [8]Immunology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA

P2–Poster 132 2556856

PAX3-FOXO1 KNOCKDOWN REDUCES PD-L1 EXPRESSION IN AN ALVEOLAR RHABDOMYOSARCOMA CELL LINES

Yoshihiro Nitta; Mitsuru Miyachi; Kazutaka Ouchi; Hideki Yoshida; Shigeki Yagyu; Ken Kikuchi; Kunihiko Tsuchiya; Tomoko Iehara; Hajime Hosoi
Pediatrics, Kyoto Pref. Univ. Med., Kyoto, Japan

P2–Poster 133 2557919

INTRATUMORAL IMMUNE-RESPONSE AND MISMATCH REPAIR STATUS IN LEIOMYOSARCOMA: A PILOT STUDY

Jonathan E. Cohen[1]; Eli Pikarsky[2]; Feras Eleyan[1]; Tamar Hamburger[1]; Adi Levi[1]; Tamar Peretz[1]; Daniela Katz, MD[1]

[1]Oncology, Hadassah Hebrew University Medical Center, Jerusalem, Israel; [2]Pathology Department, Hadassah Hebrew University Medical Center, Jerusalem, Israel

P2–Poster 134 2570678

SPLIT ANERGY OF NATURAL KILLER CELLS IN RECURRENT OR REFRACTORY SOFT TISSUE SARCOMA

Paulo Rodrigues-Santos[1]; Jani Sofia Almeida[2]; Patrícia Couceiro[2]; José Rui Simplício[2]; Vera Alves[1]; Manuel Santos-Rosa[1]; Paulo F. Tavares[3]

[1]Instituto de Imunologia, Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal;
[2]Laboratório de Imunologia e Oncologia, Centro de Neurociências e Biologia Celular, Coimbra, Portugal;
[3]Unidade de Tumores do Aparelho Locomotor, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

P2–Poster 135 2558611

BIOINFORMATIC IDENTIFICATION OF NOVEL TARGETS FOR SARCOMA IMMUNOTHERAPY

Micheala Baldauf[1]; Franziska Blaeschke[2]; Andreas Kirschner[3]; Merve M. Kiran[1]; Marlene Dallmayer[1]; Martin F. Orth[1]; Julia S. Gerke[1]; Julian Musa[1]; Rebeca Alba Rubio[1]; Aruna Marchetto[1]; Giuseppina Sannino[1]; Thomas Kirchner[1]; Uwe Thiel[3]; Tobias Feuchtinger[2]; Thomas G. Grünewald, Group-Leader[1]

[1]Laboratory for Pediatric Sarcoma Biology, Institute of Pathology, LMU Munich, Munich, Bavaria, Germany; [2]Pediatric Hematology, Oncology and Stem Cell Transplantation, Dr. von Hauner University Children's Hospital, LMU Munich, Munich, Germany; [3]Children's Cancer Research Center, Klinikum rechts der Isar, Technische Universität München, Munich, Germany

P2–Poster 136 2558012

TRABECTEDIN IN ADVANCES UTERINE SARCOMAS: A FIVE-YEARS EXPERIENCE OF A CANCER CENTER

Ana S. Patrão, MD; Miguel Henriques Abreu; Susana Sousa; Deolinda Pereira

Oncologia Médica, Instituto Português de Oncologia do Porto, Barcelos, Portugal

P2–Poster 137 2565754

THE ROLE OF ESTROGEN AND PROGESTERONE AS PROGNOSTIC FACTORS FOR ADENOSARCOMA OF THE UTERUS

Michael J. Nathenson, MD; Vinod Ravi; Heather Y. Lin; Wei-Lien Wang; Alexander Lazar; Dejka Araujo; Neeta Somaiah; Maria A. Zarzour; Ravin Ratan; SR Patel; Robert S. Benjamin; Anthony P. Conley

Sarcoma, MD Anderson, Houston, TX, USA

P2–Poster 138 2542471

SELECTIVE MARGINAL RESECTIONS IN THE MANAGEMENT OF AGGRESSVE ANGIOMYXOMAS

Henry G. Smith, MRCS[1]; Khin Thway[1]; Christina Messiou[1]; Desmond Barton[2]; Joseph Meirion Thomas[1]; Andrew J. Hayes[1]; Dirk C. Strauss[1]; Myles J. Smith[1]

[1]The Sarcoma Unit, The Royal Marsden Hospital, London, United Kingdom; [2]The Gynaecology Unit, The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom

P2–Poster 139 2569998

TREATMENT OF RETROPERITONEAL LIPOSARCOMAS AT A REFERAL CENTER: RETROSPECTIVE ANALYSIS OF PROGNOSTIC FACTORS

Alexandre M. Sousa, Resident; Ana Isabel Ferreira; Catia Ribeiro; Ana Ferreira; Sofia Conde; Marta Soares; Mariana Afonso; Flavio Videira; Jorge Guimaraes; Augusto Moreira; Joaquim Abreu de Sousa

Surgical Oncology, IPO PORTO, Vila Nova de Gaia, Portugal

P2–Poster 140 2569963

NATIONAL TREATMENT PATTERNS OF RETROPERITONEAL SARCOMA IN IRELAND

Meagan E. Wiebe[1]; Gerry Kelliher[2]; Una Hayden[1]; Charles Gillham[1]; Gary O'Toole[1]; Amy Gillis[1]; Paul F. Ridgway[2]

[1]Irish Sarcoma Group, at St. Vincent's University, St Luke's and Tallaght Hospitals, Dublin, Ireland; [2]National Clinical Programme in Surgery, RCSI, Dublin, Ireland

P2–Poster 141 2540926

DOES EXTENDED SURGICAL RESECTION IMPROVE OUTCOMES IN PRIMARY RETROPERITONEAL WELL- DIFFERENTIATED LIPOSARCOMA?

Naruhiko Ikoma, MD; Christina Roland; Keila E. Torres; Gary Mann; Kelly K. Hunt; Janice Cormier; Barry W. Feig

Surgical Oncology, MD Anderson Cancer Center, Houston, TX, USA

P2–Poster 142 2561942

PHASE I TRIAL OF PRE-OPERATIVE IMAGE-GUIDED INTENSITY MODULATED PROTON RADIATION THERAPY (IMPT) WITH SIMULTANEOUSLY INTEGRATED BOOST TO THE HIGH RISK MARGIN FOR RETROPERITONEAL SARCOMAS

Thomas F. DeLaney, MD[1]; Yen-Lin Chen[1]; Judith Adams[1]; Shea Hickey[2]; Dian Wang[3]; Elizabeth H. Baldini[4]; Karen De Amorim Bernstein[1]; Beow Yeap[2]; Stephen M. Hahn[5]; Petur Nielsen[6]; Edwin Choy[7]; John T. Mullen[8]; Sam S. Yoon[9]

[1]Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [2]Cancer Center, Massachusetts General Hospital, Boston, MA, USA; [3]Radiation Oncology, Rush University Medical Center, Chicago, IL, USA; [4]Radiation Oncology, Brigham and Women's Hospital, Dana Farber Cancer Institute, Boston, MA, USA; [5]Radiation Oncology, M.D. Anderson Cancer Center, Houston, TX, USA; [6]Pathology, Massachusetts General Hospital, Boston, MA, USA; [7]Medical Oncology, Massachusetts General Hospital, Boston, MA, USA; [8]Surgical Oncology, Massachusetts General Hospital, Boston, MA, USA; [9]Surgical Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA

P2–Poster 143 2562787

A COMPARISON OF RADIOTHERAPY TARGET VOLUMES DELINEATED WITH MRI AND CT IN PATIENTS HAVING PRE- OPERATIVE RADIOTHERAPY FOR RETROPERITONEAL SARCOMA IN THE PIRS STUDY

Daniel R. Henderson, FRCR[1]; Gabriele Poillucci[2]; Jessica Winfield[2]; Dirk C. Strauss[3]; Shane Zaidi[1]; Christina Messiou[2]; Aisha Miah[1]

[1]Radiotherapy, Royal Marsden Hospital, London, United Kingdom; [2]Radiology, Royal Marsden Hospital, London, United Kingdom; [3]Surgery, Royal Marsden Hospital, London, United Kingdom

P2–Poster 144 2569916

TREATMENT OF RETROPERITONEAL SARCOMA IN GERMANY - RESULTS OF A SURVEY OF THE GERMAN INTERDISCIPLINARY SARCOMA STUDY GROUP AND THE GERMAN SOCIETY OF GENERAL AND VISCERAL SURGERY

Jens Jakob, MD[1]; Anna Gerres[1]; Bernd Kasper[4]; Markus Wartenberg[2]; Ulrich Ronellenfitsch[1]; Hans-Rudolf Raab[3]; Peter Hohenberger[1]

[1]Department of Surgery, University Medical Center Mannheim, University of Heidelberg, Germany, Mannheim, Germany; [2]Das Lebenshaus, Wölfershausen, Germany; [3]Department of Surgery, University Hospital Oldenburg, Oldenburg, Germany; [4]Interdisciplinary Tumor Center Mannheim, University Medical Center Mannheim, Mannheim, Germany

P2–Poster 145 2529180

SURGERY FOR RETROPERITONEAL SARCOMAS IN THE ELDERLY

Henry G. Smith, MRCS; Joseph Meirion Thomas; Myles J. Smith; Andrew J. Hayes; Dirk C. Strauss

Sarcoma Unit, Academic Surgery, The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom

P2–Poster 146 2567751

IS RESECTION INDICATED FOR SCHWANNOMA OF THE RETROPERITONEUM/PELVIS?

Sally M. Burtenshaw[1]; Rebecca Gladdy[1]; Brendan C. Dickson[2]; Peter Ferguson[1]; Carol Swallow[1]

[1]General Surgery, Mount Sinai Hospital, Toronto, ON, Canada; [2]Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada

P2–Poster 147 2565613

PRIMARY RADIATION THERAPY FOR ABDOMINO-PELVIC SOFT-TISSUE SARCOMA ACHIEVES GOOD RESULTS IN PATIENTS WITH INOPERABLE DISEASE

Priyanka Patel; Natalie Nobar; Shane Zaidi; Dirk C. Strauss; Andrew J. Hayes; Myles J. Smith; Christina Messiou; Charlotte Benson; Ian Judson; Aisha Miah

Sarcoma Unit, The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom

P2–Poster 148 2570592

OUTCOMES IN PRIMARY ABDOMINAL OR RETROPERITONEAL LEIOMYOSARCOMA MANAGED WITH A MULTIDISCIPLINARY APPROACH

Fernando A. Angarita, MD, MSc[1]; Ana Olteanu[1]; Brendan C. Dickson[2]; Martin E. Blackstein[3]; Charles Catton[3]; Ian McGilvray[4]; Peter Chung[5]; Abha Gupta[6]; Rebecca Gladdy[1]

[1]Department of Surgery, Mount Sinai Hospital, Toronto, ON, Canada; [2]Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada; [3]Department of Medical Oncology, Mount Sinai Hospital, Toronto, ON, Canada; [4]Department of Surgery, University Health Network, Toronto, ON, Canada; [5]Department of Radiation Oncology, University Health Network, Toronto, ON, Canada; [6]Department of Medical Oncology, University Health Network, Toronto, ON, Canada

P2–Poster 149 2558023

A PHASE II CLINICAL TRIAL OF CONCURRENT AXITINIB AND PEMBROLIZUMAB IN SUBJECTS WITH ADVANCED ALVEOLAR SOFT PART SARCOMA AND OTHER SOFT TISSUE SARCOMAS

Breelyn A. Wilky, MD[1]; Jonathan Trent II[1]; Rosenberg Andrew[2]; Ty K. Subhawong[3]; Eric Wieder[1]; Despina Kolonias[1]; Deukwoo Kwon[4]; Efrosyni Sfakianaki[3]; Krishna Komanduri[1]

[1]Hematology/Oncology, Sylvester Comprehensive Cancer Center, Miami, FL, USA; [2]Pathology, University of Miami, Miami, FL, USA; [3]Radiology, University of Miami, Miami, FL, USA; [4]Biostatistics, Sylvester Comprehensive Cancer Center, Miami, FL, USA

P2–Poster 150 2570389

ALVEOLAR SOFT PART SARCOMA (ASPS) DISPLAYS A STRUCTURALLY ORGANIZED INFILRATING MYELOID CELLS

Silvia Stacchiotti, MD[1]; Marcella Tazzari[2]; Tiziana Negri[3]; Paolo Casali[1]; Silvia Brich[3]; Silvana Pilotti[3]; Chiara Castelli[2]

[1]Cancer Medicine, Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy; [2]Unit of Immunotherapy of Human Tumors, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [3]Laboratory of Experimental Molecular Pathology, Department of Diagnostic Pathology and Laboratory, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

P2–Poster 151 2556593

ALVEOLAR SOFT PART SARCOMA IN CHILDREN AND YOUNG ADULTS

Ricardo J. Flores[1]; Douglas J. Harrison[2]; Noah Federman[3]; Winston Huh[2]; Murali Chintagumpala[1]; Rajkumar Venkatramani[1]

[1]Pediatrics, Baylor College of Medicine, Houston, TX, USA; [2]Pediatrics, MD Anderson Cancer Center, Houston, TX, USA; [3]Pediatrics, Ronald Reagan UCLA Medical Center, Los Angeles, CA, USA

P2–Poster 152 2570365

EPITHELOID SARCOMA IN CHILDREN AND YOUNG ADULTS: RESULTS OF THE COOPERATIVE SOFT TISSUE SARCOMA (CWS) STUDIES

Ewa Koscielniak, MD, PhD[1]; Erika Hallmen[1]; Ivo Leuschner[2]; Monika Sparber-Sauer[1]; Monika Scheer[1]; Marc Münter[3]; Thekla von Kalle[4]; Steffan Loff[5]; Stefan Bielack[1]; Thomas Klingebiel[6]

[1]Ped. Oncology and Haematology, Klinikum Stuttgart, Olgahospital, Stuttgart, Baden-Württemberg, Germany; [2]Paidopathology, University Kiel, Kiel, Germany; [3]Radiation Oncology, Klinikum Stuttgart, Stuttgart, Germany; [4]Pediatric Radiology, Klinikum Stuttgart, Stuttgart, Germany; [5]Pediatric Surgery, Klinikum Stuttgart, Stuttgart, Germany; [6]Pediatric Oncology/Hematology and Hemostasis, University Children's Hospital, Frankfurt, Germany

P2–Poster 153 2522194

LONG-TERM RESULTS OF TREATMENT OF ADVANCED DERMATOFIBROSARCOMA PROTUBERANS (DFSP) WITH IMATINIB MESYLATE

Piotr Rutkowski, MD, PhD[1]; Anna Klimczak[1]; Tomasz Switaj[1]; Iwona Lugowska[1]; Beata Jagielska[2]; Michal Wagrodzki[3]; Renata Woroniecka[3]; Barbara Pienkowska-Grela[3]; Maria Debiec-Rychter[4]

[1]Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland, Warszawa, Poland; [2]Department of Oncology, Cardiooncology and Internal Medicine, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland, Warszawa, Poland; [3]Department of Pathology, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland, Warszawa, Poland; [4]Department of Human Genetics, KU Leuven and University Hospitals Leuven, Leuven, Belgium

P2–Poster 154 2570392

INSIGHTS ON THE BIOLOGY OF EWSR1 AND TAF15-POSITIVE EXTRASKELETAL MYXOID CHONDROSARCOMA

Monica Brenca[1]; Maurizio Polano[1]; Tiziana Negri[2]; Gian Paolo Dagrada[2]; Dominga Racanelli[1]; Sabrina Rossi[3]; Silvia Brich[2]; Kelly Fassetta[1]; Angelo Paolo Dei Tos[3]; Maria A. Pantaleo[4]; Alessandro Gronchi[2]; Paolo Casali[2]; Silvia Stacchiotti[2]; Silvana Pilotti[2]; Roberta Maestro[1]

[1]Experimantal Oncology 1, National Cancer Institute CRO Aviano, Aviano, Italy; [2]National Cancer Institute INT Milano, Milano, Italy; [3]Treviso General Hospital, Treviso, Italy; [4]University of Bologna, Bologna, Italy

P2–Poster 155 2560514

OUTCOMES AND SURVEILLANCE IMAGING (SI) PATTERNS FOLLOWING DEFINITIVE TREATMENT OF LOCALIZED EXTREMITY/TRUNK SOFT TISSUE SARCOMA (STS) WITH RADIATION THERAPY (RT) AND LIMB-SPARING SURGERY (LSS)

Sagar A. Patel[1]; Trevor J. Royce[1]; Constance M. Barysauskas[2]; Katherine Thornton[3]; Chandrajit Raut[4]; Elizabeth H. Baldini[1]

[1]Department of Radiation Oncology, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA, USA; [2]Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Boston, MA, USA; [3]Department of Medical Oncology, Dana- Farber/Brigham and Women's Cancer Center, Boston, MA, USA; [4]Department of Surgery, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA, USA

P2–Poster 156 2554411

WHAT MARGIN CLASSIFICATION SYSTEM BEST DISCRIMINATES THE RISK OF LOCAL RECURRENCE AFTER SOFT TISSUE SARCOMA RESECTION?

Kenneth R. Gundle, MD[1]; Lisa Kafchinski[2]; Sanjay Gupta[2]; Anthony Griffin[2]; Rita Kandel[3]; Brendan C. Dickson[3]; Peter Chung[4]; Charles Catton[4]; Brian O'Sullivan[4]; Jay Wunder[2]; Peter Ferguson[2]

[1]Orthopaedics & Rehabilitation, Oregon Health & Science University, Portland, OR, USA; [2]Dept of Surgery, University of Toronto, Mount Sinai Hospital, Toronto, ON, Canada; [3]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada; [4]Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada

P2–Poster 157 2569559

PREDICTION OF LOCAL AND METASTATIC RECURRENCE IN SOLITARY FIBROUS TUMOR: CONSTRUCTION OF A RISK CALCULATOR IN A MULTICENTER COHORT FROM THE FRENCH SARCOMA GROUP DATABASE

Corinne Bouvier, MD, PhD[1]; Noemie Resseguier[3]; Jean Yves Blay[4]; Axel Le Cesne[5]; Antoine Italiano[6]; Christine Chevreau[7]; Philippe Rosset[8]; Nicolas Isambert[9]; Dominique Ranchère-Vince[10]; Philippe Terrier[5]; Sylvie Bonvalot[5]; Nicolas Macagno[1]; Coralie Lemoine[3]; Jean Michel Coindre[6]; Sebastien Salas[2]

[1]Pathology, Timone Hospital, Marseille, France; [2]Oncology, Timone Hospital, Marseille, France; [3]Support unit for Clinical Research and Economic Evaluation, Faculty of Medecine Timone, Marseille, France; [4]Centre Léon Bérard, Lyon, France; [5]Institut Curie, Paris, France; [6]Institut Bergonié, Bordeaux, France; [7]IUCT Oncopole, Toulouse, France; [8]Orthopedic Surgery, CHU Tours, Tours, France; [9]Oncology, Centre Georges-François Leclerc, Dijon, France; [10]Pathology, Centre Léon Bérard, Lyon, France

P2–Poster 158 2565708

MALIGNANT PEROPHERAL NERVE SHEET TUMORS (MPNST) IN CHILDREN AND ADOLESCENTS: REPORT OF THE EUROPEAN PEDIATRIC SOFT TISSUE SARCOMA GROUP (EPSSG) STUDY NRSTS-2005

Max M. van Noesel[1]; Bernadette Brennan[2]; Gian Luca de Salvo[4]; Ilaria Zanetti[4]; Nadine Francotte[5]; Rita Alaggio[6]; Daniel Orbach[7]; Anna Kelsey[3]; Gianni Bisogno[8]; Michela Casanova[9]; Andrea Ferrari[9]

[1]Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands; [2]Pediatric Oncology, Royal Manchester Children's Hospital, Manchester, United Kingdom; [3]Department of Pathology, Royal Manchester Children's Hospital, Manchester, United Kingdom; [4]EpSSG Data Centre Istituto Oncologico Veneto IRCCS, Padova, Italy; [5]Department of Pediatrics, CHC-Clinique Esperance, Montegnée, Belgium; [6]Pathology Department, Padova University, Padova, Italy; [7]Pediatric Adolescent Young Adult Department, Institut Curie, Paris, France; [8]Pediatric Hematology and Oncology Division, Padova University, Padova, Italy; [9]Pediatric Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

P2–Poster 159 2558414

NEUROPATHIC PAIN AFTER SURGERY FOR EXTREMITY SARCOMA: PREVALENCE AND PREDISPOSING FACTORS

Jong Woong Park; Han-Soo Kim; Ilkyu Han, MD, PhD
Orthopedic Surgery, Seoul National University Hospital, Seoul, Korea (the Republic of)

P2–Poster 160 2557340

CONDITIONAL SURVIVAL OF PATIENTS WITH SOFT TISSUE SARCOMA (STS) AFTER CURATIVE SURGERY

Florian Posch[1]; Lukas Leitner[3]; Michael Stotz[1]; Bernadette Liegl-Antzager[2]; Angelika Bezan[1]; Martin Pichler[1]; Joerg Friesenbichler[3]; Armin Gerger[1]; Herbert Stoeger[1]; Andreas Leithner[3]; Joanna Szkandera[1]
[1]Clinical Division of Oncology, Department of Medicine, Medical University of Graz, Graz, Austria; [2]Institute of Pathology, Medical University of Graz, Graz, Austria; [3]Department of Orthopaedics and Orthopaedic Surgery, Medical University of Graz, Graz, Austria

P2–Poster 161 2570657

PATTERNS OF CARE AND OUTCOME OF METATASTIC SOFT-TISSUE SARCOMA PATIENTS (PTS) ACCORDING TO HISTOLOGICAL SUBTYPE AND TREATMENT SETTING: THE METASARC STUDY

Antoine Italiano[1]; Axel Le Cesne[2]; Jean Yves Blay[3]; Isabelle Ray-Coquard[3]; Olivier Mir[2]; Maud Toulmonde[1]; Philippe Terrier[2]; Marion Savina[1]; Jean Michel Coindre[1]
[1]Institut Bergonie, Bordeaux, France; [2]Institut Gustave Roussy, Villejuif, France; [3]Centre Léon Bérard, Lyon, France

P2–Poster 162 2528187

SARCOMA TUMOR SIZE (T) STAGING: HOW MUCH DO TUMORS DEFORM BETWEEN RADIOLOGY AND SURGERY?

Angela Pang, MBBS, MRCP[1]; Mariana Carbini[2]; Robert G. Maki[2]
[1]Medical Oncology, National University Hospital of Singapore, Singapore, Singapore; [2]Tisch Cancer Institute, Mount Sinai Medical Center, New York, NY, USA

P2–Poster 163 2566439

DEVELOPING A PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH 4 SUBTYPES OF SOFT TISSUE SARCOMA

Anne Skalicky[1]; Sameer Ghate[2]; Jose Perez[2]; Anne Rentz[1]
[1]Evidera, Seattle, WA, USA; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA

P2–Poster 164 2566592

A NEW SYMPTOM-SPECIFIC PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH SOFT TISSUE SARCOMA

Anne Rentz[1]; Anne Skalicky[1]; Sameer Ghate[2]; Sant P. Chawla[3]; Anthony P. Conley[4]; Victor M. Villalobos[5]; Jose Perez[2]
[1]Evidera, Seattle, WA, USA; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [3]Sarcoma Oncology Center, Santa Monica, CA, USA; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]University of Colorado School of Medicine, Aurora, CO, USA

P2–Poster 165 2565362

THE PROGNOSTIC VALUE OF LYMPHOVASCULAR INVASION IN TRUNCAL AND EXTREMITY SOFT TISSUE SARCOMAS: A U.S. ANALYSIS FROM THE NATIONAL CANCER DATA BASE (NCDB)

Cecilia G. Ethun, MD[1]; Alexandra G. Lopez-Aguiar[1]; Jeffery M. Switchenko[2]; Theresa W. Gillespie[1]; Keith Delman[1]; Charles Staley[1]; Shishir K. Maithel[1]; Kenneth Cardona[1]
[1]Division of Surgical Oncology, Department of Surgery, Emory University, Winship Cancer Institute, Atlanta, GA, USA; [2]Department of Biostatistics, Rollins School of Public Health, Emory University, Winship Cancer Institute, Atlanta, GA, USA

P2–Poster 166 2570200

COMORBIDITY IN SARCOMA PATIENTS: A NATIONWIDE POPULATION-BASED STUDY

Mathias Raedkjaer[1]; Katja Maretty-Kongsted[1]; Michael M. Petersen[3]; Peter Vedsted[2]; Johnny Keller[1]
[1]Dept. of Orthopedic Surgery, Aarhus University Hospital, Aarhus C, Denmark; [2]Aarhus University, Aarhus, Denmark; [3]Dept. of Orthopedic Surgery, Copenhagen University Hospital, Copenhagen, Denmark

P2–Poster 167 2561892

THE INFLUENCE OF CLINICOPATHOLOGICAL FACTORS ON RECURRENCE PATTERN AND SURVIVAL OF EXTREMITY LIPOSARCOMA PATIENTS IN A LARGE SINGLE CENTER STUDY COHORT

Melissa Vos, MD[1]; Kees Verhoef[2]; Arno van Leenders[3]; Stefan Sleijfer[4]; Dirk Grünhagen[2]
[1]Medical Oncology/Surgical Oncology, Erasmus MC, Rotterdam, Netherlands; [2]Surgical Oncology, Erasmus MC, Rotterdam, Netherlands; [3]Pathology, Erasmus MC, Rotterdam, Netherlands; [4]Medical Oncology, Erasmus MC, Rotterdam, Netherlands

P2–Poster 168 2570491

PATTERNS OF RELAPSE OR DISEASE PROGRESSION IN PATIENTS WITH METASTATIC RHABDOMYOSARCOMA: A SINGLE INSTITUTION EXPERIENCE

Beatriz Rozo[1]; Hatel Moonat[1]; Andrea Hayes-Jordan[2]; Anthony P. Conley[3]; Dejka Araujo[3]; Douglas J. Harrison[1]; Anita Mahajan[4]; Lianchun Xiao[5]; Winston Huh[1]
[1]Pediatrics, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Medical Sarcoma, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]Biostatistics, University of Texas MD Anderson Cancer Center, Houston, TX, USA

P2–Poster 169 2570488

PULMONARY METASTASECTOMY IN SARCOMA PATIENTS: OUTCOMES AND PROGNOSTIC FACTORS

Umberto Cariboni; Rita De Sanctis, MD; Marta Giaretta; Emanuele Voulaz; Pierluigi Novellis; Piergiuseppe Colombo; Emanuela Morenghi; Chiara Mussi; Andrea Marrari; Luca Balzarini; Vittorio Quagliuolo; Armando Santoro; Marco Alloisio
Humanitas Cancer Center, Rozzano (Milan), Italy

P2–Poster 170 2558648

ANALYSIS OF METASTASIS IN PATIENTS WITH SOFT TISSUE SARCOMA: IS EXTRA-PULMONARY METASTSIS RARE?

Yuki Yada; Tomoki Nakamura; Kazuma Okuno; Tomohito Hagi; Takao Matsubara; Kunihiro Asanuma; Akihiko Matsumine; Akihiro Sudo
Orthpeadic Surgery, Mie University, Tsu, Mie, Japan

P2–Poster 171 2544812

PATTERNS OF DISEASE RELAPSE IN PRIMARY EXTREMITY SOFT TISSUE SARCOMA

Henry G. Smith, MRCS; Nikolaos Memos; Joseph Meirion Thomas; Myles J. Smith; Dirk C. Strauss; Andrew J. Hayes
Academic Surgery, The Royal Marsden Hospital, Ashford, United Kingdom

P2–Poster 172 2570133

SERUM BIOMARKERS AS PROGNOSTIC FACTORS FOR METASTATIC SARCOMA

Ninna Aggerholm-Pedersen, MSc, MD, PhD; Katja Maretty-Kongsted; Steen Baerentzen; Johnny Keller; Akmal Safwat
Aarhus University Hospital, Aarhus, Denmark

P2–Poster 173 2569961

ADVANCED SOFT-TISSUE SARCOMA–RELATED TREATMENT PATTERNS AND OUTCOMES IN ELDERLY PATIENTS IN THE UNITED STATES

Maria Lorenzo[1]; Lisa Hess[2]; Steven Nicol[2]; Rohan Parikh[3]; Sean D. Candrilli[3]; James A. Kaye[4]
[1]Eli Lilly and Company Limited, Windlesham, Surrey, United Kingdom; [2]Eli Lilly and Company, Indianapolis, IN, USA; [3]RTI Health Solutions, Research Triangle Park, NC, USA; [4]RTI Health Solutions, Waltham, MA, USA

P2–Poster 174 2570650

CLINICAL FEATURES, TREATMENT AND PROGNOSIS OF ANGIOSARCOMA INVOLVING THE SPINE

Takeshi Hirose; Makoto Endo; Akihiko Yoshida; Rie Nakano; Shunichi Toki; Takenori Uehara; Masato Sugawara; Yoshihiro Araki; Tomoaki Mori; Koki Shimizu; Eisuke Kobayashi; Yoshikazu Tanzawa; Fumihiko Nakatani; Hirokazu Chuman
Akira Kawai National Cancer Center, Tokyo, Japan

P2–Poster 175 2570518

AYA PATIENT AND PROVIDER PERCEPTIONS OF FERTILITY PRESERVATION

Holly Spraker-Perlman[3]; Jennifer Wright[2]; Samantha Pannier[1]; Brynn Fowler[1]; Echo L. Warner[1]; Douglas Fair[3]; William Sause[4]; Jeffrey Yancey[2]; R. L. Randall[2]; Anne C. Kirchhoff[1]

[1]Cancer Control and Population Sciences, Huntsman Cancer Institute, Salt Lake City, UT, USA; [2]Huntsman Cancer Institute, Salt Lake City, UT, USA; [3]Primary Children's Hospital, Salt Lake City, UT, USA; [4]Intermountain Healthcare, Salt Lake City, UT, USA

P2–Poster 176 2570502

PATIENTS' PERSPECTIVES OF SARCOMA TREATMENT: RESULTS FROM A NATIONAL SARCOMA SURVEY IN ENGLAND

Eugenie Younger[3]; Jeremy Whelan[2]; Robin Jones[3]; Lindsey Bennister[1]; Winette Van der Graaf[3]

[1]Sarcoma UK, London, United Kingdom; [2]UCLH, London, United Kingdom; [3]Royal Marsden Hospital, London, United Kingdom

P2–Poster 177 2542312

IMPACT OF GERIATRIC FACTORS ON SURGICAL AND PROGNOSTIC OUTCOMES IN ELDERLY PATIENTS WITH SOFT- TISSUE SARCOMA

Yusuke Tsuda, MD[1]; Koichi Ogura[1]; Eisuke Kobayashi[2]; Toru Hiruma[3]; Shintaro Iwata[4]; Naofumi Asano[5]; Akira Kawai[2]; Hirokazu Chuman[2]; Takeshi Ishii[4]; Hideo Morioka[5]; Hiroshi Kobayashi[1]; Yusuke Shinoda[1]; Hirotaka Kawano[6]

[1]Orthopaedic Surgery, The University of Tokyo, Tokyo, Japan; [2]Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [3]Musculoskeletal Tumor Surgery, Kanagawa Cancer Center, Kanagawa, Japan; [4]Orthopedic Surgery, Chiba Cancer Center, Chiba, Japan; [5]Orthopedic Surgery, Keio University, Tokyo, Japan; [6]Orthopedic Surgery, The University of Teikyo, Tokyo, Japan

P2–Poster 178 2535716

BALANCING PROLONGED SURVIVAL WITH QUALITY OF LIFE USING LOW-DOSE PAZOPANIB MAINTENANCE: A COMPARISON WITH THE PALETTE STUDY

Kensaku Abe; Norio Yamamoto; Katsuhiro Hayashi; Akihiko Takeuchi; Takashi Higuchi; Yuta Taniguchi; Hisaki Aiba; Hiroyuki Tsuchiya

Orthopaedic Surgery, Kanazawa University, Kanazawa, Ishikawa, Japan

P2–Poster 179 2529114

WELL DIFFERENTIATED / DEDIFFERENTIATED LIPOSARCOMA: ARE SOME PATIENTS AT RISK OF DEVELOPING A SECOND CANCER?

Eric E. Jung[1]; Shefali Chopra[2]; Ann Hamilton[3]; William W. Tseng[1]

[1]Surgery, Surgical Oncology, Keck School of Medicine, University of Southern Calfiornia, Los Angeles, CA, USA; [2]Pathology, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; [3]Preventative Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

P2–Poster 180 2533243

ONCOLOGIC OUTCOMES IN PATIENTS WITH EXTREMITY MYXOFIBROSARCOMA AND UNDIFFERENTIATED PLEOMORPHIC SARCOMA: A MATCHED CASE-CONTROL STUDY

Christina Roland, MD[1]; Kelsey Watson[1]; Yi-Ju Chiang[1]; Yu Liang[2]; Nicole de Rosa[1]; Gary Mann[1]; Janice Cormier[1]; Kelly K. Hunt[1]; Barry W. Feig[1]; Wei-Lien Wang[2]; Alexander Lazar[2]; Keila E. Torres[1]

[1]Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Pathology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

P2–Poster 181 2570714

ADHERENCE TO EXTREMITY SARCOMA STANDARDS OF CARE VARIES BY CASE VOLUME: A NATIONAL CANCER DATABASE (NCDB) ANALYSIS

John Charlson, MD[1]; Manpreet Bedi[1]; Rahul Rajeev[1]; David M. King[1]; John Neilson[1]; T. Clark Gamblin[1]; Kiran Turaga[2]

[1]Medical College of Wisconsin, Wauwatosa, WI, USA; [2]University of Chicago, Chicago, IL, USA

P2–Poster 182 2570699

FAMILY HISTORY OF CANCER AND ITS INCIDENCE ON ADULT ALVEOLAR RHABDOMYOSARCOMA (ARMS): AN MD ANDERSON CANCER CENTER (MDACC) SERIES

Branko Cuglievan, MD[1]; April DePombo[1]; Winston Huh[2]; Douglas J. Harrison[2]; Andrea Hayes-Jordan[3]; Joseph A. Ludwig[4]; Dejka Araujo[4]; Vinod Ravi[4]; SR Patel[4]; Cindy L. Schwartz[2]; Robert S. Benjamin[4]; Anthony P. Conley[4]
[1]Pediatric Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Sarcoma Pediatric Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Pediatric Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Sarcoma Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

P2–Poster 183 2570265

INCIDENCE OF SARCOMAS AND HISTOLOGICAL SUBTYPES IN GERMANY – FIRST NATIONAL SURVEY

Meike Ressing[2]; Eva Wardelmann[3]; Peter Hohenberger, MD, PhD[1]; Jens Jakob[1]; Bernd Kasper[4]; Katharina Emrich[2]; Andrea Eberle[5]; Maria Blettner[2]; Sylke Zeisig[2]
[1]Division of Surgical Oncology and Thoracic Surgery, Department of Surgery, University Medical Center Mannheim, University of Heidelberg, Mannheim, Germany; [2]Institute for Medical Biostatistics, Epidemiology and Informatics, University Medical Center, Johannes Gutenberg University, Mainz, Mainz, Germany; [3]Gerhard-Domagk-Institute for Pathology, University Hospital Münster, Münster, Germany; [4]Interdisciplinary Tumor Center Mannheim, University Medical Center Mannheim, University of Heidelberg, Mannheim, Germany; [5]Cancer Registry Bremen, Bremen, Germany

P2–Poster 184 2566255

LOCAL RECURRENCE, DISTANT METASTASIS, AND DEATH IN PATIENTS WITH SOFT TISSUE SARCOMA AFTER CURATIVE RESECTION: A MULTI-STATE MODEL

Florian Posch[1]; Lukas Leitner[2]; Michael Stotz[1]; Bernadette Liegl-Antzager[3]; Angelika Bezan[1]; Martin Pichler[1]; Armin Gerger[1]; Marko Bergovec[2]; Herbert Stoeger[1]; Andreas Leithner[2]; Joanna Szkandera[1]
[1]Clinical Division of Oncology, Department of Medicine, Medical University of Graz, Graz, Austria; [2]Department of Orthopaedics and Orthopaedic Surgery, Medical University of Graz, Graz, Austria; [3]Institute of Pathology, Medical University of Graz, Graz, Austria

P2–Poster 185 2566492

THERAPY AND OUTCOME OF PATIENTS FOLLOWING UNPLANNED EXCISIONS IN SOFT TISSUE SARCOMA: A MULTI- CENTRE EXPERIENCE

Maria A. Smolle, Medical Student[1]; Elisabeth Goldenitsch[2]; Felix Machacek[2]; Marko Bergovec[1]; Bernadette Liegl-Antzager[3]; Florian Posch[4]; Joanna Szkandera[4]; Andreas Leithner[1]
[1]Department of Orthopaedic Surgery, Medical University of Graz, Graz, Austria; [2]Orthopaedic Hospital Gersthof Vienna, Vienna, Austria; [3]Institute of Pathology, Medical University of Graz, Graz, Austria; [4]Division of Clinical Oncology, Internal Medicine, Medical University of Graz, Graz, Austria

P2–Poster 186 2565082

FEASIBILITY OF BIOPSIES IN METASTATIC SOFT TISSUE SARCOMAS - RELEVANCE FOR TRANSLATIONAL TRIALS

Philipp Ammon; Sebastian Bauer
West German Cancer Center, Essen, Germany

P2–Poster 187 2565081

PREOPERATIVE ASSESSMENT OF INFILTRATIVE HISTOLOGIC GROWTH PATTERN IN EXTREMITY SOFT TISSUE SARCOMA

Jong Woong Park[1]; Han-Soo Kim[1]; Cheol Lee[2]; Ji Yeon Yun[1]; Ilkyu Han[1]
[1]Seoul National University Hospital, Seoul, Korea (the Republic of); [2]Seoul National University College of Medicine, Seoul, Korea (the Republic of)

P2–Poster 188 2561423

NEUTROPHIL-LYMPHOCYTE RATIO AS PROGNOSTIC PREDICTORS IN PATIENTS WITH SOFT TISSUE SARCOMA

Tomohito Hagi; Tomoki Nakamura; Yuki Yada; Takuya Kakimoto; Takao Matsubara; Kunihiro Asanuma; Akihiko Matsumine; Akihiro Sudo
Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Tsu, Mie, Japan

P2–Poster 189 2557539
RISK FACTORS INCREASING IN-HOSPITAL MORTALITY AFTER CHEMOTHERAPY FOR PATIENTS WITH MALIGNANT MUSCULOSKELETAL TUMORS
Toru Akiyama, MD, PhD; Kazuo Saita
Departments of Orthopaedic Surgery, Saitama Medical Center, Jichi Medical University, Saitama, Japan

P2–Poster 190 2545084
REAL-WORLD TREATMENT PATTERNS OF PATIENTS WITH METASTATIC SOFT TISSUE SARCOMA IN THE UNITED STATES
Victor M. Villalobos, MD, PhD[1]; Stacey DaCosta Byfield[2]; Sameer Ghate[3]; Oluwakayode Adejoro[2]; Jose Perez[3]
[1]University of Colorado Anschutz Medical Campus, Denver, CO, USA; [2]Optum, Eden Prairie, MN, USA; [3]Novartis, East Hanover, NJ, USA

P2–Poster 191 2529964
TREATMENT OF BONE AND SOFT-TISSUE SARCOMA PATIENTS IN JAPAN – THE DISTRIBUTION OF PATIENTS AND MEDICAL SPECIALTIES BY CANCER TOPOGRAPHY AND TREATMENT MODALITY
Makoto Endo, MD, PhD; Momoko Iwamoto; Shunichi Toki; Takeshi Hirose; Takenori Uehara; Masato Sugawara; Tomoaki Mori; Koki Shimizu; Eisuke Kobayashi; Yoshikazu Tanzawa; Fumihiko Nakatani; Hirokazu Chuman; Takahiro Higashi; Akira Kawai
National Cancer Center, Tokyo, Japan

P2–Poster 192 2541168
IMPACT OF SUPERVISED PHYSICAL EXERCISE ON FATIGUE AND QUALITY OF LIFE IN ADULT SARCOMA PATIENTS
Leopold Hentschel[1]; Wadim Kisel[3]; Michael Kramer[2]; Frank Kroschinsky[2]; Martin Bornhäuser[2]; Hornemann Beate[1]; Markus K. Schuler[2]
[1]University Cancer Center, University Hospital Carl Gustav Carus, Dresden, Germany; [2]Department of Internal Medicine I, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [3]Department of Orthopaedics and Trauma Surgery, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

P2–Poster 193 2540447
PATIENT-DIRECTED INTERVENTION TO IMPROVE QUALITY OF LIFE (QOL) FOR PATIENTS WITH SOFT TISSUE SARCOMA (STS) UNDERGOING PALLIATIVE TREATMENT: A MULTICENTER, CLUSTER-RANDOMIZED, CONTROLLED TRIAL OF THE GERMAN INTERDISCIPLINARY SARCOMA GROUP
Leopold Hentschel[1]; Ulrich Schuler[2]; Hornemann Beate[1]; Andrea Schilling[3]; Janet Freitag[4]; Stephan Richter[4]; Markus K. Schuler[4]
[1]University Cancer Center, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [2]University Palliative Center, University Hospital Carl Gustav Carus, Dresden, Germany; [3]Department of Social Work, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [4]Department of Internal Medicine I, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

P2–Poster 194 2529827
USING A MODIFIED DELPHI PROCESS TO IDENTIFY QUALITY INDICATORS FOR SARCOMA SERVICES
Michelle Ghert, MD, FRCSC[1]; Cassandra McKay[2]; Amanda Wong[2]; Sherrie Hertz[2]; Charles Catton[4]; Jonathan Irish[4]; Rita Kandel[3]
[1]Surgery, McMaster University, Hamilton, ON, Canada; [2]Cancer Care Ontario, Toronto, ON, Canada; [3]Mount Sinai Hospital, Toronto, ON, Canada; [4]University Health Network Princess Margaret Hospital, Toronto, ON, Canada

P2–Poster 195 2565122
SURVIVAL IN SOFT TISSUE SARCOMA (STS) FOLLOWING PRESENTATION OF FIRST METASTASIS OR OLIGOMETASTASES
Gerard Walls; Shane Zaidi; Omar Al-Muderis; Komel Khabra; Charlotte Benson; Robin Jones; Ian Judson; Aisha Miah
The Royal Marsden NHS Foundation Trust, London, Surrey, United Kingdom

P2–Poster 196 2570715

ADULT RHABDOMYOSARCOMA: A RETROSPECTIVE ANALYSIS OF 40 PATIENTS TREATED AT A SINGLE INSTITUTION

Ann Raldow[1]; Alex Jacobson[2]; Saveli Goldberg[2]; Haotong Wang[2]; Edwin Choy[3]; Gregory M. Cote[3]; Francis Hornicek[4]; Thomas F. DeLaney[2]; Yen-Lin Chen[2]

[1]Department of Radiation Oncology, UCLA, Los Angeles, CA, USA; [2]Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [3]Department of Medical Oncology, Massachusetts General Hospital, Boston, MA, USA; [4]Department of Surgical Oncology, Massachusetts General Hospital, Boston, MA, USA

P2–Poster 197 2569029

A MODEL FOR INTERNATIONAL MULTIDISCIPLINARY TEAMS TO ADDRESS THE SARCOMA DISEASE BURDEN IN LOW- AND MIDDLE-INCOME SETTINGS

Theoneste Nkurunziza[1]; Dayo Fadelu[3]; Cyprien Shyirambere[6]; Djamilla Uwimanzi[1]; Raphael Kalengayi[5]; Belson Rugwizangoga[2]; Thierry Zawadi [4]; Faustin Ntirenganya[2]; Jennifer Kreshak[7]

[1]Inshuti Mu Buzima/Partners in Health, Kigali, Rwanda; [2]Centre Hospitalier Universitaire de Kigali, Kigali, Rwanda; [3]Dana Farber Cancer Institute, Boston, MA, USA; [4]Kanombe Military Hospital, Kigali, Rwanda; [5]King Faisal Hospital, Kigali, Rwanda; [6]Inshuti Mu Buzima/Partners in Health, Butaro, Rwanda; [7]Harvard Medical School, Boston, MA, USA

P2–Poster 198 2544196

THE OUTCOME OF LIMB SALVAGE SURGERY IN DEVELOPING COUNTRY, KHCC EXPERIENCE

Ahmad Shehadeh

KHCC, Amman, Jordan

P2–Poster 199 2565841

THE NOSARC PROJECT, A NATIONAL, PROSPECTIVE AND POPULATION-BASED STUDY OF MUTATIONS AND MECHANISMS IN SARCOMAS, AND PRECLINICAL VALIDATION OF NOVEL TARGETED THERAPIES, WITH THE INTENTION TO LEAD TO CLINICAL TRIALS

Ola Myklebost, Dr Philos[2]; Bodil Bjerkehagen[3]; Kjetil Boye[4]; Heidi Glosli[5]; Kirsten S. Hall[4]; Nina Jebsen[6]; Heidi A. Korsmo[1]; Heidi Knobel[7]; Susanne Lorenz[1]; Leonardo A. Meza-Zepeda[1]; Else Munthe[1]; Stine Næss[4]; Eivind Smeland[8]; Eva W. Stratford[1]; Olga Zaikova[4]

[1]Inst. for Cancer Research, Oslo Univertsity Hospital, Oslo, Norway; [2]Clinical Science, University of Bergen, Bergen, Norway; [3]Pathology, Oslo University Hospital, Oslo, Norway; [4]Oncology, Oslo University Hospital, Oslo, Norway; [5]Pediatrics, Olso University Hospital, Oslo, Norway; [6]Oncology, Haukeland University Hospital, Bergen, Norway; [7]Oncology, St Olav University Hospital, Bergen, Norway; [8]Oncology, University Hospital for Northern Norway, Tromsø, Norway

P2–Poster 200 2558371

OUTCOME AFTER SURGERY FOR EXTREMITY SOFT TISSUE SARCOMA IN PATIENTS PRESENTING WITH METASTASIS AT DIAGNOSIS

Chandra Kumar Krishnan[2]; Han-Soo Kim[1]; Ilkyu Han, MD, PhD[1]

[1]Orthopedic Surgery, Seoul National University Hospital, Seoul, Korea (the Republic of); [2]Cancer Institute (WIA), Chennai, India

P2–Poster 201 2565590

CLINICAL FEATURES OF HIGH-GRADE EXTREMITY AND TRUNK SARCOMAS IN PATIENTS AGED 80 YEARS OR OLDER: THE REASONS FOR INFERIOR OUTCOMES

Jungo Imanishi, MD[1]; Lester W. Chan[2]; Matthew Broadhead[2]; Samuel Y. Ngan[4]; John Slavin[3]; Grant Pang[2]; Peter F. Choong[2]

[1]Orthopaedic Oncology and Surgery, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [2]Orthopaeics, St. Vincent's Hospital Melbourne, Fitzory, Victoria, Australia; [3]Pathology, St. Vincent's Hospital Melbourne, Fitzory, Victoria, Australia; [4]Radiation Oncology, Peter MacCallum Cancer Center, East Melbourne, Victoria, Australia

P2–Poster 202 2525004
DISTANT METASTASIS IN PATIENTS WITH MYXOFIBROSARCOMA
Hiroyuki Tsuchie[1]; Mitsunori Kaya[2]; Hiroyuki Nagasawa[1]; Makoto Emori[2]; Naohisa Miyakoshi[1]; Toshihiko Yamashita[2]; Yoichi Shimada[1]
[1]Orthopedic Surgery, Akita University Graduate School of Medecine, Akita, Akita, Japan; [2]Orthopedic Surgery, Sapporo Medical University School of Medicine, Sapporo, Japan

P2–Poster 203 2569809
A WHOLE BODY MRI STUDY IN TP53 MUTATION CARRIERS AT RISK OF MULTI-ORGAN CANCER
Mandy L. Ballinger, PhD[1]; Sue Shanley[2]; Nicholas Ferris[7]; Kate Moodie[3]; Marion Harris[4]; Alison Trainer[2]; Eveline Niedermayr[5]; Mary-Anne Young[2]; Kate McBride[6]; Bimal Parameswaran[3]; Paul James[2]; David Thomas[1]
[1]Cancer Division, Garvan Institute of Medical Research, Darlinghurst, New South Wales, Australia; [2]Familial Cancer Centre, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [3]Cancer Imaging, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [4]Familial Cancer Centre, Monash Health, Melbourne, Victoria, Australia; [5]Research Division, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [6]University of Sydney, Sydney, New South Wales, Australia; [7]Monash Imaging, Monash Health, Melbourne, Victoria, Australia

P2–Poster 204 2570538
PLEOMORPHIC RHABDOMYOSARCOMA: A SINGLE INSTITUTION EXPERIENCE
Anna Maria Frezza[1]; Paola Collini[2]; Chiara Colombo[3]; Carlo Morosi[4]; Silvia Stacchiotti[1]; Salvatore Renne[2]; Claudia Sangalli[5]; Marco Fiore[3]; Stefano Radaelli[3]; Paolo Casali[1]; Alessandro Gronchi[3]
[1]Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [2]Pathology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [3]Surgery, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [4]Radiology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [5]Radiation Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

P2–Poster 205 2570674
PEDIATRIC-TYPE RHABDOMYOSARCOMA IN ADULTS: A RETROSPECTIVE ANALYSIS FROM THE SPANISH GROUP FOR RESEARCH ON SARCOMA (GEIS)
Nadia Hindi, MD[1]; Pablo Luna[2]; Antonio Lopez-Pousa[3]; Jordi Rubio[4]; Claudia Valverde[5]; Javier Martinez-Trufero[6]; Jeronimo Martinez[7]; Maria Angeles Sala[8]; Juan Luis Arranz[9]; Fatima Toscano[10]; Rosa Alvarez[11]; Juana Maria Cano[12]; Nuria Lainez[13]; Ana de Juan[14]; Javier Martin-Broto[1]
[1]University Hospital Virgen del Rocio, Seville, Spain; [2]University Hospital Son Espases, Palma de Mallorca, Spain; [3]San Pau University Hospital, Barcelona, Spain; [4]Instituto Catalan de Oncologia (ICO), Girona, Spain; [5]University Hospital Vall d'Hebron, Barcelona, Spain; [6]University Hospital Miguel Servet, Zaragoza, Spain; [7]University Hospital La Arrixaca, Murcia, Spain; [8]University Hospital Basurto, Bilbao, Spain; [9]Fundacion Jimenez Diaz, Madrid, Spain; [10]Hospital Juan Ramon Jimenez, Huelva, Spain; [11]University Hospital Gregorio Marañon, Madrid, Spain; [12]University Hospital Ciudad Real, Ciudad Real, Spain; [13]Navarra Hospital, Pamplona, Spain; [14]University Hospital Marques de Valdecilla, Santander, Spain

P2–Poster 206 2570340
PRIMARY PSEUDOMYOGENIC HEMANGIOENDOTHELIOMA OF BONE: AN ANALYSIS OF 21 CASES TREATED AT ISTITUTO ORTOPEDICO RIZZOLI
Alberto Righi[1]; Marco Gambarotti[1]; Marta Sbaraglia[2]; Daniel Vanel[1]; Angelo Paolo Dei Tos[2]; Piero Picci[1]
[1]Department of Pathology, Rizzoli Institute, Bologna, Italy, Bologna, Italy; [2]Department of Pathology, Treviso Regional Hospital, Treviso, Italy

P2–Poster 207 2554120
SARCOMA CLINICAL RESEARCH IN THE LAST DECADE: A CLINICALTRIAL.GOV REGISTRY REVIEW
Emanuela Marchesi, PhD[2]; Irene Quattrini[2]; Piero Picci[1]
[1]Laboratry of Experimental Oncology, Isituto Ortopedico Rizzoli, Bologna, BO, Italy; [2]Italian Sarcoma Group, Bologna, Italy

P2–Poster 208 2570720

SYSTEMATIC MULTIDISCIPLINARY APPROACH TO RADIATION ASSOCIATED ANGIOSARCOMAS (RAAS) OF THE BREAST

Ivy A. Petersen, MD[1]; Amy Degnim[3]; Steven I. Robinson[2]; Robert Mutter[1]; Scott Okuno[2]
[1]Radiation Oncology, Mayo Clinic, Rochester, MN, USA; [2]Medical Oncology, Mayo Clinic, Rochester, MN, USA; [3]Surgery, Mayo Clinic, Rochester, MN, USA

P2–Poster 209 2570216

THYROXINE DEPLETION MODULATED BY EXOGENOUS L-TRIIODOTHYRONINE MAY EXTEND SURVIVAL IN ADVANCED SARCOMA PATIENTS

Rony Weitzen[1]; Aleck Hercbergs[2]
[1]Oncology, Sheba Medical Center, Ramat Gan, Israel; [2]Radiation Oncology, Cleveland Clinic, Beachwood, OH, USA

P2–Poster 210 2521934

MARRIAGE AND FERTILITY IN LONG-TERM SURVIVORS OF CHILDHOOD, ADOLESCENT AND YOUNG ADULT (AYA) HIGH- GRADE SARCOMA: A JAPANESE SINGLE-CENTER EXPERIENCE

Tsukasa Yonemoto[1]; Miyako Takahashi[2]; Mitsue Maru[3]; Akiko Tomioka[4]; Masahiro Saito[5]; Yuko Araki[6]; Makiko Tazaki[2]; Miyako Tsuchiya[2]; Shintaro Iwata[1]; Hiroto Kamoda[1]; Takeshi Ishii[1]
[1]Chiba Cancer Center, Chiba, Japan; [2]National Cancer Center, Tokyo, Japan; [3]Konan Women's University, Kobe, Japan; [4]Tokyo Healthcare University, Tokyo, Japan; [5]Oizumi Gakuen Child & Adolescence Clinic, Tokyo, Japan; [6]NEC Corporation, Kawasaki, Japan

P2–Poster 211 2527022

SARCOMA AND TYPE 1 DIABETES

William Breen, BA[1]; Yogish Kudva[3]; Scott Okuno[2]
[1]Mayo Medical School, Mayo Clinic, Rochester, MN, USA; [2]Medical Oncology, Mayo Clinic, Rochester, MN, USA; [3]Endocrinology, Mayo Clinic, Rochester, MN, USA

P2–Poster 212 2565859

BMI AS A RISK FACTOR FOR TOXICITIES IN ADVANCED STS PATIENTS TREATED WITH TRABECTEDIN

B. Vincenzi[1]; G. Armento[1]; M. Silletta[1]; M. Spalato Ceruso[1]; G. Catania[1]; D. Santini[1]; G. Tonini[1]; G. Badalamenti[2]; L. Incorvaia[2]; G. Maltese[3]
[1]Oncology, Campus Bio-Medico, Rome, Lazio, Italy; [2]Section of Medical Oncology, University of Palermo, Palermo, Italy; [3]Gynecology Oncology Unit, Fondazione IRCCS National Cancer Institute, Milan, Italy

PO 001 2565549

MDM2 RNA EXPRESSION IS ASSOCIATED WITH TUMOR PROGRESSION IN DEDIFFERENTIATED LIPOSARCOMA

Kate Lynn Bill[2]; Manojkumar Bupathi[3]; Raphael Pollock[2]; James Chen[1]
[1]Department of Biomedical Informatics and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA; [2]Department of Surgical Oncology, The Ohio State University, Columbus, OH, USA; [3]Department of Medical Oncology, The Ohio State University, Columbus, OH, USA

PO 002 2568095

SARCOIDOSIS MIMICKING PULMONARY METASTATIC LIPOSARCOMA

Takeshi Ishii; Tsukasa Yonemoto; Shintaro Iwata; Hiroto Kamoda
Chiba Cancer Center, Chiba, Japan

PO 003 2540770

SOFT-TISSUE SARCOMAS: IMAGING CHARACTERIZATION AND RADIOLOGISTS ROLE

Rui T. Gil, Resident
Radiologia, Instituto Português de Oncologia de Lisboa, Lisboa, Lisboa, Portugal

PO 004 2565808

MAGNETIC RESONANCE (MR) IMAGING INVESTIGATION OF SOFT TISSUE SARCOMA MISDIAGNOSED AS CHRONIC HEMATOMA

Naomasa Fukase, MD, PhD[1]; Ikuo Fujita[2]; Teruya Kawamoto[1]; Hitomi Hara[1]; Takuya Fujimoto[2]; Masayuki Morishita[1]; Etsuko Kamata[1]; Toshiyuki Takemori[1]; Ryosuke Kuroda[1]; Toshihiro Akisue[1]
[1]Orthopaedic Surgery, Kobe University, Kobe, Hyogo, Japan; [2]Orthopaedic Surgery, Hyogo Cancer Center, Akashi, Japan

PO 005 2565935

INTRAOSSEOUS SYNOVIAL OF THE BODY OF SCAPULA

Pedro M. Serrano[1]; João Esteves[1]; Vânia Oliveira[1]; André Coelho[2]; Pedro F. Cardoso[1]
[1]Orthopaedics, Centro Hospitalar do Porto, Porto, Portugal; [2]Pathology, Centro Hospitalar do Porto, Porto, Portugal

PO 006 2537662

SOFT TISSUE SARCOMA: PREDICTING CLINICAL BEHAVIOR BASED ON TRADITIONAL HISTOLOGIC GRADE

Whitney M. Guerrero, MD[2]; Richard A. Erali[1]; Martin D. Fleming[3]
[1]College of Medicine, UTHSC Memphis, Memphis, TN, USA; [2]Surgery, UTHSC-Memphis, Memphis, TN, USA; [3]Surgical Oncology, UTHSC-Memphis, Memphis, TN, USA

PO 007 2568396

CLEAR CELL SARCOMA-LIKE TUMOR OF THE GASTROINTESTINAL TRACT

Idoia B. Peris, Resident; Vicenç Artigas; Silvia Bagué; Manuel Rodríguez; Gemma Cerdán; Ana Sevio; Ana Virgili; Antonio Lopez
General Surgery, Hospital Santa Creu i Sant Pau, Barcelona, Spain, Spain

PO 008 2544200

CORE NEEDLE BIOPSY IS A SAFE AND ACCURATE METHOD TO DIAGNOSE BONE AND SOFT TISSUE SARCOMA

Ahmad Shehadeh
KHCC, Amman, Jordan

PO 009 2561466

THE VALUE OF CORE NEEDLE BIOPSY IN THE APPROACH TO MUSCULOSKELETAL TUMOURS

Pedro F. Cardoso[1]; João Esteves[1]; Vânia Oliveira[1]; André Coelho[2]; Tiago Couto[3]
[1]Orthopaedics, Centro Hospitalar do Porto, Porto, Portugal; [2]Pathology, Centro Hospitalar do Porto, Porto, Portugal; [3]Radiology, Centro Hospitalar do Porto, Porto, Portugal

PO 010 2565661

LONGITUDINAL CHANGE IN QUADRICEPS CROSS-SECTIONAL AREA AFTER WIDE RESECTION OF QUADRICEPS MUSCLE FOR SOFT TISSUE SARCOMA: CT SCAN BASED STUDY

Munenori Watanuki; Masami Hosaka; Kou Hayashi; Shinichirou Yoshida; Eiji Itoi
Orthopaedic, Tohoku University Hospital, Sendai, Japan

PO 011 2544197

SOFT TISSUE SARCOMAS ABUTTING THE BONE, WHERE SHALL THE KNIFE STOPS? A PROPOSED GUIDELINE FOR SURGICAL TREATMENT

Ahmad Shehadeh
KHCC, Amman, Jordan

PO 012 2570690

THE ROLE OF ISOLATED LIMB PERFUSION IN THE TREATMENT OF SOFT TISSUE SARCOMAS OF THE EXTERMITIES

Hugo Vasques; Vitor Farricha; Joana Bartolo; Nuno Abecassis
Surgery, Instituto Português Oncologia (IPO), Lisbon, Portugal

PO 013 2570154

LYMPHATICOVENULAR ANASTOMOSES FOR LYMPHOEDEMA COMPLICATED WITH SEVERE LYMPHORRHEA FOLLOWING RESECTION OF SOFT-TISSUE SARCOMAS OF THE ADDUCTOR COMPARTMENT

Hiroshi Kobayashi[1]; Takuya Iida[1]; Masachika Ikegami[1]; Ryoko Sawada[1]; Yusuke Shinoda[1]; Sakae Tanaka[1]; Hirotaka Kawano[2]
[1]The University of Tokyo Hospital, Tokyo, Japan; [2]University of Teikyo, Tokyo, Japan

PO 014 2565868

OUTCOMES OF AMPUTATION FOR TREATING SARCOMAS OF THE LIMBS

Marta S. Silva; Pedro M. Serrano; Luis Barros; João Esteves; Pedro Leite; Vânia Oliveira; Pedro F. Cardoso
Centro Hospitalar do Porto, Porto, Portugal

PO 015 2570687

SURGICAL OUTCOME OF SOFT TISSUE SARCOMA OF THE ADDUTOR COMPARTMENT

Yoshikazu Tanzawa, PhD; Eisuke Kobayashi; Makoto Endo; Fumihiko Nakatani; Hirokazu Chuman; Akira Kawai
Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan

PO 016 2540073

CLINICAL MANAGEMENT OF SKIN INVOLVEMENT OF SOFT TISSUE SARCOMA

Manabu Hoshi; Naoto Oebisu; Yoshitaka Ban; Hiroaki Nakamura
Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Osaka, Japan

PO 017 2570552

TIMING OF RADIOTHERAPY INFLUENCES OUTCOME OF LIPOSARCOMA

Daniela Greto, MD[1]; Mauro Loi[1]; Domenico Campanacci[2]; Giovanni Beltrami[2]; Guido Scoccianti[2]; Icro Meattini[1]; Isacco Desideri[1]; Pierluigi Bonomo[1]; Lorenzo Livi[1]
[1]Sperimental Biomedical and Clinical Sciences, University of Florence, Florence, Italy; [2]Ortopedical Oncological Surgery, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence, Italy

PO 018 2570528

POSTOPERATIVE RADIOTHERAPY FOR SARCOMA OF FOOT, HAND, ANKLE AND WRIST

Yeon Joo Kim[1]; Si Yeol Song[1]; Wonsik Choi[2]; Hyung Uk Je[3]; Jin-Hee Ahn[1]; Hye Won Chung[1]; Wanlim Kim[1]; Jong-Seok Lee[1]
[1]Asan Medical Center Univ. of Ulsan College of Medicine, SEOUL, Korea (the Republic of); [2]Gangneung Asan Hospital, Univ. of Ulsan College of Medicine, Gangneung, Korea (the Republic of); [3]Ulsan University Hospital, Univ. of Ulsan College of Medicine, Ulsan, Korea (the Republic of)

PO 019 2569722

NEOADJUVANT TRABECTEDIN PLUS RADIOTHERAPY IN HIGH GRADE SARCOMA OF THE LEG – CASE REPORT

Carolina Carvalho[1]; Antonio L. Silva[1]; João Freitas[2]; Ruben Fonseca[2]; Paulo F. Tavares[2]; Helena Garcia[3]; Jose M. Casanova[2]

[1]Department of Radiotherapy, Coimbra University Hospital, Coimbra, Portugal; [2]Bone and Soft Tissue Tumor Unit, Coimbra University Hospital, Coimbra, Portugal; [3]Department of Anatomical Pathology, Coimbra University Hospital, Coimbra, Portugal

PO 020 2570583

TRABECTEDIN IN THE CLINICAL MANAGEMENT OF METASTATIC SARCOMA

Daniela Greto, MD[1]; Mauro Loi[1]; Domenico Campanacci[2]; Giovanni Beltrami[2]; Guido Scoccianti[2]; Icro Meattini[1]; Pierluigi Bonomo[1]; Isacco Desideri[1]; Lorenzo Livi[1]

[1]Sperimental Biomedical and Clinical Sciences, University of Florence, Florence, Italy; [2]Ortopedical Oncological Surgery, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence, Italy

PO 021 2547462

ADMINISTRATION OF TRABECTEDIN INFUSION IN AN AMBULATORY SETTING IN TREATING SOFT TISSUE SARCOMA - A SINGLE CENTRE EXPERIENCE

Sarah Welby

Christie NHS Foundation Trust, Manchester, United Kingdom

PO 022 2559232

GEMCITABINE AND DOCETAXEL CHEMOTHRAPY FOR METASTASIS OF SARCOMA

Ryu Terauchi; Toshiharu Shirai; Shinji Tsuchida; Naoki Mizoshiri; Yuki Mori; Toshikazu Kubo

Department of Orthopaedics, Kyoto Prefectural University of Medicine, Kyoto, Kyoto, Japan

PO 023 2570507

TRABECTADIN ADN PROPHYLATIC REGIMENT: THE EXPERIENCE OF A CENTER

Ana M. Ferreira, MD[1]; Ana M. Simas[1]; Marta Soares[1]; Jose Dinis[1]; Mariana Afonso[2]; J. Flávio Videira[3]; Jorge Guimarães[3]

[1]Medical Oncology, Ipo-Porto, Porto, Portugal; [2]Pathology, Ipo-Porto, Porto, Portugal; [3]Surgery, Ipo-Porto, Porto, Portugal

PO 024 2570524

PATTERN OF HEPATIC TOXICITY IN TRABECTEDIN TREATED PATIENTS – A SINGLE INSTITUTION STUDY

Paulo F. Tavares, Head of Medical Oncology; João Freitas; Ruben Fonseca; Sandra Santos; Jose M. Casanova

Bone and Soft Tissue Tumor Unit, CHUC, Coimbra, Portugal

PO 025 2568888

THE MTOR PATHWAY IS AN EVOLUTIONARILY CONSERVED MECHANISM MEDIATING RESISTANCE TO TARGETED ANTI- CANCER THERAPY

Arcadi Cipponi[2]; David L. Goode[1]; David Thomas, FRACP, PhD[2]

[1]Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [2]Garvan Institute of Medical Research, Sydney, New South Wales, Australia

PO 026 2565257

CHARACTERIZATION OF PAZOPANIB USE IN SARCOMA

Makala Pace[2]; Melissa Shepherd[2]; Jennifer Wright, MD[1]

[1]University of Utah, Salt Lake City, UT, USA; [2]Huntsman Cancer Institute, Salt Lake City, UT, USA

PO 027 2567241

COMPLIANCE AND PERSISTENCE OF PAZOPANIB IN METASTATIC SOFT TISSUE SARCOMA PATIENTS IN THE UNITED STATES

Victor M. Villalobos, MD, PhD[1]; Stacey DaCosta Byfield[2]; Sameer Ghate[3]; Oluwakayode Adejoro[2]; Jose Perez[3]

[1]University of Colorado Auschutz Medical Campus, Denver, CO, USA; [2]Optum, Eden Prairie, MN, USA; [3]Novartis, East Hanover, NJ, USA

PO 028 2570985

VERY PROLONGED RESPONSE TO TRABECTEDIN IN REFRACTORY UTERINE LEIOMYOSARCOMA: A CASE REPORT

Vanda Salutari, MD[1]; Ida Paris[1]; Anna Fagotti[1]; Maurizio D'Incalci[2]; Gian F. Zannoni[1]; Caterina Ricci[1]; Maria G. Distefano[1]; Gabriella Ferrandina[1]; Giovanni Scambia[1]

[1]Gynecology Oncology, Fondazione Policlinico Universitario A Gemelli, Rome, Italy; [2]Department of Oncology, IRCCS - Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy

PO 029 2557833

UNIDIRECTIONAL INTRAOPERATIVE RADITION THERAPY TO TREAT RETROPERITONEAL SARCOMA USING CIVATECH SHEET PLANAR BRACHYTHERAPY: A CASE REPORT

Dian Wang, MD, PhD[1]; Minh Luu[2]; Heming Zhen[1]; Neilayan Sen[1]; Julius Turian[1]; James Chu[1]; Ross Abrams[1]

[1]Radiation Oncology, Rush University Medical Center, Brookfield, WI, USA; [2]Surgery, Rush University Medical Center, Chicago, IL, USA

PO 030 2565143

PROGNOSTIC RELEVANCE OF SUBTYPE IN LOCALLY ADVANCED SYNOVIAL SARCOMA WITH NEOADJUVANT CHEMOTHERAPY

Tatsunori Shimoi[1]; Kan Yonemori[1]; Emi Noguchi[1]; Mayu Yunokawa[1]; Ayumu Arakawa[2]; Chitose Ogawa[2]; Akira Kawai[3]; Hirokazu Chuman[3]; Akihiko Yoshida[4]; Kenji Tamura[1]

[1]Breast and Medical Oncology, National Cancer Center, Tokyo, Japan; [2]Pediatric Oncology, National Cancer Center, 5-1-1 Tsukiji, Tokyo, Japan; [3]Musculoskeletal Oncology and Rehabilitation Medicine, National Cancer Center, 5-1-1, Tsukiji Chu-o-ku Tokyo, Japan; [4]Pathology and Clinical Laboratories, National Cancer Center, 5-1-1, Tsukiji Chu-o-ku Tokyo, Japan

PO 031 2570531

PRIMARY AND SECONDARY ANGIOSARCOMAS: A SINGLE-CENTER EXPERIENCE

Daniela Greto, MD[1]; Mauro Loi[1]; Calogero Saieva[2]; Domenico Campanacci[3]; Giovanni Beltrami[3]; Guido Scoccianti[3]; Laura Trombetta[1]; Isacco Desideri[1]; Pierluigi Bonomo[1]; Lorenzo Livi[1]

[1]Sperimental Biomedical and Clinical Sciences, University of Florence, Florence, Italy; [2]Molecular and Nutritional Epidemiology Unit, ISPO (Cancer Research and Prevention Institute), Florence, Italy; [3]Ortopedical Oncological Surgery, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence, Italy, Florence, Italy

PO 032 2564890

AN UNUSUAL LOCAL INVASION OF MYXOID LIPOSARCOMA

Yusuke Minami, Dr, PhD[2]; Eisuke Kobayashi[1]; Akira Kawai[1]; Hirokazu Chuman[1]; Atsushi Okawa[2]

[1]Division of Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [2]Orthopedic Surgery, Tokyo Medical and Dental University, Tokyo, Japan

PO 033 2570457

PRIMARY CARDIAC SARCOMA: REPORT OF 3 CASES TREATED WITH COMBINED MODALITY

Eduardo C. Netto, MD[1]; Margarida Ferreira[2]; Maria Teresa Alexandre[2]; Antonio Mota[1]; Rute Pocinho[1]; João Freire[2]

[1]Radioterapia, IPO Lisboa, Lisbon, Lisbon, Portugal; [2]Oncologia Médica, IPO Lisboa, Lisbon, Portugal

PO 034 2564927

THE POTENTIAL RISK OF THE SUPERFICIAL SOFT TISSUE SARCOMA

Takashi X. Shimoji, PhD; Jun X. Manabe; Hirotaka X. Koyanagi

Orthopaedic Surgery, Saitama Cancer Center, Ina Town, Saitama Pref., Japan

PO 035 2565235

A RETROSPECTIVE CHART REVIEW OF ADULTS DIAGNOSED WITH SOFT TISSUE AND BONE SARCOMA AS TREATED AT A NON-ACADEMIC COMMUNITY CANCER CENTER

Shawn L. Price, MD; Kelsey Holmes

Orthopaedic Surgery, Norton Cancer Institute, Louisville, KY, USA

PO 036 2570669

GASTRIC METASTASE OF LUNG SYNOVIAL SARCOMA - A RARE ENTITY

Daniela V. Macedo; Isabel Fernandes; Andre Mansinho; Luis Costa
Oncologia Médica, Hospital Santa Maria - Centro Hospitalar Lisboa Norte, Lisbon, Portugal

PO 037 2569544

TUMOR-VOLUME DOUBLING TIME OF SOFT TISSUE SARCOMAS

Masachika Ikegami, MD; Hiroshi Kobayashi; Yusuke Shinoda;
Ryoko Sawada Orthopedics, The University of Tokyo Hospital, Tokyo, Japan

PO 038 2544097

FERTILITY PRESERVATION OF MALE PATIENTS WITH HIGH-GRADE MALIGNANT BONE AND SOFT TISSUE TUMOR BEFORE CHEMOTHERAPY IN JAPANESE SINGLE INSTITUTION

Manabu Hoshi; Naoto Oebisu; Yoshitaka Ban; Hiroaki Nakamura
Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Osaka, Japan

PO 039 2565901

REAL-WORLD TREATMENT PATTERNS AND SURVIVAL FOR PATIENTS WITH ADVANCED SOFT TISSUE SARCOMA RECEIVING SYSTEMIC THERAPY IN SPAIN

Daniel S Mytelka[1]; Maria Lorenzo[2]; Dana Stafkey-Mailey[3]; Yulia D'yachkova[4]; Saurabh P. Nagar[5]; Sean D. Candrilli[5]; James A. Kaye[6]; Jose A. López-Martín[7]
[1]Eli Lilly and Company, Indianapolis, IN, USA; [2]Lilly Research Center, Windlesham, United Kingdom; [3]Formerly RTI-HS, Durham, NC, USA; [4]Eli Lilly GmbH, Vienna, Austria; [5]RTI Health Solutions, Durham, NC, USA; [6]RTI Health Solutions, Waltham, MA, USA; [7]12 de Octubre University Hospital, Madrid, Spain

PO 040 2553241

EXTRASKELETAL MYXOID CHONDROSARCOMA: AN EVALUATION OF 20 CASES

Jared L. Harwood; Paul E. Wakely; Tom Scharschmidt
Ohio State University, Delaware, OH, USA

PO 041 2566323

ADVANCED SOFT TISSUE SARCOMA: SYSTEMIC TREATMENT PATTERNS AND SURVIVAL IN FRANCE

Daniel S Mytelka[1]; Maria Lorenzo[2]; Dana Stafkey-Mailey[3]; Yulia D'yachkova[4]; Saurabh P. Nagar[5]; Sean D. Candrilli[5]; James A. Kaye[6]
[1]Eli Lilly and Company, Indianapolis, IN, USA; [2]Lilly Research Centre, Windlesham, United Kingdom; [3]Formerly RTI-HS, RTP, NC, USA; [4]Eli Lilly GmbH, Vienna, Austria; [5]RTI Health Solutions, Durham, NC, USA; [6]RTI Health Solutions, Waltham, MA, USA

PO 042 2565639

SOFT TISSUE SARCOMAS: PROGNOSTIC FACTORS AND OUTCOME IN A SERIES OF 278 PATIENTS TREATED AT THE PORTUGUESE INSTITUTE OF ONCOLOGY IN LISBON

Maria Teresa Alexandre, Medical Doctor[1]; Susana Esteves[2]; Ana Luís[1]; João Freire[1]; António Moreira[1]; Filipa Santos[3]; Maria Lemos[3]; Vitor Farricha[4]; Hugo Vasques[4]; Nuno Abecassis[4]; Eduardo Netto[5]; Margarida Ferreira[1]
[1]Medical Oncology, Instituto Portugues de Oncologia de Lisboa, Lisbon, Portugal; [2]Biostatistics, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [3]Pathology, Instituto Português de Oncologia de Lisboa, Lisbon, Portugal; [4]General Surgery, Instituto Português de Oncologia de Lisboa, Lisbon, Portugal; [5]Radiation Oncology, Instituto Português de Oncologia de Lisboa, Lisbon, Portugal

PO 043 2569587

REGORAFENIB USE IN 3 PATIENTS WITH GIST IN THIRD LINE

Marta Soares, MD[1]; Ana M. Ferreira[1]; Jose Dinis[1]; Mariana Afonso[2]; Jorge Guimarães[3]
[1]Medical Oncology, IPOPORTOFG, Porto, Portugal; [2]Pathology, IPOPORTOFG, Oporto, Portugal; [3]Surgery, IPOPORTOFG, Oporto, Portugal

PO 044 2545184

FOLLOW UP OF METASTATIC GIST PATIENTS ON TARGETED TREATMENTS WITH ABDOMINAL ULTRASOUND: REDUCING RISKS WITHOUT JEOPARDIZING SURVIVAL

Branko Zakotnik, MD, PhD[1]; Simona Jereb[2]; Mojca Unk[1]; Erika Matos[1]; Darja Erzen[3]
[1]Medical Oncology, Institute of Oncology Ljubljana, Ljubljana, Slovenia; [2]Department of Radiology, Institute of Oncology Ljubljana, Ljubljana, Slovenia; [3]Department of Surgery, Institute of Oncology Ljubljana, Ljubljana, Slovenia

PO 045 2566331

MARGINS DEFINITION AND FRENCH GUIDELINES (GFPO, GSF-GETO) FOR THE PATHOLOGICAL REPORTING OF THE SURGICAL RESECTION SPECIMEN OBTAINED AFTER CHEMOTHERAPY IN BONE SARCOMAS

Anne Gomez-Brouchet, Pathologist[1]; François Gouin[2]; Gonzague de Pinieux[3]; Perrine Marec-Berard[4]; Corinne Bouvier[5]; Frédérique Larousserie[6]; Jean-Marc Guinebretiere[7]; Nathalie Gaspar[8]; Fabrice Fiorenza[9]; Philippe Anract[6]; Jérôme Sales de Gauzy[1]; Laurence Brugieres[8]; Eric Mascard[10]
[1]France, University of Toulouse (IUCT Oncopole), Toulouse, France; [2]CHU Nantes, Nants, France; [3]CHU Tours, Tours, France; [4]Institut Leon Berard, Lyon, France; [5]CHU La Timone, Marseille, France; [6]CHU Cochin, Paris, France; [7]Institut Curie, Paris, France; [8]Institut Gustave Roussy, Paris, France; [9]CHU Limoges, Limoges, France; [10]Hôpital Necker, Paris, France

PO 046 2566498

ADOLESCENTS AND YOUNG ADULTS (AYA) OSTEOSARCOMA (OST) OF THE JAW: THE CHALLENGE IN MANAGEMENT

Christopher Kuo; Paul Kent
Pediatrics, Rush University, Chicago, IL, USA

PO 047 2540371

COMPUTER ASSISTED PLANNING FOR SURGICAL RESECTION OF BONE TUMORS

Amir Sternheim, MD[1]; Prakash R. Nayak[1]; Michelle Arkhangorodsky[2]; Michael Daly[2]; Jimmy Qiu[2]; Harley Chan[2]; Robert Weersink[2]; Jonathan Irish[2]; David Jaffray[2]; Peter Ferguson[1]; Jay Wunder[1]
[1]Mount Sinai Hospital, Toronto, ON, Canada; [2]UHN Network TECHNA Institute, Toronto, ON, Canada

PO 048 2544249

A QUALITATIVE STUDY TO DETERMINE BARRIERS AND FACILITATORS ENCOUNTERED IN COLLABORATIVE PROSPECTIVE RESEARCH IN ORTHOPAEDIC ONCOLOGY

Marilyn Swinton[1]; Juan Pablo Zumárraga[2]; Walter Parizzia[3]; Michele Boffano[4]; Werner Hettwer[5]; Nicholas Bernthal[6]; Kurt Weiss[7]; Timothy Damron[8]; Marcos Galli Sera[3]; Peter Ferguson[9]; Andre Spiguel[10]; Benjamin Miller[11]; Lukas Nystrom[12]; Roberto Velez[13]; Michelle Ghert, MD, FRCSC[1]
[1]Surgery, McMaster University, Hamilton, ON, Canada; [2]Universidade Sao Paulo, Sao Paulo, Brazil; [3]Austral University, Buenos Aires, Argentina; [4]CTO Hospital, Torino, Italy; [5]National University Hospital, Copenhagen, Denmark; [6]UCLA, Los Angeles, CA, USA; [7]University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [8]SUNY, Syracuse, NY, USA; [9]University of Toronto, Toronto, ON, Canada; [10]University of Florida, Gainesville, FL, USA; [11]University of Iowa, Iowa City, IA, USA; [12]Loyola University, Chicago, IL, USA; [13]Hospital Vall D'Hebron, Barcelona, Spain

PO 049 2544202

DOES METHOTREXATE HAS AN IMPACT ON SURVIVAL OF PATIENTS WITH OSTEOSARCOMA?

Ahmad Shehadeh
KHCC, Amman, Jordan

PO 050 2567863

RADIATION RECALL COMPLICATING TREATMENT OF METASTATIC OSTEOSARCOMA

Caleb Oh; Antonio Logan; Caroline Kelmis; Graham A. Zolkowski; Paul Kent
Hematology/Oncology, Rush Hospital, Kildeer, IL, USA

PO 051 2541869

THE EWS-FLI1 FUSION TRANSCRIPT AND THE PROGNOSIS OF NORTHEASTERN MOROCCAN PATIENTS SUFFERING FROM EWING'S SARCOMA

Sara LOUATI[1]; Nadia Senhaji[1]; Meryem Azegrar[2]; Samia Arifi[2]; Khalid Amrani Joutei[1]; Laila Chbani[3]; Sanae Bennis[4]
[1]Laboratory of Bioactive Molecules, Structure and Functions, Faculty of Sciences and Techniques of Fez, Fez, Morocco; [2]Oncology Medical Department of Hassan II University Hospital, Fez, Morocco; [3]Pathology Department of Hassan II University Hospital, Fez, Morocco; [4]Biomedical and Translational Research Laboratory, Faculty of Medicine and Pharmacy, Fez, Morocco

PO 052 2570217

OSTEOFIBROUS DYSPLASIA OF THE HUMERUS: A CASE REPORT

Shinichirou Yoshida[1]; Masami Hosaka[1]; Munenori Watanuki[1]; Kou Hayashi[1]; Kentaro Suzuki[3]; Eiji Itoi[1]; Masahito Hatori[2]; Mika Watanabe[1]; Shin Hitachi[4]
[1]Orthopaedic Surgery, Tohoku University Graduate School of Medicine, Sendai, Japan; [2]Orthopaedic Surgery, Tohoku kosai hospital, Sendai, Japan; [3]Orthopaedic Surgery, Miyagi Cancer Center, Sendai, Japan; [4]Diagnostic Radiology, Tohoku University Graduate School of Medicine, Sendai, Japan

PO 053 2565973

UNDIFFERENTIATED SARCOMA MASQUERADING AS A SACROCOCCYGEAL TERATOMA

Adam P. Kidwell, MD; Robert Hartemayer; Kacie Steinbrecher; Destiny Hause; Srikumar Pillai; Brett Mahon; Paul Kent
Rush Medical College, Chicago, IL, USA

PO 054 2565915

A SINGLE INSTITUTION EXPERIENCE OF 14-YEARS TREATING EWING SARCOMA - FOCUS ON LOCALIZED DISEASE

Ana Catarina Freitas, Resident[5]; Duarte Machado[5]; Cátia Pedro[4]; Marco Ramos[2]; Maria Teresa Alexandre[5]; Margarida Ferreira[5]; João Freire[5]; João Conceição e Silva[1]; Maria José Ribeiro[3]; Filomena Pereira[3]; António Moreira[5]
1Radiology, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [2]Biostatistics, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [3]Pediatrics, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [4]Radiotherapy, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [5]Oncology, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal

PO 055 2570260

GIANT CELL TUMOR OF BONE – CASE REPORT OF AN UNUSUAL TUMOR LOCATION WITH A MULTIDISCIPLINARY APPROACH

Maria Inês S. Sequeira[1]; Ana M. Simas[1]; Ana M. Ferreira[1]; Jose Dinis[1]; Mariana Afonso[2]; Sofia Conde[2]; Machado Carvalho[2]; Marta Soares[1]
[1]Medical Oncology, Instituto Português de Oncologia do Porto, Porto, Portugal; [2]Instituto Português de Oncologia do Porto, Porto, Portugal

PO 056 2537845

IS SYMPTOM WORSENING (SW) ASSOCIATED WITH RECIST RESPONSE IN PATIENTS (PTS) WITH DESMOID TUMORS (DT)?

Nuria Kotecki; Armelle Renaud; Meriem Ben Haj Amor; Anne-Sophie Thomassin Defachelles; Thomas Ryckewaert; Vincent Gamblin; Yves-Marie Robin; Sophie Taieb; Nicolas Penel
Centre Oscar Lambret, Lille, France

PO 057 2571294

INTRALESIONAL CURETTAGE OF GRADE I CHONDROSARCOMA OF LONG BONES: 2 YEAR FOLLOW UP OF 8 CASES

Bhaskar S. Sugath, Fellowship Orthopaedic Oncology
Orthopaedics, Aster Medcity, Kochi, India, Trivandrum, Kerala, India

PO 058 2535985

BIGH3 IS A UNIQUE AND NOVEL MECHANISM OF OSTEOLYSIS IN KIDNEY CANCER BONE METATASIS

Robert Satcher, MD, PhD[1]; Tianhong Pan[1]; Sue-Hwa Lin[2]
[1]Orthopaedic Oncology, MD Anderson Cancer Center, Houston, TX, USA; [2]Translational Molecular Pathology, MD Anderson Cancer Center, Houston, TX, USA

PO 059 2570485

LYMPHOMA OF BONE AND SOFT TISSUES: DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS

Annika Müller[1]; Martin Dreyling[2]; Falk Roeder[3]; Andrea Baur-Melnyk[4]; Alexander Klein[1]; Thomas Knösel[5]; Volkmar Jansson[1]; Hans R. Dürr[1]
[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany; [2]Medical Clinic III, LMU Munich, Munich, Germany; [3]Institute of Radiotherapy, LMU Munich, Munich, Germany; [4]Institute of Radiology, LMU Munich, Munich, Germany; [5]Institute of Pathology, LMU Munich, Munich, Germany

PO 060 2563993

THE IMPROVEMENT OF HYPOXIA BY TRANSCUTANEOUS CO2 APPLICATION BLOCKS THE PROGRESSIVE BONE DESTRUCTION IN A METASTATIC BONE TUMOR MODEL

Toshiyuki Takemori; Teruya Kawamoto; Takeshi Ueha; Mitsunori Toda; Etsuko Kamata; Masayuki Morishita; Naomasa Fukase; Hitomi Hara; Masahiro Kurosaka; Ryosuke Kuroda; Toshihiro Akisue
Kobe University Graduate School of Medicine, Kobe, Japan

PO 061 2552781

SURGICAL TREATMENT FOR METASTATIC BONE TUMOR OF EXTREMITY

Hitomi Hara[1]; Toshihiro Akisue[2]; Yoshitada Sakai[3]; Teruya Kawamoto[1]; Naomasa Fukase[1]; Masayuki Morishita[1]; Etsuko Kamata[1]; Toshiyuki Takemori[1]; Kenichiro Kakutani[1]; Yasuo Ejima[4]; Ryohei Sasaki[4]; Kotaro Nishida[1]; Ryosuke Kuroda[1]
[1]Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan; [2]Rehabilitation Science, Kobe University Graduate School of Health Sciences, Kobe, Hyogo, Japan; [3]Rehabilitation Medicine, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan; [4]Radiation Oncology, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan

PO 062 2570495

INSUFFICIENCY FRACTURE AFTER RADIATION THERAPY

Michihito Miyagi, MD, PhD[1]; Hiroaki Ogihara[1]; Yoji Shido[2]
[1]Orthopedics Surgery, Hamamatsu Red Cross Hospital, Hamamatsu, Shizuoka, Japan;
[2]Orthopedics Surgery, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan

PO 063 2570603

AYTPICAL LOCATIONS OF AVASCULAR NECROSIS FROM ZOLEDRONIC ACID IMITATING METASTASIS

Graham A. Zolkowski; Antonio Logan; Caroline Kelmis; Caleb Oh; Paul Kent
Pediatric Hematology/Oncology, Rush University Medical Center, Chicago, IL, USA

PO 064 2552797

A CASE OF A PATIENT WITH AN ADENOCARCINOMA OF THE DISTAL FEMUR: IS IT TRULY A METASTASIS FROM UNKNOWN ORIGIN?

Hideto Obata
Orthopedic Surgery, Yukoukai General Hospital, Ibaraki, Osaka, Japan

PO 065 2570639

THE ILLUMINOSS INTRAMEDULLARY STABILIZATION DEVICE: POTENTIAL BENEFITS OVER STANDARD NAIL FIXATION FOR PATHOLOGIC HUMERUS FRACTURES

Jason Hoellwarth, MD; Kurt Weiss; Mark Goodman; Alma Heyl; Richard McGough
Orthopedics, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

A

C

D

G

H

K

L

M

N

S

W

Z

2:00 pm – 3:35 pm

– SOFT TISSUE SARCOMAS –
Adjuvant & Neoadjuvant Therapies

2:00 pm Paper 001 #2566582

RADIOMIC FEATURES EXTRACTED FROM T1-WEIGHTED MAGNETIC RESONANCE IMAGES PREDICT OUTCOMES IN SOFT TISSUE SARCOMA

Matthew B. Spraker[1]*; Landon Wootton*[1]*; W. Art Chaovalitwongse*[2]*; Meghan W. Macomber*[1]*; Seth M. Pollack*[3]*; Edward Y. Kim*[1]*; Matthew Nyflot*[1]
[1]Radiation Oncology, University of Washington, Seattle, WA, USA; [2]Radiology, University of Washington, Seattle, WA, USA; [3]Division of Oncology, University of Washington, Seattle, WA, USA

Objective: Soft tissue sarcomas (STS) exhibit variable behavior ranging from indolent to aggressive and widely metastatic. Surgical resection and radiotherapy remains the cornerstone of treatment for localized disease, but accurate prediction of individual patient outcome remains a critical challenge.

Radiomics is an emerging research field that quantifies complex aspects of tumor images, such as shape and texture, under the assumption that this information is related to tumor biology. Other studies have validated the use of radiomics to predict patient outcomes in lung and head and neck cancers. This study examined the relationship between radiomics measures extracted from T1-weighted magnetic resonance images (MRI) and overall (OS) and progression free survival (PFS) in STS.

Methods: Pre-treatment T1-weighted magnetic resonance images (MRI) were collected from 44 patients with biopsy-proven STS that were treated with RT and/or chemotherapy prior to resection. Patients younger than 18 years old were excluded. Characteristics for each patient were collected from our institutional electronic medical record. A radiation oncologist evaluated segmented the tumor volume. A total of 41 different radiomics features were calculated for the segmented tumor in each image. Machine learning was used to generate a predictive model of OS and PFS based on logistic regression of clinical features alone, radiomic features alone, and both together. Receiver operator characteristics (ROC) curves were generated and the corresponding c-index (area under the ROC curve) was calculated for each predictive model.

Results: Patient and tumor characteristics are shown in table 1. Median age was 57 year old (range: 28-83) and median follow up was 30 months (range 3-114). Figure 1 depicts ROCs for models including clinical (blue), radiomic (green), and both (red) types of features that predict 1- and 3-year PFS and 1- and 3-year OS. Radiomic features greatly improved predictive power and their use with or without clinical features were far more predictive than clinical features alone (Figure 1). This model was most predictive of progression free survival at 1 year (Figure 1A).

Conclusion: This study demonstrates that radiomic features extracted from pre-treatment T1-weighted MRIs improve prediction of PFS and OS over clinical features alone in a cohort of patients with STS. This technique can be used to stratify patients by risk of relapse, with an ultimate goal of tailoring therapy based on individual tumor radiomic profiles.

Patient and Tumor Characteristics

N (%)	
Sex	
Male	20 (46)
Female	24 (54)
Location	
Extremity	38 (86)
Central	4 (9)
Retroperitoneal	2 (5)
Surgical Margins	
Positive	7 (16)
Negative	37 (84)
FNCLCC Grade	
1	6 (14)
2	16 (36)
3	19 (43)
Not reported	3 (7)
Size	
>5cm	33 (75)
<5cm	11 (25)
Histology	
Spindle Cell Sarcoma	12 (27)
Pleomorphic Sarcoma	7 (16)
Synovial Sarcoma	6 (14)
Leiomyosarcoma	5 (11)
Myxoid Liposarcoma	4 (10)
Myxofibrosarcoma	2 (5)
Ewing	1 (2)
Undifferentiated sarcoma	1 (2)
Rhabdomyosarcoma	1 (2)
Other	5 (11)

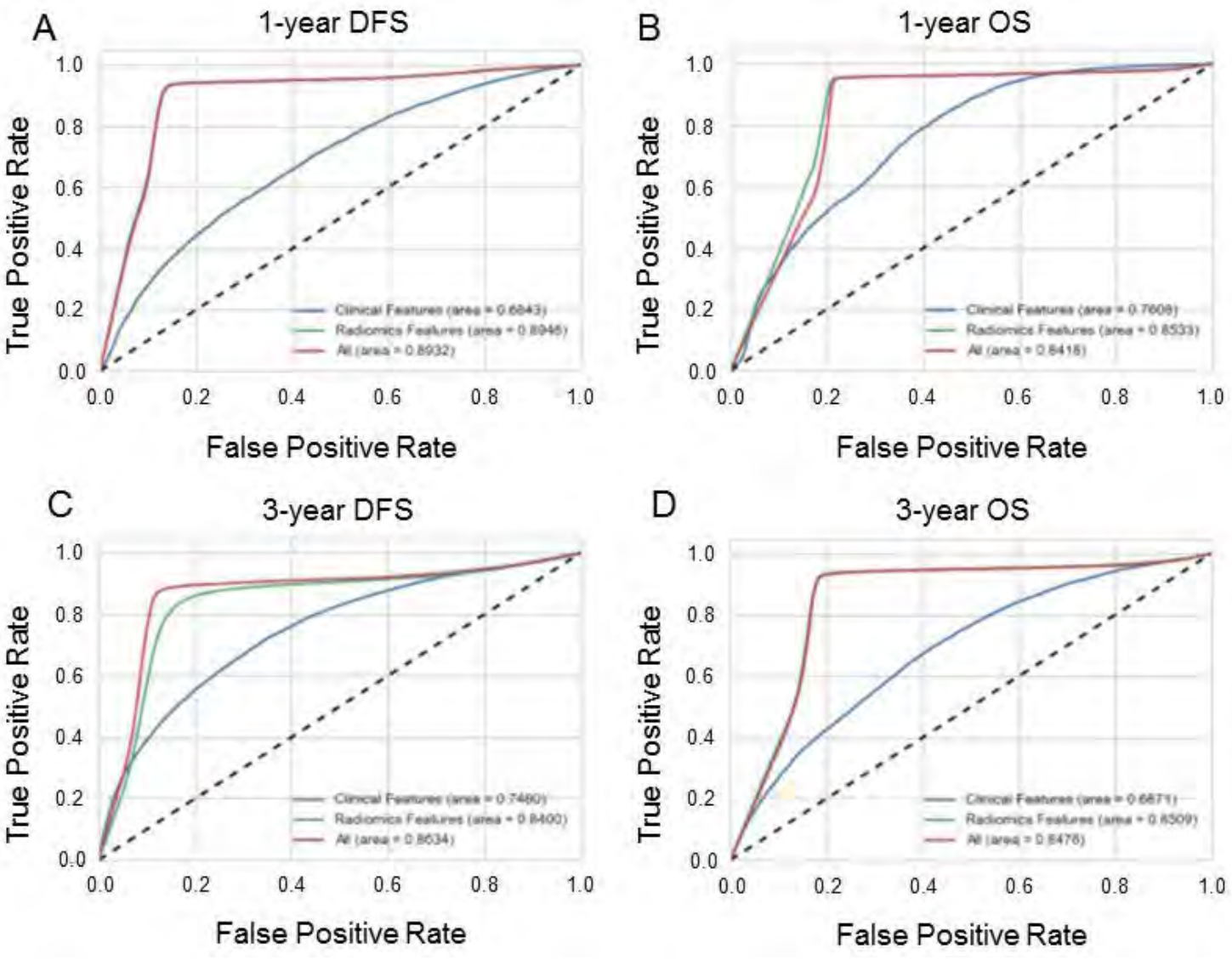


Figure 1. Corrected receiver operator curves (ROC) for 1-year disease free survival (DFS) **(A)**, 1-year overall survival **(B)**, 3-year DFS **(C)**, and 3-year OS **(D)**.

2:40 pm Paper 002 #2546312

HISTOLOGIC RESPONSE TO RADIATION IN SOFT TISSUE SARCOMA (STS): HYALINIZATION/FIBROSIS IS ASSOCIATED WITH FAVORABLE OUTCOME

Inga-Marie Schaefer[1]*; Jason Hornick*[1]*;*
Constance M. Barysauskas[2]*; Chandrajit Raut*[3]*;*
Sagar A. Patel[4]*; Trevor J. Royce*[4]*;*
Christopher D.M. Fletcher[1]*; Elizabeth H Baldini*[4]
[1]Department of Pathology, Brigham and Women's Hospital, Boston, MA, USA; [2]Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Boston, MA, USA; [3]Department of Surgery, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA, USA; [4]Department of Radiation Oncology, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA, USA

Objective: Histologic response (HR) is a known predictor of outcome for osteosarcoma, but has not been systematically studied in STS. We examined HR following pre-operative radiation therapy (pre-op RT) for STS and its association with outcomes.

Methods: Resection specimens from 100 patients with primary, localized STS of the extremity/trunk treated with pre-op RT followed by resection from 2006-2014 were evaluated histologically by at least 2 dedicated sarcoma pathologists. Representative gross sampling to include viable and non-viable areas was performed. Extent (%) of residual viable tumor, coagulative necrosis, hyalinization/fibrosis, and infarction were determined. Patients without a definitive tumor bed post-radiation or those who received chemotherapy were excluded. Local recurrence free (LRF), recurrence free survival (RFS), and overall survival (OS) were compared with log-rank tests. Logistic regression was used for multivariable analysis (MVA).

Results: Patient and tumor characteristics are shown in Table 1. Median follow-up was 60 months. There were 5 local recurrences and 26 distant metastases. 5-yr LRF was 96%, 5-yr RFS was 68%, and 5-yr OS was 75%. After pre-op RT, 9 patients (9%) had a complete histologic response (no residual viable tumor). Ninety-three (93%) showed some non-viable tumor (median extent 70%), 27 showed necrosis (median 20%), 78 showed hyalinization/fibrosis (median 23%), and 64 showed infarction (median 33%). The only univariate predictor for LR was tumor size. On MVA for RFS, hyalinization/fibrosis was a significant favorable predictor (HR 0.48, P = 0.006); tumor size (HR 1.56, P = 0.01), and high grade (HR 6.39, P = 0.01) were unfavorable predictors. For OS, hyalinization/fibrosis was again a favorable predictor (HR 0.36, P = 0.02); necrosis (HR 1.62, P = 0.04) and infarction (HR 1.54, P = 0.02) were unfavorable predictors. RFS and OS rates by extent of hyalinization/fibrosis are shown (Table 2).

Conclusion: Histologic evaluation after pre-op RT showed a low complete response rate. Hyalinization/fibrosis was a favorable predictor of RFS and OS while necrosis and infarction were unfavorable predictors for OS. These findings suggest that hyalinization/fibrosis indicates response to treatment associated with favorable outcome, whereas necrosis and infarction may be inherent adverse tumor factors and not directly related to treatment response. Assessment of treatment response defined as hyalinization/fibrosis may be a valid endpoint for neoadjuvant trials of STS.

Table 1. Patient and tumor characteristics (n=100)

Gender	52% female 48% male
Median age, years (range)	58 (20 - 88)
Median tumor size, cm (range)	7.5 (1.8 - 25)
FNCLCC Grade	8% 1 21% 2 71% 3
HISTOLOGIC SUB-TYPE	
Unclassified sarcoma	36%
Myxofibrosarcoma	23%
Leiomyosarcoma	8%
Myxoid liposarcoma	6%
Pleomorphic liposarcoma	6%
Dedifferentiated liposarcoma	5%
Other	16%

Table 2.
5-year RFS and OS rates by extent of hyalinization/fibrosis following pre-operative RT and resection for STS (n=100)

Extent of Hyalinization/Fibrosis	5-year RFS	p-value	5-year OS	p-value
0%	50%		54%	
5 - 10%	57%		64%	
10 - 22.5%	57%		71%	
22.5% - 55%	84%		84%	
55% - 100%	92%	0.04	100%	0.05

2:50 pm Paper 003 #2570259

EXTREMITY SOFT TISSUE SARCOMA: THE IMPACT OF ADJUVANT THERAPIES ACROSS THE MAJOR HISTOLOGICAL SUBTYPES. A RETROSPECTIVE ANALYSIS OF A LARGE MULTI-INSTITUTIONAL DATA BASE

Dario Callegaro[3]*; Rosalba Miceli*[1]*; Sylvie Bonvalot*[5]*; Peter Ferguson*[2]*; Dirk C. Strauss*[4]*; Antonin Levy*[6]*; Anthony Griffin*[2]*; Andrew J. Hayes*[4]*; Cecile Le Péchoux*[6]*; Marco Fiore*[3]*; Angelo Paolo Dei Tos*[7]*; Charles Catton*[10]*; Paolo Casali*[8]*; Jay Wunder*[9]*; Alessandro Gronchi*[3]
[1]Department of Clinical Epidemiology and Trial Organisation, Istituto Nazionale dei Tumori, Milan, Italy; [2]Department of Surgery, Mount Sinai and Princess Margaret Hospitals, University of Toronto, Toronto, ON, Canada; [3]Department of surgery, Istituto Nazionale dei Tumori, Milan, Italy; [4]Department of Surgery, Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom; [5]Department os Surgery, Institut Curie, PSL Research University, Paris, France; [6]Department of Radiation Oncology, Gustave Roussy Cancer Campus, Paris Sud University, Villejuif, France; [7]Department of Pathology, General Hospital of Treviso, Treviso, Italy; [8]Department of Cancer Medicine, Istituto Nazionale dei Tumori, Milan, Italy; [9]University Musculoskeletal Oncology Unit, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; [10]Department of Radiation Oncology, Princess Margaret Hospital/ University Health Network, Toronto, ON, Canada

Objective: While quality of surgery is similar, the overall use of radiotherapy (RT) and chemotherapy (CT) for different extremity soft tissue sarcoma (eSTS) subtypes may vary broadly across different referral institutions. Aim of the present study was to explore whether these differences impacted the outcomes of patients affected by the commonest eSTS histological subtypes.

Methods: All consecutive adult patients with primary eSTS surgically treated at 3 European and 1 North American centers between January 1994 and December 2013 were included in this retrospective analysis (desmoids, soft-tissue Ewing's sarcoma, alveolar or embryonal rhabdomyosarcoma, DFSP, and ALT were excluded). 5- and 10-yr overall survival (OS) and crude cumulative incidence (CCI) of local recurrence (LR) and distant metastases (DM) were calculated. Multivariate analyses for OS, CCI of LR and DM were performed.

Results: In all, 3752 patients were included. The number of patients and the median follow-up by center were respectively 444 and 54mo (30-71); 1452 and 86mo (47-123); 420 and 75mo (46-117); 1436 and 85mo (44-121). Adjuvant/neoadjuvant (ad/neoad) RT and ad/neoad CT were administered to 50% and 2%, 48% and 26%, 82% and 52%, 68% and 2% of the patients among the four participating institutions respectively.

10-yr CCI of LR were 0.196 (95% CI: 0.113-0.339); 0.095 (0.080-0.113); 0.086 (0.058-0.128); 0.051 (0.040-0.065) respectively. Grade, histological subtype, surgical margins and administration of ad/neoad RT were significant predictors for LR. A higher LR risk was associated to a lesser use of ad/neoad RT in all histology subtypes, particularly in myxoid liposarcoma, myxofibrosarcoma and vascular sarcoma. However this was not associated to a higher mortality.

10-yr CCI of DM were 0.319 (0.26-0.391); 0.25 (0.227-0.275); 0.312 (0.267-0.364); 0.299 (0.273-0.328), respectively. Size, grade and histological subtype were significant predictors for DM. The use of CT was not associated to a lesser risk of DM, although a trend in favor of the use of CT was seen for vascular sarcoma, myxofibrosarcoma, myxoid liposarcoma and undifferentiated pleomorphic sarcoma.

Conclusion: The use of ad/neoad RT seems to be particularly effective in selected histotypes to reduce the risk of local recurrence, with no effect on OS. Likewise the use of CT has a minor impact, if any, on the metastatic risk, which also varies according to the different histological subtypes.

4:05 pm – 5:10 pm

– SOFT TISSUE SARCOMAS –
Radiation Therapy

4:05 pm Paper 004 #2542801

VORTEX TRIAL: A RANDOMISED CONTROLLED MULTI-CENTRE PHASE III TRIAL OF VOLUME OF POST-OPERATIVE RADIOTHERAPY GIVEN TO ADULT PATIENTS WITH EXTREMITY SOFT TISSUE SARCOMA (STS)

Martin Robinson[2]*; Piers Gaunt*[5]*; Robert Grimer*[3]*; Beatrice Seddon*[1]*; James Wylie*[10]*; Aileen Davis*[7]*; David Hughes*[8]*; David Peake*[4]*; Anna Cassoni*[1]*; David Spooner*[4]*; Aisha Miah*[6]*; Ana Hughes*[5]*; Catharine West*[11]*; Karen Venables*[9]*; Lucinda Billingham*[5]
[1]University College Hospital, London, United Kingdom; [2]University of Sheffield, Sheffield, United Kingdom; [3]The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, United Kingdom; [4]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [5]University of Birmingham, Birmingham, United Kingdom; [6]The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom; [7]University of Toronto, Toronto, ON, Canada; [8]Royal Hallamshire Hospital, Sheffield, United Kingdom; [9]Mount Vernon Cancer Centre, Middlesex, United Kingdom; [10]The Christie NHS Foundation Trust, Manchester, United Kingdom; [11]University of Manchester, Manchester, United Kingdom

Objective: To assess whether reducing the volume of tissue irradiated post-operatively improves limb function in patients with extremity STS without impairing local control.

Methods: Eligible patients had proven extremity STS for whom tumour resection and post-operative radiotherapy without adjuvant chemotherapy was indicated. Patients were registered pre-operatively for tumour and normal tissue collection and baseline TESS questionnaire. Patients eligible for radiotherapy after surgery were randomised to either of the trial arms in a 1:1 ratio (stratified by surgical margin, tumour grade and treatment centre). Patients were treated either in the Control arm (C): 50Gy in 25 fractions to CTV1 (GTV + 5cm cranio-caudally and 2cm axially) followed by 16Gy in 8 fractions to CTV2 (GTV + 2cm c-c and axially) or the Research arm (R): 66Gy in 33 fractions to CTV2 alone.

Co-primary outcome measures were a difference in limb function at 2 years (TESS score) and time to local recurrence (non-inferiority margin of 1.6). The trial required 210 patients to detect a difference in mean TESS of 10 (SD 20) with a two-sided alpha of 5% and power of 95%.

Secondary outcomes were soft tissue and bone toxicity, disease-free and overall survival and level of disability.

Results: 216 patients were randomised,108 in each arm. Tissue was collected from 206 randomised and 301 registered patients.There were 176 lower limb tumours; C;96, R;80 and 40 upper limb; C;12, R;28. Median baseline TESS was 92 (22-100) for C and 97 (10-100) for R.

Mean change in TESS at 2 years was -5.0 (SD 18) in C and -4.9 (SD 18) in R (p=0.97). In both arms the TESS scores dropped post-operatively followed by recovery over subsequent months.

Median follow up was 4.8yr (C & R). The 5yr local recurrence free survival (LRFS) rates were; for C:86% (95%CI;75,93) and for R:84% (95% CI;74,90) HR;1.5 (95%CI; 0.7-3.3). For C the 5-year overall survival was 72% (95%CI;61,81) and for R 67% (95%CI;56,76) HR=1.2 (95% CI; 0.7,2.0). No statistical differences between the arms in late radiation toxicity grade 2+ at 2 years; skin (C 34% vs R 37% p=0.77), subcutaneous (C 47% vs R 41%, p=0.39), bone (C 11% vs R 15%, p=0.48) and joint (C 18% vs R 18%, p=0.91).

Conclusion: There was no difference in limb function at 2

years between control and research arms. Because of the small number of events it was not possible to state that the research arm was non inferior for LRFS.

Currently we are not able to recommend the smaller volumes used in the research arm as standard of care.

4:15 pm Paper 005 #2570451

PREOPERATIVE HYPOFRACTIONATED RADIATION THERAPY +/- INTRAOPERATIVE RADIATION THERAPY FOR SOFT TISSUE SARCOMAS OF EXTREMITIES AND SUPERFICIAL TRUNK: AN INSTITUTIONAL EXPERIENCE

Antonino De Paoli[1]*; Federico Navarria*[1]*; Gianni Boz*[1]*; Roberto Innocente*[1]*; Vincenzo Canzonieri*[2]*; Angela Buonadonna*[3]*; Marco Forlin*[4]*; Franco Gherlinzoni*[5]*; Giulio Bertola*[4]

[1]Radiation Oncology , National Cancer Institute - C.R.O. Aviano, Aviano, , Italy; [2]Pathology, National Cancer Institute - C.R.O. Aviano, Aviano, , Italy; [3]Medical Oncology, National Cancer Institute - C.R.O. Aviano, Aviano, Italy; [4]Surgical Oncology, National Cancer Institute - C.R.O. Aviano, Aviano, Italy; [5]Orthopedic Department, General Hospital Gorizia, Gorizia, Italy

Objective: Radiation Therapy (RT) and Conservative Surgery (S) is a well established approach for Soft Tissue Sarcomas (STS) of Extremities and Superficial Trunk. Preoperative RT is emerging as the preferred combined modality for the potential decrease in late morbidity and better functional results compared to postoperative approach. Recent advances in RT techniques allow more conformal treatment volumes and, eventually, to explore unconventional, potentially more effective fractionation schedules.

Methods: A retrospective analysis of a series of patients (pts) with STS treated with preoperative hypofractionated RT at our Institute is reported. Pts selection included no high-risk pts candidate to adjuvant chemotherapy or no critical tumor sites. Advanced RT techniques such as 3D-CRT and IMRT-IGRT were used. A moderate hypofractionation of RT dose of with 40.5y/18 frs was planned. Individualised dose constraints were used for bone and skin corridor. A IORT boost was planned for expected close or positive surgical margins.

Results: Between June 2007 and December 2015, 123 pts (M/F:78/45, median age: 58yrs (20-89) with extremity (102 pts) and superficial trunk (21 pts) underwent to RT with 40.5Gy/18 frs. Disease presentation was primary tumor in 95 (77%) and recurrent in 28 pts (23%). Most common histologic types were Liposarcoma (34%), Pleomorphic sa.(14%), Mixofibrosa (12%) and Leiomiosa (10%). Overall, 45 pts (36%) had G1, 32 (27%) G2 and 46 (37%) G3 disease. All but 2 pts completed the planned 40.5Gy. At surgery, 98 pts (79%) had R0 resection, 25 (21%) R1 resection; 71 pts (58%) underwent IORT for close or positive margins. No concomitant adjuvant chemotherapy was planned in this series. Only 3 pts had G3 acute skin toxicity. Major postoperative complications (SR2criteria) were reported in 16/123 pts (13%). At a median follow-up of 60 mos (7-108), 103 pts (83%) are alive; 11/123 (9%) had local recurrence and 18/123 (15%) had metastatic recurrence. No difference in incidence of complications and patterns of recurrences was observed in IORT vs No-IORT pts.

Conclusion: Preoperative moderate Hypofractionation RT with 40.5Gy/18frs for Extremities and Superficial Trunk STS demonstrated feasible with acceptable risk of complications and comparable local control rates of more standard fractionation. Dose escalation with IORT is possible, when needed. We continue this experience to confirm this data in larger series of pts and to evaluate also long-term toxicity.

4:25 pm Paper 006 #2546357

BENEFIT OF ADJUVANT RADIOTHERAPY FOR LOCAL CONTROL, DISTANT METASTASIS, AND SURVIVAL OUTCOMES IN PATIENTS WITH LOCALIZED SOFT TISSUE SARCOMA: COMPARATIVE EFFECTIVENESS ANALYSIS OF AN OBSERVATIONAL COHORT STUDY

Florian Posch[1]*; Lukas Leitner*[2]*; Bernadette Liegl-Antzager*[3]*; Anna Wink*[4]*; Michael Stotz*[1]*; Angelika Bezan*[1]*; Martin Pichler*[1]*; Armin Gerger*[1]*; Marko Bergovec*[2]*; Herbert Stoeger*[1]*; Andreas Leithner*[2]*; Joanna Szkandera*[1]

[1]Clinical Division of Oncology, Department of Medicine, Medical University of Graz, Graz, Austria; [2]Department of Orthopaedics and Orthopaedic Surgery, Medical University of Graz, Graz, Austria; [3]Institute of Pathology, Medical University of Graz, Graz, Austria; [4]Department of Therapeutic Radiology and Oncology, Medical University of Graz, Graz, Austria

Objective: Adjuvant radiotherapy (ARTX) is an accepted strategy for improving local control in patients with localized soft tissue sarcoma (STS) undergoing curative surgery. However, the magnitude of benefit of this intervention regarding local control, and its impact on non-local treatment outcomes such as distant metastasis and survival are ill-defined. In this study, we aim to quantify the contribution of ARTX to long-term outcomes in STS patients after surgical resection.

Methods: In this historical cohort study, we included 443 STS patients who were operated in curative intent between 1995 and 2015 at a single academic center (Table 1). Two-hundred-sixty (58.7%) patients received ARTX. After a median follow-up period of 5.5 years (range: 18 days - 18.2 years), we observed 41 (9.3%) local recurrences, 74 (16.7%) occurrences of distant metastasis, 64 (14.5%) STS-related deaths, and 59 (13.3%) deaths adjudicated

to other causes (Fig.1). An inverse-probability-of-treatment-weighting (IPTW) analysis was implemented to rigorously account for imbalances in prognostic variables between adjuvant treatment groups.

Results: As expected, patients receiving ARTX were more likely to have high-grade G3 tumors (p<0.0001) than patients not receiving ARTX. In naïve analysis, ARTX did not emerge to be associated with an improved recurrence-free survival experience (Hazard ratio (HR)=0.99, 95%CI:0.72-1.36, p=0.96). However, after IPTW, ARTX was associated with a 35% relative reduction in the risk of recurrence or death (HR=0.57, 95%CI:0.37-0.89, p=0.01, Fig.2). This benefit was driven by a strong reduction in the risk of local recurrence (Subdistribution hazard ratio (SHR)=0.46, 95%CI:0.23-0.89, p=0.02), whereas relative risks of distant metastasis (SHR=0.71, 95%CI:0.43-1.19, p=0.20) and overall survival (HR=0.79, 95%CI:0.52-1.20, p=0.27) were only non-significantly in favor of ARTX. Subgroup analyses demonstrated that patients with G3 tumors undergoing ARTX appeared to have not only a benefit regarding local recurrence, but also regarding overall survival (HR=0.54, 95%CI:0.36-0.83, p=0.005).

Conclusion: In this large cohort of patients with STS after curative surgery, ARTX was associated with a 54% reduction in the relative risk of local recurrence. Our data suggest that in the subset of patients with high-grade STS, ARTX may not only improve local control but also confer an overall survival benefit. No consistent association between ARTX and a lower risk of distant metastasis was observed.

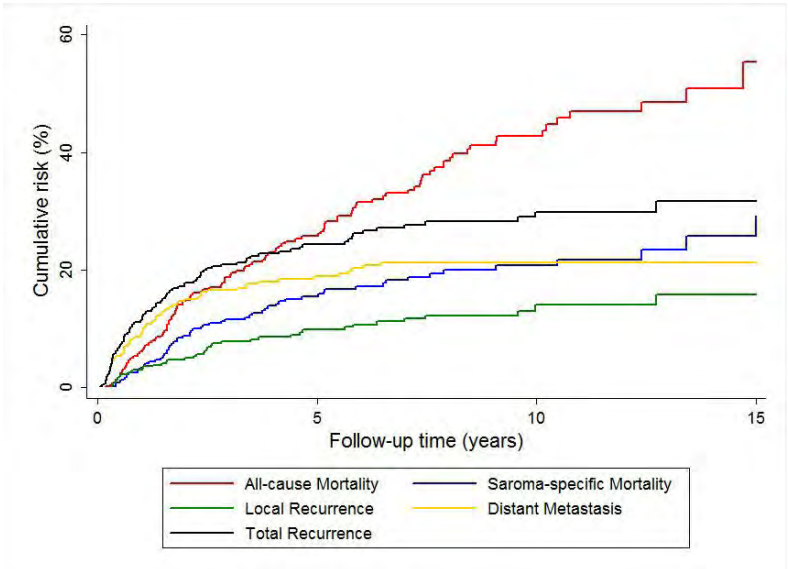


Figure 2. Recurrence-free survival according to ARTX (n=443)

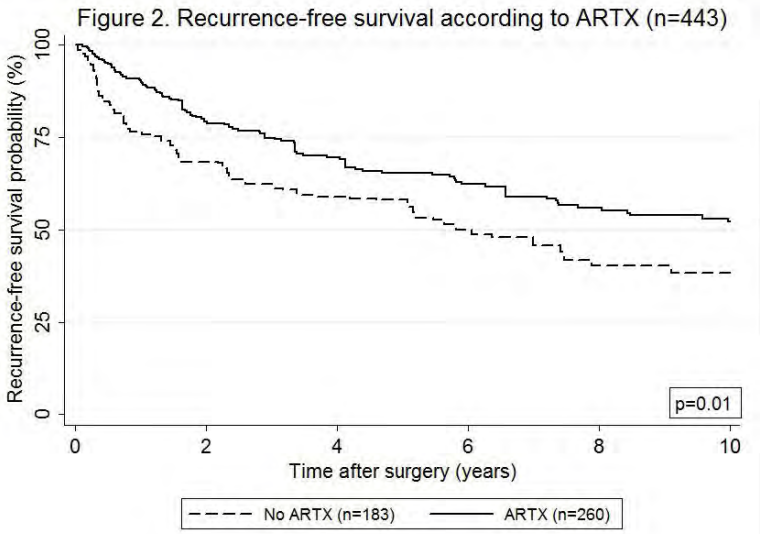


Table 1. Baseline characteristics of the study population

Variable	Overall (n=443)
Age at entry (years)	62.3 (47.2-73.5)
Female Gender	217 (49.0%)
Non-extremity location	84 (19.0%)
Deep tumor	284 (64.1%)
Tumor size >5cm	310 (70.0%)
Histology	
- Myxofibrosarcoma	131 (29.6%)
- Liposarcoma	113 (25.5%)
- Leiomyosarcoma	44 (9.9%)
- Synovial sarcoma	31 (7.0%)
- Malignant peripheral nerve sheath tumor	15 (3.4%)
- Other	109 (24.6%)
Tumor grade	
- G1	97 (21.9%)
- G2	82 (18.5%)
- G3	264 (59.6%)
AJCC stage	
- I	98 (22.1%)
- II	175 (39.5%)
- III	170 (38.4%)
Adjuvant chemotherapy	40 (9.1%)
Adjuvant radiotherapy	260 (58.7%)

META-ANALYSIS OF THE EFFECT OF RADIATION THERAPY ON LOCAL RECURRENCE AND OVERALL SURVIVAL IN SOFT TISSUE SARCOMA

Markus Albertsmeier[1]*; Falk Roeder*[2]*;*
Alessandro Gronchi[3]*; Alexandra Rauch*[4]*;*
Martin K Angele[1]
[1]General, Visceral and Transplantation Surgery, Ludwig Maxilian University, Munich, Germany; [2]Department of Radiation Oncolgy, Ludwig Maxilian University, Munich, Germany; [3]Department of Surgery, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy; [4]Institute for Medical Informatics, Biometry and Epidemiology, Ludwig Maxilian University, Munich, Germany

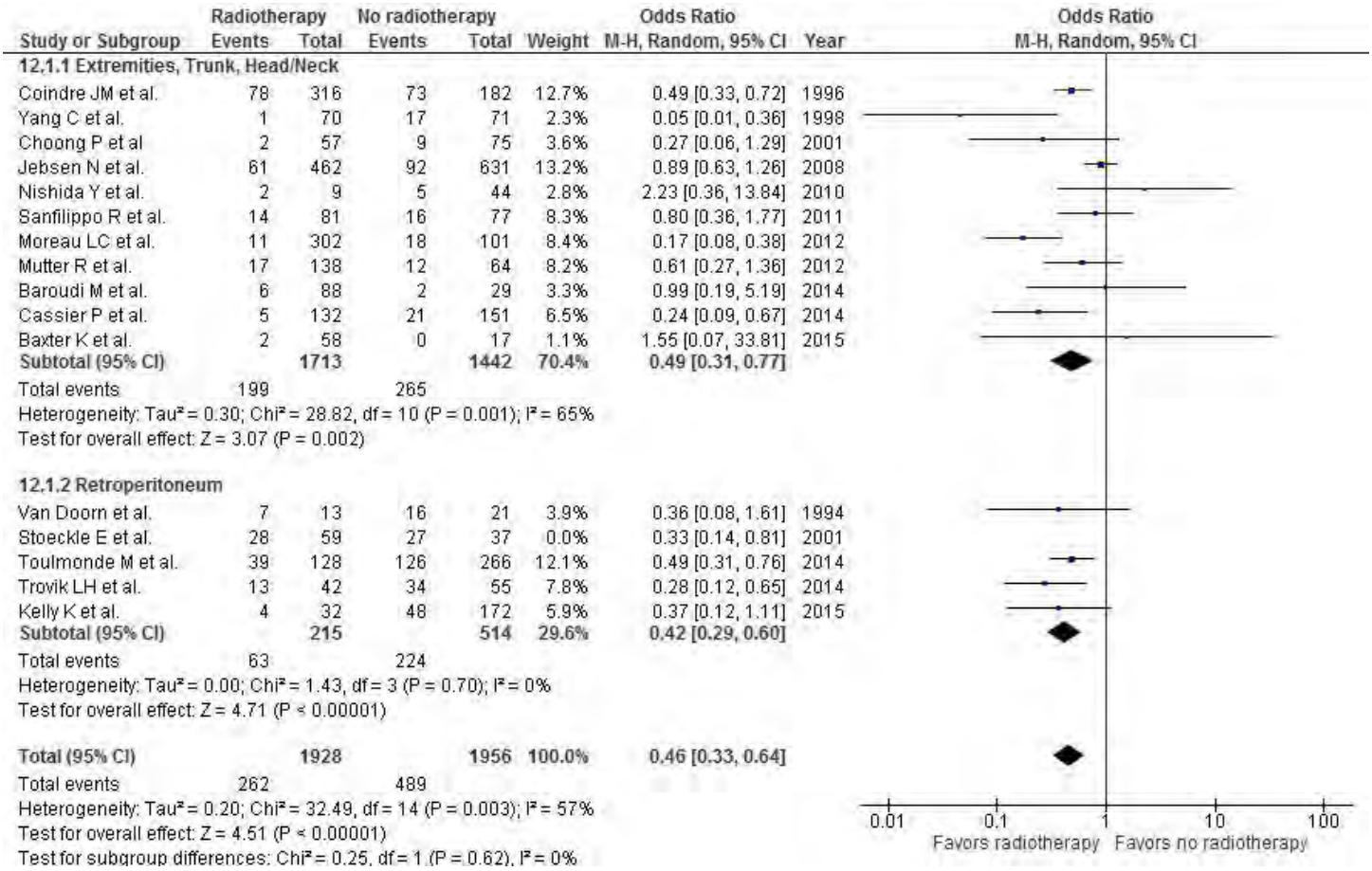
Objective: External beam radiation therapy (EBRT) is frequently used to improve local control in soft tissue sarcoma of different locations. The objective of the present meta-analysis was to quantitavely summarize for the first time the existing evidence for the effectiveness of EBRT in resectable soft tissue sarcoma and to determine whether the preferred timing should be preoperative or postoperative.

Methods: We conducted a systematic search of the PubMed and Embase databases, identifying studies that compared the effect of EBRT vs. no EBRT on local recurrence and overall survival and studies comparing preoperative with postoperative EBRT. Meta-analyses estimating combined odds ratios for each outcome and tumor location were performed using random effect models.

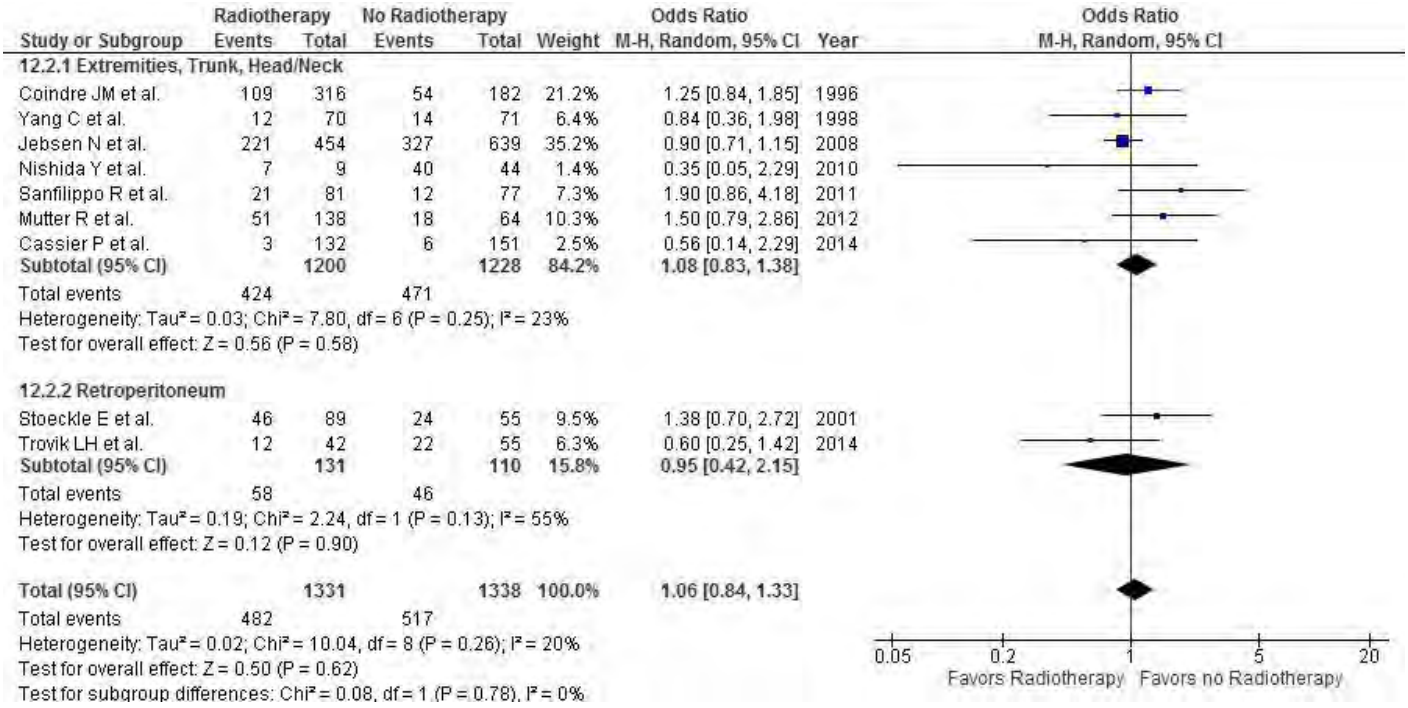
Results: In a meta-analysis of 5 studies including 729 patients with retroperitoneal tumors, a significant combined effect of EBRT on local recurrence was found (HR 0.42 (0.29-0.60), P < 0.00001) while 11 studies including 3155 patients demonstrated a positive effect in extremities and other tumor locations (HR 0.49 (0.31-0.77), P = 0.002, Figure 1). For neither tumor location, a significant effect of EBRT on overall survival could be shown (Figure 2). Only one randomized-controlled trial was included in this analysis while most studies beard a high risk of bias and included heterogenous patient cohorts. A meta-analysis of 8 studies including 1012 patients with extremity ≠and trunk tumors found a significant advantage of preoperative EBRT over postoperative EBRT (HR0.66 (0.49-0.01), P = 0.01, Figure 3).

Conclusion: The existing evidence suggests that EBRT reduces the risk of local recurrence in both extremity and retroperitoneal sarcomas while overall survival appears to be unchanged. EBRT should be applied preoperatively if possible. More prospective trials including specific tumor entities need to be conducted.

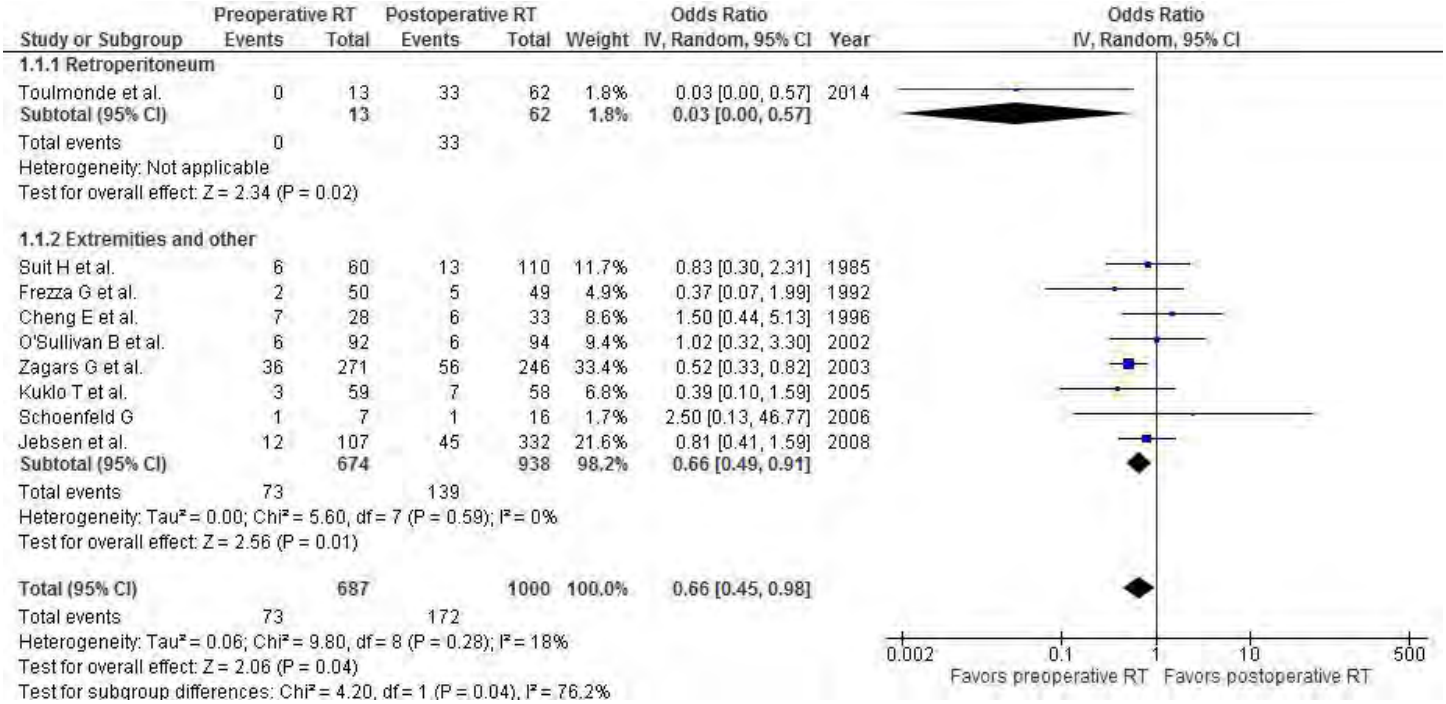
Meta-analysis on the effect of external beam radiation therapy on local recurrence in retroperitoneal soft tissues sarcomas and soft tissue sarcomas of the extremities, head/neck and trunk.



Meta-analysis on the effect of external beam radiation therapy on overall survival in retroperitoneal soft tissues sarcomas and soft tissue sarcomas of the extremities, head/neck and trunk.



Meta-analysis comapring the effect of preoperative vs. postoperative external beam radiation therapy on local recurrence in retroperitoneal soft tissues sarcomas and soft tissue sarcomas of the extremities, head/neck and trunk.



5:10 pm – 5:50 pm

– SOFT TISSUE SARCOMAS –
Retroperitoneal STS

5:10 pm Paper 008 #2565241

SECOND SAFETY ANALYSIS OF A PHASE III RANDOMIZED STUDY OF PRE OPERATIVE RADIOTHERAPY (RT) PLUS SURGERY VERSUS SURGERY ALONE FOR PATIENTS WITH RETRO PERITONEAL SARCOMA (RPS)
- EORTC 62092-22092- STRASS -

Sylvie Bonvalot[1]*; Rick Haas*[2]*; Saskia Litiere*[3]*; Cecile Le Péchoux*[4]*; Dirk C. Strauss*[5]*; Carol Swallow*[6]*; Piotr Rutkowski*[7]*; Chan Raut*[8]*; Pierre Meeus*[9]*; Eberhard Stoekle*[10]*; Sandrine Marreaud*[3]*; Alessandro Gronchi*[11]

[1]Surgery, Institut Curie, Paris, France; [2]Radiation Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; [3]Statistics department, EORTC, Brussels, Belgium; [4]Radiation oncology, Gustave Roussy, Villejuif, France; [5]Surgery, The Royal Marsden NHS Foundation Trust, London, United Kingdom; [6]Surgery, Princess Margaret Cancer Centre , Toronto, ON, Canada; [7]Surgery, Sklodowska-Curie Memorial Cancer Center, Warsaw, Poland; [8]Surgery, Brigham and Women's Hospital, Boston, MA, USA; [9]Surgery, Centre Léon Bérard, Lyon, France; [10]Surgery, Bergonié, Bordeaux, France; [11]Surgery, Istituto Nazionale dei Tumori, Milan, Italy

Objective: Surgery alone is the standard of care for RPS. Abdominal recurrences (AR) are the most common cause of death. STRASS, an EORTC randomized trial investigating preoperative RT (50.4Gy) followed by surgery (Arm R) versus surgery alone (Arm S) in primary RPS, resectable and suitable for RT, aims to investigate whether preoperative RT is able to reduce the rate of AR. Acute toxicity profile of preoperative RT, perioperative and late complications are among the secondary endpoints. We present the second early safety check, focusing on the first 66 patients (pts) who have been treated in each arm.

Methods: In arm S, surgery was planned within 4 weeks after randomization, and between 4 and 8 weeks after completing RT in Arm R. More than 12% difference of tumors becoming non-operable or more than 20% difference in the rate of reoperation were safety stopping rules. Clinical cut-off date was 04/09/2015.

Results: At the cut off date, a total of 179 pts/ 256 required were registered since January 2012. Median tumor size on CT was 168 mm. There were n = 40/57/17/18 well-differentiated/dedifferentiated liposarcoma/LMS/others. The RT was prematurely stopped for 1 pt (pt's request) and temporarily interrupted for 9. During RT, 5 (7.8%), 34 (53.1%), 5 (7.8%), and 3 pts (4.7%) had a grade 3 anemia, lymphopenia, hypo albuminemia and anorexia, respectively; and 18 pts (28.1%) had a grade 4 lymphopenia. There was no difference between the rate of tumors becoming non-operable in the two arms (p = 0.970) neither between the rate of re-operations (p = 0.340). Median duration of surgery (mn) was 290/300 in arms S/R, macroscopically complete in one bloc (%) in 98/94 in arms S/R. No peroperative complications (%) in 68/56 (arm S/R). Transfusion during surgical procedure (%) was done in 24/32 pts in arm S/R. Two pts (arm S) died post operatively. There was no difference in the rate of post-operative complications. Post-operative grade 3 and 4 elevation of creatinine was observed in 3/0 pts in arms S/R.

Conclusion: In general, compliance is good, and the safety profiles observed did not suggest any safety issue. The safety monitoring committee authorized to continue the study as planned.

5:20 pm Paper 009 #2555264

POST-RELAPSE OUTCOMES AFTER PRIMARY EXTENDED RESECTION OF RETROPERITONEAL SARCOMA: A REPORT FROM THE TRANS-ATLANTIC RPS WORKING GROUP (TARPSWG)

Andrea J MacNeill[1]*; Rosalba Miceli*[12]*; Dirk C. Strauss*[2]*; Sylvie Bonvalot*[3]*; Peter Hohenberger*[4]*; Frits van Coevorden*[5]*; Piotr Rutkowski*[6]*; Dario Callegaro*[7]*; Rick Haas*[8]*; Marco Fiore*[7]*; Paolo Casali*[9]*; Raphael Pollock*[10]*; Chandrajit Raut*[11]*; Alessandro Gronchi*[7]*; Carol Swallow*[1]

[1]Department of Surgical Oncology, Mount Sinai Hospital and Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada; [2]Department of Surgery, Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom; [3]Department of Surgery, Insitute Curie, Paris, France; [4]Division of Surgical Oncology & Thoracic Surgery, Mannheim University Hospital, Mannheim, Germany; [5]Department of Surgical Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; [6]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; [7]Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [8]Department of Radiation Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; [9]Department of Cancer Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [10]Division of Surgical Oncology, Ohio State University Medical Center, Columbus, OH, USA; [11]Division of Surgical Oncology, Brigham and Women's Hospital and Center for Sarcoma and Bone Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [12]Department of Biostatistics, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Objective: Despite a radical surgical approach to primary retroperitoneal sarcoma (RPS), many patients develop

locoregional and/or distant recurrence. The objective of this study was to analyze post-relapse outcomes in patients with RPS treated with extended surgical resection at high-volume referral centers.

Methods: All consecutive patients who underwent resection for primary RPS at eight high-volume centers from January 2002 to December 2011 were identified and those who developed recurrent disease were included in the current study. Overall survival (OS) was calculated, as well as crude cumulative incidence (CCI) of a second event after the first local recurrence. Multivariable analyses for OS were performed.

Results: From an initial series of 1007 patients who underwent resection for primary RPS, 444 patients developed recurrent disease during the follow-up period. Patients were grouped into three cohorts according to pattern of first recurrence: LR only (n=249), DM only (n=148), and synchronous LR and DM (n=47), with median follow-up of 38, 42, and 65 months, respectively. Median OS after LR was 33 months, after DM 25 months, and after LR+DM 13 months, while five-year OS was 28%, 20%, and 12%, respectively. Predictors of OS after LR were time interval to LR, resection for LR, histologic grade, and receipt of chemotherapy for LR. In the cohort with DM, predictors of OS were time interval to DM, resection for DM, and histologic subtype. OS was extended by a median of 32, 9, and 21 months for the LR, DM, and LR+DM cohorts, respectively, in patients who underwent resection for recurrent disease as compared to those who did not.

Conclusion: Relapse of RPS is associated with considerable disease-specific mortality; thus every effort should be made to optimize upfront control of primary disease. Surgery for recurrent and metastatic disease may confer a survival benefit and should be considered in appropriately selected patients.

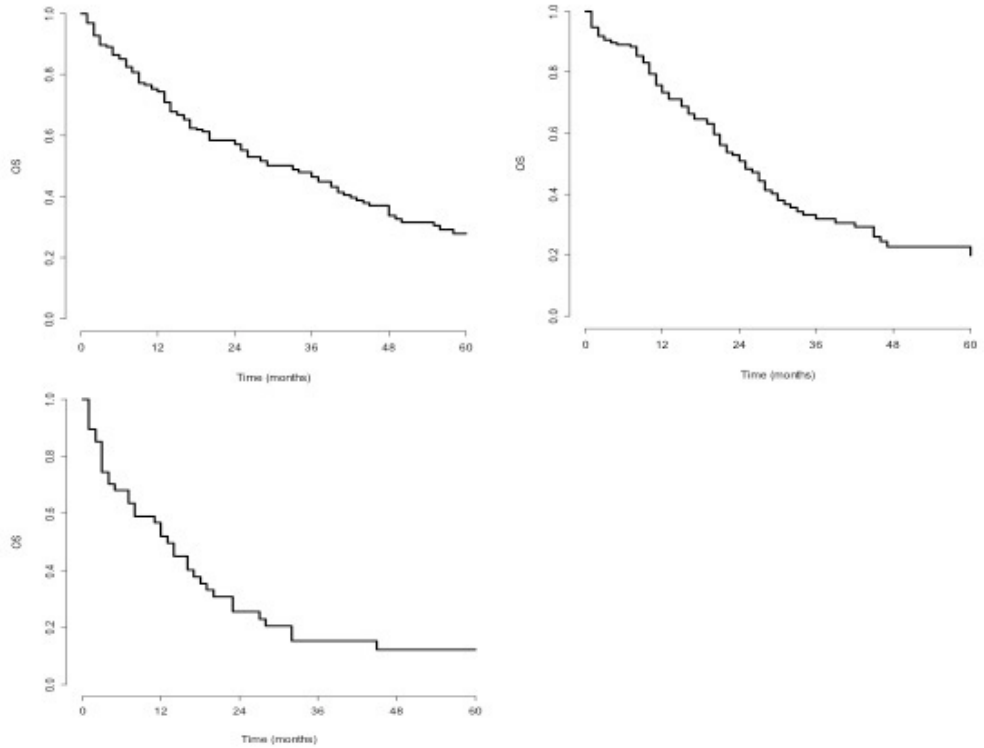


Figure 1. Overall survival curves for patients with A) local recurrence B) distant metastases, and C) synchronous local recurrence and distant metastases

8:00 am – 9:15 am

– OSTEOSARCOMA & EWING SARCOMA –
Immune Therapy of Osteosarcoma

8:00 am Paper 010 #2565919

PD-1, PD-L1 AND CD8 EXPRESSION IN HUMAN EWING SARCOMA AND OSTEOSARCOMA PATIENT TUMOR SAMPLES SUGGESTS PUTATIVE ROLE FOR TARGETED CHECKPOINT INHIBITION

Noah Federman[1]*; Ryan Akiyama*[1]*; Arun S. Singh*[2]*; Sarah M Dry*[3]*; Nicholas Bernthal*[4]*; Frederick C. Eilber*[5]*; Susan Bukata*[4]*; Christopher Denny*[1]
[1]Department of Pediatrics, University of California, Los Angeles, Los Angeles, CA, USA; [2]Department of Medicine, UCLA, Los Angeles, CA, USA; [3]Department of Pathology, UCLA, Los Angeles, CA, USA; [4]Department of Orthopaedics, UCLA, Los Angeles, CA, USA; [5]Department of Surgery, UCLA, Los Angeles, CA, USA

Objective: The outcomes for refractory, recurrent and/or metastatic osteosarcoma (OS) and Ewing sarcoma (ES) are dismal and overall survival has not improved significantly over the past few decades with conventional cytotoxic chemotherapy. Immunotherapy through checkpoint inhibition has rapidly improved outcomes for several cancers most notably advanced melanoma, though it has a potential therapeutic role across all cancer types. In this study, we describe the tumor immune microenvironment by characterization of expression of programmed cell death-1 (PD-1), programmed cell death-ligand 1 (PD-L1), and CD8(+) T-lymphocyte infiltration in human OS and ES tumor samples.

Methods: 70 unique patient tumor samples with OS and ES treated at UCLA over 15 years (2000-2015) were identified through the UCLA Tissue Procurement Core Laboratory and microscopy sections re-cut from FFPE: OS (n=40, localized n=20, pulmonary mets n=20); ES (n=30, localized n=15, pulmonary mets n=15). Slides were stained with antibodies to PD-1, PD-L1, and CD8 and expression was assayed by fluorescence immunohistochemistry.

Results: In OS, PD-L1 was expressed in 12/20(60%) primary tumors, in 15/20(75%) pulmonary metastases (1 with low expression); PD-1 was expressed strongly in 12/20(60%) primary tumors, 16/20(80%) pulmonary metastases with 2 having low expression; and CD8 was expressed strongly in 11/20(55%) primary bone lesions and 16/20(80%) pulmonary metastases. In ES, PD-L1 was expressed in 6/15(40%) primaries and 9/15(60%) metastases; PD-1 was expressed in 6/15(40%) primary tumors and 9/15(60%) pulmonary metastatic lesions; and CD8 infiltration was present in 6/15(40%) primary lesions and 11/15(73%) metastases. Overall, Co-localization of PD-1, PD-L1 and CD8 was present in 5/15(33%) of the primary ES and 10/15(67%) of metastatic ES tumors; with 9/20(45%) primary OS and 15/20(75%) OS pulmonary metastases.

Conclusion: PD-L1 is expressed in a large subset of primary and metastatic Ewing sarcoma and osteosarcoma human patient samples. Moreover, co-localization of PD-1, PD-L1 and CD-8 was shown in the majority of pulmonary metastases suggesting development of an inflamed tumor immune microenvironment in metastatic OS and ES, and a potential role for targeting the immune checkpoint pathway as a therapeutic modality in these aggressive sarcomas.

8:10 am Paper 011 #2570021

TARGETING THE PD-1/PDL-1 SIGNALING PATHWAY FOR THE TREATMENT OF OSTEOSARCOMA LUNG METASTASIS

Pooja Dhupkar; Eugenie S Kleinerman; Nancy Gordon
Pediatrics-Research, UT MD Anderson Cancer Center, Houston, TX, USA

Objective: The *main objective* of this study is to determine if blocking the PD-1-PDL-1 immunosuppressive signaling pathway using a PD-1 checkpoint inhibitor will have an impact in OS lung metastasis. Upregulation of PDL-1 on tumor cells and its enhanced interaction with PD-1 immune-inhibitory receptor is one of the acquired mechanisms of tumor cells to decrease immune-therapeutic efficacy. We *hypothesize* that the disruption of the PD-1-PDL-1 signaling pathway using an anti-PD-1 antibody will have an effect against OS lung metastasis and improve the overall survival.

Methods: Flow cytometry and western blot were used to analyze PDL-1 expression in 7 different OS cell lines. The MDA-MB-231 breast cancer cell line was the positive control. Immunohistochemistry(IHC) analysis was used to determine PDL-1 expression in OS lung metastases from patients and mice. The LM7 human OS mouse model was used to test the effect of blocking murine PD-1 in OS lung metastases. Therapeutic effect of anti-PD-1 treatment was measured by the number of macro and micrometastases. IHC was used to measure cell proliferation (Ki67), apoptosis(TUNEL) and caspase 3 expression in addition to NK cells and macrophages infiltration. Western blot was used to address the downstream components of the signal transduction pathway such as p-Stat3 and p-Erk1/2. The anti-asialo GM1 antibody and/or clrodronate or carrageenan were used for NK cells and macrophage depletion respectively. The Simple PCI software was used to quantify the IHC data.

Results: Our studies confirm surface and total PDL-1

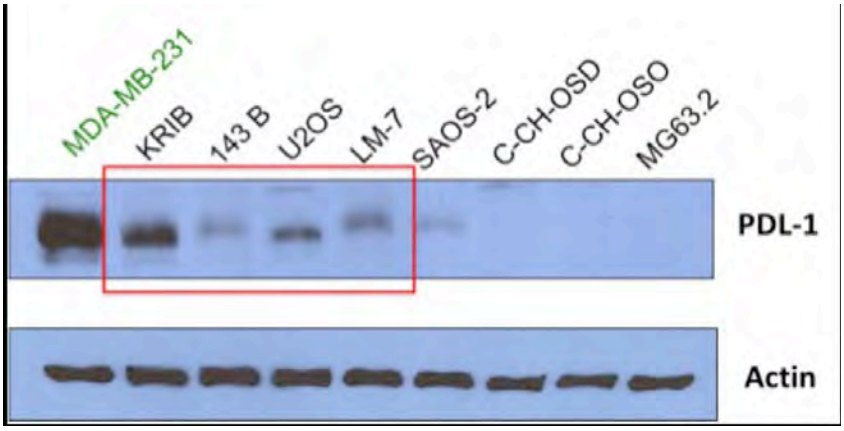
expression in five out of seven osteosarcoma cell lines. Primary and metastatic lung tumor samples from patients and mice demonstrated membranous and cytoplasmic PDL-1 expression. Using a human OS mouse model we demonstrated therapeutic effect of anti-PD-1 therapy. We demonstrated that anti-PD-1 treatment led to a significant increase in the number of NK cells and macrophages in the lung tumors and that the decrease in PDL-1 expression in the lung tumors after anti-PD-1 treatment could be attributed to a decrease in p-ERK1/2 and p-Stat3 expression.

Conclusion: We conclude that targeting the PD-1/ PD-L1 axis could be used to treat OS lung metastasis. Therapeutic efficacy of anti-PD-1 may be due to the increase activity of the local NK cells and/or macrophages in the lung tumors and that inhibition of the p-Stat3/ PDL-1 pathway may be the mechanism implicated in OS lung metastases response to anti-PD-1 treatment.

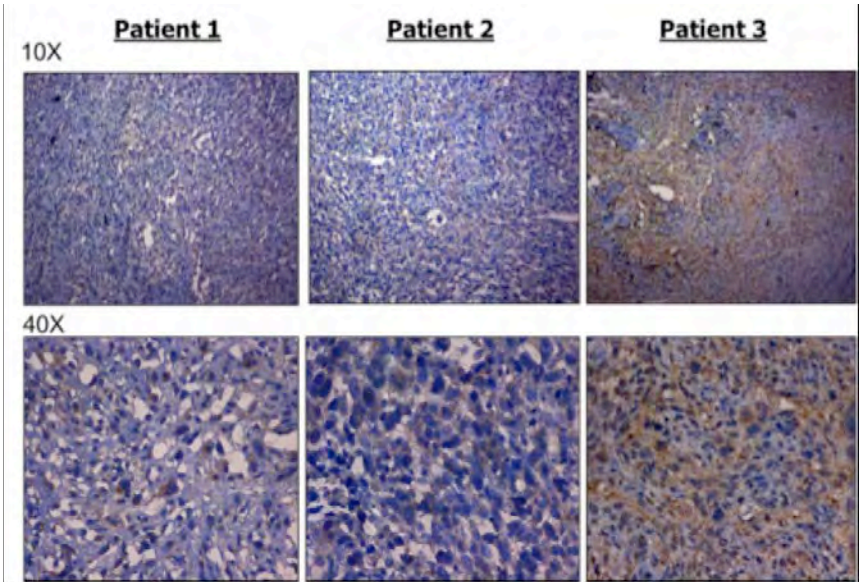
PDL-1 expression in OS cell lines

Cell Line	% PDL-1 expression
KRIB	97.5%
U2OS	98.8%
143B	97.2%
LM7	71.4%
SAOS-2	63.2%
CCH-OS-D	27.3%

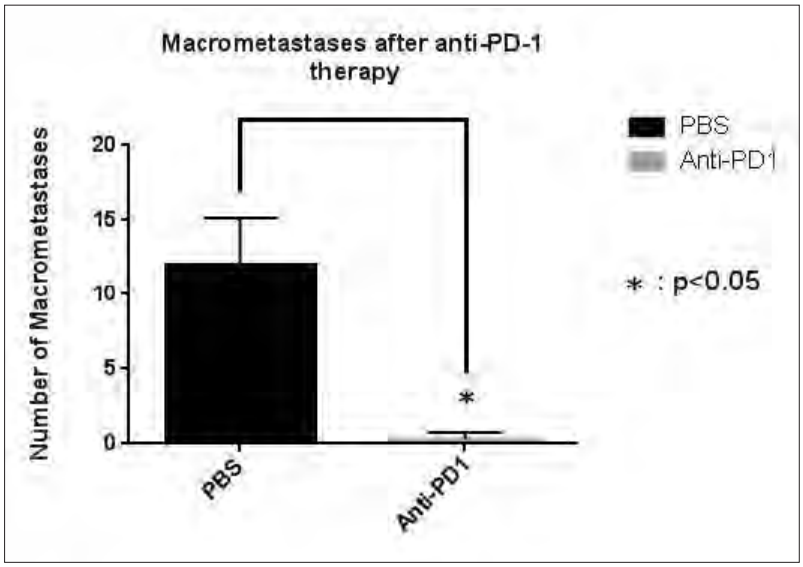
PDL-1 is highly expressed in KRIB, U2OS, 143B, LM-7 and SAOS-2 OS human cell lines as determined by flow cytometry analysis.



PDL-1 is expressed in KRIB, 143B, U2OS, LM-7, and SAOS-2 OS human cell lines as determined by Western Blotting



Membrane and cytoplasmic PDL-1 expression was observed in human OS lung metastases by IHC



Anti-PD-1 therapeutic effect is evidenced by a significant decrease in the number of lung macrometastases

8:20 am Paper 012 #2569674

TUMOR ASSOCIATED MACROPHAGES BUT NOT PD1/PDL1 CHECKPOINTS ARE CRUCIAL EVENTS IN THE INHIBITION OF OSTEOSARCOMA PROGRESSION

Claire Illac[1]*; Corinne Bouvier*[2]*;*
Sophie Piperno-Neumann[3]*; Sebastien Aubert*[4]*;*
Marie-Françoise Heymann[5]*; Jean-Marc Guinebretiere*[3]*;*
Béatrice Marie[7]*; Frédérique Larousserie*[6]*;*
Gonzague de Pinieux[12]*; Eric Mascard*[10]*;*
François Gouin[11]*; Dominique Heymann*[9]*,*
Laurence Brugieres[8]*; Françoise Redini*[9]*;*
Anne Gomez-Brouchet[1]
[1]France, University of Toulouse (IUCT Oncopole), Toulouse, France; [2]CHU la Timone, Marseille, France; [3]Institut Curie , Paris, France; [4]CHRU Lilles, Lilles, France; [5]University of Nantes, Nantes, France; [6]CHU Cochin, Paris, France; [7]CHU Nancy, Nancy, France; [8]Institut Gustave Roussy, Paris, France; [9]INSERM UMR 947, Nantes, France; [10]Hopital Necker, Paris, France; [11]CHU Nantes, Nantes, France; [12]CHU Tours, Tours, France

Objective: Recently it has been demonstrated that Tumor-infiltrating macrophages (TAMs) can exert direct anti-tumor activity against osteosarcoma cells and that activation of the receptor programmed cell death (PD)-1/PD1Ligand (PDL)-1 checkpoint is involved in tumor immune tolerance and escape. The phase 3 trial (OS 2006) conducted in France, that combined Zoledronate (an inhibitor of the osteoclast activity) with chemotherapy and surgery was stopped for futility. To understand the unexpected result of this trial we investigated the role of osteosarcoma-infiltrating immune cells in the biopsies of patients included in the OS 2006 trial.

Methods: in 113 biopsies of the OS 2006 trial, we analyzed by immunohistochemistry, the percentage of TAMs with CD 163 and CD 206 (M2-like macrophages) antibodies, and in 54 patients the expression of PD1 and PDL1. The expression of CD 68 was associated with the presence of osteoclastic cells. The expression of these markers was correlated with the response to chemotherapy, metastases and survival.

Results: patients with a highly infiltrated osteosarcoma by positive CD 163 macrophages (M2-like macrophages) significantly presented less metastases than patients with low macrophages infiltration ($p<0.0022$). The higher level of CD163 macrophages was correlated to a higher overall survival and metastasis-free survival ($p< 0.0032$ and 0.00223 respectively) than those infiltrated by few CD 163 macrophages. The CD 206 and CD 163 macrophages staining showed the same distribution, with less stained cells with CD 206. There was a significant correlation between the absence of osteoclast cells (negative CD 68 cells) and the absence of metastases ($p<0.04$). Only 9 and 4 patients presented respectively an overexpression of PDL1 and PD1 and no correlation was found with metastases and prognosis. For all markers no correlation was found with the response to chemotherapy.

Conclusion: Our study demonstrated that, in contrast to the negative effect of TAMs on survival in patients with other solid tumors, the presence of TAMs in osteosarcoma at diagnosis is positively correlated with a favorable outcome. Much more, osteoclastic cells are associated to metastases. The role of the PD1/PDL1 checkpoint seems to be minor in the development of osteosarcomas. These results show that by decreasing the TAMs, bisphosphonates may be toxic in osteosarcomas and that specific macrophage-activating drugs, is an attractive option to complement current chemotherapy in osteosarcomas.

8:30 am Paper 013 #2569712

COMBINED TARGETING OF IL6 AND IL8 AXES PREVENTS OSTEOSARCOMA LUNG METASTASIS

Ryan D. Roberts[1]; Amy Gross[2]; Hakan Cam[2];
Mary Frances Wedekind[1]; Sarah Winget[2];
Peter Houghton[3]
[1]Pediatric Hematology/Oncology/BMT, Nationwide Children's Hospital, Columbus, OH, USA; [2]Center for Childhood Cancer and Blood Disorders, Nationwide Children's Hospital, Columbus, OH, USA; [3]Greehey Children's Cancer Research Institute, San Antonio, TX, USA

Objective: To identify the biological processes driven by IL6- and IL8-mediated interactions within the lung and to evaluate the therapeutic potential of IL6 and IL8 signal disruption for preventing osteosarcoma metastasis.

Methods: Given previous results suggesting a mechanistic role for IL6 and IL8 in the colonization of lung tissue by osteosarcoma cells, we sought to identify the particular biological processes involved. Using combinations of therapeutic agents and cell lines expressing inducible shRNAs targeting IL6 and IL8 pathways, we studied their effects on: 1) the growth of osteosarcoma in soft agar, 2) growth in traditional cell culture, 3) the ability to migrate and invade through Matrigel layers, and 4) the ability to induce angiogenesis. To verify that our previous observations resulted from on-target drug effects, we compared the effects of shRNA knockdown on lung metastasis to those seen with drug treatment. To determine the generalizability of our observations, we tested the same drugs in a number of murine models of osteosarcoma metastasis, including syngeneic (immunocompetent) models, PDX models, canine osteosarcomas, and other models of human osteosarcoma.

Results: Disruption of IL6, but not IL8 prevented the emergence of colonies in soft agar. Neither drug affected growth in traditional cell culture at physiologically-relevant concentrations. Targeting either pathway affected migration

and invasion, though markedly greater effects were seen with combined inhibition. shRNA experiments validated these findings as representing on-target effects. Angiogenesis induced by cell-free supernatants was impaired much more with blockade of IL8 signaling than IL6. Pre-clinical studies using varied models of osteosarcoma showed that combined blockade could prevent metastatic lung colonization broadly and that effects endure long beyond termination of therapy.

Conclusion: IL6 and IL8 mediate biological processes representative of particular steps in the metastatic cascade. Tumor-lung interactions mediated by these cytokines likely drive behaviors critical to lung metastasis. Targeting these pathways in a number of preclinical mouse models of metastasis suggests that such drugs could be helpful for preventing the evolution from circulating tumor cell to clinically-significant metastasis. It remains to be seen how these drugs might affect primary or established metastatic disease and whether they could be combined safely with other cytotoxic regimens.

8:40 am Paper 014 #2564941

CHANGES IN HLA CLASS I EXPRESSION, PD-L1 AND T-CELLS DURING OSTEOSARCOMA PROGRESSION: A RETROSPECTIVE STUDY USING IMMUNOHISTOCHEMISTRY

Yayan T. Sundara[1]*; Marie Kostine*[1]*;*
Marco W. Schilham[2]*; Judith V.M.G. Bovée*[1]*;*
Anne-Marie Cleton-Jansen[1]
[1]*Pathology, LUMC, Leiden, Netherlands;* [2]*Pediatrics, LUMC, Leiden, Netherlands*

Objective: Genomic instability of osteosarcoma (OS) may be beneficial for immunotherapy as it may generate specific tumor neo-antigens, with the prerequisite of intact antigen processing machinery and HLA molecules expression. We aim to investigate the heterogeneity of HLA class I and PD-L1 expression, as well as tumor-infiltrating lymphocytes (TILs) between primary OS and relapses/metastases.

Methods: Samples from multiple stages of the disease were available (pre-treatment biopsy, resection, relapse and metastasis). Overall, 87 formalin-fixed, paraffin-embedded blocks from 26 OS patients treated in the Leiden Medical University Center were collected and stained for HCA2 (HLA-A), HC10 (HLA-B/C), β2-microglobulin and PD-L1 using immunohistochemistry and CD3-CD8-FoxP3 using triple immunofluorescence. HLA class I expression was categorized as negative/focal weak, heterogeneous (both negative and positive regions on the same slide) and positive. PD-L1 positivity was defined as ≥1% of tumor cells showing a membranous staining of any intensity. TILs subtypes were counted manually within four high power fields. Kaplan-Meier analyses were used for investigating a correlation with patient survival.

Results: HLA class I expression was strongly positive in 56%, heterogeneous in 38%, and negative or weakly positive in 6% of OS, without differences between the stages of the disease. In primary tumors, these patterns of HLA expression associated with disease-free survival (p=0.003). A selective down-regulation of HLA-A expression was more frequently observed than HLA-B/C. TILs were highly heterogeneous and mainly observed in tumor areas with strong expression of HLA class I. Density of TILs was significantly higher in metastases (mean ± SE = 75 ± 13) than in primary tumors (19 ± 6) and local relapses (18 ± 4), with a proportion of cytotoxic $CD8^+$ T-cells of 47%, 46% and 52% respectively. T-regulatory ($FoxP3^+$) cells were most frequently observed in tumors with high $CD8^+$ infiltrate (p=0.001). Positive PD-L1 expression was found in 13% of primary tumors, 25% of relapses and 48% of metastases, and correlated with a high T-cell infiltrate (p=0.002).

Conclusion: Altogether, our data indicate an increased TILs and PD-L1 expression during disease progression, suggesting that T-cell based immunotherapy with adoptive cell transfer, peptide vaccines or checkpoint blockade could be a suitable approach for metastatic OS patients. However, the downregulation of HLA-A molecules may be a limiting factor in some patients.

9:15 am – 10:10 am

– OSTEOSARCOMA & EWING SARCOMA –

Amid Surgery and Dose Intensity: What Matters in Ewing Sarcoma?

9:15 am Paper 015 #2570256

FACTORS INFLUENCING LOCAL CONTROL IN EWING SARCOMA (EWS) PATIENTS: AN ANALYSIS OF THE DATA OF THE EURO-EWING99 TRIAL

Dimosthenis Andreou[1]*; Andreas Ranft*[2]*; Sander Dijkstra*[3]*; Hans Gelderblom*[4]*; Georg Gosheger*[1]*; Jendrik Hardes*[1]*; Ruth Ladenstein*[5]*; Andreas Leithner*[6]*; Michael Paulussen*[7]*; Arne Streitbuerger*[1]*; Beate Timmermann*[8]*; Per-Ulf Tunn*[9]*; Eva Wardelmann*[10]*; Heribert Juergens*[2]*; Uta T Dirksen*[2]

[1]Department of General Orthopedics and Tumororthopedics, Münster University Hospital, Münster, Germany; [2]Department of Pediatric Hematology and Oncology, Münster University Hospital, Münster, Germany; [3]Department of Orthopaedic Surgery, Leiden University Medical Center, Leiden, Netherlands; [4]Department of Medical Oncology, Leiden University Medical Center, Leiden, Netherlands; [5]Department of Pediatric Hematology and Oncology, St. Anna Kinderkrebsforschung e.V. and St. Anna Kinderspital, Vienna, Austria; [6]Department of Orthopedics and Orthopedic Surgery, University Hospital Graz, Graz, Austria; [7]University Children's Hospital, Basel, Switzerland; [8]Clinic for Particle Therapy, West German Proton Therapy Centre, Essen, Germany; [9]Department of Orthopedic Oncology, Sarcoma Center Berlin-Brandenburg, HELIOS Klinikum Berlin-Buch, Berlin, Germany; [10]Department of Pathology, Münster University Hospital, Münster, Germany

Objective: Local recurrence (LR) is associated with very poor prognosis in EwS patients. We sought to identify factors associated with LR in patients undergoing multimodal treatment.

Methods: Retrospective analyses of the medical files of 1207 patients with previously untreated EwS registered in the Euro-EWING99 trial (NCT00020566) from centers in D, A, B, CH, CZ und NL between 1998 and 2009 were performed. The primary outcome was local recurrence-free survival (LRFS), defined as the interval between diagnostic biopsy and LR. A secondary outcome was overall survival (OS).

Results: With a median follow-up of 3.9 years for all patients and 5.9 years for survivors, LRFS was 81.6% at 5 years, and OS was 59.9%. Pelvic tumors (PT) ($p < 0.0001$), primary tumor volume ≥200ml ($p < 0.0001$), locoregional tumor extension ($p = 0.005$), primary metastases ($p < 0.0001$), tumor regression ≤ 90% after neoadjuvant treatment (NT) ($p < 0.0001$) and deviations from protocol treatment ($p = 0.001$) were associated with a poorer LRFS. Complete removal of the involved bone was associated with improved LRFS ($p = 0.007$) and OS ($p = 0.001$) in PT, but not extremity tumors (ET) ($p = 0.068$; $p = 0.848$). Patients with PT undergoing surgery (S) and local radiation (RT) had an improved LRFS compared to patients undergoing only S ($p = 0.01$) or RT only ($p < 0.0001$). No differences in LRFS between S and S + RT were found in chest wall (CWT) ($p = 0.239$) and ET ($p = 0.957$); both provided better local control compared to RT only ($p = 0.007$ and $p = 0.037$ for CWT; $p = 0.0002$ and $p = 0.001$ for ET). PT with >90% histological response to NT had a higher LRFS after S + RT compared to S only ($p = 0.04$) ($n = 118$), but not PT with ≤ 90% response ($p = 0.564$) ($n = 38$).

Intralesional resections were associated with a poorer LRFS than marginal resections ($p = 0.009$), which also correlated with a poorer LRFS compared to wide or radical resections ($p = 0.0002$). Patients with soft tissue infiltration prior to surgery had a poorer LRFS ($p = 0.001$) and OS ($p < 0.0001$). Additional RT did not improve LRFS compared to S alone in these patients ($p = 0.799$).

Conclusion: PT were associated with a poorer LRFS in this study, but appear to benefit from a complete removal of the involved bone and additional RT, even in cases with >90% response to NT. RT additional to S does not appear to influence LRFS in CWT and ET.

9:25 am Paper 016 #2570181

DO TREATMENT DELAYS IMPACT PROGNOSIS IN PATIENTS WITH EWING SARCOMA (EWS)? AN ANALYSIS OF THE DATA OF THE EURO-EWING99 TRIAL AND REGISTRY

Uta T. Dirksen[1]*;Andreas Ranft*[1]*; Daniel Baumhoer*[2]*; Beate Timmermann*[3]*; Georg Gosheger*[4]*; Jendrik Hardes*[4]*; Wolfgang Hartmann*[5]*; Ruth Ladenstein*[6]*; Andreas Leithner*[7]*; Hans Roland Dürr*[9]*; Arne Streitbuerger*[4]*; Per-Ulf Tunn*[8]*; Hans Eich*[10]*; Heribert Juergens*[1]*; Dimosthenis Andreou*[4]

[1]Pediatric Hematology and Oncology, University Hospital Muenster, Muenster, Germany; [2]Pathology, Unierest Hospital Basel, Basel, Switzerland; [3]WestGermanProton Centre, University Hospital Essen, Essen, Germany; [4]Orthopedics, University Hospital Muenster, Muenster, Germany; [5]Gerhard Domagk Institute for Pathology, University Hospital Muenster, Muenster, Germany; [6]Pediatric Hematology and Oncology, St. Anna Children`s Hospital, Vienna, Austria; [7]Orthopedics, University Hospital Graz, Graz, Austria; [8]Orthopedics, Helios, Berlin, Germany; [9]Orthopedic Oncology, Ludwig Maximilian University, Munic, Germany; [10]Radiooncology, University Hospital Muenster, Muenster, Germany

Objective: The aim of this study was to evaluate the prognostic impact of treatment delays after surgical procedures

in EwS patients.

Methods: Retrospective analysis of the files of 692 patients with previously untreated EwS of the extremities, the pelvis and the chest wall registered in the Euro-EWING99 trial (NCT00020566) between 1998 and 2009 from centers in D, A, B, CH, CZ und NL, who presented with localized disease and underwent surgical treatment of the primary tumor. Receiver operating characteristic (ROC) curves were used to analyze the influence of various intervals on EFS and OS. Survival curves were calculated with the Kaplan-Meier method and compared with the log-rank test.

Results: With a median follow-up of 4.8 years in all patients and 5.9 years in survivors, event-free survival (EFS) was 67% at 5 years and overall survival (OS) 73%. The median interval between diagnostic biopsy and begin of systemic chemotherapy amounted to 14 days and was not associated with EFS (area under the curve (AUC) 0.506, p=0.797) or OS (AUC 0.509, p=0.721).

In 485 patients surgical treatment was performed after 6 cycles of neoadjuvant chemotherapy, according to the protocol. The median interval between start of the first cycle of chemotherapy and surgery (startCTX-SURG) in these patients amounted to 141 days and was significantly associated with EFS (AUC 0.566, p=0.016), but not OS (AUC 0.546, p=0.109). ROC curve analysis showed that the optimal cut-off to predict an improved EFS was 146.5 days. Patients with a startCTX-SURG interval of <146.5 days had an EFS at 5 years of 70%, compared to 56% in patients with an interval of >146.5 days (p=0.006), and an OS of 74% compared to 66% (p=0.048).

The median interval between surgery and start of adjuvant chemotherapy (SURG-ADJCTX) was 17 days. ROC curve analysis showed a significant association with EFS (AUC 0.582, p=0.004) and OS (AUC 0.560, p=0.042), with an optimal cut-off at 16.5 days. Patients with a SURG-ADJCTX interval of <16.5 days had a 5-year EFS of 71%, compared to 61% in patients with an interval of >16.5 days (p=0.007), and a 5-year OS of 79% compared to 66% (p=0.030).

Conclusion: The interval between diagnostic biopsy and begin of systemic chemotherapy does not significantly influence OS or EFS in EwS patients . However, shorter intervals between start of neoadjuvant chemotherapy and surgery, as well as surgery and start of adjuvant chemotherapy in patients receiving 6 cycles of neoadjuvant treatment are associated with an improved EFS and OS.

10:40 am – 11:30 am

– OSTEOSARCOMA & EWING SARCOMA –
The Spectrum of Ewing Sarcoma

10:40 am Paper 017 #2570427

FREQUENT INACTIVATING GERMLINE MUTATIONS IN DNA REPAIR GENES IN PATIENTS WITH EWING SARCOMA

Andrew Scott Brohl[1]; *Rajesh Patidar*[2]; *Clesson Turner*[3]; *Xinyu Wen*[2]; *Berkley Gryder*[2]; *Jun Wei*[2]; *Kathleen Calzone*[2]; *Javed Khan*[2]
[1]*Sarcoma, H. Lee Moffitt Cancer Center, Tampa, FL, USA;*
[2]*National Cancer Institute, Bethesda, MD, USA;*
[3]*Walter Reed National Military Medical Center, Bethesda, MD, USA*

Objective: Ewing sarcoma is a highly malignant small round blue cell tumor that predominantly affects the adolescent and young adult population. It has long been suspected that a genetic predisposition exists for this cancer, but the germline genetic underpinnings of this disease have not been well established. In this study, we perform the largest and most comprehensive germline mutational analysis in Ewing sarcoma to date.

Methods: We utilized whole genome or whole exome sequencing from 175 patients affected by Ewing sarcoma, drawing from multiple studies in which the somatic mutational spectrum has previously been reported. Sequencing variants were filtered for analysis using an in-house pipeline that relies on population databases and curated variant archives including ClinVar and the Human Gene Mutation Database. Resultant variants of interest were manually reviewed by a medical oncologist and medical geneticist and classified using American College of Medical Genetics and Genomics guidelines.

Results: We discovered pathogenic or probably pathogenic germline mutations in 13.1% of our cohort. Twenty two different genes were affected, with only a single gene having pathogenic mutations in multiple patients (Table 1). Pathogenic mutations were highly enriched for genes involved with DNA repair pathways and for genes associated with cancer predisposition syndromes (Table 2). There was no significant association between presence of a pathogenic germline mutation and somatic mutation in *STAG2*, *TP53*, or *CDKN2A*. There was a trend towards younger age amongst patients with pathogenic germline mutation, but this did not reach statistical significance.

Conclusion: We report a higher than previously anticipated rate of pathogenic or probably pathogenic germline mutation in patients with Ewing sarcoma. We found that pathologic germline mutations in Ewing sarcoma are not highly recurrent in a single gene, but rather spread across a number of genes with potentially similar functional cluster-

ing. Genetic counseling should be considered for patients and families affected by this disease to take advantage of existing risk management strategies. Our study also highlights the importance of germline sequencing for patients enrolled on precision medicine protocols.

Table 1: Pathogenic/probably pathogenic variants Identified in Ewing sarcoma patients

Gene	Variant	dbSNP
APC	NM_001127511:c.806_807insAACAGCC:p.E269fs	
BLM	NM_000057:c.3384_3385insTATTTGTATACTT:p.S1128fs	
BLM	NM_000057:c.C1933T:p.Q645X	rs373525781
BRCA1	NM_007300:c.3481_3491del:p.E1161fs	rs80357877
BRIP	NM_032043:c.C2392T:p.R798X	rs137852986
ERCC3	NM_000122:c.1421dupA:p.D474fs	
EXT2	NM_000401:c.69+2insAGGG (splice site)	
FANCC	NM_000136:c.C553T:p.R185X	rs121917783
FANCD2	NM_033084:c.2715+1G>A (splice site)	rs201811817
FANCM	NM_020937:c.2191_2192del:p.L731fs	
FLCN	NM_144606:c.G918A:p.W306X	rs142934950
MITF	NM_000248:c.G952A:p.E318K	rs149617956
PMS2	NM_000535:c.G137T:p.S46I	rs121434629
POLE	NM_006231:c.4090dupC:p.R1364fs	
PTCH2	NM_001166292:c.3311_3312insA:p.L1104fs	
PTPN11	NM_002834:c.A1529G:p.Q510R	rs121918470
RAD51	NM_001164269:c.G452A:p.R151Q	rs121917739
RAD51D	NM_001142571:c.293delA:p.D98fs	
RET	NM_020630:c.G2370C:p.L790F	rs75030001
SLX4	NM_032444:c.C5242T:p.Q1748X	
TINF2	NM_001099274:c.C936A:p.Y312X	rs201677741
TP53	NM_001126115:c.C451T:p.R151C	rs149633775
WRAP53	NM_018081:c.1558dupG:p.C519fs	

Table 2: Top enriched pathways affected by pathogenic/probably pathogenic germline variants in Ewing sarcoma patients.

Ingenuity Canonical Pathway	p value
Hereditary Breast Cancer Signaling	3.16E-13
Role of BRCA1 in DNA Damage Response	7.94E-13
ATM Signaling	3.02E-09
Ovarian Cancer Signaling	1.70E-07
Molecular Mechanisms of Cancer	1.20E-06
Basal Cell Carcinoma Signaling	5.01E-05
DNA Double-Strand Break Repair by Homologous Recombination	8.71E-05
Mouse Embryonic Stem Cell Pluripotency	1.15E-04
GADD45 Signaling	1.62E-04
DNA damage-induced 14-3-3σ Signaling	1.62E-04

10:50 am Paper 018 #2570156

EWSR1-CREB FUSIONS IN SARCOMAS

Sherri Z. Millis[1]*; Vivek Subbiah*[3]*; Oliver Holmes*[1]*;*
Alexa Schrock[1]*; David Stockman*[2]*; Julia Elvin*[1]*;*
Philip Stephens[1]*; Vincent Miller*[1]*; Jeffrey Ross*[1]*; Siraj Ali*[1]
[1]*Medical Affairs, Foundation Medicine, Phoenix, AZ, USA;*
[2]*Ortho Path Labs, Kalamazoo, MA, USA;*
[3]*MD Anderson Cancer Center, Houston, TX, USA*

Objective: We sought to identify genomic alterations (GA) in rare, aggressive cancers that have been successfully matched to targeted therapies in the management of other cancers. Using an example case, a malignant gastrointestinal neuroectodermal tumor (GNET) harboring a rare *EWSR1-CREB1* fusion that featured a durable response crizotinib/pazopanib treatment, we interrogated our 80,000 patient database for *EWSR1-CREB* fusions.

Methods: Samples were submitted as FFPE blocks for comprehensive genomic profiling (CGP) in the course of clinical care to identify biomarkers associated with targeted therapies. Relapsed and refractory sarcomas were assayed for 405 genes by DNA sequencing and additional RNA sequencing of 265 genes frequently altered in cancer, to evaluate GA (base substitutions, indels, amplifications, copy number alterations and fusions/rearrangements). Forty-two cases with *EWSR1-CREB* fusions were further evaluated, to identify patterns that might inform therapeutic opportunities.

Results: Review of genomic profiles of 1355 cases harboring *EWSR1* fusions identified 42 tumors with rare *EWSR1-CREB* fusions (3% of *EWSR1* fusions). In addition to the previously identified GNET case, 8 other clear cell sarcomas (20%), 12 (29%) fibrosarcomas, 5 sarcomas of unknown primary (12%), 4 bone osteosarcomas (10%), and 9 other sarcoma subtypes were found (only 2 of which were Ewing sarcomas, which commonly exhibit other EWSR1 fusions). Additionally, 3 non-sarcomas harbored *EWSR1-CREB* fusions. The majority of the fusions were with *CREB3L1* (18; chr11) or *CREB1* (16; chr2); however, 6 were to *CREB3L2* (chr7), and 1 each was with *CREB3L3* and *CREB3L4* (chr19 and 1, respectively). The GNET patient had a 1.5 year durable near-complete response to crizotinib and pazopanib.

Conclusion: An unexpected number of sarcomas harbor rare *EWSR1-CREB* fusions. While other non-*CREB*-*EWSR1* fusions have not historically shown great response to targeted therapies, the GNET patient with an exceptional response suggests that tumors with *CREB*-specific alterations, including the 16 cases with *EWSR1-CREB1* fusion, might respond well to targeted therapies. Further study of targeted therapies for patients with *EWSR1-CREB* driven sarcomas potentially combining drugs impacting both transcriptional and PIK3CA/mTOR pathways appears warranted.

1:30 pm – 2:25 pm

– SOFT TISSUE SARCOMAS –

WSN "Sarcoma of the Year"

Alveolar Soft Part Sarcoma

1:30 pm Paper 019 #2548431

LONG-TERM RESULTS OF THERAPY WITH SUNITINIB IN METASTATIC ALVEOLAR SOFT PART SARCOMA (ASPS) PATIENTS

Piotr Rutkowski*; Katarzyna Kozak; Anna Klimczak;*
Hanna Kosela-Paterczyk; Slawomir Falkowski;
Tomasz Switaj
Soft Tissue/Bone Sarcoma and Melanoma,
Maria Sklodowska-Curie Memorial Cancer Center and
Institute of Oncology, Warsaw, Poland,
Warszawa, Poland

Objective: Alveolar soft part sarcoma (ASPS) is a rare highly vascularized soft tissue sarcomas characterized by indolent growth but with a high frequency of metastatic disease and resistance to classic chemotherapy. ASPS harbours an unbalanced recurrent t(X;17)(p11;q25) translocation, resulting in fusion protein ASPL-TFE3. Sunitinib is an oral multi targeted RTK inhibitor, with high antiangiogenic properties. The purpose of our analysis was to assess long-term sunitinib activity in treatment of metastatic ASPS based on the largest assessed group of patients.

Methods: Between 2009 and 2015, 15 patients have been diagnosed with metastatic ASPS and received therapy with sunitinib in initial continuous daily dosing 37.5mg (one patients started treatment at 50mg/d on a 4/2 week schedule). All patients' initial performance status according to ECOG was 0-1. Median age at time of diagnosis was 32 years (range 18-57), gender distribution Male/Female was 5/10. Primary localization of the tumor was: lower extremity (8), trunk retroperitoneum/pelvis (2), upper extremity (3), other (2). Primary tumor size ranged from 5 to 13 cm (median 10 cm). All patient had unresectable disease (primary or relapse in the form of metastases to the lungs +/ bones). Five patients received systemic therapy before initiating sunitinib . Median time from diagnosis to start of sunitinib therapy was 6 months (range: 2-156). Median follow-up time from start of sunitinib therapy was 38 months (range 5-69 months).

Results: At the time of present analysis 4 patients continue therapy, and 9 is still alive, 2 patients received pazopanib after progression. Six patients had RECIST PR (partial remission) as the best response, 8 - SD (stable disease) and one progression of the disease. Median PFS (progression free survival) was 19 months with 86% patients free of progression of the disease at 6 months. Median OS (overall survival) was 56 months; 5-year OS rate was 49%. Five patients were treated with sunitinib longer than 2 years. Toxicity was rather moderate. All patients experienced some side effects, 8 patients (53%) had toxicity

grade 3/4 CTC, 7 patients required dose reduction. The common treatment toxicity was neutropenia, thrombocytopenia, hypothyroidism, arterial hypertension, hand and foot syndrome.

Conclusion: Our analysis confirms long-term efficacy of sunitinib in some patients with advanced ASPS.

1:40 pm Paper 020 #2569540

PAZOPANIB (P) AND TRABECTEDIN (T) IN ALVEOLAR SOFT PART SARCOMA (ASPS)

Silvia Stacchiotti[1]*; Olivier Mir*[2]*; Bruno Vincenzi*[3]*; Alexander Fedenko*[4]*; Robert G Maki*[5]*; Neeta Somaiah*[6]*; Mehdi Brahmi*[6]*; Kjetil Boye*[7]*; Nadia Hindi*[8]*; Hanna Kosela Paterczyk*[9]*; Antoine Italiano*[10]*; Eisuke Kobayashi*[11]*; Salvatore Provenzano*[1]*; Akira Kawai*[12]

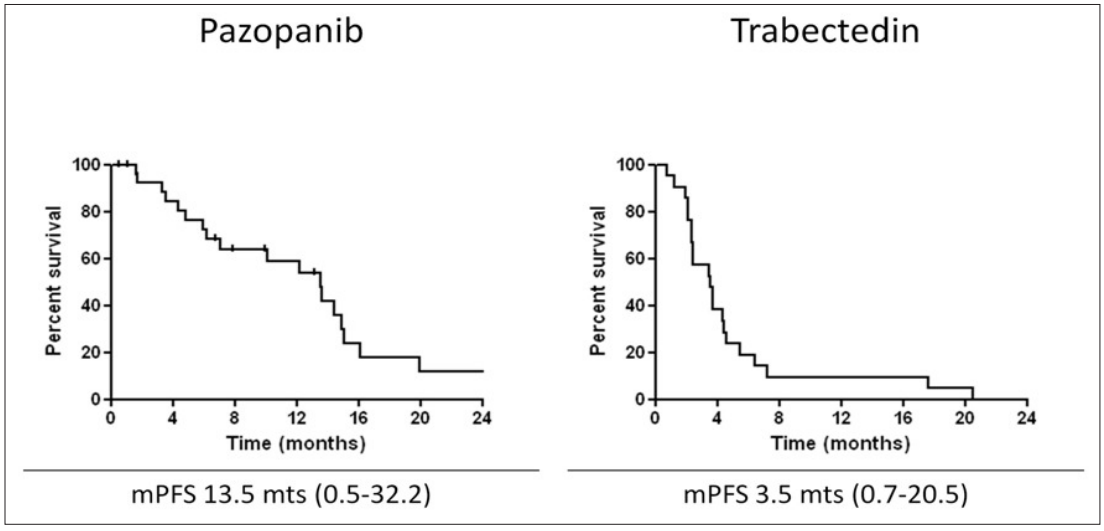
[1]Cancer Medicine, Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy; [2]Cencer Medicine, Gustave Roussy Cancer Institute , Paris, France; [3]Cancer Medicine, University Hospital Campus Biomedico, Rome, Italy; [4]Cancer Medicine, N.N. Blokhin Russian Cancer Research Centre , Moscow, Russian Federation; [5]Cancer Medicine, The Mount Sinai Medical Center, New York, NY, USA; [6]Cancer Medicine, Centre Léon Bérard, Lyon, France; [7]Department of Oncology, Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway; [8]Cancer Medicine, Istituto de Biomedicina de Sevilla, Sevilla, Spain; [9]Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsav, Poland; [10]Institut Bergonié, Bordeaux, France; [11]National Cancer Center, Tokyo, Japan; [12]Musculoskeletal Oncology and Rehabilitation Medicine, National Cancer Center, Tokio, Japan

Objective: ASPS is a rare soft tissue sarcoma (STS), with no active agent available. This is a multi-institutional retrospective case series analysis to review the activity of T and P, both approved for further-line treatment of STS, in advanced ASPS, carried out among 21 reference centres for sarcoma within the World Sarcoma Network effort.

Methods: Between May 2007 and May 2016, 12 sites from Europe, US and Japan identified 44 ASPS patients (pts) treated with T (21) or P (28). Five pts received both treatments. Demographics and past clinical history were collected. Tumor response was evaluated by RECIST. PFS and OS were computed by Kaplan-Meier method. Progression according to RECIST and death were considered PFS events.

Results: Among 28 pts treated with P (14 M/14 F, mean age 33 yrs), 18 were pretreated, 11 also with other antiangiogenic agent(s) (sunitinib and/or cediranib). P was administered in second/third/further line in 17/9/2 pts, respectively. All pts started P at the dose of 800 mg/day, except 3 who received 600 mg/day. Response was evaluable in 26/28 pts. Best responses were 1 CR, 5 PR, 16 SD, 4 PD. Of note, 2 pts responded after having PD to another antiangiogenic drug. At a 16.2-mo median follow-up, median PFS was 13.5 mos (range 0.5-32.2), with 59% of pts progression-free at 1 year. Median OS was not reached. At the time of the analysis, 8 pts are still on P. Reasons for P discontinuation were PD in 16 and toxicity in 4 pts.

Among 21 pts treated with T (14 M/7 F, mean age 32 yrs), all were pretreated, 13 with at least one antiangiogenic agent (sunitinib, cediranib, sorafenib, pazopanib). Sixteen pts received T as third-line therapy, 4 beyond. Starting dose of T was 1.2/1.3/1.5 mg/sqm in 3/3/15 cases, respectively, administered every 3 weeks. Response was evaluable in all cases. Best responses were 0 CR, 1 PR, 14 SD, 6 PD. At a median follow up of 22 mos, median PFS was 3.5 mos (range 0.7-20.5), with 2 pts progression-free at 1 year. Median OS was 9 mos. At the time of the analysis, no pts are still on T, being withdrawn for PD in 21, for pt choice in one.



Progression free survival curves of ASPS patients treated with pazopanib and with trabectedin

Conclusion: These data confirm the value of P in pts with advanced ASPS. Responses can be long-lasting, although they tend to be shorter than reported with cediranib and sunitinib (*Kummar, JCO 2013; Stacchiotti, Ann Oncol 2010*). The proportion of pts who had been pre-treated with other target-overlapping TKIs may have been one reason. The value of T in advanced ASPS seems limited.

1:50 pm Paper 021 #2570689

EXPLORATORY ANALYSIS OF IMMUNOMODULATION AND APOPTOSIS FACTORS IN ALVEOLAR SOFT-PART SARCOMA: A RETROSPECTIVE STUDY FROM THE SPANISH GROUP FOR RESEARCH ON SARCOMA (GEIS)

Nadia Hindi[1]*; Javier Martinez-Trufero*[2]*; Andres Carranza*[6]*; Antonio Lopez-Pousa*[7]*; Ramiro Alvarez*[2]*; Juan Luis Arranz*[3]*; Jeronimo Martinez*[4]*; Claudia Valverde*[8]*; Juana Maria Cano*[5]*; Cristina Tous*[1]*; Romina Ribas*[7]*; Ricardo Gonzalez-Campora*[6]*; Javier Martin-Broto*[1]

[1]HUVR-IBIS, Sevilla, Spain; [2]Hospital Universitario Miguel Servet, Zaragoza, Spain; [3]H.U. Fundacion Jimenez Diaz, Madrid, Spain; [4] HCU Virgen de la Arrixaca, Murcia, Spain; [5]Hospital Universitario de Ciudad Real, Ciudad Real, Spain; [6]HUVR, Sevilla, Spain; [7]Hospital San Pau, Barcelona, Spain; [8]HU Vall d'Hebron, Barcelona, Spain

Objective: Alveolar soft-part sarcoma (ASPS) is an exceedingly rare neoplasm. Expression of programmed death-1/ programmed death-1 ligand (PD-1/PD-L1) and apoptotic pathway Fas/FasL in this entity has not been reported. The aim of this study is to analyze the expression of these factors in a series from the Spanish Group for Research on Sarcoma (GEIS) and to explore its possible prognostic role.

Methods: Patients (pts) diagnosed with ASPS from October 2003 to December 2015 were reviewed. Data regarding clinical and histopathological characteristics, therapy and survival were collected. Kaplan-Meier method was used for overall survival (OS) and relapse-free survival (RFS). Immunohistochemical expression was tested on archived Formalin-Fixed Paraffin-Embedded (FFPE) blocks using PD-L1 (ab58810;Abcam); PD-1 (ab52587; Abcam); FAS (C18C12; Cell Signaling); FASL (sc-73974; Santa Cruz) antibodies.

Results: We identified twelve pts with ASPS: Median age at diagnosis 23.5y (6-52), M/F=3/9. Site of primary tumor was limbs in 9/12 (thigh in 7 pts, arm in 1 pt, gluteus in 1 pt), other sites in 3/9. Stage at diagnosis was localized/ metastatic in 8/4. All metastatic pts had lung metastasis and 1 pt also had bone metastasis. Nine pts underwent surgery of primary tumor. With a median follow-up from diagnosis of 87 mos (12-135), 5/8 pts (62%) have relapsed, with a median RFS of 20.5 mos (95% CI 1-72) and no pts have died. Among those patients diagnosed with advanced disease, 2 pts have died, at 17 and 27 mos from diagnosis respectively. PD-L1 staining was positive on tumor cells in 5/11 pts. FasL staining was positive in 2/9 pts. No association with stage at diagnosis or OS was found. Further analysis are ongoing.

Conclusion: ASPS is a rare and aggressive disease, with >50% of pts with localized disease suffering disease relapse. Identification of prognostic and predictive factors is needed. PD-L1 expression on tumor cells could identify patients with potential benefit from anti PD-1 therapies.

2:25 pm – 3:50 pm

– SOFT TISSUE SARCOMAS –
Immune Therapy of STS

2:25 pm Paper 022 #2566350

OPEN LABEL NON-RANDOMIZED MULTI-COHORT PILOT STUDY OF GENETICALLY ENGINEERED NY-ESO-1 SPECIFIC NY- ESO-1^{C259} SPEAR T-CELLS™ IN HLA-A*02^{+} PATIENTS WITH SYNOVIAL SARCOMA (NCT01343043)

Crystal Mackall[4]*; Sandra D'Angelo*[2]*; Stephan Grupp*[3]*; John Glod*[5]*; Mihaela Druta*[6]*; Warren Chow*[7]*; Karen Chagin*[1]*; Michael Mehler*[1]*; Gabor Kari*[1]*; Trupti Trivedi*[1]*; Tom Holdich*[8]*; Lini Pandite*[1]*; Rafael Amado*[1]

[1]Clinical Development, Adaptimmune LLC, Philadelphia, PA, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Children's Hospital of Philadelphia, Philadelphia, PA, USA; [4]Stanford Cancer Institute, Stanford, CA, USA; [5]Center for Cancer Research, NCI, Bethesda, MD, USA; [6]Moffitt Cancer Center, Tampa, FL, USA; [7]City of Hope Medical Center, Duarte, CA, USA; [8]Adaptimmune LTD, Abingdon, United Kingdom

Objective: NY-ESO-1, a member of the cancer-testis family of tumor antigens, is expressed in ~ 70% of synovial sarcoma (SS) cases. NY-ESO-1^{c259} SPEAR T-cells™ recognizing the NY-ESO-1 derived SLLMWITQC peptide complexed with HLA-A*02 have been developed for study in SS.

Methods: The primary endpoint of overall response rate [ORR (CR+PR)] will be evaluated in high NY-ESO expressers [2+, 3+ NY-ESO in ≥50% of tumor cells by IHC (Cohorts 1, 3, and possibly, 4)] and low expressers [1+ in >1%, 2+, 3+ in <50% (Cohort 2)] in the context of different lymphodepleting regimens (Table). Secondary endpoints include safety, duration of response (DOR), PFS, OS, and persistence of gene-marked cells. Subjects are HLA-A*02:01, :05 or :06^{+}, with unresectable, metastatic or recurrent SS expressing NY-ESO-1, and have failed at least one regimen of ifosfamide and/or doxorubicin. Eligible subjects are leukapheresed; T-cells are isolated, activated, transduced and expanded. Target dose is 1×10^{9} – 6×10^{9} transduced T-cells. Disease assessments (RECIST v1.1 via independent review) occur at wks 4, 8 and 12 post-T-cell infusion and every 3 months thereafter.

Results: Enrollment in cohort 1 is complete (15 pts) and ongoing in cohorts 2 and 3 (2 in each). ORR in cohort 1 is 6/12 or 50% (1 CR; 5 PR) in subjects who received the TCR (N=12) with a 95% CI (25%, 75%). Two pts receiving

Cohort	NY-ESO-1 Expression	Lymphodepleting Regimen
1	high	A: Fludarabine (FL) 30 mg/m2/day × 4 cyclophosphamide (CTX) 1800 mg/m2/day × 2
2	low	A: Fludarabine (FL) 30 mg/m2/day × 4 cyclophosphamide (CTX) 1800 mg/m2/day × 2
3	high	B: CTX 1800 mg/m2/day × 2
4 (to open if B not effective)	high	C: FL 30 mg/m2/day × 3, CTX 600 mg/m2/day × 3

non-target doses (<1 x 10^9 transduced T-cells) did not respond. Excluding these, the ORR is 6/10 or 60% with a 95% CI (31%, 83%). The median DOR was 31.5 wks (max of 47.3 wks). The most common treatment-emergent AEs reported in all cohorts are leukopenia, lymphopenia (94% each), neutropenia (88%), anemia (81%), nausea (81%), and thrombocytopenia (88%) as of January 2016. Six events of CRS were reported; all resolved with supportive therapy. One fatal SAE (BM failure) occurred in cohort 2.

Conclusion: The NY-ESO-1^{c259} SPEAR T-cells™ have promising efficacy and acceptable safety profile in pts with SS who highly express NY-ESO. Efficacy and safety data will be further evaluated and presented from subjects enrolled in all cohorts.

2:35 pm Poster View 1 #2570708

PEMBROLIZUMAB (P) IN PATIENTS WITH ADVANCED SOFT TISSUE (STS) AND BONE SARCOMAS (BS): UPDATED EFFICACY RESULTS OF MULTICENTER PHASE II STUDY SARC028 AND CORRELATES OF RESPONSE

Melissa Burgess[1]*; John Crowley*[2]*; Brian Van Tine*[3]*; James Hu*[4]*; Scott Schuetze*[5]*; Sandra D'Angelo*[6]*; Steven Attia*[7]*; Dennis Priebat*[8]*; Scott Okuno*[9]*; Richard Riedel*[10]*; Lara Davis*[11]*; Sujana Movva*[12]*; Damon Reed*[13]*; Denise K Reinke*[14]*; Hussein Tawbi*[15]
[1]University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [2]Cancer Research and Biostatistics, Seattle, WA, USA; [3]Washington University in St. Louis, St. Louis, MO, USA; [4]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [5]University of Michigan, Ann Arbor, MI, USA; [6]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [7]Mayo Clinic, Jacksonville, FL, USA; [8]Washington Hospital Center Washington Cancer Institute, Washington, USA; [9]Mayo Clinic, Rochester, MN, USA; [10]Duke University Medical Center, Durham, NC, USA; [11]Oregon Health and Sciences University, Portland, OR, USA; [12]Fox Chase Cancer Center, Philadelphia, PA, USA; [13]Moffitt Cancer Center, Tampa, FL, USA; [14]SARC, Ann Arbor, MI, USA; [15]University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: Targeting the programmed death-1 (PD-1)-PD-ligand 1 (PD-L1) pathway has changed the therapeutic landscape of both solid tumors and hematologic malignancies. In this study, we aimed to evaluate the safety and efficacy of the anti-PD-1 antibody P in patients with advanced STS and BS.

Methods: SARC028 is a multicenter phase II open-label study of P monotherapy in patients with STS (Arm A) or BS (Arm B). P was given 200mg IV every 21 days. The primary endpoint for each arm was objective response rate (ORR) by RECIST 1.1 (target ORR=25%, 82% power vs 10% ORR, $\alpha = 0.042$). The study was also powered to detect an improvement in 3-month progression free rate (PFR) from 20 to 40% (87% power, $\alpha = 0.04$). Safety and tolerability, progression free survival, overall survival, and ORR by immune-related response criteria were evaluated as secondary endpoints. Tumor biopsies were obtained in screening, at 8 weeks of therapy (mandatory), and at progression (optional). Exploratory objectives were to evaluate correlates of response in tissue and in the circulation before and during therapy. Arm A enrolled 4 subtypes in balanced cohorts: leiomyosarcoma (LMS), liposarcoma (LPS), undifferentiated pleomorphic sarcoma (UPS) and synovial sarcoma (SS). Arm B enrolled osteosarcoma (OS), Ewing sarcoma (ES) and high-grade/ dedifferentiated chondrosarcoma (CS).

Results: 86 patients were enrolled (6 were replaced) at 12 centers and evaluated for response. In Arm A, 7 partial responses (PR) were seen with an ORR of 17.5%: UPS (4/10), LPS (2/10), LMS (0/10), and SS (1/10). In Arm B, the ORR was 5% (2/40). 2 PR were seen: 1/19 OS and 1/6 CS. No objective responses were seen in ES (0/13). For Arm A, 3-month PFR rate was 55% (39-71%) 95% CI. The toxicity profile of P was consistent with previous published data. 78 (90%) baseline and 62 (72%) post-treatment tumor biopsies were collected, as well as, peripheral blood samples. Correlative data including correlation of response with PD-L1 status will be presented. Planned analyses include the assessment of T-cell populations in circulation and within the tumor.

Conclusion: P monotherapy was safe in patients with advanced sarcomas. Encouraging activity was observed in unselected STS patients with ORR of 17.5% and 55% 3-month PFR. Particularly promising results in the UPS and LPS subgroups warrant further study. There was no activity observed in the LMS or ES subgroups. Translational studies should offer unique insights into the biology of PD-1 blockade in sarcoma.

2:35 pm Poster View 2 #2562782

ANTI-PD1 THERAPY WITH NIVOLUMAB IN SARCOMA

Luca Paoluzzi[1]*; Adrienne Cacavio*[1]*; Munir Ghesani*[2]*; Ajit Karambelkar*[2]*; Amy Rapkiewicz*[3]*; Gerald Rosen*[1]
[1]*Medicine, New York University, New York, NY, USA;* [2]*Radiology, New York University, New York, NY, USA;* [3]*Pathology, New York University, New York, NY, USA*

Objective: Manipulation of immune checkpoints such as CTLA4 or PD-1 with targeted antibodies, has recently emerged as an effective anticancer strategy in multiple malignancies. Sarcomas are a heterogeneous group of diseases in need of more effective treatments. Different subtypes of soft tissue and bone sarcomas have been shown to express PD-1 ligand.

Methods: We retrospectively analyzed a cohort of patients (pts) with relapsed metastatic/unresectable sarcomas, who were treated with nivolumab provided under a patient assistance program from the manufacturer. Pts underwent CT or PET/CT imaging at baseline and after at least 4 doses of nivolumab; RECIST 1.1 criteria were used for response assessment.

Results: Twenty-seven pts with soft tissue (STS, N=23) or bone sarcoma (N=4), received IV nivolumab 3mg/kg every 2 weeks from July 2015 to June 2016. Median age was 58 (24-78), male to female ratio was 13:14; the median number of nivolumab cycles was eight; eighteen pts concomitantly received the tyrosine kinase inhibitor pazopanib at 400-800mg daily. The most common side effect was grade 1-2 LFT elevations; grade 3-4 toxicity occurred in 5 pts (1 colitis, 1 anemia, LFT elevations in 3 pts with one pt who also had pneumonitis). Twenty pts received at least 4 cycles so far and were evaluable for response. We observed three partial responses: one dedifferentiated chondrosarcoma, one proximal epithelioid sarcoma and one maxillary osteosarcoma (last 2 on pazopanib); 8 pts had stable disease: 1 intimal sarcoma, 1 alveolar soft part, 1 synovial sarcoma (SS), 1 osteosarcoma, 1 malignant peripheral sheet tumor and 3 leiomyosarcoma (LMS); 9 pts had progression: 4 LMS, 1 SS, 1 mesenchymal chondrosarcoma, 1 desmoplastic small round cell tumor, 1 liposarcoma and 1 undifferentiated pleomorphic sarcoma. Clinical benefit (response + stability) was observed in 11/20 pts.

Conclusion: Collectively, our data provide a rationale for further exploring the efficacy of nivolumab and other checkpoint inhibitors in soft tissue and osteosarcoma.

2:35 pm Poster View 3 #2570703

PD-1 AND CTLA-4 INHIBITORS IN UNSELECTED METASTATIC SARCOMA PATIENTS

Elizabeth Trice Loggers[1]*; Seth M Pollack*[1]*; Kathryn Hammer*[2]*; Catherine Lee*[2]*; Lee D Cranmer*[2]
[1]*Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA;* [2]*University of Washington, Seattle, WA, USA*

Objective: Until trial data mature and are reported, the activity of PD-1 and CTLA-4 inhibitors in sarcoma patients remains uncertain. Therefore, this study presents preliminary activity data for these agents in unselected, metastatic sarcoma patients.

Methods: Single institution, retrospective study comparing the progression free survival (PFS) of unselected, metastatic sarcoma patients receiving pembrolizumab (P), nivolumab (N) or nivolumab plus ipilimumab (NI) as part of an off-label, compassionate access program.

Results: 33 patients (19 male), mean age 53 years (range [R] 26-87), 82% Caucasian, received P (n=2), N (n=18), and NI (n=13). Subtypes included: leiomyosarcoma (8), chondrosarcoma (4), rhabdomyosarcoma (4), osteosarcoma (3), GIST (3), synovial (2), other (9); none were radiation associated. Average ECOG performance status at therapy initiation was 1 (R 0-2) with 2.7 mean prior lines of therapy (R 0-8). To-date patients have received an average of 4 doses (R 1-11) with 70 days mean on therapy (standard deviation 42, R 7-153). Disease stabilization have been observed in patients with gastrointestinal stromal tumor, non-uterine leiomyosarcoma and myxoid liposarcoma. Notable toxicities included: nephritis, diabetes type 1, infusion reaction.

Conclusion: Activity of PD-1 and CTLA-4 inhibitors in unselected sarcoma patients remains uncertain, however the fact that some patients appear to be responding suggest these treatment may have a role for some sarcoma patients. Toxicity was consistent with prior trial results. Updated results will be presented.

2:35 pm Poster View 4 #2570261

COMBINATION OF PEMBROLIZUMAB AND METRONOMIC CYCLOPHOSPHAMIDE IN PATIENTS WITH ADVANCED SARCOMAS: A FRENCH SARCOMA GROUP STUDY

Antoine Italiano[1]*; Nicolas Penel*[2]*; Christine Chevreau*[7]*; Jean-Yves Blay*[4]*; Axel Le Cesne*[5]*; Emmanuelle Bompas*[8]*; Sophie Piperno-Neumann*[3]*; Sophie Cousin*[1]*; Thomas Ryckewaert*[2]*; Marina Pulido*[1]*; Alban Bessede*[6]*; François Ghiringhelli*[9]*; Maud Toulmonde*[1]
[1]Institut Bergonie, Bordeaux, France; [2]Centre Oscar Lambret, Lille, France; [3]Institut Curie, Paris, France; [4]Centre Léon Bérard, Lyon, France; [5]Institut Gustave Roussy, Villejuif, France; [6]Immusmol, Bordeaux, France; [7]Oncopole, Toulouse, France; [8]Institut Cancerologie de l'Ouest, Nantes, France; [9]Centre Georges François Leclerc, Dijon, France

Objective: To assess safety and efficacy of the anti-PD-1 antibody pembrolizumab (P) in combination with metronomic chemotherapy in patients (pts) with advanced sarcomas.

Methods: This open-label multicenter phase II study included 5 arms: leiomyosarcoma (Arm A), undifferentiated pleiomoprhic sarcoma (Arm B), gastrointestinal stromal tumors (Arm C), osteosarcomas (Arm D) and other sarcomas (Arm E). All pts received pembrolizumab 200mg IV q21 days and cyclophosphamide 50 mg BID 1week on, 1 week off. For Arms A, B, D, and E, the primary endpoint was a dual one encompassing non-progression and objective response at 6 months (as per RECIST 1.1). For Arm C, the primary efficacy endpoint was 6-month non-progression (as per RECIST 1.1). Based on the following hypotheses for Arm A, B, D and E: 40% 6-month non-progression rate (H0), 60% acceptable 6-month non-progression rate (H1), or 5% objective response rate (H0), 20% objective response rate (H1), 5% type I error rate, 80% power, a total of 30 assessable patients were necessary (1st stage: n=15; 2nd stage: n=15). Following the inclusion of the first 15 patients, if ≥ 3 patients had objective response or ≥ 7 were progression-free at 6 months, the accrual was planned to continue. Based on the following hypotheses for Arm C: 30% 6-month non-progression rate (H0), 60% acceptable 6-month non-progression rate (H1), 5% type I error rate, 90% power, a total of 28 assessable patients were necessary (1st stage: n=10; 2nd stage: n=18). Following the inclusion of the first 10 patients, if ≥ 4 patients were progression-free at 6 months, the accrual was planned to continue.

Results: 41 patients (22 males, 19 females) have been included between June 19 2015 and June 17 2016 in Arm A (15), C (n=10) and E (n=16). Median age was 59.5 years (18.4 – 84.1). 27 pts (67.5%) and 7 patients had grade 1/2 and grade 3/4 adverse events (AE) related to the experimental regimen respectively. No objective responses were observed. 3 patients had stable disease (SD) at 6 months (Arm C n=1, Arm E n=2: solitary fibrous tumor, low grade endometrial stromal sarcoma). Pembrolizumab + low dose CP had not reached the pre-specified endpoint to justify continuing accrual after the 1st step of the study in Arm A, C and E. Accrual is ongoing in Arm B and D.

Conclusion: Pembrolizumab + low dose cyclophosphamide regimen has no activity in leiomyosarcoma ,gastrointestinal stromal tumors and miscellaneous sarcomas. Comprehensive efficacy, safety and molecular analyses will be presented at the meeting.

– YOUNG INVESTIGATOR AWARD WINNERS –

3:05 pm Paper 023 #2570351

INCREASED INFILTRATION OF M2-MACROPHAGES, T-CELLS AND PD-L1 EXPRESSION IN HIGH GRADE LEIOMYOSARCOMAS SUPPORTS IMMUNOTHERAPEUTIC STRATEGIES

Marie Kostine[1]*; Arjen H.G. Cleven*[1]*; Carly Vervat*[2]*; Willem E. Corver*[1]*; Marco W. Schilham*[2]*; Anne-Marie Cleton-Jansen*[1]*; Judith V.M.G. Bovée*[1]
[1]Pathology, LUMC, Leiden, Netherlands; [2]Pediatrics, LUMC, Leiden, Netherlands

Objective: The growing interest in cancer immunotherapy is reaching the sarcoma field and may be a rational strategy in leiomyosarcoma (LMS), a tumor known for its genomic complexity. As an important prerequisite for therapeutic applications, we aimed to characterize the immunological microenvironment in LMS, as well as its prognostic value.

Methods: Primary tumors (n=75), local relapses (n=6) and metastases (n=19) of LMS patients treated at the Leiden University Medical Center were included in this study, as well as benign leiomyomas (n=7). Using immunohistochemistry, we evaluated $CD3^+$ T-cells, $CD163^+$ macrophages, PD-L1/PD-L2 and HLA class I expression (HCA2, HC10 and β2m) on whole tumor sections. T-cells were further characterized using CD3-CD8-FoxP3 combination in immunofluorescence. Correlation with clinicopathological parameters and Kaplan-Meier survival analyses were assessed. To explore the effect of LMS cells on macrophage differentiation, $CD14^+$ monocytes from healthy donors (n=3) were cocultured with the LMS cell lines LMS04 and LMS05 (transwell) or their conditioned media. Macrophage markers were analyzed by flow cytometry after 6 days and compared to GM-CSF and M-CSF-differentiated macrophages (respectively M1 and M2 phenotype).

Results: 52% of the tumors were highly infiltrated with T-cells (>5 cells/HPF), mainly cytotoxic $CD8^+$ T-cells, and 58% were highly infiltrated with $CD163^+$ macrophages (>20%). PD-L1 expression on ≥1% of tumor cells was found in 31 samples (30%). PD-L2 expression was also detected in some of the PD-L1-positive tumors, but was not related

to degree of macrophage infiltrate. HLA class I was strongly or heterogeneously expressed in 84% of tumors. Interestingly, all these immune markers were interrelated and their presence correlated with high tumor grade. $CD163^+$ infiltrate was the only immune marker associated with overall survival (p=0.0003) and disease-specific survival (p=0.041). *In vitro*, the macrophage marker CD163 was upregulated in the presence of LMS cells or their conditioned media, suggesting that this tumor drives macrophages towards the M2/pro-tumoral phenotype.

Conclusion: The clinical significance of M2 macrophages, possibly induced by LMS cell-secreted factors, suggests that LMS patients may benefit from macrophage-targeted agents. Furthermore, PD-L1 expression together with high T-cell infiltrate and HLA class I expression in around 30% of high grade LMS reflects an active immune microenvironment, which may be targeted with immune checkpoint inhibitors.

3:15 pm Paper 024 #2556786

INCREASE IN PD-L1 EXPRESSION AFTER PRE-OPERATIVE RADIATION THERAPY FOR SOFT TISSUE SARCOMA

***Kirtesh R. Patel**; Anthony Martinez; Stephen Byron Huff; Mandy Ford; Keith Delman; David Monson; Shervin Oskouei; Nickolas Reimer; Kenneth Cardona; Melinda Yushak; Eugene Fortune; Richard Cassidy; Mark Edgar; Jerome Landry; Karen Godette*
Emory University, Atlanta, GA, USA

Objective: Soft tissue sarcomas (STS) have minimal expression of PD-L1, a biomarker for PD-1 checkpoint blockade therapy; recently, the SARC028 trial of PD-1 inhibition in metastatic STS demonstrated only a 5.2% (2/38) objective response rate. Radiation therapy (RT) has been shown to increase PD-L1 expression pre-clinically. We investigate the expression of PD-L1 pre and post radiation in STS patient samples.

Methods: We reviewed records of adult, stage II-III, node negative STS patients treated with pre-operative RT (50Gy in 25 fraction) alone followed by surgical resection 4-6 weeks later at our institution. Patients treated with pre-operative chemotherapy were excluded. 39 patients with baseline clinical information and both tissue sample prior to radiation (i.e. biopsy sample) and post radiation therapy (i.e. resection sample) were identified. PD-L1 expression was evaluated by immunochemistry using the anti PD-L1 monoclonal antibody (E1L3N clone; Cell Signaling). PD-L1 expression was considered positive when greater than 1% membranous staining was present. Changes in PD-L1 expression were analyzed via the Fisher exact test.

Results: The median age was 61 years old, with 61.5% male. The majority of patients were T2 (92.3%) and high grade (66.6%). Histologic subtypes include undifferentiated pleomorphic sarcoma (41.0%), liposarcoma (20.5%), leiomyosarcoma (7.7%), and other (30.8%). 84.6% were from the extremities, with the remaining 15.4% from the pelvis or trunk. Prior to RT, no patients (0%, 0/39) demonstrated PD-L1 tumor expression. After irradiation, 4 patients (10.3%) demonstrated PD-L1 tumor expression. This increase in expression after irradiation reached borderline statistical significance (p=0.115) All 4 of these tumors were grade 3 of the lower limbs, with 3 being pleomorphic sarcomas, and 1 an epitheloid sarcoma. On macrophages within the tumor, PD-L1 expression increased after radiation, from 17.9% to 48.7% (p=0.007).

Conclusion: Overall PD-L1 expression in soft tissue sarcoma was low; however, pre-operative RT may increase tumor and macrophage PD-L1 expression, even at 4-6 weeks after radiation. Further studies are needed to investigate the optimal peak expression of PD-L1 after irradiation and if this increase can improve efficacy of PD-1 inhibition in locally advanced STS.

4:20 pm – 5:05 pm

– SOFT TISSUE SARCOMAS – Uterine Sarcomas

4:20 pm Paper 025 #2570383

A PHASE II RANDOMIZED – NON COMPARATIVE – STUDY ON THE ACTIVITY OF TRABECTEDIN OR GEMCITABINE + DOCETAXEL IN METASTATIC OR LOCALLY RELAPSED UTERINE LEIOMYOSARCOMA (MLRUL) PRETREATED WITH CONVENTIONAL CHEMOTHERAPY

***Federica Grosso**[8]; Giovanni Scambia[2]; Francesco Raspagliesi[3]; Nicoletta Colombo[5]; Giovanni Grignani[6]; Paolo Casali[3]; Angela Buonadonna[7]; Armando Santoro[9]; Domenica Lorusso[3]; Emanuele Negri[1]; Maurizio D'Incalci[1]; Ilaria Pacchetti[1]; Elena Biagioli[1]; Roldano Fossati[1]; Angiolo Gadducci[4]*
[1]IRCCS Mario Negri Institute, Milan, Milan, Italy; [2]Policlinico Gemelli, Rome, Italy; [3]Istituto Nazionale Tumori, Milan, Italy; [4]Azienda Ospedaliera Universitaria Pisana, Pisa, Italy; [5]Istituto Europeo di Oncologia, Milan, Italy; [6]Istituto di Candiolo-IRCCS, Turin, Italy; [7]Centro di Riferimento Oncologico-IRCCS, Aviano (PN), Italy; [8]Azienda Ospedaliera Nazionale SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy; [9]Istituto Clinico Humanitas-IRCCS, Rozzano (MI), Italy

Objective: Patients with metastatic disease at diagnosis or who recur after initial treatment have a dismal prognosis and, except for a subset of pts with completely resectable disease, the median survival is less than one year. Treatment options for MLRUL are limited. The most active drugs are doxorubicin ± ifosfamide and gemcitabine + docetaxel

(GD) with response rate of 25-55% and 27-53%, respectively. So far no phase II studies have specifically tested the activity of trabectedin in uterine leiomyosarcoma.

Methods: Pts were eligible if they had received ≥ 1 line of chemotherapy either in adjuvant setting or as first line in advanced/recurrent disease. Pts who had not already received GD were randomized to *Arm A*: trabectedin 1.3 mg/m^2 or *Arm B*: gemcitabine 900 mg/m^2, on days 1 and 8, and docetaxel 75 mg/m^2 on day 8. Pts randomized to *Arm B* served as calibration group. Pts who had already received GD were directly included in *Arm A*. At progression, pts randomized to *Arm B* could be crossed to *Arm A*. Primary end-point was the 6-months progression free rate (PFS-6 rate). Assumptions for *Arm A* sample size calculation: 1) expected PFS-6 rate for trabectedin is similar in 2nd or further line 2) trabectedin is inactive if PFS-6 rate < 14% and clinically active if PFS-6 rate ≥ 25% 3) one sided alpha=.05 and power=90%. According to an exact single-stage phase II design 109 patients were to be enrolled in *Arm A*. Long-lasting responding pts will be the target of specific translational analyses.

Results: 168 pts were accrued between 04/2010 and 01/2016 from 26 sites: 126 entered *Arm A* (45 from randomization and 81 directly) and 42 *Arm B. Arm A* pts characteristics: median age 57; 64%, 33% and 3% had received 1, 2, 3 previous chemotherapic lines, respectively; site of disease was only pelvic (8%), only distant metastasis (61%) and both (31%). Data for PFS-6 analysis are currently available for 113 pts (*Arm A*): 37 pts successfully reached the target end-point (PFS-6) (33%, 90% Confidence Intervals (CI): 25.5% to 40.7%). The PFS-12 mos. rate was 20%. In the randomization part of the study there are 40 pts and 34 pts currently evaluable for *Arm A* and *B*, respectively. PFS-6 rate were 33% (95% CI 18.6 to 49.1) for *Arm A* and 44% (95% CI 27.2 to 62.1) for *Arm B*. No toxic deaths occurred.

Conclusion: Trabectedin met the study criteria for activity in MLRUL pretreated with conventional chemotherapy. Its efficacy seems to remain unchanged across one to three previous lines of chemotherapy.

4:30 pm Paper 026 #2544038

PROGNOSTIC FACTORS FOR ADENOSARCOMA OF THE UTERUS

Michael Jason Nathenson*; Anthony Paul Conley; Heather Yan Lin; Wei-Lien Wang; Alexander Lazar; Dejka Araujo; Neeta Somaiah; Maria Alejandra Zarzour; Ravin Ratan; SR Patel; Robert S. Benjamin; Vinod Ravi*
Sarcoma, MD Anderson, Houston, TX, USA

Objective: Uterine adenosarcoma is the rarest of sarcomas to characteristically involve the uterus. Standard treatment involves surgical resection with hysterectomy and BSO, resulting in a 50-70% 5-yr overall survival (OS). Retrospective data suggests no OS benefit of adjuvant radiation therapy. The role of adjuvant chemotherapy is undefined in uterine adenosarcomas. Previously identified pathologic prognostic factors for adenosarcoma include myometrial invasion (MI), sarcomatous overgrowth (SO), mitosis, tumor size, lymphovascular invasion (LVI), age, necrosis, heterologous elements and rhabdomyosarcoma elements The objective of this study was to retrospectively examine pathologic prognostic factors in the MDACC uterine adenosarcoma experience.

Methods: Patients with uterine adenosarcoma seen in consultation between 1982 and 2014 were identified from the institutional tumor registry. Clinical data was collected retrospectively. The Kaplan-Meier method was employed to estimate OS and disease-free survival (DFS). The Log-rank test compared the difference in survival between groups. Regression analyses of survival data utilized the Cox proportional hazards model.

Results: Of 165 pts identified, 85 had SO, 72 had no SO, and 8 were unknown. MI was present in 64 pts, absent in 53 pts, and unknown in 48 pts. LVI invasion was present in 8 pts and absent in 157 pts. Tumor size was <5cm in 49 pts, and ≥ 5cm in 62 pts, and unknown in 54 pts. Mitosis were < 5 per 10 hpf in 36 pts, ≥ 5 in 38 pts, and unknown in 91 pts. Median OS for all pts was 8.5 yrs. Median DFS for all pts was 4.7 yrs. Median OS for adenosarcoma pts with SO was 4.9 yrs vs 14.5 yrs for pts without SO. Median DFS for adenosarcoma pts with SO was 2.5 yrs vs 10.9 yrs for pts without SO. On univariate analysis, age, SO, MI, LVI, mitosis, and tumor size were significant, Table 1. On multivariate analysis, SO, MI, and LVI were significant, Table 2.

Conclusion: Outcomes after surgical resection of uterine adenosarcoma vary greatly. It is of paramount importance to identify patients at high risk of recurrence, who may benefit from adjuvant therapy. The most important pathologic prognostic factors for uterine adenosarcoma are sarcomatous overgrowth, myometrial invasion, and lymphovascular invasion. Patients with sarcomatous overgrowth have inferior outcomes and could receive consideration for adjuvant therapy. Additionally, patient with sarcomatous overgrowth,

myometrial invasion, and lymphovascular invasion should be closely monitored for recurrence.

Uterine Adenosarcoma Prognostic Factors for Overall Survival: Univariate Analysis

Prognostic Factor	p value	Hazard Ratio	95% Confidence Interval
Tumor Size	0.0009	3.23	1.62 to 6.45
Myometrial Invasion	0.0005	3.32	1.68 to 6.53
Sarcomatous Overgrowth	<0.0001	3.01	1.80 to 5.04
Lymphovascular Invasion	0.0021	3.47	1.57 to 7.67
Mitosis	0.036	2.38	1.06 to 5.35
Age	0.0017	1.03	1.01 to 1.04

Uterine Adenosarcoma Prognostic Factors for Overall Survival: Multivariate Analysis

Prognostic Factor	p value	Hazard Ratio	95% Confidence Interval
Sarcomatous Overgrowth	0.016	2.17	1.15 to 4.08
Myometrial Invasion	0.011	2.51	1.23 to 5.12
Lymphovascular Invasion	0.0001	6.53	2.50 to 17.07

5:05 pm – 6:15 pm

– SOFT TISSUE SARCOMAS –
Desmoplastic Small Round Cell Tumor (DSCRT)

5:05 pm Paper 027 #2565759

THERAPEUTIC TRIAL FOR PATIENTS WITH DESMOPLASTIC SMALL ROUND CELL TUMORS

***Sara M. Federico**; Mary Elizabeth McCarville; Mike Doubrovin; Matthew Krasin; Michael W. Bishop; Catherine Lam; Wayne Furman; Fariba Navid; Alberto Pappo*
Oncology, St. Jude Children's Research Hospital, Memphis, TN, USA

Objective: Desmoplastic small round cell tumor (DSRCT) is a rare malignancy with a poor prognosis. In this study we investigated a therapeutic approach for newly-diagnosed patients.

Methods: Patients with newly-diagnosed DSRCT were eligible to receive two 21 day cycles of window therapy (irinotecan 20mg/m^2 IV days 1-5 and 8-12, temozolomide 100mg/m^2 po days 1-5 and temsirolimus 35mg/m^2 IV days 1, 8). Response to window therapy was assessed using WHO and volumetric measurements (primary tumor) and RECIST 1.1 (metastases). Following window therapy, patients received 13 cycles of dose-compressed vincristine/doxorubicin/cyclophosphamide alternating with ifosfamide/etoposide. Local control measures included surgery with hyperthermic interperitoneal chemotherapy (HIPEC) and radiation. At the completion of therapy, patients were eligible to receive 6 cycles of maintenance (bevacizumab 15mg/m^2 IV day 1, sorafenib 90mg/m^2 po BID and cyclophosphamide 50mg/m^2 po daily).

Results: Six patients (5 males; median age 14.8yrs; range 9.4-20.9yrs) were enrolled between 12/2013-6/2015. Five patients completed window therapy (1 patient was not eligible due to resected localized disease). There were 4 grade 3 toxicities (neutropenia (2), diarrhea, and mucositis) to window therapy. All patients had stable disease (SD) following the window with a median volumetric decrease of 44.5% (range: 37.9-53%) and WHO decrease of 30.6% (range: 11.3-44.5%) in the primary tumor. RECIST 1.1 confirmed a median 18.6% (range: 12.6-22.4%) decrease in the size of the metastatic lesions. Two patients developed progressive disease during dose-compressed chemotherapy. Two patients discontinued the trial during the dose-compressed chemotherapy (1 with a partial response (PR) and 1 with a complete response (CR) removed due to toxicity related to HIPEC); both of these patients received more window therapy off trial with continued benefit. One patient completed all therapy with a CR, but did not receive maintenance therapy (physician discretion). The final patient with localized disease completed dose-compressed chemotherapy and radiation to the primary tumor site. This patient had a CR, received 1 course of maintenance therapy, but developed grade 4 neutropenia and was removed from the trial.

Conclusion: The window regimen including irinotecan, temozolomide and temsirolimus administered to newly-diagnosed patients with DSRCT was well-tolerated and demonstrated clinically meaningful responses. Further studies of this approach are warranted.

5:15 pm Paper 028 #2570178

RELAPSE OR DISEASE PROGRESSION IN 45 DESMOPLASTIC SMALL ROUND CELL TUMOR PATIENTS FOLLOWING CYTOREDUCTION AND HYPERTHERMIC INTRAPERITONEAL PERFUSION OF CISPLATIN (HIPEC)

Laura Salvador[1]*; Winston Huh*[1]*; Joseph A Ludwig*[2]*; Mary McAleer*[6]*; Ajaykumar Morani*[3]*; Lianchun Xiao*[4]*; Andrea Hayes-Jordan*[5]

[1]Pediatrics, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Medical Sarcoma, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Diagnostic Radiology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Biostatistics, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [6]Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: Desmoplastic small round cell tumor (DSRCT) is a rare sarcoma believed to arise from the peritoneum, and patients typically present with numerous intra-abdominal tumors. Our institution uses multimodal therapy involving chemotherapy, hyperthermic intraperitoneal perfusion of cisplatin (HIPEC) and whole abdominal radiation therapy (WART). The pattern of treatment failure for DSRCT patients is poorly understood. The purpose of our study is to describe the pattern of treatment failure in our DSRCT cohort following HIPEC which may provide insight for improving multimodal therapy.

Methods: Retrospective medical record review of DSRCT patients treated at the University of Texas MD Anderson Cancer Center from 2006 to 2015.

Results: There were 72 patients who received HIPEC, and 45 had evaluable relapse or disease progression. Mean age at diagnosis was 20.5 years (range 4.9 – 52.9 years). There were 39 males, and mean duration of follow-up was 35.5 months (range 12 – 71 months). Metastasis at diagnosis was noted in 33 patients (73%) with liver (n=22) and distant lymph node (n=17) as most common sites. Progression of disease during therapy was noted in 24 patients (53%) at mean duration of 17.6 months from diagnosis (range 8-32 months), while 21 patients had recurrence at mean duration of 28.1 months from diagnosis (range 15-49 months) and 11 months from end of treatment (range 1-30 months). Liver (n=24), intra-abdominal (n=22) and distant lymph node (n=18) were most common sites of failure, and 18 patients had multiple sites of failure. Intra-abdominal-only failure in patients with complete cytoreduction was seen in only 8 patients. Of patients with liver metastasis at diagnosis, 68% had treatment failure involving the liver. Six of 8 patients (75%) not achieving complete cytoreduction had progression during therapy. Adjuvant irinotecan/temozolomide (I/T) therapy was given in 23 patients (51%). Progression during therapy was noted to be higher in patients with delay in I/T therapy compared to no delay (67% vs. 36%) but patient numbers were small. Status included 29 patients who died from disease, 10 who are alive with disease, 4 lost to follow-up with disease, and only 2 without evidence of disease.

Conclusion: Treatment failure remains a problem in treating DSRCT patients. Improved systemic therapies and local therapies for liver metastases are needed. More study is required for the role of I/T adjuvant therapy.

5:25 pm Paper 029 #2543656

ABDOMINAL DESMOPLASTIC SMALL ROUND CELL TUMOR WITHOUT EXTRAPERITONEAL METASTASES: IS THERE A BENEFIT OF HIPEC AFTER MACROSCOPICALLY COMPLETE SURGERY?

Charles Honoré[1]*; Vincent Atallah*[2]*; Olivier Mir*[3]*; Daniel Orbach*[4]*; Gwenael Ferron*[5]*; Cecile Le Péchoux*[6]*; Philippe Terrier*[7]*; Olivier Glehen*[8]*; Veronique Minard-Colin*[9]*; François Bertucci*[10]*; Jean-Yves Blay*[11]*; Sylvie Bonvalot*[12]*; Axel Le Cesne*[3]*; Paul Sargos*[2]

[1]Surgical Oncology, Gustave Roussy Cancer Campus, Villejuif, France; [2]Radiotherapy, Institut Bergonié, Bordeaux, France; [3]Medical Oncology, Gustave Roussy Cancer Campus, Villejuif, France; [4]Pediatric, Adolescent and Young Adult Oncology, Institut Curie, Paris, France; [5]Surgical Oncology, Institut Claudius Regaud, Toulouse, France; [6]Radiotherapy, Gustave Roussy Cancer Campus, Villejuif, France; [7]Pathology, Gustave Roussy Cancer Campus, Villejuif, France; [8]Surgical Oncology, Hospices civils de Lyon, Lyon, France; [9]Pediatric Oncology, Gustave Roussy Cancer Campus, Villejuif, France; [10]Medical oncology, Institut Paoli Calmette , Marseille, France; [11]Medical oncology, Centre Leon Berard, Lyon, France; [12]Surgery, Institut Curie, Paris, France

Objective: Desmoplastic Small Round Cell Tumor (DSRCT) is a rare disease affecting predominantly children and young adults and for which the benefit of hyperthermic intraperitoneal chemotherapy (HIPEC) after complete cytoreductive surgery (CCRS) remains unknown.

Methods: To identify patients with DSRCT without extraperitoneal metastases (EPM) who underwent CCRS between 1991 and 2015, a retrospective nation-wide survey was conducted by crossing the prospective and retrospective databases of the French Network for Rare Peritoneal Malignancies, French Sarcoma Group, French Reference Network in Sarcoma Pathology, French Sarcoma Clinical Network and French Pediatric Cancer Society.

Results: Among the 107 patients with DSRCT, 48 had no EPM and underwent CCRS. The median peritoneal cancer index (PCI) was 9 (range: 2-27). Among these 48 patients,

38 (79%) had pre- and/or postoperative chemotherapy and 23 (48%) postoperative whole abdominopelvic radiotherapy (WAP-RT). Intraperitoneal chemotherapy was administered to 11 patients (23%): two received early postoperative intraperitoneal chemotherapy (EPIC) and nine HIPEC. After a median follow-up of 30 months, the median overall survival (OS) of the entire cohort was 42 months. The 2-y and 5-y OS were 72% and 19%. The 2-y and 5-y disease-free survival (DFS) were 30% and 12%. WAP-RT was the only variable associated with longer peritoneal recurrence-free survival and DFS after CCRS. HIPEC/EPIC did not influence OS and DFS, although PCI was significantly higher in the HIPEC/EPIC group (16 vs. 9).

Conclusion: The benefit of HIPEC is still unknown and should be evaluated in a prospective trial. The value of postoperative WAP-RT is confirmed.

5:35 pm Paper 030 #2554404

INTRAPERITONEAL RADIOIMMUNOTHERAPY FOR DESMOPLASTIC SMALL ROUND CELL TUMOR: PRELIMINARY RESULTS OF A PHASE I STUDY (CLINICALTRIALS.GOV NCT01099644)

Shakeel Modak[1]*; Michael LaQuaglia*[1]*; Neeta Pandit-Taskar*[2]*; Pat Zanzonico*[3]*; Todd Heaton*[1]*; Jason Lewis*[2]*; Nai-Kong V. Cheung*[1]*; Jorge Carrasquillo*[2]
[1]Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: Desmoplastic small round cell tumor (DSRCT), a rare sarcoma of adolescents and young adults, has a long-term survival of <20% despite aggressive multimodality therapy, warranting a search for novel treatments. The murine monoclonal IgG1 antibody 8H9 recognizes cell surface antigen 4Ig-B7H3, binds to several solid tumors including 96% of DSRCTs with restricted normal tissue reactivity. DSRCT recurrences often present as multifocal peritoneal implants. We hypothesized that IP radioimmunotherapy (RIT) by virtue of prolonged residence time and slow transfer to the circulation, may selectively target IP DSRCT. We tested the hypothesis in a phase I study of IP RIT with radioiodinated 8H9: objectives were evaluation of toxicity, pharmacokinetics (PK), biodistribution and efficacy.

Methods: After debulking surgery, cohorts of 3-6 patients received ^{131}I-8H9 at escalated doses from 30-90mCi/m^2 as a single IP injection. A prior tracer dose of IP 2mCi^{124}I-8H9 was used to acquire PET images and biodistribution data. Toxicity was monitored clinically and biochemically. PK was studied with serial blood draws. Patients were followed for progression-free (PFS) and overall survival (OS).

Results: Thirty DSRCT patients received 30-90mCi/m^2 IP ^{131}I-8H9. Maximum tolerated dose was not reached; there were no dose-limiting toxicities. Adverse events were rare and transient: grade 3 transaminitis (n=1), neutropenia (n=1), and thrombocytopenia (n=1). Blood and peritoneal half-times were 32.5h and 14.6h respectively. Mean projected absorbed doses to blood, kidney, liver, lung and spleen were 0.7, 1.72, 1.92, 0.64 and 1.03 rad/mCi respectively (n=12 patients analyzed). Dehalogenation was insignificant: >80% of ^{131}I remaining protein-bound in blood. The proposed dose for the phase II study was established at 80mCi/m^2. 12/15 (80%) patients with gross residual disease post-surgery progressed after RIT. In contrast, 10/15 patients (67%) who underwent a gross total resection (GTR) plus RIT were disease-free at last follow-up. For patients undergoing GTR+RIT, 2-yr PFS and OS are 50±14% and 83±11%, respectively. Median PFS is 23.4±4 months; median OS has not been reached.

Conclusion: ^{124}I-8H9-directed radioimmuno-PET successfully determined biodistribution and whole-body and organ radiation exposure. ^{131}I-8H9 IP RIT had a satisfactory safety profile. Early survival data in patients treated with RIT after GTR indicate marked improvement in survival compared to historical controls. A phase II trial will commence shortly.

8:00 am – 8:40 am

– OTHER BONE & ST NEOPLASMS – Giant Cell Tumor of Bone

8:00 am Paper 031 #2563920

DENOSUMAB TREATMENT OF INOPERABLE OR LOCALLY ADVANCED GIANT CELL TUMOR OF BONE (GCTB) - MULTICENTER RETROSPECTIVE ANALYSIS OUTSIDE CLINICAL TRIAL

Piotr Rutkowski[1]*; Louie Gaston*[2]*; Aneta Borkowska*[1]*; Silvia Stacchiotti*[3]*; Giacomo Giulio Baldi*[4]*; Emanuela Palmerini*[5]*; Paolo Casali*[3]*; Alessandro Gronchi*[6]*; Michael Parry*[2]*; Hans Gelderblom*[7]*; Stefano Ferrari*[5]*; Andrzej Pienkowski*[1]*; Robert Grimer*[2]
[1]Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland, Warszawa, Poland; [2]The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, United Kingdom; [3]Sarcoma Unit, Medical Oncology, Istituto Nazionale Tumori, Milan, Italy; [4]UO Oncologia Medica, Nuovo Ospedale di Prato "S.Stefano", Prato, Italy; [5]Chemotherapy Unit, Istituto Ortopedico Rizzoli, Bologna, Italy; [6]Sarcoma Unit, Surgery, Istituto Nazionale Tumori, Milan, Italy; [7]Department of Medical Oncology, Leiden University Medical Center, Leiden, Netherlands

Objective: This is retrospective study evaluating a large series of GCTB patients (pts) treated with denosumab(D) in routine practice in 5 European reference centers.

Methods: 100 pts with histologically confirmed, locally advanced/metastatic GCTB treated with D outside clinical trials (2011-2016) were included. Treatment was conducted until tumor progression, unacceptable toxicity or tumor resection if feasible.

Results: Primary tumor was located in lower limb (46%; n=46) -mostly in tibia (20.4%), in pelvis/axial skeleton (28%; n=28) and in upper limb (26%; n=26). 75(75%) pts had primary tumors, 25(25%) recurrent tumors after previous surgery. 23/23 analyzed cases showed H3F3A mutation. All cases were evaluated by multidisciplinary team before start of D therapy. 79 pts had locally advanced tumors (mostly with soft tissue involvement +/-penetration to the joint- grade 3 according to Campanacci), not amenable for limb-sparing surgery or with high risk of tumor recurrence. 18 pts were assessed as definitively unresectable (18%) – mostly in axial location, 3 were metastastic. The average D treatment duration was 7 months (median number of cycles 9). 58 pts were surgically treated after D, 27 had wide en-block resection (+ implantation of prosthesis in 15 pts), the other pts had intralesional curettage. Progression after surgical treatment was observed in 7 patients, six of them after intralesional curettage, 4 received rescue D. Moreover progression was observed in 3 pts during D treatment, 2 of them had applied radiotherapy in the past. One-year progression-free survival was 91%. The median number of D doses in group of pts operated after neoadjuvant therapy was 9 (range 4-16), 15 pts had received D postoperatively. In pts, who had not yet had surgery (or those definitively unresectable), and continued on D, the median number of D doses was 16. Treatment was well tolerated with only 3 cases of grade 3 toxicity.

Conclusion: Our study confirms that D is active in both neoadjuvant and in advanced setting, and it became the standard therapy in multidisciplinary management of GCTB with excellent short-term tolerability. Our data suggest that neoadjuvant therapy with D may become the option for treatment of initially locally advanced tumors to facilitate complete surgical resection or avoid mutilating surgery, but the risk of recurrences after curettage of GCTB following D raises the question about the preoperative treatment duration and rescue D immediately after surgery or at time of progression/relapse.

8:40 am – 9:20 am

– OTHER BONE & ST NEOPLASMS – Pigmented Villonodular Synovitis (PVNS)

8:40 am Paper 032 #2570093

PRELIMINARY RESULTS ON THE INTERNATIONAL MULTICENTER RETROSPECTIVE TENOSYNOVIAL GIANT CELL TUMOUR DATABASE

Emanuela Palmerini[2]*; Monique Mastboom*[3]*; Floortje Verspoor*[4]*; Hans Gelderblom*[3]*; Silvia Stacchiotti*[5]*; Primo Daolio*[6]*; Eric Staals*[1]*; R G Maki*[7]*; Marta Fiocco*[3]*; Alessandro Gronchi*[5]*; Stefano Ferrari*[2]*; Piero Picci*[8]*; Bart Schreuder*[4]*; Michiel van de Sande*[3]
[1]Clinica 3 - Musculoskeletal Oncology, Istituto Ortopedico Rizzoli Bologna, Bologna, Italy; [2]Chemotherapy, Istituto Ortopedico Rizzoli, Bologna, , Italy; [3]LUMC, Leiden, Netherlands; [4]Radboud UMC, Nijmegen, Netherlands; [5]INT, Milan, Italy; [6]Istituto Gaetano Pini, Milan, Italy; [7]Mount Sinai School of Medicine, New York, NY, USA; [8]Experimental Oncology Laboratory, Istituto Ortopedico Rizzoli, Bologna, Italy

Objective: Tenosynovial Giant Cell Tumour(TGCT), previously named Pigmented Villonodular Synovitis(PVNS), is a rare, locally aggressive neoplasm that can either present as a single nodule(nodular-type), or as multiple nodules(-diffuse-type) along a synovial layer or tendon sheath.

Current literature consists relatively small cohort studies containing inhomogeneous data. Our goal is to set up a large retrospective multicenter cohort to evaluate current treatment protocols, as well as risk factors for progressive disease and local recurrence (LR).

Methods: (Un)published data of individual patients from 5 tertiary orthopedic oncology centers included 407 (239 female, median age at operation 34.7years) TGCT cases treated between 1990 and 2014 (minimal follow-up 2 yrs): 276 affected knee-joints (69% are diffuse-type), 131 other joints (64% are diffuse-type). TGCT of fingers and toes are excluded.
Median follow-up time overall is 6.39 (95%CI 5.19-7.59) years.
A multivariate cox-regression model with risk factors: gender(male/female), age at first operation(years), surgical treatment(arthroscopic/open), affected joint(knee/other) and TGCT-type(diffuse/nodular) is estimated. LR free survival at 2-and 5-years is calculated from the time of 1st surgical resection to 1st LR.

Results: Total number of 1st LR is 157(39%); Knee: diffuse-type 103(54%) and nodular-type 13(15%); Other affected joints: diffuse-type 30(35%) and nodular 7(15%). Mean time to LR is 11.68(95%CI 9.57-13.80)years.
LR was significantly more frequent in male patients (p=0.018) and in diffuse-type(p=0.0001).

Median time to LR in males 5.16 (95%CI 3.10-7.20) years, in females 16.05 (95%CI 4.82-27.36) years (p=0.017); after arthroscopy 5.00(95%CI 2.36-7.64) years, after open-resection 10.56(95%CI 7.52-13.53) years (p=0.089).

Local recurrence free survival at 2-and 5-years is 0.74(95%CI 0.69-0.80) and 0.59(95%CI 0.54-0.65) respectively. At final follow-up 343 patients(84%) show no evidence of disease (49 alive with disease, 5 death of other disease, 10 lost).

Conclusion: Preliminary results on the international multicenter TGCT database show high risk of first local recurrence, especially for diffuse-type. Open resection is advocated, especially in young patients with TGCT of the knee and in diffuse or recurrent cases.

A multicenter international database, to better determine risk factors of recurrence, is essential for proper treatment planning in an era of new systemic and (neo)adjuvant treatment possibilities.

9:20 am – 10:25 am
– OTHER BONE & ST NEOPLASMS –
Desmoid Fibromatosis

9:20 am Paper 033 #2549467
AGGRESSIVE FIBROMATOSIS RESPONSE TO TAMOXIFEN: MRI FEATURES WITH SYMPTOMATIC CORRELATION - THE ROYAL MARSDEN EXPERIENCE
***Indu Mitra**; Zoltan Szucs; Michela Libertini; Cyril Fisher; Khin Thway; Ian Judson; Aisha Miah; Van der Graaf Winette; Eleanor Moskovic; Christina Messiou; Charlotte Benson; Robin Jones*
Royal Marsden Hospital, London, United Kingdom

Objective: Data on efficacy of tamoxifen use in aggressive fibromatosis (AF) is limited, consisting of small case series. The aim of this study is to assess treatment response to tamoxifen in AF in a large series, including MRI and symptom correlation.

Methods: A retrospective study was undertaken at the RMH, London. All adults treated with tamoxifen for histologically confirmed AF between 2007-2014 were identified. Inclusion criteria included a minimum of one baseline and one follow up MRI. MR images were reviewed by a soft tissue sarcoma radiologist, who recorded size and response by RECIST 1.1 and T2 signal changes. Symptom changes were obtained from electronic records.

Results: 35 patients were identified (21F, 14M, mean age 41, age range 26-68). Average duration of tamoxifen use was 304 days. 17 patients were also treated with naproxen. 3 patients did not have a baseline MR for comparison and were excluded. Of the remaining 32 patients follow up MRI demonstrated partial response in 1(3%), stable disease in 22(69%) and progressive disease in 9(28%) patients. In 11 of the 32 cases (34%) there was no change in symptoms; 9 had stable disease and 2 progressive disease. 12 patients (38%) reported an improvement in symptoms: 1 had partial response, 7 stable disease and 4 progressive disease. 9 patients (28%) reported worsening symptoms: 6 had stable disease and 3 had progressive disease. Of all 32 patients, 8 (25%) demonstrated a decrease in T2 signal, and of these 3 reported no change in symptoms, 3 had symptom improvement and 2 worsening symptoms. All reported symptom improvement occurred within 6 months of starting tamoxifen. Pre-baseline imaging was available for 14 of the 32 patients. In 13 patients disease was increasing in size before starting tamoxifen: in 10 the fibromatosis continued to increase, in 2 it stabilised and in 1 it showed a decrease in size.

Conclusion: Disease shrinkage is rare with tamoxifen treatment. Symptom improvement was seen in 38% but concomitant naproxen treatment may have contributed.

There was a poor correlation between MRI changes in volume, T2 signal changes and symptoms in this series, which illustrates the difficulty of reporting treatment efficacy in this disease.

9:30 am Paper 034 #2544509

IMATINIB INDUCES SUSTAINED PROGRESSION ARREST IN RECIST PROGRESSIVE DESMOID TUMORS - FINAL RESULTS OF A PHASE II STUDY OF THE GERMAN INTERDISCIPLINARY SARCOMA GROUP (GISG)

Bernd Kasper[1]*; Viktor Gruenwald*[2]*; Peter Reichardt*[3]*; Sebastian Bauer*[4]*; Michaela Sommer*[1]*; Geraldine Rauch*[5]*; Florian Haller*[6]*; Peter Hohenberger*[1]
[1]Interdisciplinary Tumor Center, Sarcoma Unit, Mannheim University Medical Center, Mannheim, Germany; [2]Department of Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany; [3]Sarcoma Center Berlin-Brandenburg, HELIOS Klinikum Berlin-Buch, Berlin-Buch, Germany; [4]Sarcoma Center, West German Cancer Center, Essen, Germany; [5]Institut of Medical Biometry and Informatics, University of Heidelberg, Heidelberg, Germany; [6]Institute of Pathology, University of Erlangen-Nuremberg, Erlangen, Germany

Objective: Desmoid tumors describe a rare monoclonal, fibroblastic proliferation characterized by an often unpredictable clinical course. Surgery is one therapeutic option for progressing patients, except if mutilating and associated with considerable function loss. Different systemic treatment approaches have been investigated for advanced disease and promising results could be demonstrated using imatinib.

Methods: Therefore, we initiated a phase II trial within the GISG evaluating imatinib to induce progression arrest in the subset of desmoid tumor patients being RECIST progressive, not amenable to surgical resection with R0 intent or accompanied by unacceptable function loss (NCT01137916). 38 patients (median age 44 years [range: 19 - 80]; 68 % female; 90 % ECOG 0) were treated with a daily dose of 800 mg imatinib planned over two years - the longest treatment period published so far. The progression arrest rate after six months of imatinib treatment (PAR_{6mo}) was the primary endpoint. Patients showing disease progression under imatinib could be treated with nilotinib 800 mg daily until subsequent RECIST progression. Accrual started in July 2010 in four GISG centers and finalized in September 2013.

Results: The final analysis for the primary endpoint in the full analysis set revealed a PAR_{6mo} of 65 %. Subsequent progression arrest rates at 12, 15, 18, 21 and 24 months were 65 % [90 % CI: 49-76], 61 % [CI: 46-74], 61 % [CI: 46-74], 54 % [CI: 39-67] and 54 % [CI: 39-67], respectively. None of the patients died within the study observational period. Best reported response was six partial responses at 21 months revealing an overall response rate of 16 %. Results on the mutational analysis identified a patient cohort characterized by an aggressive clinical course (*Ann Surg Oncol 2016; 23: 1924-7*). Interestingly, eight patients treated with nilotinib as 2nd line therapy after progression or imatinib intolerance demonstrated a PAR at 3 months of 88 % (7/8); no more disease progressions occurred until end of study at 24 months. In general imatinib adverse events were mild to moderate; results on quality of life will be presented.

Conclusion: Imatinib induces sustained progression arrest in RECIST progressive desmoid tumor patients. In addition, nilotinib had the potential to stabilize desmoid tumor growth after treatment failure with imatinib.

9:40 am Paper 035 #2566869

LONG TERM FOLLOW UP OF DESMOID FIBROMATOSIS TREATED WITH PF-03084014, A GAMMA SECRETASE INHIBITOR

Victor Manuel Villalobos*; Antonio Jimeno; Lia Gore; Anthony Elias; Brianna Hoffner; Wells Messersmith*
Medical Oncology, University of Colorado Denver, Aurora, CO, USA

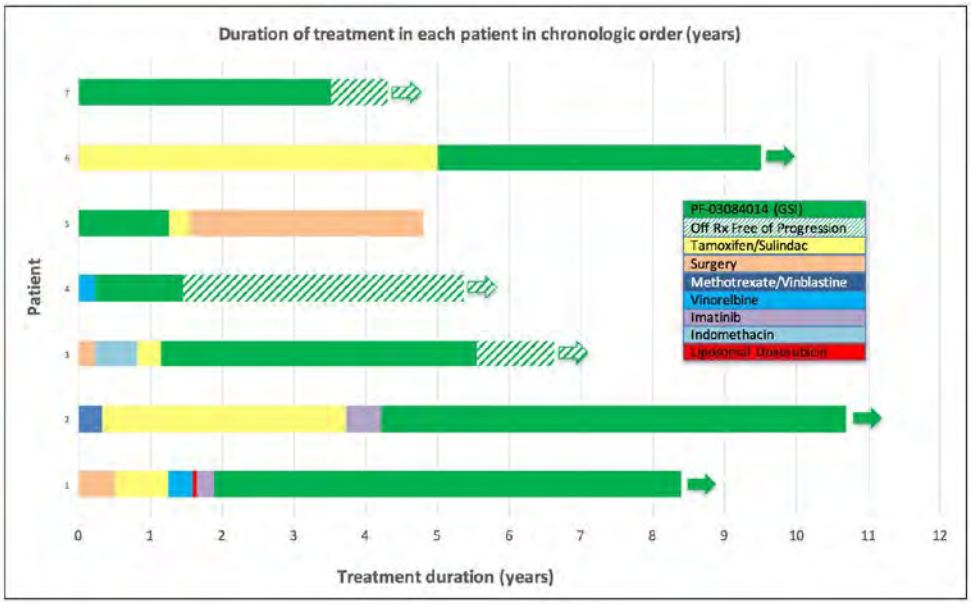
Objective: Desmoid fibromatosis is a fibroblastic “benign” neoplasm with high risk for local recurrence. These tumors are often driven by aberrations within the WNT signaling pathway; 85% of tumors exhibiting mutations in beta-catenin and others harboring mutations in APC. We review long term follow up of patients treated with an oral gamma secretase inhibitor, PF-03084014, as part of a phase-I dose finding study.

Methods: PF-03084014 was administered at doses ranging from 20 to 330 mg BID. Study drug was continued until disease progression, unacceptable toxicity, a treatment delay of >2 weeks or more than two dose reductions in the absence of clinical benefit. Tumor assessments were performed using CT/MRI at 4 weeks, at cycle 3, and every 2 cycles thereafter. After cycle 9, patients were scanned every 3 months until disease progression and beyond.

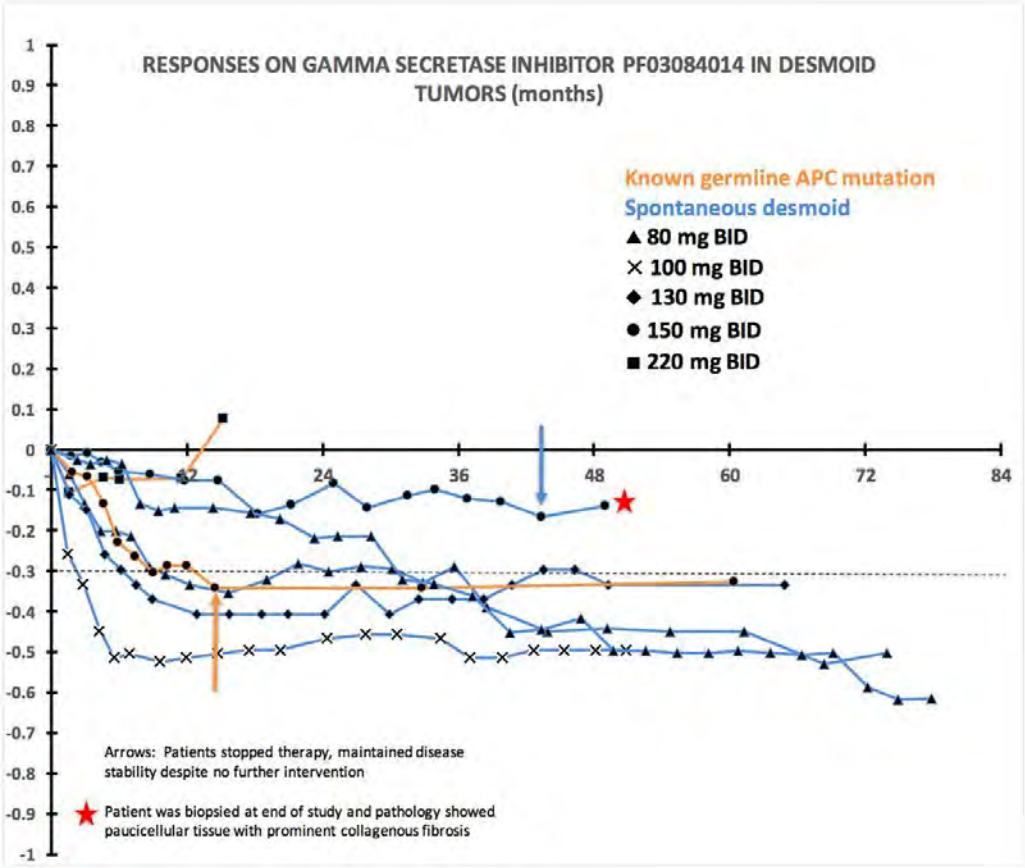
Results: Of the 64 patients treated on the initial study, 7 patients with progressive desmoid fibromatosis were treated at UC-Denver from Dec-2009 through Jun-2016. 71.4% of desmoid patients achieved a partial response (PR) with median time to achieving response of 8.7 mo. (5.9-30.3 mos.). All patients who achieved a PR continue to maintain responses between 47.4 – 67+ months with persistent disease control. Three of these patients stopped treatment yet continue off therapy, free of progression between 9 - 47 months. One patient had stable disease for 50+ months with 17% decrease in tumor volume and

a biopsy performed at end of study showed paucicellular collagenous fibrosis with no active desmoid. In addition, in patients who had MRI scans, we observed a dramatic decrease in T2 pre-contrast and T1 post-contrast enhancement of the tumor. The one patient with progressive disease had stable measurable disease but came off due to increase tumor pain. Effective treatment doses ranged from 80 -220 mg dosed orally twice daily.

Conclusion: The gamma-secretase inhibitor, PF-03084014, proved highly effective in treating desmoid tumors with an objective response rate of 71.4% in this small cohort of patients. PF-03084014 exhibits excellent activity even at relatively low doses (80mg BID) with high tolerability leading to prolonged responses and/or stability even long after therapy was halted. Further, response assessment by size criteria alone may not adequately characterize the depth of pathologic response, whereas MRI based assessments of T2 pre- and T1 post-contrast enhancement may more appropriately gauge response and should be prioritized in this tumor type.



This bar graph show the representative efficacy of PF-03084014 compared to other prior therapies. Additionally it demostrates the prolonged efficacy even when therapy was stopped.



This spider plot shows RECIST response rate of 71.2%. However, the patient with prolonged stable disease (red star) had complete loss of enhancement on MRI, despite lack of shrinkage, and a post treatment biopsy showed paucicellular tissue consistent with dramatic pathologic response to disease. If included as a response, this would raise response rate to 85.7%.

9:50 am Paper 036 #2562590

SORAFENIB TARGETS THE MAPK/ERK PATHWAY AND RECEPTOR TYROSINE KINASES AND INHIBITS TUMOR GROWTH BY INDUCING TWO DIFFERENT DEATH PATHWAYS IN DESMOID TUMOR CELLS

Danielle De Almeida Braggio[1]*; Abeba Zewdu*[1]*; Gonzalo Lopez*[1]*; Kara Batte*[1]*; Lucia Casadei*[1]*; Nanda Siva*[6]*; O. Hans Iwenofu*[2]*; Anne M Strohecker*[3]*; Dina Lev*[4]*; Raphael Pollock*[5]

[1]CCC, The Ohio State University, Columbus, OH, USA; [2]Department of Pathology, The Ohio State University, Columbus, OH, USA; [3]Department of Molecular Virology, Immunology, and Medical Genetics, The Ohio State University, Columbus, OH, USA; [4]Surgery B, Sheba Medical Center, Tel Aviv, Israel; [5]Surgical Oncology, The Ohio State University, Columbus, OH, USA; [6]Department of Chemical and Biomedical Engineering, West Virginia University Statler College of Engineering and Mineral Resources, Morgantown, WV, USA

Objective: Sorafenib is a multikinase inhibitor that targets the MAPK/ERK pathway and several receptor tyrosine kinases, including vascular endothelial growth factor receptor 2 (VEGFR2) and platelet-derived growth factor receptor (PDGFR). Recently, the antitumor activity of sorafenib has been clinically demonstrated in desmoid tumor (DT) patients. However, no *in vitro* investigations have been performed to elucidate the sorafenib mechanism of action, so we investigated the mechanism of sorafenib-induced death in desmoid tumor cells.

Methods: The expression/activation of pro-angiogenic proteins and MAPK/ERK pathway were analyzed in DT cell strains using western blot. A panel of DT cells was exposed to increasing concentrations of sorafenib *in vitro* and evaluated for cell survival, cell cycle, and apoptosis. To assess autophagic dynamics, autophagy flux was measured with bafilomycin, an inhibitor of late phase autophagy. The autophagic responsiveness between DTs harboring different *CTNNB1* mutations was compared under autophagy enhancing conditions.

Results: Sorafenib down-regulated the activation of PDGFR-β and ERK, but not MEK. Sorafenib also markedly inhibited proliferation of DT cells. No difference was observed in the cell cycle. Interestingly, the induction of apoptosis was only observed in *CTNNB1* T41A mutated and wild-type DTs. Immunoblotting of LC3B in S45F mutated DTs showed that sorafenib (10uM) significantly increased LC3-II expression, suggesting that this concentration of sorafenib alters autophagy in these cells. Chemical inhibition of autophagy by bafilomycin led to a significant decrease of sorafenib-induced cell death in DT cells harboring the *CTNNB1* S45F mutation, whereas no effect was seen in T41A mutated DT cells or wild-type DTs, indicating that autophagy may promote cell death in the specific setting of S45F mutated DTs.

Conclusion: Our results suggest that the antitumor activity of sorafenib in DTs cells may happen by acting directly on the tumor (inhibition of MAPK/ERK pathway) and on tumor angiogenesis (inhibition of PDGFR-β signaling). Moreover, our results show that the cell death response to sorafenib differs when comparing DTs harboring the *CTNNB1* S45F mutation and T41A mutated or wild-type DTs. Caspase 3/7 seems to have a key role in triggering sorafenib-induced apoptosis in T41A mutated or wild-type DTs, whereas sorafenib-induced cell death in S45F mutated DTs appears to be associated with altered autophagy signaling pathways.

Effective concentration (EC50) values of sorafenib against normal cell lines and 14 DT cell strains

Cell line / strain	EC 50 values (μM)
NDF-α	ND
HuMSC	95.18
OSU-Des9	6.05
OSU-Des13	9.80
OSU-Des23	7.12
OSU-Des23.2	6.37
OSU-Des76	3.95
OSU-Des91	7.16
OSU-Des93	6.95
OSU-Des148	6.50
OSU-Des157	7.92
OSU-Des168	6.69
Desm4	6.87
Desm8	7.26
Desm14	7.44
Desm38	7.02

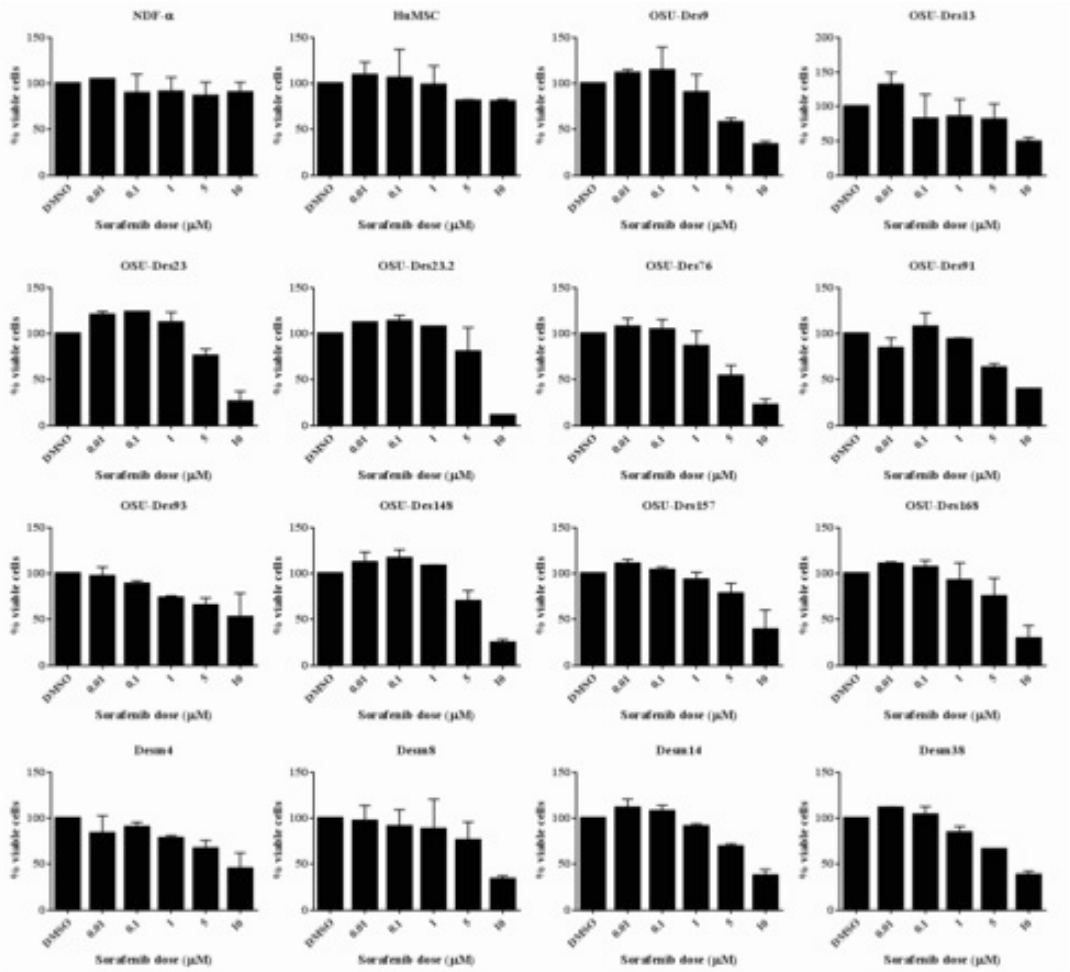


Figure 2. Treatment with Sorafenib inhibits cell proliferation. Desmoid tumor cells strains were exposed to the indicated concentrations of Sorafenib. The proliferation of desmoid cells is significantly inhibited.

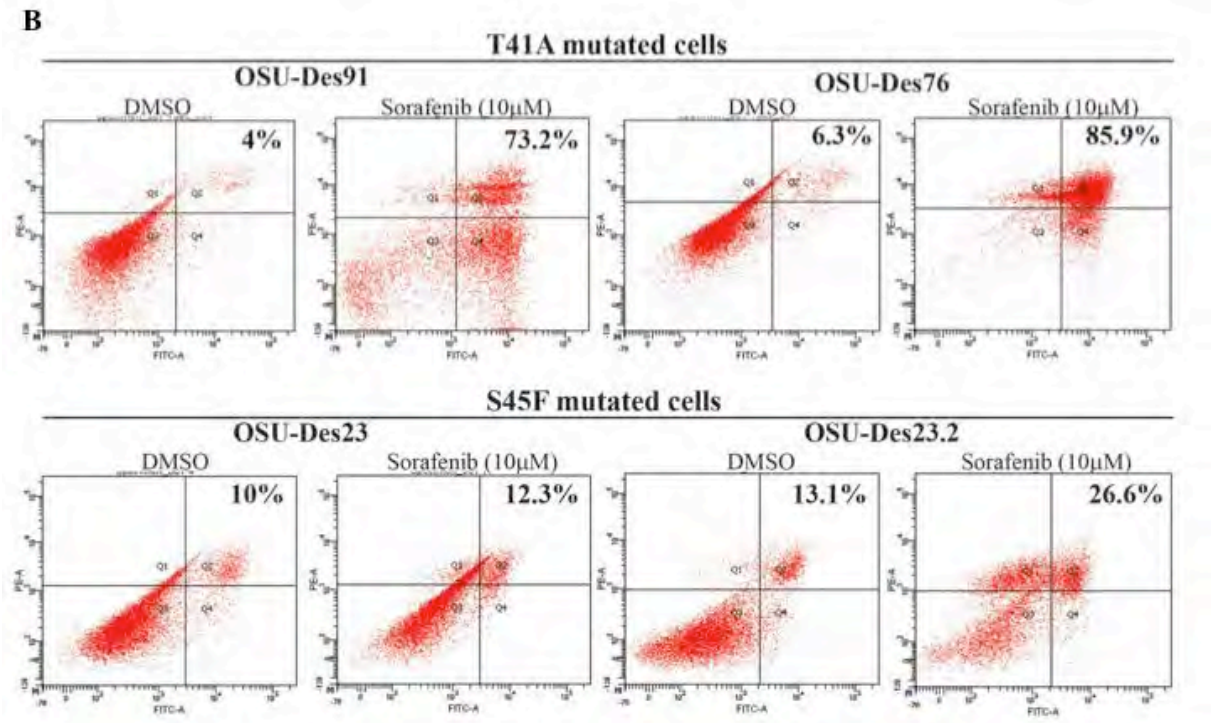


Figure 3. Sorafenib induces different mechanisms of cell death between desmoid cells. Cleaved caspase was analyzed by Incucyte Zoom (A). Apoptosis (Annexin V / PI) was analyzed by flow cytometry (B).

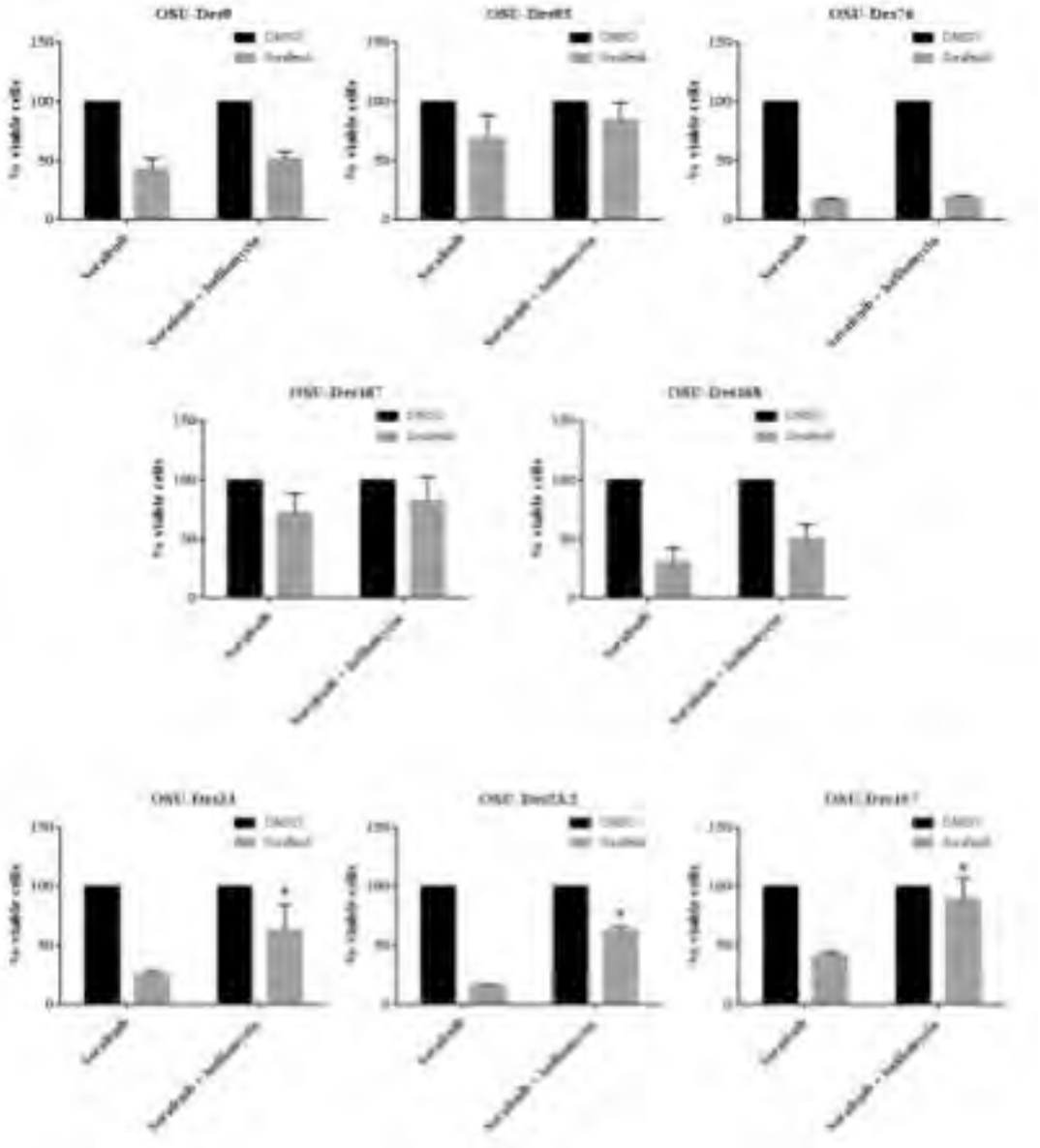


Figure 4. Bafilomycin reduces sorafenib anti-proliferative effects.

Figure 4.
Bafilomycin reduces sorafenib anti-proliferative effects. Bafilomycin treatment decreased sorafenib-induced cell death in DT cells harboring the *CTNNB1* S45F mutation, but not in T41A mutated DT cells or wild-type DTs.

10:50 am – 11:30 am

– OTHER BONE & ST NEOPLASMS – Extraskeletal Osteosarcoma

10:50 am Poster View 5 #2565699

THE ROLE OF CHEMOTHERAPY AND RADIATION IN SOFT TISSUE OSTEOSARCOMA

Marilyn Heng[2]*; Takafumi Ueda*[3]*; John Healey*[4]*; Peter Rose*[13]*; Peter Ferguson*[1]*; Abha Gupta*[5]*; Albiruni Abdul Razak*[5]*; Ginger Holt*[6]*; David Blau*[8]*; Xiaohui Niu*[7]*; Nicholas Bernthal*[9]*; Sophie Mottard*[10]*; Darin Davidson*[11]*; Robert Turcotte*[12]*; Jay Wunder*[1]
[1]Orthopaedic Surgery, University of Toronto, Toronto, ON, Canada; [2]Orthopaedic Surgery, Massachusetts General Hospital, Boston, MA, USA; [3]Japanese Musculoskeletal Oncology Group, Osaka, Japan; [4]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [5]Medical Oncology, University of Toronto, Toronto, ON, Canada; [6]Vanderbilt University, Nashville, TN, USA; [7]Peking University, Beijing, China; [8]Hopital Cochin, Paris, France; [9]UCLA, Los Angeles, CA, USA; [10]Hopital Maisonneuve-Rosemont, Montreal, QC, Canada; [11]University of Washington, Seattle, WA, USA; [12]McGill University, Montreal, QC, Canada; [13]Mayo Clinic, Rochester, MN, USA

Objective: The role of chemotherapy in bone osteosarcoma and of radiation in soft tissue sarcoma are well defined. However, soft tissue osteosarcoma (STO) is a rare entity which lacks consensus on the role of similar adjuvants. Our objective was to describe the disease outcomes in a large series of STO and to investigate for an association between use of chemotherapy or radiation with disease recurrence and cause-specific survival.

Methods: Retrospective review of 16 international institutions identified patients 18yrs+ treated for STO from 1971-2015. Patient and tumor characteristics, treatment, complications, local/systemic recurrence, and survival were reviewed. Chi-square tests and multiple logistic regression analyzed for associations with local or systemic recurrence. Survival analysis with Kaplan-Meier and Cox proportional hazards regression was performed.

Results: 330 pts median aged 59yrs and 57% male presented with mainly deep (82%) and localized disease (86%). 320 pts (97%) underwent surgery–28 treated with amputation (9%); 292 received limb-salvage (88%). 94 pts (29%) received chemotherapy; 61 (18%) received radiation, and 67 (20%) had both. 26% got a complication.

Of 280 pts with localized disease who had definitive surgery,19% developed a local recurrence and 39% developed a systemic one. Median time to recurrence was 7.9 months. Margin status (Micro+ p=0.004; Gross+ p<0.001) and radiation (p=0.03) were significantly associated with local recurrence. Chemotherapy was not independently

Predictors of Local and Systemic Recurrence

Outcome	Variable		OR	95% CI	p-value
Local Recurrence					
	Radiation	No Yes	Ref 0.45	- 0.21 – 0.91	- 0.03 *
	Chemotherapy	No Yes	Ref 1.05	- 0.54 – 2.05	- 0.88
	Margin Status	Negative Micro + Gross +	Ref 3.9 14.4	- 1.49 – 9.73 3.79 – 70.7	- 0.004 * <0.001 *
	Depth	Superficial Deep	Ref 2.19	- 0.83 – 7.0	- 0.14
	Maximal Diameter	(cm)	1.02	0.99 – 1.05	0.14
Systemic Recurrence					
	Chemotherapy	No Yes	Ref 0.77	- 0.46 – 1.31	- 0.34
	Radiation	No Yes	Ref 1.50	- 0.88 – 2.55	- 0.14
	Margin Status	Negative Micro + Gross +	Ref 1.22 1.21	- 0.50 – 2.90 0.33 – 4.54	- 0.66 0.77
	Depth	Superficial Deep	Ref 2.58	- 1.18 – 6.13	- 0.02 *
	Maximal Diameter	(cm)	1.07	1.03 – 1.12	0.001 *

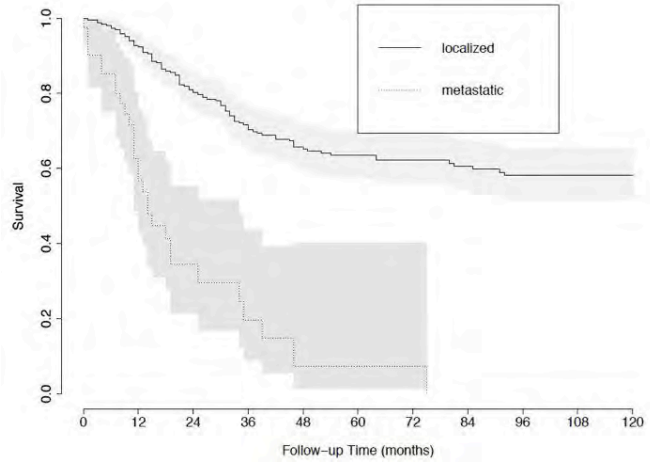
Multiple Logistic Regression analysis controlling for radiation, chemotherapy, margin status, depth, and size of tumor

associated with systemic recurrence (p=0.34); only depth (p=0.02) and tumor size (p=0.001) were significant.

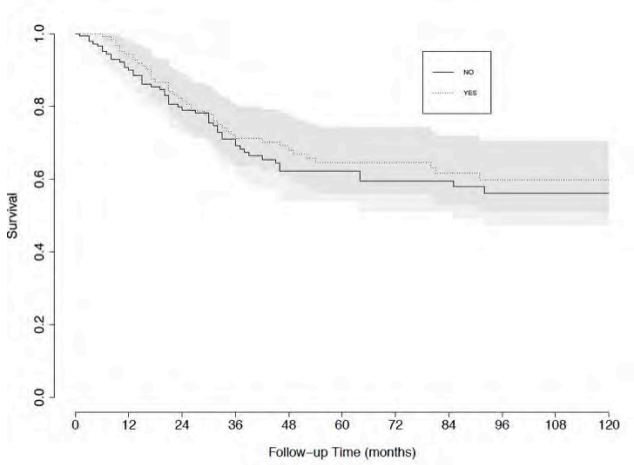
Cause-specific 5-year survival was 58% (64% and 7% for pts presenting with localized and metastatic disease, respectively). For 280 pts with localized disease undergoing resection, adding chemotherapy (p=0.36), radiation (p=0.09) or both adjuvants (p=0.25) had no difference in survival. Only age (p=0.02), deep tumors (p<0.001) and larger size (p<0.001) were independent predictors of mortality.

Conclusion: Our series of 330 STO patients is one of the largest to date. 64% 5-yr survival in those presenting with localized disease is of the higher reported. Our results suggest that STO behaves more like soft tissue sarcoma than conventional bone osteosarcoma. While radiation was significantly associated with decreased local recurrence, chemotherapy was not associated with differential survival in patients with localized disease and thus should only be considered with careful multi-disciplinary discussion.

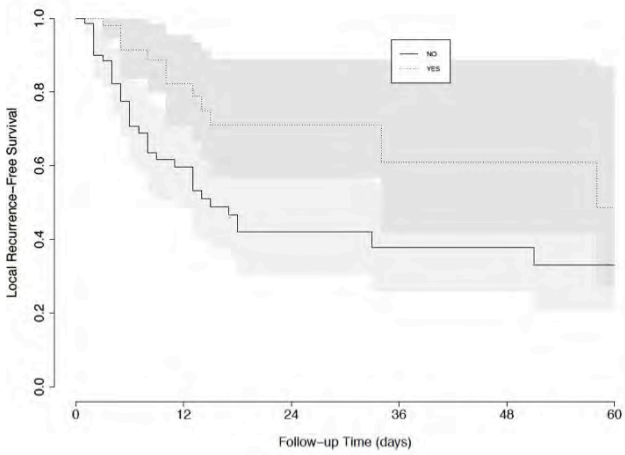
Survival Based on Presenting Status



Survival Based on Chemotherapy



Local Recurrence Based on Radiation



Predictors of Disease-Specific Time to Mortality

Variable		HR	95% CI	p-value
Age	(yrs)	1.02	1.00 – 1.04	0.02 *
Sex	Female Male	Ref 1.09	- 0.70 – 1.69	- 0.69
Depth	Superficial Deep	Ref 4.87	- 1.93 – 12.3	< 0.001 *
Maximal Diameter	(cm)	1.02	1.01 – 1.02	< 0.001 *
Surgery	Amputation Limb Salvage	Ref 0.90	- 0.46 – 1.77	- 0.77
Margin status	Negative Micro + Gross +	Ref 1.77 1.94	- 0.94 – 3.35 0.77 – 4.91	- 0.08 0.16
Radiation	No Yes	Ref 1.13	- 0.74 – 1.73	0.56
Chemotherapy	No Yes	Ref 0.83	- 0.54 – 1.30	0.42

Multiple Cox Proportional Hazards Regression analysis controlling for age, sex, type of surgery, depth of tumor, size of timor, margin status, radiation and chemotherapy

10:50 am Poster View 6 #2554781

EXTRASKELETAL OSTEOSARCOMA: A RETROSPECTIVE ANALYSIS OF 28 PATIENTS TREATED AT A SINGLE INSTITUTION

Haotong Wang[1]*; Ruoyu Miao*[1]*; Alex Jacobson*[1]*; Saveli Goldberg*[1]*; David Harmon*[2]*; Edwin Choy*[2]*; Gregory Cote*[2]*; Francis Hornicek*[3]*; Petur Nielsen*[4]*; Joseph Schwab*[3]*; Kevin Raskin*[3]*; Thomas F DeLaney*[1]*; Yen-Lin Chen*[1]

[1]Radiation Oncology, MGH, Billerica, MI, USA; [2]Medical Oncology, MGH, Boston, MA, USA; [3]Surgical Oncology, MGH, Boston, MA, USA; [4]Pathology, MGH, Boston, MA, USA

Objective: Extraskeletal osteosarcoma is a very rare soft-tissue sarcoma (<1%). There is very little known about this tumor. The purpose of this retrospective study is to review the clinical outcomes of patients diagnosed with extraskeletal osteosarcoma.

Methods: The clinicopathologic features, treatment methods, and disease outcomes were reviewed retrospectively for 28 patients with extraskeletal osteosarcoma treated between 1960 and 2015 at a single institution. Overall survival (OS) and recurrence-free survival (RFS) were estimated using the Kaplan-Meier method.

Results: The mean age was 60.5 (range: 22 - 85), median follow-up time was 26 months, (range 1 - 213 months) and 10 (36%) of patients were female. Patients presented with AJCC stage 2 (10, 36%), Stage 3 (14, 50%), Stage 4 (3, 11%), and unstaged (1, 4%). Tumor sites included lower extremity (17, 61%), abdomen/pelvis/peritoneum/gastrointestinal tract (soft tissue) (4, 15%), upper extremity / shoulder (2, 7%), trunk (4, 14%), and thorax (1, 4%). 21 (75%) patients presented with primary tumor larger than 5cm. 23 (82%) patients had high grade (Grade 3) tumors. Patients were treated according to the following treatment categories: No Surgery & No radiation (RT) (1, 4%), Surgical Treatment, No RT (11, 39%), Preoperative RT -> Surgery (9, 32%), Preoperative RT -> Surgery -> Postoperative RT (2, 7%), Surgery -> Postoperative RT (3, 11%). 16 (57%) patients received chemotherapy: pre-operatively (2, 7%), post-operatively (7, 25%) and both pre- and post-operatively (4, 14%). Methotrexate-Adriamycin-Cisplatin is the most common regimen. 1-year OS and RFS were 68% (95% CI: 58%-78%) and 59% (95% CI: 49%-69%), respectively. 11 (39%) patients had recurrence during follow-up, among which, three had local recurrence, seven had distant metastasis and one had progression of disease.

Conclusion: Extraskeletal osteosarcoma is an aggressive tumor with a high risk of recurrence. Further studies are needed to determine which treatments are associated with better survival.

10:50 am Poster View 7 #2555544

ADJUVANT CHEMOTHERAPY FOR PATIENTS WITH EXTRASKELETAL OSTEOSARCOMA

Shigeki Kakunaga[1]*; Toru Wakamatsu*[2]*; Hidetatsu Otani*[3]*; Kenichiro Hamada*[2]*; Norifumi Naka*[2]*; Nobuhito Araki*[3]*; Ikuo Kudawara*[1]*; Takafumi Ueda*[1]*; Yasuaki Aoki*[4]*; Hideki Yoshikawa*[2]

[1]Osaka National Hospital, Osaka, Japan; [2]Osaka University, Suita, Japan; [3]Osaka Medical Center for Cancer, Osaka, Japan; [4]Himeji Red Cross Hospital, Himeji, Japan

Objective: Extraskeletal osteosarcoma is a rare malignant neoplasm accounting for about 1% of all soft tissue sarcoma. It typically occurs in late adults and the prognosis is very poor. Diagnosis is difficult and often inadequate surgery is performed or there is delay in referral to sarcoma center. Prognosis has improved with the introduction of chemotherapy, but its role is still controversial. We retrospectively reviewed the clinical outcome of extraskeletal osteosarcoma treated at our institute.

Methods: We identified 17 patients with extraskeletal osteosarcoma treated at our institute between 1992 and 2012. Gender was male 9, female 8; age at presentation was 25-79 years (median 60 years); site of tumor was thigh 4, chest wall 2, forearm 2, shoulder girdle 2, retroperitoneum 2, buttock 2, lower leg 2, upper arm 1. Disease AJCC stage was II 4, III 10, IV 3. Six patients had inadequate treatment before referral. Adjuvant chemotherapy, consisting mainly of doxorubicin and ifosfamide was administered to 12 patients. For statistical analysis, the following variables were considered: disease stage at presentation, inadequate initial treatment, adjuvant chemotherapy.

Results: Median follow-up period was 36 months (range 1-138 months). At last follow-up, the clinical outcome was CDF 5, NED 2, DOD 10. Five patients had local recurrence (mean 27 months after treatment), and 9 patients developed metastasis (mean 17 months after treatment). The 5 year overall survival (5YOS) for all patients was 41.2%. The 5YOS for stage II, stage III and stage IV patients were 75%, 40%, and 0% respectively. Patients with inadequate initial treatment had a 5YOS of 16.7% compared with 54.1% for patients treated systematically. Patients who received chemotherapy had a 5YOS of 46.2% compared with 25% for those who did not receive chemotherapy.

Conclusion: Extraskeletal osteosarcoma is a rare malignant neoplasm with very poor prognosis. The prognosis improved with adjuvant chemotherapy and adequate wide resection surgery in our study. Diagnosis is difficult therefore inadequate surgery or delay in treatment is common. Due to the rarity of extraskeretal osteosarcoma, a multi-institutional study is needed to clarify the role of chemotherapy in treatment of this tumor.

1:30 pm – 2:05 pm

– GASTROINTESTINAL STROMAL TUMORS (GIST) –
Surgery of Residual Disease to TKIs

1:30 pm Paper 037 #2567795

SURGICAL COMPLEXITY SCORE PREDICTS MORBIDITY FOLLOWING SURGERY FOR METASTATIC GASTROINTESTINAL STROMAL TUMOR (GIST) ON TYROSINE KINASE INHIBITOR (TKI) THERAPY

***Mark Fairweather**; George Li; Monica Bertagnolli; Chandrajit Raut*
Surgery, Brigham and Women's Hospital, Boston, MA, USA

Objective: While TKIs remain the mainstay treatment for patients with metastatic GIST, metastasectomy has been shown to be effective in a select group of patients (pts). The potential benefit of surgery must be balanced against risks associated with a challenging operation that often involves multivisceral resection. While survival data after metastasectomy are available, data predictive of morbidity are not. A surgical complexity score has been shown to be predictive of morbidity in patients with advanced ovarian cancer. We evaluated the use of a surgical complexity score in predicting postoperative morbidity in GIST pts undergoing metastasectomy.

Methods: We reviewed all GIST pts treated with any TKI and metastasectomy between 2001-2014 at our institution. Patient factors, organs resected, procedures performed, and disease burden were evaluated to develop a surgical complexity score (low, intermediate, and high) (Table 1). Postoperative complications were graded using the Clavien-Dindo classification system. Prognostic ability of clinicopathologic factors and surgical complexity for postoperative morbidity and overall survival (OS) were assessed.

TABLE 1. Surgical complexity scoring system based on the sum of points determined from patient factors, procedures performed, organs resected and disease burden.

PATIENT FACTORS		**ORGANS RESECTED**	
Age ≥65	1	Stomach	1
Emergency	2	Duodenum	1
Clean-contaminated case	1	Small bowel[b]	1
Diabetic	1	Right colon	1
Current smoker	1	Left colon	1
Prior abdominal surgery	1	Pancreas	1
SURGICAL PROCEDURE		Liver[b]	1
Abdominoperineal resection	3	Diaphragm	1
Low anterior resection	2	Spleen	1
Liver lobectomy	3	Peritoneum/abdominal wall	1
Liver wedge resection	1	Adrenal gland	1
Left lateral segmentectomy	1	Kidney	1
Caudate resection	2	Gallbladder[c]	1
Whipple[a]	3	Bladder	1
Distal pancreatectomy	2	Major vessel	1
Duodenectomy	2	Ovary	1
Total gastrectomy	3	Uterus	1
Subtotal gastrectomy	2	Omentum	1
Distal gastrectomy	2		
Gastric wedge resection	1	**DISEASE BURDEN[d]**	
Lysis of adhesions (>45 min)	1	Low (<10cm)	0
Laparoscopic approach	1	Medium(10-20cm)	1
Vascular dissection/repair	1	High (>20cm)	2
Vascular reconstruction	2		
Hysterectomy	2	**SURGICAL COMPLEXITY SCORE**	
Nephrectomy	1	Low	≤4
Complex bladder repair	1	Intermediate	5-7
Cystectomy	2	High	≥8

a, Whipple includes duodenum/pancreas only; b, 1 point assigned for each resection;
c, Gallbladder removal not counted if part of hepatectomy or whipple;
d, Cumulative size of resected tumor.

Results: We performed 210 operations on 158 pts with metastatic GIST on TKI. Fifty-seven pts developed 68 post-operative complications (any grade) following 59 operations (28%). Of these complications, 37 were grade 3/4 requiring percutaneous intervention (n=17) or re-operation (n=18). There were 3 peri-operative deaths (1.4%). The use of sunitinib or other TKI at time of metastasectomy, R2 resection, and a high surgical complexity score (median 7, range 1-15) were significant predictors of morbidity on univariate analysis (Table 2). A high surgical complexity score was the only independent prognosticator of increased risk of postoperative morbidity (odds ratio 3.6, 95% confidence interval 1.02-12.75, P=0.047). The number of metastatic lesions and number of organs resected did not significantly impact morbidity. Surgical complexity score was not predictive of OS (P=0.053).

Conclusion: To our knowledge, this is the first study

TABLE 2. Univariate and multivariate analysis of treatment and surgical variables on morbidity for all patients with gastrointestinal stromal tumor treated with TKI at time of metastasectomy (n = 210).

Variables	Univariate analysis		Multivariate analysis	
	Odds Ratio (CI)	***P*-value**	**Odds Ratio (CI)**	***P*-value**
TKI at time of metastasectomy				
Imatinib	Ref	-	Ref	-
Sunitinib	2.6 (1.2-5.5)	0.01	2.2	NS
Other	2.2 (1.0-4.6)	0.05	1.5	NS
Duration of preoperative TKI				
≤24 mo	Ref	-	Ref	-
>24 mo	0.9	NS	0.6	NS
Radiographic response[a]				
Stable	Ref	-	Ref	-
Responsive	1.5	NS	4.0	NS
Unifocal progression	0.6	NS	0.5	NS
Multifocal progression	1.4	NS	0.9	NS
Metastatic mitotic index				
<5/50 HPF	Ref	-	Ref	-
≥5/50 HPF	1.7	NS	4.2	NS
Extent of resection				
R0	-	-	-	-
R1	Ref	-	Ref	-
R2	2.1 (1.1-3.9)	0.02	1.6	NS
Number of metastases				
≤5	Ref	-	Ref	-
>5	1.2	NS	0.6	NS
Number of organs resected				
≤2	Ref	-	Ref	-
>2	1.6	NS	0.9	NS
Surgical complexity score				
Low	Ref	-	Ref	-
Intermediate	2.2	NS	2.3	NS
High	3.4 (1.4-8.6)	0.008	3.6 (1.0-12.8)	0.05

a, At time of metastasectomy. Abbreviations: CI, 95% confidence interval; TKI, tyrosine kinase inhibitor; Ref, reference; HPF, high-power field; NS, not significant.

to investigate predictors of postoperative morbidity following metastasectomy in GIST pts treated with TKI. We demonstrate the utility of a surgical complexity score that combines patient-related factors and surgical factors in predicting morbidity. The use of this score can allow preoperative risk stratification in order to determine optimal treatment planning.

2:05 pm – 2:50 pm

– GASTROINTESTINAL STROMAL TUMORS (GIST) –

Long-term Survival of Metastatic GIST

2:05 pm Paper 038 #2556232

PREDICTION OF LONG-TERM SURVIVAL IN METASTATIC GASTROINTESTINAL STROMAL TUMOUR: ANALYSIS FROM A LARGE, SINGLE-INSTITUTION PATIENT COHORT

Ivar Hompland[1]*; Øyvind Sverre Bruland*[1]*; Jan Peter Poulsen*[1]*; Stephan Stoldt*[2]*; Toto Hølmebakk*[2]*; Kirsten Sundby Hall*[1]*; Kjetil Boye*[1]

[1]*Department of Oncology, Oslo University Hospital, Norwegian Radium Hospital, Oslo, Norway;*

[2]*Department of Abdominal and Pediatric Surgery, Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway*

Objective: Treatment of metastatic gastrointestinal stromal tumour (GIST) has improved considerably after the introduction of imatinib. A subset of patients become long-term survivors, and a more precise outcome prediction could improve clinical decision-making. The aim of this study was to identify factors associated with long-term survival in metastatic GIST.

Methods: Patients diagnosed with metastatic GIST from 1995 to 2013 were identified from the sarcoma database at Oslo University Hospital. Clinical data were prospectively registered in the database and supplemented with retrospective review of medical records. Factors associated with survival were analysed using Kaplan-Meier curves, log-rank test and uni- and multivariate Cox regression analysis.

Results: One-hundred thirty-three patients with metastatic GIST were identified, and 115 were included in the final study cohort. First-line treatment with imatinib was given to 111 patients, two received nilotinib and two never received systemic treatment. Second-line treatment was administered to 35 patients and third-line therapy to 19 patients. Median overall survival (OS) was 6.9 years (95 % CI 5.6-8.3). After a median follow-up of 9.0 years 52 patients (43 %) were still alive. Factors associated with long-term survival in univariate analysis were good baseline performance status (ECOG ≤1; p<0.001), young age (p=0.022), oligometastatic disease (≤3 metastases; p<0.001), maximum tumour diameter <5 cm (p<0.001), surgery for metastatic disease (p=0.005), radical surgery of the primary tumour (p<0.001), normal baseline haemoglobin level (p=0.046), normal baseline albumin level (p=0.001) and normal baseline neutrophil count (p=0.032). In multivariate analysis, good performance status and oligometastatic disease were the only factors associated with outcome. Five-year and 10-year OS for patients with oligometastatic GIST were 89 % and 71 %, respectively, compared to 38 % and 20 % for patients with more disseminated disease.

Conclusion: In the present cohort oligometastatic disease and good performance status were the most important predictors of long-term survival. Patients with oligometastatic disease had an excellent outcome, and may be regarded as a separate category among patients with metastatic GIST.

2:15 pm Paper 039 #2556314

THE DANA-FARBER CANCER INSTITUTE (DFCI) EXPERIENCE OF EXTREME LONG-TERM RESPONDERS TO IMATINIB: 16 YEARS OF FOLLOW-UP FROM THE B-2222 TRIAL OF EFFICACY AND SAFETY OF IMATININB MESYLATE IN PATIENTS WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR (GIST)

Eytan Ben-Ami*; Katherine Thornton; Priscilla Merriam; Jeffrey Mrogan; Andrew Wagner; Suzanne George; GD Demetri*

Sarcoma and Bone Oncology, Dana Farber Cancer Institution, Boston, MA, USA

Objective: To characterize advanced GIST patients with extreme long-term response to imatinib.

Methods: All patients who participated in the B-2222 trial and followed in DFCI who continue to receive imatinib as of January 2016 were included.

Results: As of January 2016,of 84 patients followed in DFCI,nine continue to receive imatinib for a period of 15 years or more as first line tyrosine kinase inhibitor for advanced GIST.Their mean age at study start was 55.9 years with a 5:4 male to female ratio.Six patients were assigned to an initial 600 mg of imatinib while three received 400 mg as initial daily dose according to the clinical trial dosing assignment.Mean time from diagnosis to treatment start was 3.2 years,baseline mean tumor size was 9.3cm.Best response by RECIST 1.1 was eight partial responses and one stable disease.Tumor genotype included five KIT exon 11 mutations,three KIT exon 9 mutations and one KIT/PDGFR wild-type SDH-deficient tumor.Two of the nine patients underwent interval surgery while on imatinib treatment due to progressive lesions.One patient (SDH-deficient) underwent a partial gastrectomy after 2.7 years of imatinib treatment.Analysis of somatic mutations of 41 genes (including KIT/PDGFRA) in the resistant lesion did not reveal any secondary mutations.The second patient (exon 9 mutation) underwent omental metastasectomy after 15 years of imatinib treatment.Mutation analysis of the progressing lesion revealed the known KIT exon 9 mutation and a KIT exon 17 p.N822K point mutation which is associated with poor response to imatinib.Both patients resumed imatinib therapy following surgical treatment.

In our follow-up cohort we also identified eight additional patients who developed progressive disease within 3 months of imatinib treatment (early resistance) and subsequently went off trial to receive other treatments. Compared with

Table 1. Clinicopathological and Molecular Characteristics of Long-Term Responders to Imatinib

Case	Age/ Gender	Site/ Size (cm)	Mitoses/High Power Field	Diagnosis to Treatment (days)	Exon Mutation	KIT mutations	Best Response
#1	52.6/M	S/13	13/10	156	11	p.Q556_V560del	PR
#2	18.6/F	S/22	2/10	2289	WT	None	SD
#3	50.9/F	S/5.5	6/10	1321	11	p.P551_Y553del	PR
#4	55.9/F	SB/5	9/10	306	11	p.W557_K558del	PR
#5	57.7/M	SB/3	5/10	539	9	p.A502_Y503ins	PR
#6	62/M	R/2	25/30	2553	11	p.W557_K558del	PR
#7	54.2/M	S/7	5/30	1652	9	p.A502_Y503ins	PR
#8	63/F	S/17	8/10	219	11	75655_75686del (splice acceptor)	PR
#9	57/M	SB/6.1	16/10	1578	9	p.A502_Y503ins	PR

S: Stomach; SB: Small bowel; R: Retroperitoneum; WT: Wild-type; PR: Partial response; SD: Stable disease.

long-term responders,these patients were older (61.2 years),had shorter interval from diagnosis to study start (median 2.1 years) and a larger mean tumor size (10.6 cm). Tumor genotype included three KIT exon 9 mutations,two KIT exon 11 mutations,one KIT exon 17 mutation,one PDGFR mutation (D842V) and one KIT/PDGFR wild-type tumor.Median survival for early progression patients was 2.07 years.

Whole Exome Sequencing (WES) of extreme long-term imatinib responders and early progressing patients is planned.

Conclusion: We provide the first report of imatinib extreme long-term responders in GIST.WES may provide insight to these patients' unique drug sensitivity.

2:50 pm – 3:50 pm

– GASTROINTESTINAL STROMAL TUMORS (GIST) – "Wild-Type" GIST

2:50 pm Paper 040 #2561543

QUADRUPLE NEGATIVE GIST IS A SENTINEL FOR UNRECOGNIZED NEUROFIBROMATOSIS TYPE 1 SYNDROME

Roberta Maestro[1]*; Daniela Gasparotto*[1]*; Sabrina Rossi*[2]*; Maurizio Polano*[1]*; Elena Tamborini*[3]*; Marta Sbaraglia*[2]*; Alessia Mondello*[1]*; Stefano Lamon*[2]*; Raffaella Bracci*[4]*; Alessandra Mandolesi*[4]*; Franco Stanzial*[5]*; Guido Mazzoleni*[5]*; Silvana Pilotti*[3]*; Alessandro Gronchi*[3]*; Angelo Paolo Dei Tos*[6]

[1]CRO Aviano National Cancer Institute, Aviano, Italy; [2]Treviso General Hospital, Treviso, Italy; [3]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano, Italy; [4]Ospedali Riuniti di Ancona, Ancona, Italy; [5]Bolzano General Hospital, Bolzano, Italy; [6]Treviso General Hospital, University of Padova, Treviso, Italy

Objective: The majority of Gastrointestinal Stromal Tumors (GISTs) are driven by *KIT*, *PDGFRA* or, less commonly, *BRAF* mutations, and *SDH* gene inactivation is involved in a limited fraction of gastric lesions. However, about 10% of GISTs are devoid of any of such alterations and are poorly responsive to standard treatments.
This study aims to shed light on the molecular drivers of quadruple-negative GISTs.

Methods: Twenty-two sporadic quadruple-negative GISTs with no prior association with Neurofibromatosis Type 1 syndrome were molecularly profiled for a panel of genes belonging to tyrosine kinase pathways or previously implicated in GISTs.

For comparison purposes, 24 GISTs carrying *KIT*, *PDGFRA*, or *SDH* gene mutations were also analyzed. Molecular findings were correlated to clinicopathological features.

Results: Most quadruple-negative GISTs featured intestinal localization, with a female predilection.

About 60% (13/22) of quadruple-negative tumors carried *NF1* pathogenic mutations, often associated with biallelic inactivation.

The analysis of normal tissues, available in 11 cases, indicated the constitutional nature of the *NF1* mutation in 7/11 cases, unveiling an unrecognized Neurofibromatosis Type 1 syndromic condition.

Multifocality and a multinodular pattern of growth were common findings in *NF1*-mutated quadruple-negative GISTs.

Conclusion: *NF1* gene mutations are frequent in quadruple-negative GISTs and are often constitutional, indicating that a significant fraction of patients with apparently sporadic quadruple-negative GISTs are affected by unrecognized Neurofibromatosis Type 1 syndrome.

Hence, a diagnosis of quadruple-negative GIST, especially if multifocal or with a multinodular growth pattern and a non-gastric location, should alert the clinician to a possible Neurofibromatosis Type 1 syndromic condition.

3:00 pm Paper 041 #2557891

NF1 IS FREQUENTLY MUTATED IN GASTROINTESTINAL STROMAL TUMORS AT THE DUODENAL-JEJUNAL FLEXURE

Martina De Siena[1]*; Adam Burgoynge*[5]*; Chih-Min Tang*[1]*; John Thorson*[2]*; Karra Jones*[2]*; Paul Fanta*[5]*; Grace Lin*[2]*; Dwayne Stupack*[2]*; Martin Belinsky*[3]*; M von Mehren*[4]*; Olivier Harismendy*[6]*; Jason K Sicklick*[1]

[1]*Division of Surgical Oncology, Department of Surgery, University of California, San Diego, La Jolla, CA, USA;* [2]*Department of Pathology, University of California, San Diego, San Diego, CA, USA;* [3]*Molecular Theraputics Program, Fox Chase Cancer Center, Philadelphia, PA, USA;* [4]*Hematology/Oncology, Fox Chase Cancer Center, Philadelphia, PA, USA;* [5]*Division of Hematology and Oncology, Department of Medicine, University of California, San Diego, La Jolla, CA, USA;* [6]*Biomedical Informatics, University of California, San Diego, La Jolla, CA, USA*

Objective: Gastrointestinal stromal tumors (GISTs) are commonly associated with somatic driver mutations in *KIT* and *PDGFRA*. However, a small subset of GISTs arises from germline mutations in *NF1* (neurofibromatosis type 1, NF-1). The first case of *NF1* mutant GIST in the absence of a germline *NF1* mutation was reported recently. We sought to validate this finding in a separate cohort of patients undergoing broad genomic sequencing.

Methods: We describe the demographics and clinicopathologic features of 40 patients with GIST whose tumors underwent next generation sequencing (NGS) for coding regions in nearly 400 cancer-related genes.

Results: We identified 6/40 GISTs (15%) with *NF1* genomic alterations. Of the 6 patients, 5 (83.3%) had unifocal tumors at the duodenal-jejunal flexure (DJF, or Ligament of Treitz). Within our institutional cohort (n=140), 2 additional patients with DJF GISTs (but no available NGS) were identified. This particular location represents an infrequent site of GIST (7/140, 5%). Of the 5 DJF GISTs with NGS, 4 (80%) had known deleterious *NF1* mutations and 1 (20%) had an *NF1* single nucleotide polymorphism (SNP) reported in NF-1 families. Paired germline *NF1* sequencing was available in 4 cases. Only 2 of 4 (50%) *NF1* mutant DJF GIST patients had germline *NF1* alterations, including the aforementioned SNP. Similar to the first reported case of somatic-only *NF1* mutant GIST, we identified 2 patients from our cohort. While 4/5 (80%) tumors at the DJF had known deleterious *NF1* mutations, only 1/35 (2.9%) tumors outside the DJF had a deleterious *NF1* mutation. Moreover, 3/5 (60%) DJF tumors with *NF1* alterations also had deleterious *KIT* mutations (exons 9/11), while 2/5 (40%) DJF tumors had Notch pathway mutations (*NOTCH2*, *MAML2*), which were not observed in the 35 non-DJF GISTs.

Conclusion: Small bowel GISTs associated with *NF1* are often multifocal and were previously thought to only arise in the setting of underlying NF-1. Broad genomic profiling of DJF GISTs has revealed frequent *NF1* mutations at this site, which may be somatic or germline (even in the absence of clinical NF-1). These tumors also may harbor concurrent deleterious *KIT* and/or Notch pathway mutations. We now provide new insights into the genomics/pathobiology of *NF1* mutant GIST, and support investigations of somatic and/or germline *NF1* testing in all patients with DJF GISTs. Taken together, these findings may also have implications for familial genetic counseling and for personalizing drug therapy in patients with DJF GISTs.

3:10 pm Paper 042 #2570353

PROGNOSTIC SIGNIFICANCE OF WNT SIGNALING PATHWAY MOLECULES IN NON-GASTRIC LOCALIZED GIST PATIENTS. A TISSUE MICROARRAY-BASED (TMA) ANALYSIS. A SPANISH GROUP FOR RESEARCH ON SARCOMA (GEIS) STUDY

Javier Martin-Broto[1]*; Marta Mendiola*[2]*; Laura Guerra*[2]*; Antonio Gutierrez*[4]*; Irene Felipe*[3]*; Javier Martinez-Trufero*[7]*; Luis Miguel de Sande Gonzalez*[5]*; Nadia Hindi*[1]*; Cristina Tous*[3]*; Claudia Valverde*[8]*; Antonio Casado*[6]*; Rafael Ramos* [4]*; Virginia Martinez-Marin*[2]

[1]*Medical Oncology, Universitary Hospital Virgen del Rocío, Sevilla, Spain;* [2]*University Hospital La Paz, Madrid, Spain;* [3]*Biomedical Research Institute Seville (IBIS), Sevilla, Spain;* [4]*University Hospital Son Espases, Palma de Mallorca, Spain;* [5]*Hospital Leon, Leon, Spain;* [6]*University Clinic Hospital Madrid, Madrid, Spain;* [7]*University Hospital Miguel Servet, Zaragoza, Spain;* [8]*University Hospital Vall d'Hebron, Barcelona, Spain*

Objective: Pathogenesis in GIST could be related to cancer stem cell hypothesis (highly chemo resistant, very uncommon complete responses, kit is stem cell marker) even though no stem cell component in GIST has been yet demonstrated. Wnt signaling regulates proliferation in some normal and cancer stem cells as it occurs with intestinal epithelium. We have explored the prognostic significance of several Wnt signaling pathway and related molecules and its correlation with relapse free survival (RFS) and overall survival (OS).

Thus, the aim was to investigate the prognostic significance of β-Catenin, CDC25A, ROR2, p53, CUL4A, AKT-p, VEGFR-2, pAKT and CD133 by immunohistochemical (IHC) analysis in TMA specimens of 79 localized non-gastric GIST.

Methods: Data of diagnostic, therapeutic and follow-up procedures derived from the GIST Registry of GEIS. Staining was deemed as weak positive (+), strong positive (++) or negative (-) for VEGFR2, β-Catenin, CUL4A, CDC25A and CD133 whereas it was positive or negative for ROR2, p53 and pAKT antibodies. Nuclear staining was considered positive for CDC25A, CUL4A, ROR2 and p53 antibodies. Kaplan–Meier estimations were used for time-to-event variables and the log-rank test was used to compare groups. Relapse free survival was the clinical endpoint.

Results: A subset of 79 localized non-gastric GIST patients was selected in this analysis. The median age was 62 y and the median follow-up was 36 months. A statistically significant difference was found for β-Catenin in RFS: 15, 86 and 110 months for (++), (+) and (-) (p=0.004) respectively. Other results showing a clear trend but not reaching statistical significance were for VEGFR2 in OS: 36, 262 and not reached for (++), (+) and (-) (p=0.085) respectively and for p53 in RFS: 24 and 86 months for (+) and (-) respectively (0.086)

Conclusion: Protein positive expression of β-Catenin seems a significant worse prognostic factor for RFS in localized non-gastric GIST. Likewise, positive VEGFR2 shows a trend toward worse RFS. This outcome points out Wnt signaling pathway as new potential molecular target in GIST.

– BONE SARCOMAS & GIST–

P1 - Poster 001 2565304

MOLECULAR EVOLUTION DURING TUMOR PROGRESSION IN GASTROINTESTINAL STROMAL TUMORS (GIST)

Milena Urbini[1]; Manuela Ianni[2]; Annalisa Astolfi[2]; Valentina Indio[1]; Margherita Nannini[1]; Maristella Saponara[1]; Lidia Gatto[1]; Guido Biasco[2]; Maria A. Pantaleo[1]
[1]Department of Specialized, Experimental and Diagnostic Medicine, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy;
[2]"Giorgio Prodi" Cancer Research Center, University of Bologna, Bologna, Italy

Objective: Most of gastrointestinal stromal tumors (GIST) are characterized by mutation on KIT or PDGFRA receptors. These mutations present an intra and inter-lesions heterogeneity in metastatic disease. Currently the molecular evolution occurring during tumor progression from primary tumor to metastatic lesion is not investigated yet. The aim of this study was to evaluate the molecular background of primary GIST compared with their corresponding metastases by the integration of exome sequencing and copy number analysis.

Methods: Fresh frozen tissues of primitive GIST and of two different metastasis were collected from two KIT mutated GIST patients. Exome sequencing (Nextera Rapid Capture Exome, Illumina) and copy number analysis (CytoScan Array, Affymetrix) were performed on DNA extracted from all the tumor tissues types collected. Sequencing of normal counterpart was performed for detection of somatic mutations.

Results: Copy number variation (CNV) analysis unveiled several alterations: GIST174 showed extreme genomic instability (average of 18 chr. with macroscopic CNV), while GIST183 carried few alterations (6 chr. with macroscopic CNV). The majority of CNV were in common between primitive and metastasis. In both patients was present the DMD intragenic deletion and in all samples tested was found homozygously deleted. Loss of heterozygosity and amplification of chr4 (from p16.3 to q22.1) was detected only in GIST174 and was conserved between the tumor tissues, leading to the expression of only the mutated allele of KIT. Coupling exome sequencing and copy number analysis, several alterations on tumor suppressor genes were detected. All three samples of GIST174 carried a mutation on LATS2 gene (p.Q937X). Homozygous loss of CDKN2A was detected in primitive and in only one metastasis. In the primitive tissue of GIST174 another mutation was detected on PTEN (p.R233X), in association with loss of chr10. In the other two metastasis no point mutation was detected on PTEN, however both maintained the macroscopic chr10 loss and one metastasis showed an additional focal loss on PTEN leading to its homozygous deletion.

Conclusion: The comparison between primary and metastatic tumor tissue within the same patient may allow the identification of the genetic events occured during the metastatic process. This better comprehension of the molecular evolution of the disease in all its phases of development and progression could lead to the identification of novel potential therapeutic targets.

P1 - Poster 002 2558139

A PILOT STUDY ON INTRA-TUMORAL HETEROGENEITY IN GASTROINTESTINAL STROMAL TUMORS

Herbert H. Loong, MBBS, MRCP, FHKCP, FHKAM[1]; Chit Chow[2]; Enders K. Ng[3]; Stephen L. Chan[1]; Anthony W. Chan[2]
[1]Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong, Hong Kong; [2]Department of Anatomical & Cellular Pathology, The Chinese University of Hong Kong, Hong Kong, Hong Kong; [3]Department of Surgery, The Chinese University of Hong Kong, Hong Kong, Hong Kong

Objective: Whilst the primary treatment for gastrointestinal stromal tumors (GISTs) is surgical resection, evidence and clinical practice supports the use of molecularly targeted therapies (MTT) in selected adjuvant and metastatic settings. Inter-tumoral clonal heterogeneity and selective pressure from treatment with prior lines of MTT has been established as one of the reasons of secondary resistance to MTT. We examined whether there may be a presence of intra-tumoral heterogeneity in larger GIST tumors on presentation as a possible source of heterogeneity. We hypothesize that larger GIST tumors may carry differing molecular signatures at presentation of disease and identification of this may be beneficial in the planning of subsequent treatments.

Methods: Patients with GISTs of > 5cm in size who have undergone primary resection at Prince of Wales Hospital, Hong Kong who have not received neoadjuvant imatinib and undergone primary resection were identified between January 2015 and March 2016 . For each case, four different representative areas from the same specimen were subjected to *KIT* mutation analyses by PCR followed by direct Sanger sequencing.

Results: A total of 10 patients with primary GIST tumors >5cm on presentation (stomach = 5, small bowel = 4, duodenum = 1). Median size = 6.5cm (range 5.5cm –

23cm). Median mitotic index = 2/50HPF (range < 1 – 27/50 HPF). Primary analysis on mutation status: exon 11 = 6 pts, exon 9 = 1 pt, exon 17 = 2 pt, WT = 1 pt. 3 additional representative blocks were identified from each specimen for individual *KIT* analyses. The concordance rate between mutational status within different representative regions of each specimen was 100%.

Conclusion: There is no evidence of intra-tumoral heterogeneity within the tested population. Clonal evolution and heterogeneity seen in clinical practice is unlikely to have been initiated prior to start of MTT treatment or at metastases. This has implications on clinical practice, as given to high rate of concordance, there is a potential that serial monitoring with liquid biopsies targeting specific mutations identified in the tumor of a particular GIST patient can serve as a personalized method for disease monitoring. Our group is currently investigating this approach.

Funding: This project is partially funded by the CUHK Direct Grant and the Young Investigators' Grant of the Hong Kong College of Physicians.

P1 - Poster 003 2570784

ABL1 IS AN ANTITARGET IN THE THERAPEUTIC RESPONSE OF GIST CELLS TO IMATINIB MESYLATE THAT ACTS THROUGH INCREASED CDK2/AKT SIGNALING

Jessica L. Rausch[1]; Sergei Boichuk[1]; Areej Ali[1]; Donna M. Lee[1]; Sneha Patil[1]; Matthew F. Brown[1]; Kathleen R. Makielski[1]; Ying Liu[1]; Takahiro Taguchi[1]; Shih-Fan Kuan[2]; Anette Duensing, MD[1]
[1]University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA; [2]University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Objective: Most gastrointestinal stromal tumors (GISTs) are caused by activating mutations of the KIT receptor tyrosine kinase. Imatinib mesylate (IM) was initially FDA-approved to target the ABL1 kinase, which is constitutively activated through chromosomal translocation in BCR-ABL1-positive chronic myeloid leukemia (CML). Because of cross-reactivity of IM against KIT, IM is successfully used for the treatment of GIST. Although inhibition of KIT has a major role in the therapeutic response of GIST cells to imatinib, the role of concomitant inhibition of ABL1 in this context needs to be explored.

Methods: GIST (GIST882, GIST-T1, GIST48, GIST48B, GIST430), leiomyosarcoma (SK-LMS, SK-UT1) and CML (K562) cell lines were used. Primary GISTs were examined by immunoblotting (IB) and immunohistochemistry (IHC; tissue microarray, TMA). KIT, ABL1, CDK2 expression levels were reduced via siRNA-mediated knockdown. Inhibitors used were IM (KIT/ABL1), GNF-2 (ABL1) and OSU-03012 (PDK1). Luminescence-based assays, FACS and IB were used to determine cell viability, apoptosis, cell cycle stage, and protein expression levels.

Results: ABL1 was expressed in all GIST cell lines and most primary GISTs (7/8 by IB, 27/28 by IHC in TMA), but not in LMS. BCR-ABL1 was expressed in K562. As previously reported, siKIT/ABL1 (mimicking IM) led to reduced apoptosis, attenuated inhibition of proliferation, attenuated KIT inhibition as well as attenuated cleaved caspase 3 and cyclin A expression when compared to siKIT alone. Interestingly, siABL1 as well as ABL1 inhibition with GNF-2 led to upregulation of AKT S473 activity. This was not due to increased PDK1 activity (the upstream kinase of AKT) or decreased AKT phosphatase expression. A recent study showed that CDK2, which acts in concert with cyclin A, has the capability to directly phosphorylate AKT. We could show that siKIT/ABL1 and treatment with GNF-2 led to increased CDK2 activity. Importantly, siCDK2/ABL1 attenuated the increase in AKT S473 activation induced by siABL1 alone .

Conclusion: Our results indicate that ABL1 is an anti-target in GIST, whose inhibition limits the therapeutic effect of IM by eliciting a pro-survival signal via activation of CDK2/AKT. Rational development of novel KIT-targeted agents to treat GIST should therefore focus on increasing their specificity for KIT while reducing their ability to inhibit ABL1.

P1 - Poster 004 2570730

THE PROTEIN TRANSLATION INHIBITOR HOMOHARRINGTONINE IS A PROMISING NEW AGENT FOR THE TREATMENT OF GASTROINTESTINAL STROMAL TUMORS (GISTS)

Sneha Patil[1]; Parker Trent[1]; Donna M. Lee[1]; Areej Ali[1]; Jessica L. Rausch[1]; Takahiro Taguchi[2]; Anette Duensing, MD[1]
[1]University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA; [2]Kochi Medical School, Kochi, Japan

Objective: Although GISTs can be effectively treated with imatinib mesylate (IM), many patients develop resistance to IM and the second- and third-line tyrosine kinase inhibitors (TKI) sunitinib (SU) and regorafenib. The main mechanism of TKI resistance in GIST involves secondary mutations in the KIT or PDGFRA kinases, and these tumors are still highly dependent on activated KIT/PDGFRA. New therapeutic strategies that target KIT/PDGFRA through a different mechanism of action are therefore especially intriguing. Homoharringtonine (HHT, omacetaxine mepesuccinate) is an inhibitor of protein translation that has recently been FDA-approved for the treatment of IM-resistant chronic myeloid leukemia (CML). HHT has also been shown to be active in KIT D816V-mutant mastocytosis models. We hypothesized that HHT could be effective in GIST through downregulation of KIT protein expression thereby abolishing KIT activation.

Methods: Studies were performed in IM-sensitive (GIST882, GIST-T1) and IM-resistant (GIST48, GIST48B, GIST430) GIST cells as well as K562 (BCR-ABL-positive CML) positive control cells. Cells were treated with varying doses of HHT compared to IM and/or SU (1 uM). Luminescence-based assays, TUNEL and immunoblotting (IB) were used to determine cell viability, apoptosis, proliferation, KIT activation/protein expression as well as translational activity. RT-PCR and qRT-PCR were used to measure mRNA levels.

Results: HHT was highly effective in GIST cells, irrespective of IM sensitivity. GIST IC50s ranged from 18-76 nM compared to 48 nM in K562. Strong induction of apoptosis and reduced cell viability was seen at 100 nM (luminescence-based assays, TUNEL, IB). HHT led to complete abolishment of KIT activation/expression (BCR-ABL expression in K562) at this concentration while mRNA levels were unaffected. The apoptotic response involved PARP and caspase 3 cleavage while reduced levels of cyclin A indicate cell cycle exit of the remaining viable cells.

Conclusion: Targeting the protein translation machinery is a promising strategy to diminish KIT activation and overcome IM resistance in GIST. Further preclinical studies to dissect the precise mechanism of action of HHT and to test the compound *in vivo* are ongoing.

P1 - Poster 005 2562622

THE HEDGEHOG PATHWAY REGULATES *KIT* EXPRESSION AND CELL VIABILITY IN HUMAN GASTROINTESTINAL STROMAL TUMORS

Chih-Min Tang[4]; Sabriya A. Syed[1]; Tracy Lee[4]; Eileen Shi[4]; Juliann Chmielecki[2]; Deborah Morosini[2]; Kai Wang[2]; Jeffrey Ross[2]; Michael Kendrick[5]; Michael Bardsley[1]; Martina De Siena[4]; Junhao Mao[3]; Olivier Harismendy[6]; Tamas Ordog[1]; Jason K. Sicklick, MD[4]

[1]Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN, USA; [2]Foundation Medicine, Inc., Cambridge, MA, USA; [3]Department of Molecular, Cell and Cancer Biology, University of Massachusetts, Worchester, Worcester, MA, USA; [4]Division of Surgical Oncology, Department of Surgery, University of California, San Diego, La Jolla, CA, USA; [5]Department of Surgery, Mayo Clinic, Rochester, MN, USA; [6]Division of Biomedical Informatics, University of California, San Diego, La Jolla, CA, USA

Objective: Gastrointestinal stromal tumors (GIST) arise within the interstitial cell of Cajal (ICC) lineage due to activating *KIT* and *PDGFRA* mutations. Both ICC and GIST possess primary cilia, which coordinate PDGFRA and Hedgehog signaling, regulators of gastrointestinal mesenchymal development. Therefore, we hypothesized that Hedgehog signaling may be altered in human GIST and modulate *KIT* expression.

Methods: Quantitative RT-PCR, microarrays, and next generation sequencing were used to describe the Hedgehog and primary cilia-related genes in purified human ICC and GIST. Genetic and pharmacologic approaches were employed to investigate the effects of *GLI* transcription factor manipulation on *KIT* expression and GIST cell viability.

Results: We report that Hedgehog pathway and primary cilia components are expressed in both ICC and GIST. Moreover, these components are subject to dysregulation during GIST oncogenesis, irrespective of *KIT* or *PDGFRA* mutation status. Using genomic profiling, 1.6% of GIST studied had deleterious genomic alterations in the *PTCH1* tumor suppressor gene. *GLI3* expression was inversely correlated with *KIT* mRNA levels in GIST cells and in non-*KIT*/non-*PDGFRA* mutant GIST. Treatment with GLI siRNA or GLI inhibitors, including arsenic trioxide, significantly decreased *KIT* expression and reduced GIST cell viability in imatinib-sensitive and imatinib-resistant lines.

Conclusion: This study discovers that genes necessary for Hedgehog signaling and primary cilia function in ICC are dysregulated in GIST. The Hedgehog pathway regulates *KIT* expression and cell viability in the ICC/GIST lineage and is dysregulated in GIST regardless of mutation status, offering a novel approach to treat imatinib-resistant GIST.

P1 - Poster 006 2563845

BRAIN METASTASIS FROM GASTROINTESTINAL STROMAL TUMOR: A CASE REPORT

Ana M. Simas; Jose Dinis; Ana M. Ferreira; Mariana Afonso; Marta Soares
Medical Oncology, IPO-Porto, Porto, Porto, Portugal

Objective: Gastrointestinal stromal tumors (GIST) are the most common type of mesenchymal tumors in the gastrointestinal tract. They frequently metastize to the liver and peritoneum; GIST metastasis to the central nervous system is extremely rare.

We describe a rare case of brain metastasis from a Gastrointestinal stromal tumor.

Methods: Case report.

Results: We report a clinical case of a 76 year-old female, with the diagnosis of a metastatic esophageal GIST since 2003. She presented liver and lung metastasis at the diagnosis.

She began Imatinib 400mg id since the diagnosis, in France, with a complete response in the liver and lung, maintaining esophageal thickening.

In February 2016 she presented with dysarthria, holocranial headache and imbalance. A brain Magnetic resonance imaging (MRI) was performed and revealed two brain lesions:

one in the left frontal lobe and the other in the right cerebellum. She was medicated with steroids with symptomatic improvement. A positron emission tomography computed tomography (PET-CT) examination didn't show any other lesions other than the esophageal thickening.

She was submitted to a craniotomy and a excisional biopsy of the frontal lesion. The pathology confirmed the suspicion of a metastasis from GIST. She was proposed to radiotherapy and maintenance of the dose of Imatinib 400mg id.

Conclusion: Metastasis from GIST outside the abdomen are uncommon and primarily seen in advanced cases only. This case shows that cerebral and cerebellum GIST metastasis can occur in patients with disease controlled in the abdomen.

P1 - Poster 007 2533131

THE TOXICITY AND EFFICACY PROFILE OF REGORAFENIB (RG) IN GASTROINTESTINAL TUMOR (GIST) PATIENTS (PTS) USING AN ALTERNATE DOSING REGIMEN

Gustavo Schvartsman, MD[1]; Michael J. Wagner[1]; Andrea G. Barbo[6]; Heather Y. Lin[6]; Behrang Amini[2]; Van A. Trinh[3]; Wei-Lien Wang[4]; SR Patel[5]; Robert S. Benjamin[5]; Neeta Somaiah[5]

[1]Department of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Department of Radiology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Department of Pharmacy Clinical Programs, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]Department of Sarcoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [6]Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: RG is an oral tyrosine kinase inhibitor approved in 2013 as third-line therapy for advanced GIST at a starting dose of 160 mg daily 3 weeks on, 1 week off, based on the results of the GRID study. Herein we summarize the MD Anderson Cancer Center's experience with RG with an alternate dosing.

Methods: The pharmacy database was queried to determine GIST pts who received RG through our pharmacy from March 2013 until October 2014. Electronic records were reviewed for mutation profile, lines of therapy, starting dose and schedule, dose reductions, response rate, survival and toxicity. An independent radiologist assessed response (by RECIST v1.1 and CHOI criteria) for all pts.

Results: Twenty-eight pts were included in this study. Median age when starting RG was 58 years (range: 21-84 years) and 17 (61%) were male. RG was given as third-line in 71% of pts (29% had 3 or more therapies). Primary mutation results were available for 27 pts; 85% had *KIT* (22 pts with exon 11 and one with exon 9 mutation), 4% had *PDGFR* and 11% were wild-type for both. Secondary mutations were available in 6 pts; 5 had mutation in exon 17 and 1 in exon 13 of *KIT*. The median follow-up time was 26.8 months (95% CI: 22.4 – 28.9 months). Median duration of treatment was 7.3 months (5 months in the GRID study) and median tolerated dose was 120 mg once daily continuously (mean dose was 103.2 mg; SD=23.5 mg). Majority of pts (79%) were started on 120 mg continuous daily dosing schedule. Partial response (PR) by RECIST was 4% and disease control rate (DCR) was 75%. PR and DCR by CHOI was 29% and 75%, respectively. Nineteen (68%) patients died within the study period and the median overall survival after initiation of RG was 18.3 months (95% CI: 7 – 23 months). No significant survival advantage was noted among pts who experienced PR vs stable disease by CHOI. Any grade adverse event (AE) was seen in 93% of pts, most common being hand-foot syndrome (61%), fatigue (50%) and weight loss (43%). Grade 3/4 AEs were noted in 43% pts (61% in the GRID study); most common were hand-foot syndrome and fatigue in 18% each. Dose reductions were required in 61% of pts and treatment interruptions were noted in 43%.

Conclusion: Continuous dosing with RG 120 mg daily is the preferred schedule for GIST pts at MD Anderson and

Summary of Median OS and PFS by RECIST and CHOI at first follow-up – Landmark Analysis

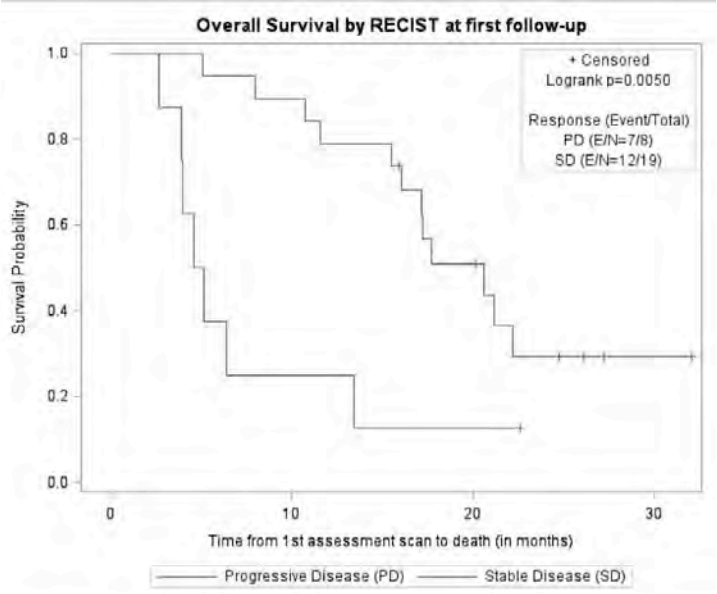
Response at first follow-up	Median OS in months by RECIST		Median PFS in months by RECIST		Median OS in months by CHOI		Median PFS in months by CHOI	
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
PD	4.8	(2.6-13.4)	1.3	(0-4.8)	3.9	(2.6-21.2)	2.6	(0-7.8)
SD	20.6	(15.5-not reached)	8.2	(6.2-20.6)	15.5	(5.1-22.2)	9.0	(0-not reached)
PR	N/A		N/A		17.7	(5.1-not reached)	6.8	(4.0-8.2)
p value (log-rank test)	0.005		<0.001		0.266		0.112	

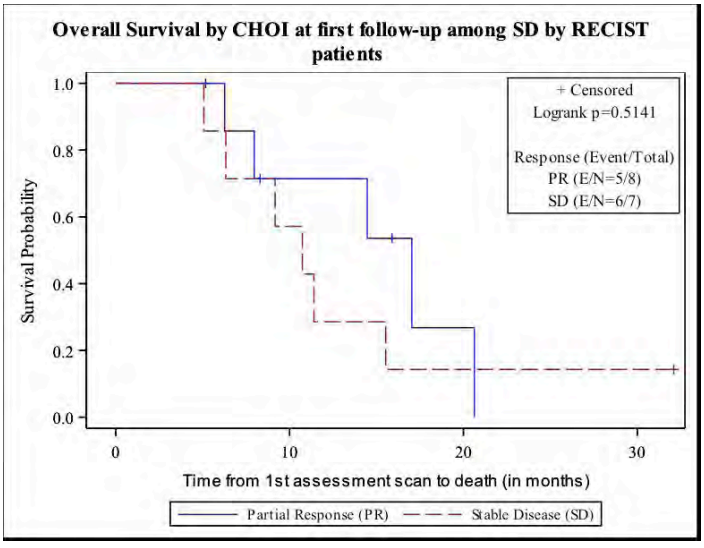
Abbreviations: PD, progressive disease; SD, stable disease; PR, partial response; OS overall survival; PFS, progression-free survival; CI, confidence interval; N/A, non applicable

compares favorably to the reported efficacy and toxicity of standard dosing. CHOI criteria was more sensitive than RECIST to detect responses, but that did not correlate with improved overall survival in this population.

Treatment-related adverse events

	Any grade n (%)	Grades 3/4 n (%)
Any event	26 (92.9)	12 (42.9)
Hand-foot skin reaction	17 (60.7)	5 (17.9)
Fatigue	14 (50.0)	5 (17.9)
Weight loss	12 (42.9)	4 (14.3)
Nausea	7 (25.0)	2 (7.1)
Diarrhea	11 (39.3)	2 (7.1)
Hypertension	7 (25.0)	2 (7.1)
Neuropathy	2 (7.1)	2 (7.1)
Arthralgia	1 (3.6)	0
Creatinine elevation	1 (3.6)	0
Liver function tests elevation	1 (3.6)	0





P1 - Poster 008 2562704

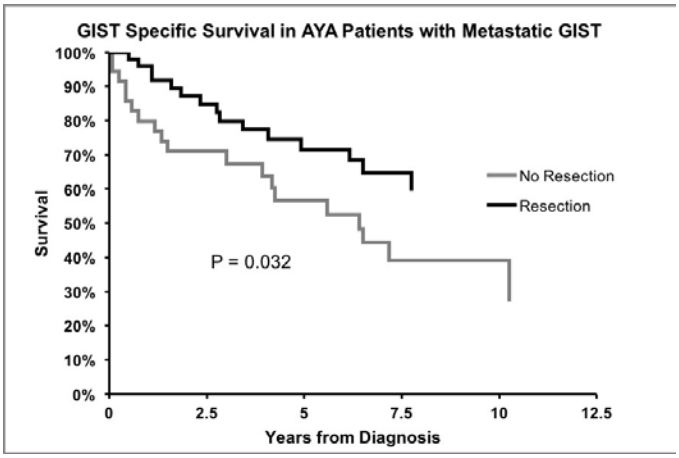
SURGICAL RESECTION IMPROVES THE SURVIVAL OF ADOLESCENTS AND YOUNG ADULTS WITH METASTATIC GASTROINTESTINAL STROMAL TUMORS: A POPULATION-BASED ANALYSIS IN THE UNITED STATES

Katherine Fero[1]; Taylor Coe[1]; Paul Fanta[3]; James Murphy[2]; Jason K. Sicklick, MD[1]
[1]Division of Surgical Oncology, Department of Surgery, University of California, San Diego, La Jolla, CA, USA; [2]Department of Radiation Oncology, University of California, San Diego, La Jolla, CA, USA; [3]Division of Hematology and Oncology, Department of Medicine, University of California, San Diego, La Jolla, CA, USA

Objective: There is a dearth of population-based evidence regarding outcomes of the adolescent and young adult (AYA) population with gastrointestinal stromal tumors (GIST). Some debate exists about whether AYA patients with metastatic GIST should undergo tumor resections in the absence of obstruction, perforation, bleeding, or pain. The aim of this study is to describe a large cohort of AYA patients with GIST, and investigate the impact of surgical resection on GIST-specific and overall survival.

Methods: This is a retrospective cohort study of patients in the Surveillance, Epidemiology and End Results (SEER) database. The database was queried for patients histologically diagnosed with GIST between 2001-2013, with follow-up through 2015. Baseline characteristics were compared between AYA (13-39 years old) and older adult (OA; ≥40 years old) patients with chi-square and t-tests; similarly, we compared characteristics among AYA patients stratified by operative management. Kaplan-Meier estimates were used for overall survival analyses. Cumulative incidence functions were used for GIST-specific survival analyses to account for the competing risk of non-cancer death. The impact of surgery on survival was evaluated with a multivariable Fine-Gray regression model.

Results: We identified 392 AYA among 5,765 patients with histologically-confirmed GIST. There was no significant difference between AYA and OA with regards to sex, race distribution, tumor size or stage at diagnosis. AYA patients more frequently had small intestine GISTs. Compared to OA, a larger proportion of AYA patients were managed operatively (78.4% vs. 84.7%, P<0.01). On subset analysis of AYA patients with metastatic disease, 60.4% were managed operatively. This AYA cohort with metastatic disease managed operatively had significantly improved GIST-specific survival (**Figure**) and overall survival as compared to those who did not undergo an operation (71.5% vs. 56.65%, P=0.032; 69.5% vs. 53.7%, P=0.039). Moreover, on multivariable analysis, among all AYA patients, operative management was associated with a 56% decreased risk of GIST-specific death, after adjusting for age, sex, race, year of diagnosis, tumor site, size, and stage.



Conclusion: We report the first population-based analysis of GIST outcomes in the AYA population. These patients are more likely to undergo surgical management than patients in the OA cohort. Tumor resection improved GIST-specific and overall survival in all AYA patients, including those with metastatic disease.

P1 - Poster 009 2565842

QUANTITATING CIRCULATING TUMOR DNA IN PEDIATRIC SARCOMA PATIENTS USING CAPP-SEQ

Avanthi T. Shah[1]; Jake Chabon[2]; Tej Azad[2]; Marcus Breese[1]; Aviv Spillinger[1]; Stanley Leung[1]; Maximilian Diehn[2]; Ash Alizadeh[2]; Alejandro Sweet-Cordero[1]
[1]Pediatrics, Stanford University, Belmont, CA, USA; [2]Stanford University, Stanford, CA, USA

Objective: To quantify circulating tumor DNA in pediatric Ewing sarcoma, osteosarcoma, synovial sarcoma, and alveolar and embryonal rhabdomyosarcoma using CAPP-Seq (CAncer Personalized Profiling by deep Sequencing).

Methods: A promising tool for non-invasive disease monitoring is analysis of circulating tumor DNA (ctDNA). Healthy individuals carry 1-10 ng/ml of cell-free DNA (cfDNA) in the blood; in oncology patients, ctDNA, which is released from tumor cells, comprises a fraction of the cfDNA and carries tumor specific alterations, such as mutations, translocations, and copy number alterations. Most existing methods for ctDNA detection require high tumor burden or are prohibitively expensive. Recent work at Stanford led to the development of CAncer Personalized Profiling by deep Sequencing (CAPP-Seq), a method capable of ultraspecific and ultrasensitive detection of ctDNA fractions as low as 0.01%. Utilizing COSMIC and TCGA data, recent sequencing publications defining the landscape of pediatric sarcomas, and our own in-house sequencing data, we designed a pediatric sarcoma CAPP-Seq selector, which is comprised of tiling biotinylated oligonucleotides that enrich for recurrently mutated regions via hybrid capture. This selector can be applied to a sequencing library prepared from patient cfDNA to enrich for genomic regions of interest and the resulting enriched library undergoes next-generation sequencing to allow for detection and quantification of circulating tumor DNA.

Results: In non-small-cell lung cancer, CAPP-Seq detected ctDNA levels highly correlated with tumor volume, distinguished residual disease and treatment-related imaging changes, and facilitated earlier therapeutic response assessment, compared to traditional imaging. We have isolated cfDNA from pediatric sarcoma patients and found that their levels are higher than levels found in adults and age-matched controls, likely due to a large fraction of contributing ctDNA. We have applied our selector to normal, healthy control cfDNA and pediatric sarcoma cell line libraries and found enrichment for regions in our selector. We have also applied our selector to primary tissue samples and patient-matched plasma samples, at diagnosis, and found enrichment for regions in our selector.

Conclusion: CAPP-Seq serves as a highly specific, ultrasensitive tool to detect circulating tumor DNA in pediatric sarcoma patients. This technology offers a promising method for more accurate diagnosis and management of pediatric sarcoma patients.

P1 - Poster 010 2570517

ERBB4 PROMOTES CELL SURVIVAL IN OSTEOSARCOMA LUNG METASTASIS THROUGH REGULATION OF NDRG1

Hongsheng Wang; Zhengdong Cai; Yingqi Hua, MD, PhD
Orthopedics, Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai, China

Objective: Osteosarcoma (OS) is the most common primary malignant bone tumor in children and adolescents. Lung metastasis is the leading cause of death in OS patients. The clarification of mechanism regarding cell survival during OS lung metastasis is important. We studied the role of ERBB4 in osteosarcoma lung metastasis.

Methods: Clinical samples of OS were evaluated by immunohistochemistry. RNA expression for ERBB4 were reviewed retrospectively. Gene knockdown and over-expression were used to explore the consequences of altered ERBB4 gene expression *in vitro* and *in vivo.* Functional assay regarding ERBB4 was performed afterward.

Results: We found ERBB4 level was highly expressed in the majority of OS tissues, and the level of ERBB4 expression correlated with metastatic progression and patient 5-year survival rate. Next, we demonstrated that ERBB4 expression increased in the adverse conditions, such as sphere culture and serum starvation culture. ERBB4 knockdown cells became more sensitive to anoikis, serum starvation, and chemotherapy. Functional studies revealed that suppression of ERBB4 inhibited OS cells growth and

induces cellular senescence *in vitro* and *in vivo* through targeting the expression of N-myc downstream regulated gene 1 (NDRG1). ERBB4 knockdown or over-expression responsively altered both the protein and mRNA levels of NDRG1. Conversely, NDRG1 can also regulate ERBB4 expression. Using orthotopic xenograft model, we found that depleted expression of ERBB4 and NDRG1 in murine and OS cells led to a significant decrease in lung metastasis, respectively.

Conclusion: Our present study indicated that ERBB4-NDRG1 axis promotes OS cells survival in the process of lung metastasis, and suggests a potential therapeutic target in OS.

P1 - Poster 011 2547973

TARGETING STRESS GRANULES AS A NOVEL THERAPEUTIC APPROACH FOR HIGH-RISK CHILDHOOD SARCOMAS

Amal M. EL Naggar, PhD[1]; Hongwei Cheng[2]; Syam Prakash Somasekharan[3]; Yemin Wang[4]; Bo Rafn[1]; Poul H. Sorensen[1]

[1]Pathology and Laboratory Medicine, The University of British Columbia, Vancouver, BC, Canada; [2]Vancouver Prostate Centre, University of British Columbia, Vancouver, BC, Canada; [3]BC Cancer Research Center, University of British Columbia, Vancouver, BC, Canada

Objective: To investigate the potential effects of HDAC class I inhibitor Entinostat (MS-275) on stress granule (SG) formation and sarcoma progression.

Background: Stress granules (SGs) are non-membrane bound cytoplasmic aggregates comprised of RNA binding proteins, select mRNAs, the 40S ribosome, and stalled translation initiation complexes. SGs are assembled in vitro and in vivo in cells exposed to diverse stress forms such as hypoxia and oxidative stress, resulting in silencing translation of SG-bound mRNAs. Recently, we showed for the first time that genetically blocking SGs dramatically inhibits metastasis of Ewing sarcoma (ES) and osteosarcoma (OS) cells in vivo. Therefore, targeting SGs represents a promising strategy to block sarcoma metastasis. We then performed in vitro cell-based drug screens for SG inhibitors and found unexpectedly that class I HDAC inhibitors (HDACi), notably Entinostat (MS-275), potently inhibit SG formation.

Methods: To confirm the in vitro effects of MS-275 on stress SG formation, ES and OS cell lines were treated with either vehicle or MS-275, and then subjected to different assays including SG immunoflourescence, Western blotting for SG proteins, migration assays, and reactive oxygen species (ROS) detection. In vivo studies were conducted using the renal subcapsular xenotransplantation model in which sarcoma cells are implanted under the kidney capsules of NOD/SCID mice, then mice are treated with vehicle alone or MS-275. Comprehensive pathological evaluation of primary tumors as well as lung metastatic lesions was then performed.

Results: We confirmed that different class 1 HDACi's block SG formation in sarcoma cells. In particular, MS-275 inhibits SG formation in vitro within a few hours of treatment. Moreover, MS-275 treated cells show enhanced ROS and are highly vulnerable to further oxidative insults such as ROS-inducing cytotoxic agents. Indeed, combining MS-275 with cisplatin or doxorubicin in vitro showed a marked synthetic lethal interaction. In vivo, we found that MS-275 treatment inhibits SG formation, enhances local ROS production in primary tumors, and induces tumor cell death in vivo. Moreover, MS-275 treatment almost completely blocked local invasion and lung metastasis of sarcoma cell lines in vivo.

Conclusion: These findings highlight a novel role for MS-275 in blocking SG formation and preventing sarcoma metastasis.

P1 - Poster 012 2565739

GENOME-WIDE MISTARGETING OF ONCOGENIC SWI/SNF(BAF) COMPLEXES IN SMARCB1(BAF47)-DEFICIENT SARCOMAS

Robert Nakayama, MD, PhD[1]; John Pulice[2]; Robert T. Williams[2]; Alfredo M. Valencia[2]; GD Demetri[3]; Cigall Kadoch[2]

[1]Orthopaedic Surgery, Keio University Hospital, Tokyo, Japan; [2]Pediatric Oncology, Dana Farber Cancer Institute, Boston, MA, USA; [3]Medical Oncology, Dana Farber Cancer Institute, Boston, MA, USA

Objective: SMARCB1/BAF47/INI1 is a core subunit of the mammalian SWI/SNF (BAF) family of ATP-dependent chromatin remodeling complexes, which remodel nucleosome architecture to achieve coordinated regulation of gene expression. Loss of BAF47 has been identified in several cancer types, including malignant rhabdoid tumor (MRT, 98%) and epithelioid sarcoma (EpS, 90%), strongly implicating this event as the oncogenic driver in these malignancies. However, the precise mechanism underpinning the tumor suppressive function of BAF47 to date remains unclear. In order to elucidate the underlying mechanism and to identify direct genetic targets of aberrant BAF complexes in this context, we comprehensively evaluated the effects of BAF47 reintroduction in BAF47-deficient sarcomas with respect to complex subunit composition, global chromatin structure, and gene regulation.

Methods: Eight MRT cell lines and Eight EpS cell lines were characterized as BAF47-deficient and subsequently modified with a constitutive BAF47 expression system by

lentiviral infection. The effects of BAF47 reintroduction into BAF47-deficient cell lines were evaluated at the levels of proliferation, BAF complex biochemical composition, global transcriptional signature (RNA-seq), and genome-wide localization (ChIP-seq).

Results: Reintroduced BAF47 stably integrated into BAF complexes, and remarkably, stabilized a highly specific set of BAF subunits. These biochemical changes were reproducibly associated with differential chromatin architecture and gene expression signatures hallmark to both MRT and EpS, and uniformly resulted in proliferative senescence of MRT and EpS cell lines in culture. BAF47 reintroduction drove genome-wide gain of BAF complex occupancy and the BAF47-specific BRG1 sites were localized to TSS-distal sites. Dramatic gain of H3K27ac occupancy and decrease of H3K27me3 and SUZ12 occupancy were observed at BAF47-specific BRG1 sites, suggesting that gain of gene activation and loss of gene repression were seen at the BAF47 specific sites.

Conclusion: These studies highlight, for the first time, the full spectrum of structural and functional contributions of the BAF47 subunit, implicating its role as a keystone in heteromorphic BAF complex assembly, which we determine govern specific genome-wide targeting mechanisms and chromatin-templated activities. These results reveal the mechanisms underlying the oncogenesis of BAF47-deficient sarcomas and point toward novel therapeutic strategies for this group of human sarcomas.

P1 - Poster 013 2544143

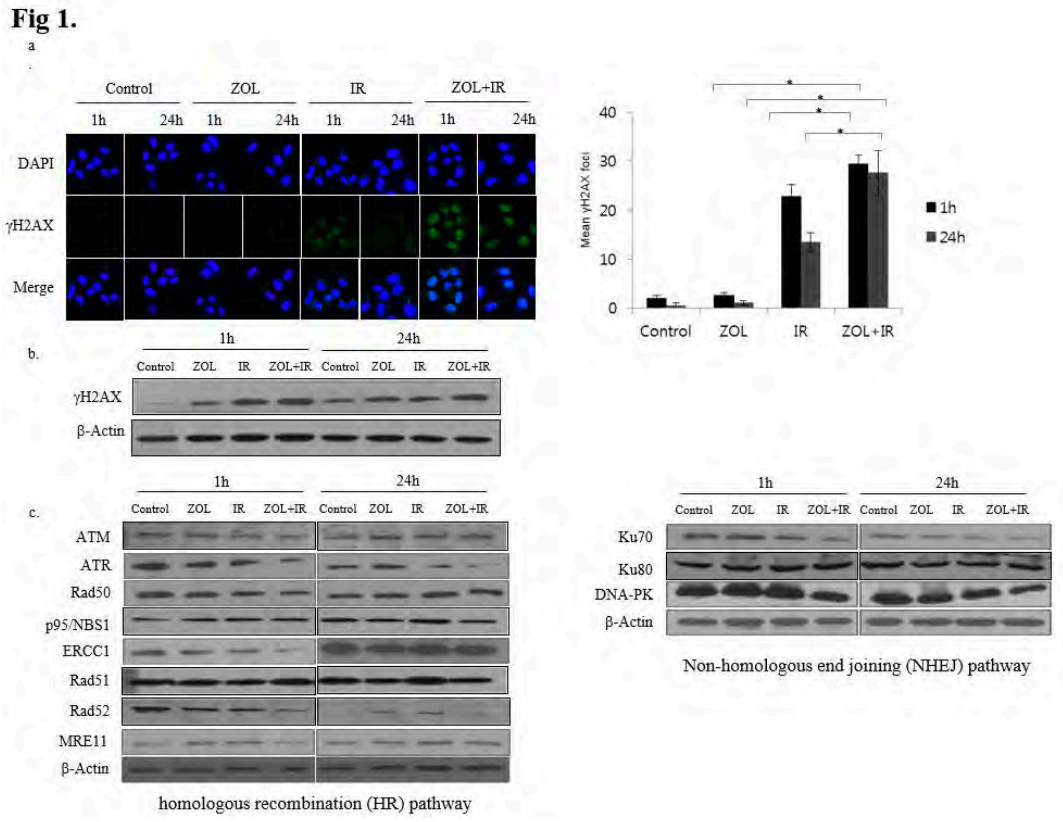
THE EFFECTIVENESS OF ZOLEDRONIC ACID AS A RADIOSENSITIZER FOR RADIOTHERAPY AGAINST OSTEOSARCOMA

Chang-Bae Kong; Kyung-Hee Lee; Eun Ho Kim
KCCH, Seoul, Korea (the Republic of)

Objective: An osteosarcoma (OS) is a primary malignant tumor of the bone derived from primitive transformed cells of mesenchymal origin. Radiotherapy (RT) in the local treatment of OS has limited benefits because of radioresistance, and thus, conventional RT is not effective in its management. The purpose of this study, therefore, was to investigate the potential of a third-generation bisphosphonate, zoledronic acid (ZOL), as a radiosensitizer against OS.

Methods: Biological effects were evaluated on the basis of cell survival, apoptosis, cell cycle, DNA damage, MAPK signaling, migration, and invasiveness.

Results: We demonstrated that the combination of ZOL with radiation showed growth inhibitory effects against human OS cells in both an orthotopic model, as well as in cells of an OS patient by enhancing the radiotoxicity of the applied radiation. Orthotopic models are essential for preclinical evaluation of therapeutic agents. Orthotopic models are used for studying the pathobiology of tumor progression and metastasis and identifying anticancer agents. For a model to have the best outcome of predicting clinical results, it should demonstrate the characteristics of the cancer in human patients, including the histologic type. Accordingly, we explored the available ZOL preclin-



ical models with an orthotopic model and a culture of OS patient–derived cells. ZOL+IR treatment showed radiosensitizing effects, as evidenced by increased apoptosis manifested as decreased Ψ_m and induced subG1, retained DNA damage through suppression of HR and NHEJ repair pathways (Fig. 1), decreased PI3K-Akt and MAPK signaling related to RT resistance of tumor cells (Fig. 2), and metastatic potential through decreased expression of EMT-related proteins (Fig. 3).

Conclusion: To conclude, our investigation for the first time demonstrates the therapeutic radiosensitizing effects of ZOL in OS cells. We attribute these effects to the inhibition of cell survival, cell cycle regulation, DNA repair activity, and tumor cell invasiveness. This radiosensitizing effect is associated with the inhibition of DNA DSB repair processes through HR repair and NHEJ repair signaling pathways, thereby enhancing radiation-induced cell apoptosis. Moreover, we provide biological evidence for the molecular basis of chemoradiation treatment for OS.

Fig 2.

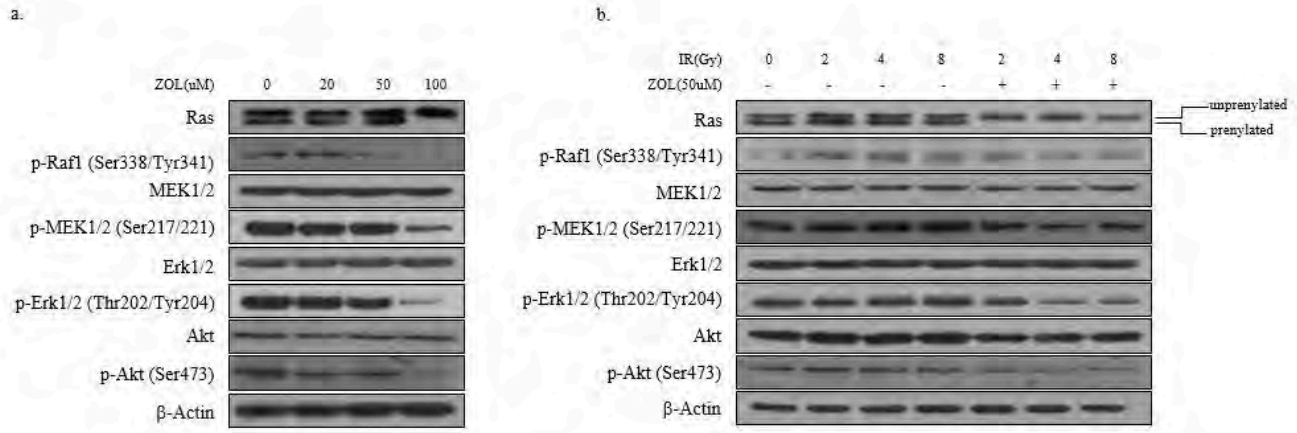
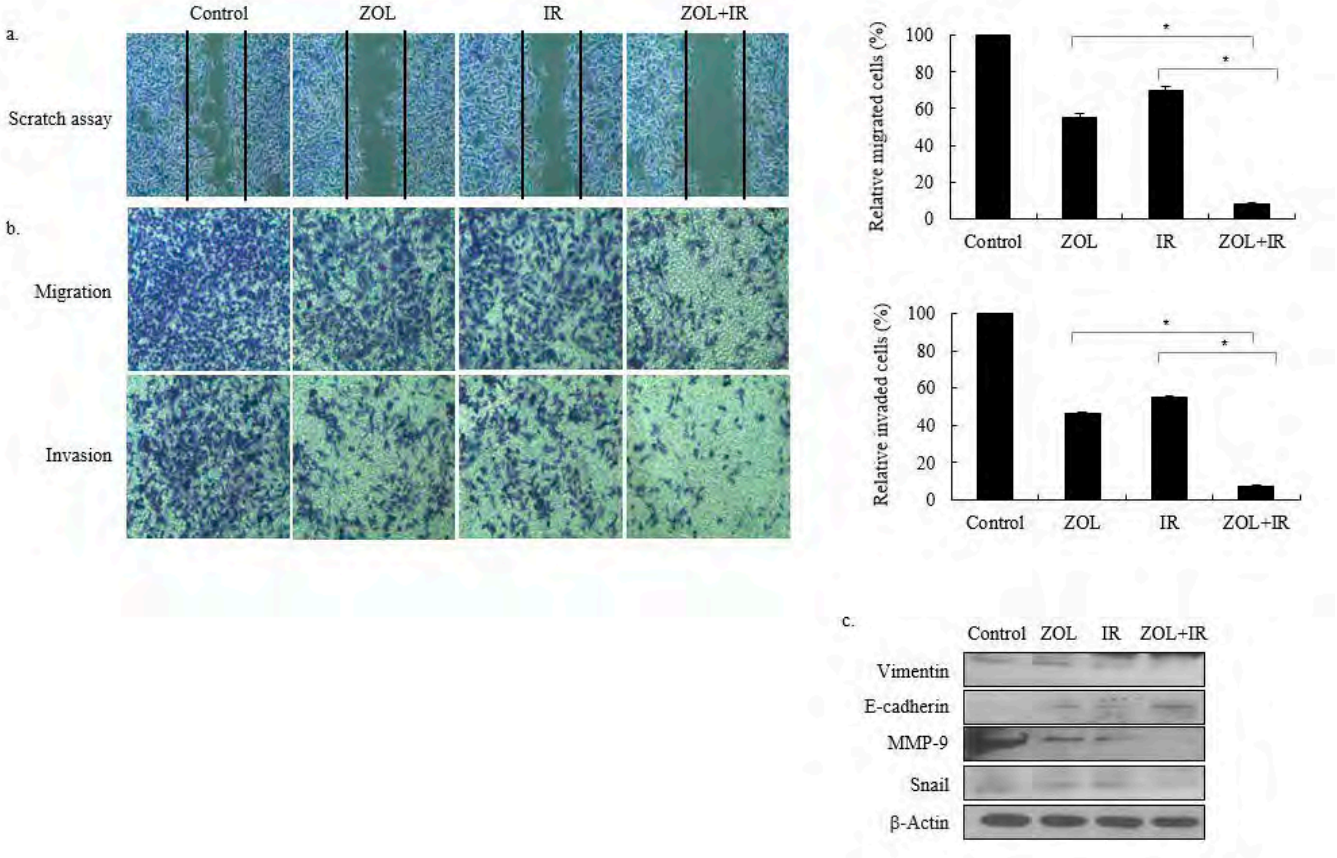


Fig 3.



P1 - Poster 014 2555397

NON-INVASIVE BIOLUMINESCENCE IMAGING OF ENGINEERED SARCOMA TUMORS IN THE LIVING CHICKEN EMBRYO

Benedict Jefferies[1]; Florian Lenze[1]; Anuja Sathe[2]; Rüdiger von Eisenhart-Rothe[1]; Roman Nawroth[1]; Philipp Mayer-Kuckuk[2]

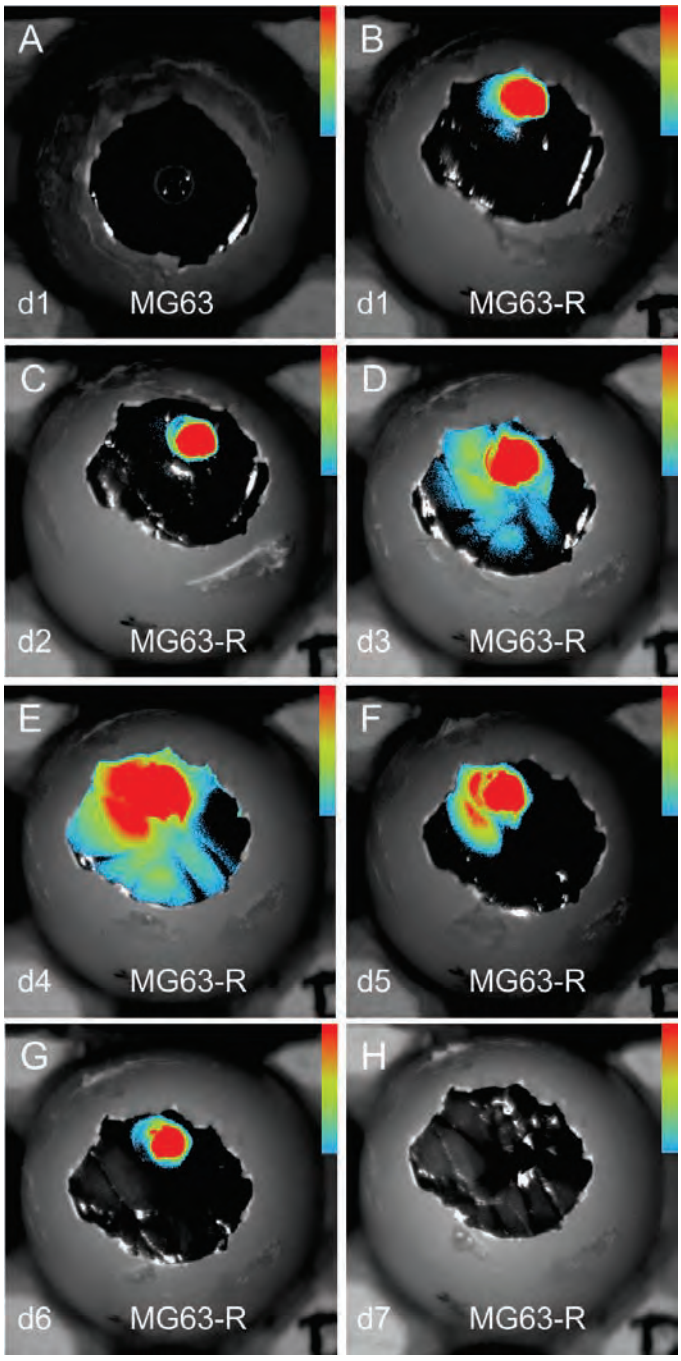
[1]Orthopedics, Technical University Munich, Munich, Germany; [2]Urology, Technical University Munich, Munich, Germany

Objective: Bioluminescence imaging (BLI) is an established mean for monitoring luciferase reporter gene expressing cells non-invasively. The growing interest in engineered tumor models prompted us to investigate BLI for the assessment of such models. Specifically, we hypothesized BLI of osteosarcoma models in the fertilized chicken egg, i.e, chick chorioallantoic membrane (CAM) assay.

Methods: We modified the human osteosarcoma cell lines MG63 and HOS with luciferase. These cell lines were termed MG63-R(reporter) and HOS-R, and data showed that bioluminescent light production correlated with cell number. Subsequently, the cells were seeded either onto basement membrane extract (BME) or gelfoam scaffolds, and these engineered tumor scaffolds were then grafted in vivo onto the CAM.

Results: BLI enabled non-invasive, specific detection of the engineered tumors on the CAM in the living chicken embryo. Further, BLI permitted daily, quantitative monitoring of the engineered tumors over the course of up to 7 days. Data showed that an extracellular matrix (ECM) composed of BME does not support tumor growth in either MG63-R or HOS-R based tumors. In contrast, the collagen-based gelfoam ECM induces a temporal proliferation burst in MG63-R cells.

Conclusion: Taken together, the data demonstrated non-invasive BLI of engineered human osteosarcoma models in living chicken embryos. The combination of CAM assay and BLI holds great potential for the examination of tumor angiogenesis, growth/apoptosis, stroma interactions and dormancy in engineered sarcomas.



P1 - Poster 015 2559102

CONCOMITANT REPROGRAMMING OF TUMOR CELL DIFFERENTIATION AND IMMUNE ENVIRONMENT INHIBITS OSTEOSARCOMA METASTATIC POTENTIAL

Claudia Chiodoni, PhD[1]; Ilaria Torselli[1]; Claudio Tripodo[2]; Chiara Ratti[1]; Cecilia Garofalo[3]; Silvia Galvan[1]; Maria Cristina Manara[3]; Katia Scotlandi[3]; Mario Paolo Colombo[1]

[1]Department of Experimental Oncology and Molecular Medicine, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [2]Department of Health Science, Human Pathology Section, University of Palermo, Palermo, Italy; [3]Experimental Oncology Lab, Istituto Ortopedico Rizzoli, Bologna, Italy

Objective: Osteosarcoma (OS) is the most common primary bone tumor in childhood and adolescence, with poor prognosis, because of the high rate of metastases, in particular to the lungs. Therapy of bone sarcomas is still firmly entrenched in conventional cytotoxic drugs; prognosis for patients with metastasis remains grim and few treatment options can be offered to patients that relapse after first line therapies. For an effective implementation of current therapy as well as for designing new therapies in OS, improved understanding of the disease biology is mandatory. Few mouse models recapitulating the human disease are currently available and xenografts of human OS lines in immune-deficient mice cannot reproduce the complex interaction of tumor cells with the surrounding stroma.

Methods: To fill such a gap, we recently developed new mouse OS cell models that grow orthotopically in the bone cavity spontaneously metastatizing to the lungs, well resembling human OS and we took advantage of these models to test the therapeutic efficacy in OS treatment of Trabectedin, a chemotherapeutic agent of marine origin, which mechanisms of action are only partially defined, and recently it has been reported that cytotoxicity on mononuclear cells is a key component of its antitumor activity.

Results: Experiments in our OS models showed significant efficacy in inhibiting primary tumor growth as well as experimental and spontaneous metastasis. We identified a double mechanism of action, targeting both tumor cells and immune microenvironment. Specifically Trabectedin induces a striking differentiation of neoplastic cells that, in turn, proliferate less and produce more bone matrix; on the other hand, it negatively affects the number of myeloid/monocytic cells, both locally at the tumor site and sistemically in peripheral blood, spleen and bone marrow, while increasing T cell tumor infiltration.

Conclusion: In conclusion we have developed new immunocompetent OS mouse models that well recapitulate the human disease and can be exploited to study OS biology and to evaluate the anti-tumor efficacy and mechanisms of action of immunotherapeutic approaches. In this context, we unveiled a dual activity of Trabectedin, which on one side induces neoplastic cell differentiation, leading to a more indolent phenotype, while, on the other, it redirects the local and systemic immune environment toward a less suppressive state.

P1 - Poster 016 2562030

EFFECT OF BONE MICROENVIRONMENT IN JAW OSTEOSARCOMA DEVELOPMENT

Hélios Bertin[1]; Romain Guiho[2]; Benoit Piot[1]; Pierre Corre[1]; Anne Brouchet-Gomez[3]; Françoise Redini[2]

[1]Oral and Maxillo-facial Surgery, CHU de Nantes, Nantes, France; [2]UMR957, Laboratoire de Physiopathologie de la Résorption Osseuse, Nantes, France; [3]Laboratoire d'Anatomie et Cytologie Pathologiques, Oncopôle - CHU de Toulouse, Toulouse, France

Objective: Osteosarcoma is the most frequent malignant bone tumor in children and adolescents. Jaw osteosarcoma (JOs) differs from the long bones osteosarcoma (LBOs) in an onset two decades later and a lower metastatic potential with better survival. The aim of our work is to develop a preclinical model of JOs in order (i) to investigate the potential role played by the bone microenvironment in the JOs development, (ii) to understand a different clinical behavior as compared with LBOs and (iii) to screen therapeutic drugs.

Methods: Using syngenic and xenogenic models from mouse and human osteosarcoma cell lines, and a tumor xenograft induced by patient derived JOs biopsy, we developed jaw osteosarcoma models in mice. The jaw model was compared to the tibia induced osteosarcoma model and characterized according to clinical parameters, microCT imaging and histologic settings. A comparative analysis of bone markers (RANK, RANKL, OPG), cells (RUNX2, TRAP) and angiogenesis (VEGF, CD146) was carried out at transcriptomic and immunohistochemical levels between the two locations in animal models and by using tissue micro-array (TMA) from human biopsies. Zoledronic acid targeted therapy was realized in jaw osteosarcoma model looking for a possible effect on the tumor growth and the metastatic development.

Results: The tumor growth was higher in LBOs models than in JOs and lung metastases were found in both models. The histological analysis of tumors in mice models showed non differentiated osteosarcoma features as described in human disease. The morphometric characterization by microCT revealed osteolytic lesions in jaw localization and osteogenic injuries in long bones. A transcriptomic overexpression of RANKL and a decreased expression of VEGF were found in JOs models. The TMA studies in human samples confirmed these observations showing a higher RANKL immunostaining and a lower

CD146 in JOs than in LBOs (72% vs 46%; p 0,02 and 55% vs 66%; ns). The CD146 angiogenic marker was associated with overall survival in JOs (HR 2.3 [0,8-6,6]). Zoledronic acid did not have a significant effect in reducing the tumor growth and lung metastasis in JOs animal models but showed a significant inhibition of the tumor osteolysis.

Conclusion: We describe the first animal model of jaw osteosarcoma in non-GM mice and its potential use in specific therapeutic targeting. The tumor angiogenesis and RANKL appear as differentiated markers of the bone tumor microenvironment between JOs and LBOs.

P1 - Poster 017 2566098

RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS INDUCED OSTEOSARCOMA CANCER STEM-LIKE CELLS WITH CO-EXPRESSION OF CD133

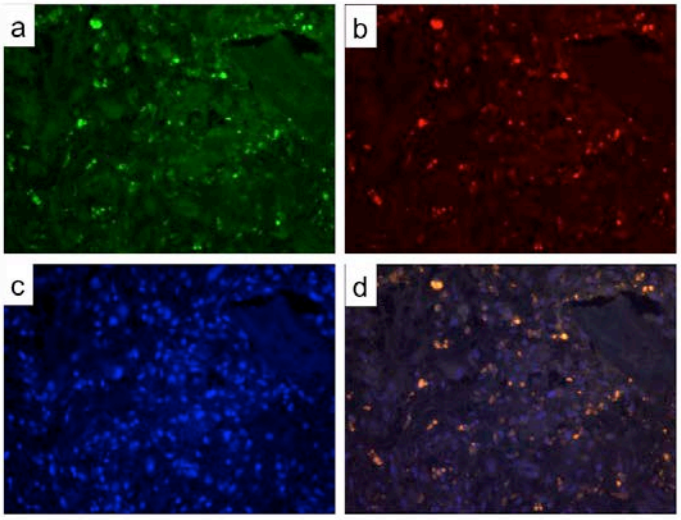
Akihiko Takeuchi, MD, PhD[1]; Yasuhiko Yamamoto[2]; Seiichi Munesue[2]; Norio Yamamoto[1]; Katsuhiro Hayashi[1]; Takashi Higuchi[1]; Kensaku Abe[1]; Yuta Taniguchi[1]; Hisaki Aiba[1]; Hiroyuki Tsuchiya[1]
[1]Orthopaedic Surgery, Kanazawa University Graduate School of Medical Science, Kanazawa, Japan;
[2]Biochemistry and Molecular Vascular Biology, Kanazawa University Graduate School of Medical Sciences, Kanazawa, Japan

Objective: Cancer stem cells (CSC) are defined as those cells that have the ability of self-renew, drive the tumorigenesis and chemoresistance. In osteosarcoma, CD133 has been reported as one of the cell surface markers for CSC in osteosarcoma and certain type of cancer such as brain, breast, pancreas, and colon, etc. Receptor for advanced glycation end-products (RAGE) is a pattern-recognition receptor and its engagement by ligands such as high mobility group box 1 (HMGB1) is implicated in tumor growth and metastasis. Recently, we found the co-localized expression of RAGE and CD133 in osteosarcoma (Fig.1). Accordingly, the purpose of this study was to analyze the relationship between RAGE expression and stemness in osteosarcoma.

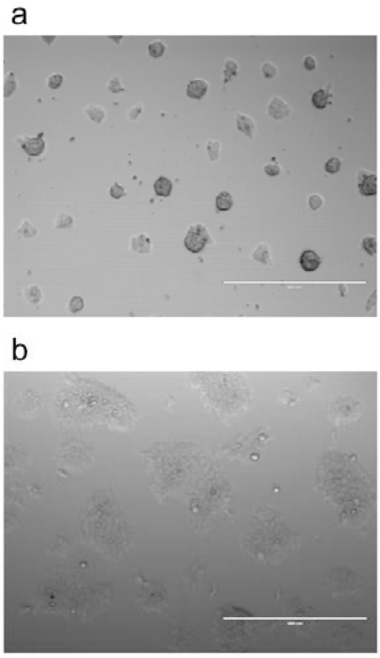
Methods: In order to establish stable transfectant, a human osteosarcoma cell line, HOS, was used; this yielding RAGE-overexpressing (HOS^{RAGE}) and mock-transfected control (HOS^{mock}) cells after stable transfection. We examined their proliferation, spheroid formation, migration, drug-resistance, expression of stem cell markers, and gene expressions *in vitro*.

Results: Cell proliferation of HOS^{RAGE} cells was significantly higher than that of HOS^{mock} cells at every time point. HOS^{RAGE} cells formed the spheroids in ultra–low attachment plates, but HOS^{mock} cells did not (Fig.2). In cell migration assay, the wound closure rate was significantly higher in HOS^{RAGE} cells than HOS^{mock} cells at 24 h after a monolayer denudation. HOS^{RAGE} cells were significantly more resistant to cisplatin and doxorubicin than HOS^{mock}. The expression of CD133 in HOS^{RAGE} was significantly higher than that in HOS^{mock} by flow cytometory. The real-time PCR showed that the stem cell marker genes expression such as *Sox2* and *Nanog* were significantly higher in HOS^{RAGE} than HOS^{mock}.

Conclusion: This study demonstrated that RAGE-transfected osteosarcoma cells showed cancer stem-like characteristics.Further analyses are required to unveil how RAGE could induce the stem cell markers and related genes. RAGE might be a novel therapeutic target against cancer stem cells of osteosarcoma.



Confocal immunocytochemistry of osteosarcoma
(a. RAGE, b. CD133, c. DAPI, d. merged).
The expression of CD133 and RAGE was co-localized.



Spheroid assay. HOS^{RAGE} formed spheroids (a), whereas HOS^{mock} did not form spheroid in ultra–low attachment plates (b).

P1 - Poster 018 2565773

TRENDS IN INCIDENCE AND OUTCOME OF GASTROINTESTINAL STROMAL TUMORS IN THE NETHERLANDS IN THE IMATINIB ERA

Ronald Tielen; Rob Verhoeven; Johannes Bonenkamp; Valery Lemmens; Winette van der Graaf; Johannes de Wilt
Radboudumc, Nijmegen, Netherlands

Objective: In this study, we aimed to study the incidence, treatment and outcome of GIST in an era known for advances in diagnosis, imaging and the introduction of effective systemic therapy in this disease.

Methods: Nationwide population-based data were retrieved from the Netherlands Cancer Registry (NCR). All patients with a GIST in the period of 2001 – 2012 were included. Primary treatment, defined as the treatment within the first 6 – 9 months after diagnosis, was studied. Age-standardized incidence was calculated according to the European standard population. Changes in incidence were evaluated by calculating the estimated annual percentage change (EAPC). Relative survival (RS) was used for survival calculations with follow-up available until December 2012.

Results: A total of 1749 (945 male and 804 female) patients were diagnosed with GIST. At primary diagnosis, 1286 (74%) patients presented with localized GIST, and 323 (18%) patients presented with metastatic GIST. In 140 patients (8%) the disease was unknown. The majority of GISTs were located in the stomach (1020 patients, 58%), followed by the small intestine (411 patients, 23%), rectum (69 patients, 4%), and other/unknown (249 patients, 14%). The incidence of localized GIST increased from 3.1 (2001) to 7.0 (2012) per 1,000,000 person-years, and the EAPC was 7,1% (95% CI 4.1 -10.2, p < 0,001). For primary metastatic GIST, the incidence was 1.3 per 1,000,000 person-years in both 2001 and 2012 (p = 0.18). The incidence for unknown disease stage decreased from 1.0 per 1,000,000 person-years in 2001 to 0.3 in 2012, EAPC was -12.1% (95% CI -20.0 - -4.3%, p 0,004). The 3-year RS for all patients improved from 77.8% (95% C.I. 73.0 – 82.1) in 2001 – 2004 to 84.1% (95% C.I. 80.1 – 87.6) in 2009 – 2012. Patients with a localized GIST had a 5-year RS of 88% (95% C.I. 84.9 – 90.0). Patients with a localized gastric GIST had the highest 5-year RS rate of 83.1% versus 78.6, 73.6, approximately 50% for GISTs of the small intestine/duodenum, rectum and other GI locations, respectively. Patients with a primary metastatic GIST had a 5-year RS of 48.3% (95% C.I. 41.0 – 55.3).

Conclusion: The present study demonstrates a stable incidence of GIST of approximately 8 per 1,000,000 person-years and one in six patients presenting with metastatic disease. Relative survival improved significantly over the years for patients with both localized and metastatic GIST.

P1 - Poster 019 2553097

THE ANDROGEN RECEPTOR (AR) IS A POTENTIAL NOVEL PROGNOSTIC MARKER AND ONCOGENIC TARGET IN OSTEOSARCOMA WITH DEPENDENCE ON CDK11

Yunfei Liao; Slim Sassi; Stefan Halvorsen; Yong Feng; Edwin Choy; Gregory Cote; Francis Hornicek; Zhenfeng Duan
Massachusetts General Hospital, Boston, MA, USA

Objective: Osteosarcoma is the most common bone cancer in children and adolescents, and has been considered as a hormone-related cancer. Previously, we have found that cyclin-dependent kinase 11 (CDK11) signaling is essential for osteosarcoma cell growth and survival. However, the signaling network of CDK11 in osteosarcoma is unknown.

Methods: CDK11 siRNA gene targeting, expression profiling, and network reconstruction of differentially expressed genes were performed between CDK11 knock down cell lines and wild type osteosarcoma cells. According to the results, we examined the expression and relationship between CDK11 and androgen receptor (AR) in osteosarcoma cell lines and patient tissues. The functional roles of AR in growth/viability and migration of osteosarcoma cell lines were evaluated as well.

Results: Reconstructed gene network pointed to the AR as key to CDK11 signaling in osteosarcoma. CDK11 increased AR-dependent transcriptional activation in osteosarcoma cell lines. AR protein was shown to be highly expressed in various osteosarcoma cell lines and in tumor tissues from osteosarcoma patients. Tissue microarray analysis showed that the disease-free survival rate for patients with high levels of AR protein expression was significantly shorter than for patients with low AR. In addition, AR gene expression knockdown via siRNA greatly inhibited cell growth and viability. Similar results were found in osteosarcoma cells treated with AR inhibitor (bicalutamide).

Conclusion: These findings suggest that CDK11 is involved in the regulation of AR pathway and AR can be a potential novel prognostic marker and therapeutic target for osteosarcoma treatment.

P1 - Poster 020 2566414

THE CDK4 & 6 INHIBITOR ABEMACICLIB BLOCKS TUMOR GROWTH IN PRECLINICAL MODELS OF PEDIATRIC EWING'S SARCOMA

Michele Dowless, BS; Caitlin May; Timothy Holzer; Wayne Blosser; Sean Buchanan; Gerard Oakley; Richard Beckmann; Louis F. Stancato
Eli Lilly and Company, Indianapolis, IN, USA

Objective: Abemaciclib (LY2835219) is an ATP-competitive inhibitor of cyclin-dependent kinases 4 and 6 (CDK4

& 6) currently undergoing clinical evaluation as a single agent or in combination trials in adults with breast cancer and non-small lung cancer; trials in children and young adults with recurrent and refractory solid tumors are now enrolling. Ewing's sarcoma (ES) is a highly aggressive pediatric solid tumor of bone and soft tissue, genetically characterized by chimeric transcription factors resulting from recurrent chromosomal translocations. Despite treatment regimens involving surgery, radiation, and chemotherapy, the 5-year disease-free survival rate is 60% and drops to 30% for patients presenting with metastatic disease. Here, we investigated abemaciclib activity preclinically to determine if single agent or combination with standard therapy effectively blocked tumor growth in ES models.

Methods: *In vitro* sensitivity to abemaciclib was assessed in a panel of 150 cancer cell lines; 4 ES cell lines were used for further characterization. Assays included high content imaging and FACS for cell cycle changes; immunoblotting and protein expression arrays to investigate the mechanism of action, resistance, and senescence-associated secreted protein phenotype (SASP); and Modaplex-based assessment of transcriptional changes. Thirteen ES patient-derived xenograft (PDX) models were used to evaluate abemaciclib activity alone and in combination with chemotherapy.

Results: ES was identified as particularly sensitive to abemaciclib *in vitro*. Several of the most sensitive cell lines harbored *CDKN2A* loss while *RB1* mutation or *CCNE1* amplification was associated with resistance. A senescence-like phenotype was observed following abemaciclib treatment whereby cell cycle was blocked in Rb wild-type cells and pro-inflammatory cytokine secretion increased. However, cells did not appear to have undergone classic irrevocable senescence as cell growth resumed upon abemaciclib removal, and resistance to increasing concentrations of drug was detected. Tumor growth of ES PDX models was strongly inhibited by abemaciclib, especially in combination with chemotherapy and objective response was observed in 50% of PDX models.

Conclusion: Preclinical models of ES are responsive to abemaciclib at clinically relevant concentrations as a single agent and in combination with chemotherapy. Therefore, cell cycle inhibition in selected pediatric tumor models of Ewing's sarcoma with abemaciclib results in anti-tumor effects.

P1 - Poster 021 2570258

TARGETING THE EIF4E-MEDIATED TRANSLATIONAL MACHINERY OF EWING SARCOMA: THERAPEUTIC CONVERGENCE OF THE MTOR AND MNK PATHWAYS

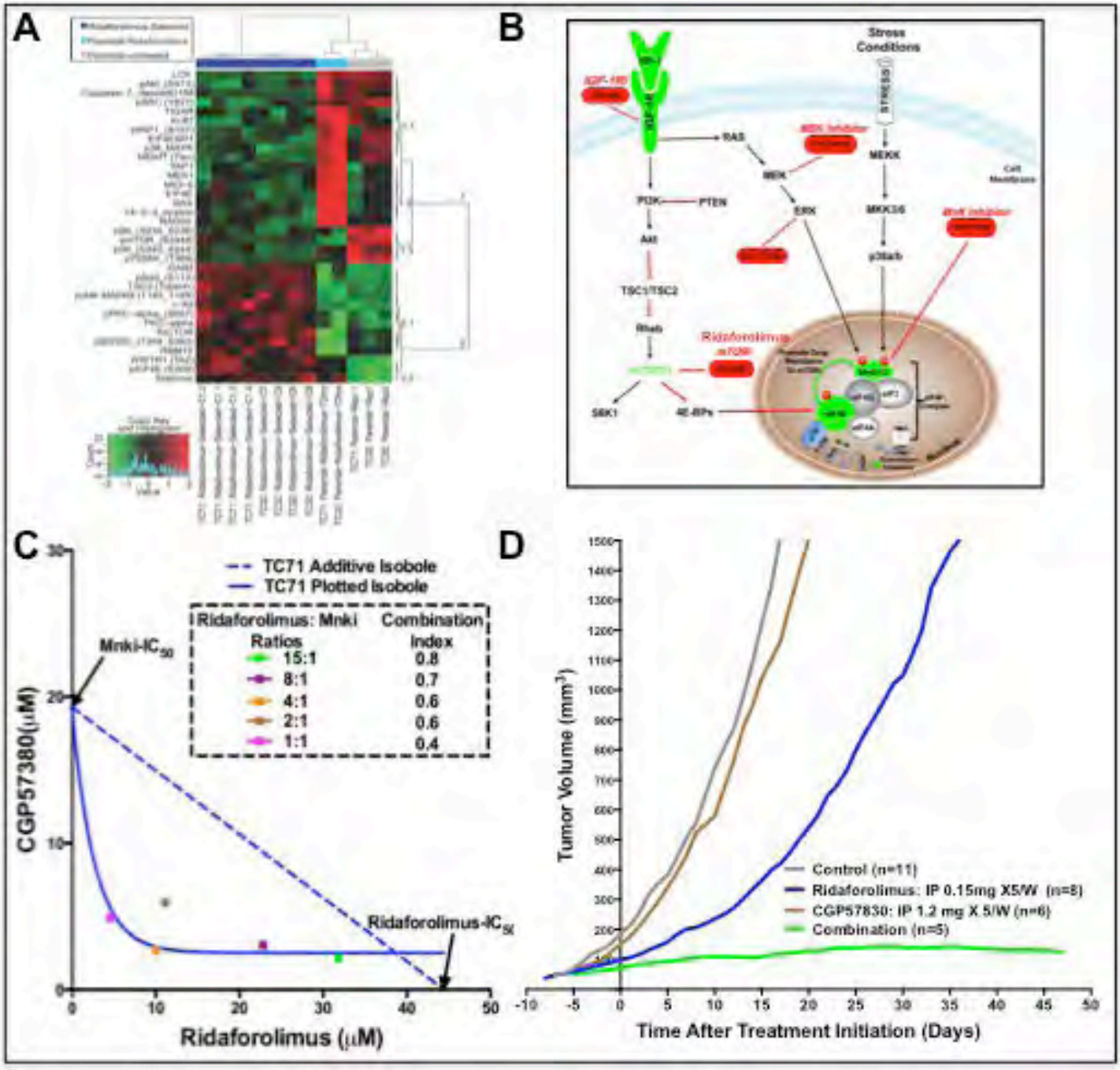
Joseph A. Ludwig, MD[1]; Brian A. Menegaz[1]; Salah Lamhamedi-Cherradi[1]; Najat Daw[2]; Ravin Ratan[1]; Vivek Subbiah[3]; Hesham Amin[4]; Alexander Lazar[4]; Robert S. Benjamin[1]

[1]Sarcoma Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA; [2]Pediatrics, MD Anderson Cancer Center, Houston, TX, USA; [3]Investigational Cancer Therapeutics, MD Anderson Cancer Center, Houston, TX, USA; [4]Pathology, MD Anderson Cancer Center, Houston, TX, USA

Objective: As the predominant oncogenic driver of Ewing sarcoma (ES), the EWS-FLI1 fusion protein acts as a transcription factor (TF) to alter transcription of more than 500 genes, including ones that activate the IGF-1R/PI3K/Akt/mTOR and MAPK signaling cascades. Though global effects of the EWS-FLI1 TF can be suppressed using inhibitors of LSD1 or RNA Helicase A, the most effective biologically targeted therapies in clinic today target downstream mediators of IGF-1R and/or mTOR. Unfortunately, even when ES patients benefit from IGF-1R- or mTOR-targeted therapies, responses rarely exceed two months. In an attempt to avert acquired mechanisms of resistance (MOR), we sought to identify novel protein targets that induce synthetic lethality in ES when the mTOR-signaling cascade is blocked.

Methods: Our research approach sought to identify MOR to ridaforolimus, a prototypical TORC1 inhibitor. Chronic ridaforolimus exposure led to mTOR-resistant ES cell lines, which were subsequently analyzed using reverse-phase protein lysate arrays (RPPA). Proteins that were strongly and consistently upregulated in mTOR-resistant cells lines were subsequently validated using Western blots, then subjected to further scrutiny in the preclinical setting using in vitro cell-based assays, xenografts, and human clinical samples.

Results: Among >200 proteins assessed by RPPA, pEIF4E was one of just three that were significantly upregulated. This protein is a key regulator of mRNA translation that sits squarely at the convergence of the mTOR and MAPK signaling cascades. When phosphorylated by mTOR, EIF4E disengages from 4E-BP1 and joins the EIF4F complex. Subsequent phosphorylation of EIF4E at Ser 209 by the MAPK interacting kinase protein (Mnk), immediately downstream of ERK and p38 MAPK pathways, is the rate-limiting step for selective cap-dependent translation of EIF4E-sensitive mRNA transcripts. Co-targeting the two pathways that activate pEIF4E—mTOR and Mnk—led to synergistic reductions cell proliferation and marked tumor regression in murine xenograft models.



Conclusion: This mechanism of pEIF4E-mediated resistance to rapalogs has been observed in select lymphomas and prostate cancers but has not previously been reported to occur in any sarcoma subtype (manuscript in press, JNCI). Therapeutic strategies that quell pEIF4E-mediated oncoprotein translation provide a universal approach to effectively overcome rare and heterogenous 'upstream' events present in ES tumors.

P1 - Poster 022 2566290

HIGH-THROUGHPUT CHEMICAL SCREENING IDENTIFIES FOCAL ADHESION KINASE (FAK) AND AURORA KINASE B INHIBITION AS A SYNERGISTIC TREATMENT COMBINATION IN EWING SARCOMA

Brian Crompton, MD[1]; Sarah Wang[1]; Elizabeth Hwang[1]; Rajarshi Guha[2]; Matthew Boxer[2]; Crystal McKnight[2]; Min Shen[2]; Nicole Melong[3]; Chansey Veinotte[3]; Jason Berman[3]; Matthew Hall[2]; Mindy Davis[2]; Kimberly Stegmaier[1]

[1]Pediatric Oncology, Dana-Farber Cancer Institute, oston, MA, USA; [2]National Center for Advancing Translational Sciences, Rockville, MD, USA; [3]Dalhousie University, Halifax, NS, Canada

Objective: Ewing sarcoma is the second most common bone malignancy of childhood. Current treatment employs chemotherapy, surgery, and radiation. Although this approach cures approximately 70% of patients with localized disease, treatments are largely ineffective for patients with metastases or relapse. Furthermore, these treatments are associated with an alarming rate of long-term toxicities. New treatment combinations are necessary to improve cures and lower toxicities for these patients.

Methods: We recently found that Ewing sarcoma is dependent on focal adhesion kinase (FAK) for cell viability and tumor proliferation. In order to identify candidate treatment combinations for Ewing sarcoma, we performed a screen of 1912 compounds to identify those with synergistic anti-Ewing activity when combined with FAK inhibition. The A673 Ewing cell line was treated with PF-562271, a FAK-specific inhibitor, in combination with compounds from the Mechanism Interrogation PlatE (MIPE) 4.0 library. Cell viability was measured after 48 hours of treatment. The activity of top scoring combinations in this screen were then validated across multiple Ewing cell lines *in vitro* and in zebrafish and murine xenograft models of Ewing sarcoma.

Results: Multiple computational metrics were utilized to identify and rank all compound combinations for synergistic impairment of cell viability. Multiple Aurora kinase inhibitors scored as synergistic with FAK inhibition in this screen. Aurora kinases are important in the regulation of mitosis and are highly expressed in Ewing sarcoma tumors and cell lines. We found that Aurora kinase B inhibitors are synergistic across a larger range of doses than Aurora kinase A inhibitors when combined with FAK inhibition in multiple Ewing cell lines. We found that the combination of AZD-1152, an Aurora kinase B-selective inhibitor, and PF-562271 induces apoptosis in Ewing cells at doses that have minimal effect on cell survival when treated with either drug alone. We also found that the combination significantly impairs tumor proliferation and prolongs survival in multiple xenograft models of Ewing sarcoma.

Conclusion: Our data demonstrate that FAK and Aurora kinase B inhibition synergistically impair Ewing sarcoma cell viability *in vitro* and significantly inhibits tumor proliferation *in vivo*. We believe this study supports the development of a clinical trial testing the safety and efficacy of the combination of FAK and Aurora kinase B inhibition for patients with Ewing sarcoma.

P1 - Poster 023 2566408

AN EWS-FLI1-SYNTHETIC LETHAL SHRNA SCREEN IDENTIFIES CANDIDATE TUMOR-CELL SPECIFIC THERAPEUTIC TARGETS IN EWING SARCOMA

Christiane Schaefer, PhD Student[1]; Nikhil Mallela[2]; Philipp Berning[1]; Jochen Seggewiß[3]; Eberhard Korsching[2]; Uta T. Dirksen[1]; Jenny C. Potratz[1]

[1]University Children's Hospital Münster, Münster, Germany; [2]Institute of Bioinformatics, Westfälische Wilhelms-Universität Münster, Münster, Germany; [3]Institute of Human Genetics, University Hospital, Münster, Münster, Germany

Objective: Ewing sarcoma (ES) is the second most common malignant bone cancer in children and young adults. To improve prognosis, particularly for high-risk patients, and to reduce treatment toxicities, novel treatment strategies are needed. ES is genetically characterized by chromosomal translocations leading to oncogenic transcription factors such as EWS-FLI1. Clinical approaches to target EWS-FLI1 remain problematic. However, targeting of EWS-FLI1 cooperating pathways could serve as alternative tumor cell-specific strategy. To identify such pathways and targets, we established a pooled EWS-FLI1-synthetic lethal shRNA screening approach.

Methods: We utilized an A673 ES cell line derivate with constitutive shRNA knockdown of EWS-FLI1 (-off) or control (-on). Cell lines were transduced with the Decode Pooled Lentiviral shRNA Screening Library consisting of 4,675 distinct shRNA sequences, targeting 709 human protein kinases.

Results: Transduction conditions were adjusted to integrate one single shRNA per cell and protein knockdown efficiency was validated. A 100-fold representation of individual shRNAs was maintained at all times. Ion Proton Next-Generation sequencing (NGS) was carried out for quantification and identification of enriched or depleted shRNA sequences in EWS-FLI1-on and -off cell populations: shRNAs depleted from surviving cell populations serve as potential targets.

Applying a model-based algorithm, we identified a hit-list of 20 potential EWS-FLI1 specific target genes, among them BUB1B, CDK4, EPHB3, PRKD2, and PTK6. First validations confirmed EPHB3 and PRKD2 protein knockdown and impaired cell proliferation and colony formation capacities specifically in the EWS-FLI1 (-on) background. Silencing of BUB1B however induced variable lethality in

ES cell lines and a primary culture, not clearly specific to EWS-FLI1 expression.

Conclusion: The established pooled shRNA screening protocol thus identified candidate targets in an EWS-FLI1 synthetic lethal setting; to be evaluated for tumor-cell specific therapeutic strategies as well as for their contribution to the molecular mechanisms of EWS-FLI1-driven sarcomagenesis.

P1 - Poster 024 2564896

COMBINATION OF EPIGENETIC DRUGS (SAHA-HCI2509) SYNERGISTICALLY AFFECTS PROLIFERATION IN EWING SARCOMA

Lourdes Hontecillas-Prieto[1]; Daniel J. Garcia-Dominguez[1]; Pablo Rodríguez-Núñez[1]; Rosa García-Mejías[1]; Guillem Pascual- Pastó[2]; Angel Montero Carcaboso[2]; Laura Romero-Pérez[1]; Juan Diaz-Martin[1]; Enrique De Álava *Casado[1]*

[1]Molecular Pathology, Instituto de Biomedicina de Sevilla (IBiS)/Hospital Virgen del Rocio/CSIC/Universidad de Sevilla, Seville, Spain; [2]Developmental Tumor Biology Laboratory, Fundacio Sant Joan de Deu, Department of Pediatric Hematology and Oncology, Hospital Sant Joan de Deu, Barcelona, Spain

Objective: Epigenetic regulation is crucial in mammalian development and maintenance of tissue-cell specific functions. Perturbation of epigenetic balance may lead to alterations in gene expression, resulting in cellular transformation and malignancy. Previous studies in Ewing sarcoma (ES) have shown that the nucleosome remodeling and histone deacetylase (NuRD) complex (histone deacetylases and Lysine-specific demethylase 1) binds directly to EWSR1-FLI1 oncoprotein modulating its activity. The role of EWSR1-FLI1 as a driver of proliferation, transformation, and cellular growth in ES is widely known. The present study was conducted to evaluate the effects of the histone deacetylase inhibitor suberoylanilidehydroxamic acid (SAHA) and Lysine-specific demethylase 1 inhibitor (HCI2509) as single agents and in combination on different biological functions in ES.

Methods: Experiments were made for both drugs in monotherapy and in combination at different times and concentrations in ES cell lines. ATP-lite assay was used to evaluate cell viability and sensitivity. We then evaluated by flow cytometry cell cycle (propidium iodide) and apoptosis (cleaved caspase 3).To study directional ES cell migration we carried out a wound healing assay. RT-qPCR and Western Blot were used to study the modulation of EWS-FLI 1 and selected EWS-FLI1 targets in treated ES cell lines. Finally, different ES patient-derived xenograft (PDX) mouse models were used to evaluate the combination effects on tumor progression.

Results: The study of cell viability and proliferation showed a synergistic effect between two drugs (SAHA and HCI2509) in most ES cell lines analyzed (4/5). Moreover, we observed a synergistic effect of this combination in the induction of apoptosis at 24 and 48 hours after treatment, together with accumulation in G1 phase of the ES cell lines and a blockage of migratory capacity. Treatment either in monotherapy or in combination caused a significant decrease in the expression of the EWSR1-FLI1 fusion mRNA and protein levels as well as in its downstream targets. The anti-tumoral effect of the combination was studied in PDX mouse models, in which we observed a significant decrease in tumor volume.

Conclusion: Preclinical data showed that SAHA and HCI2509 combination affects proliferation in ES likely by inducing a decrease in the expression of EWSR1-FLI1.

P1 - Poster 025 2556655

MOLECULAR TARGETING OF CDK4/6 AND IGF-1R IN A *FUS-ERG* FUSION DOXORUBICIN-RESISTANT EWING SARCOMA/PNET PATIENT-DERIVED ORTHOTOPIC XENOGRAFT (PDOX) MODEL

Takashi Murakami, MD[1]; Arun S. Singh[2]; Tasuku Kiyuna[1]; Sarah M. Dry[3]; Yunfeng Li[3]; Kentaro Igarashi[1]; Kei Kawaguchi[1]; Yong Zhang[1]; Tara A. Russell[4]; Mark A. Eckardt[4]; Jane Yanagawa[4]; Noah Federman[5]; Itaru Endo[6]; Frederick C. Eilber[4]; Robert M. Hoffman[1]

[1]AntiCancer, Inc., San Diego, CA, USA; [2]Division of Hematology-Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [3]Department of Pathology, University of California Los Angeles, Los Angeles, CA, USA; [4]Division of Surgical Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [5]Department of Pediatrics and Department of Orthopaedics, University of California, Los Angeles, Los Angeles, CA, USA; [6]Department of Gastroenterological Surgery, Yokohama City University, Graduate School of Medicine, Yokohama, Japan

Objective: Ewing sarcoma/PNET is a small round blue cell tumor (SRBCT) that is often characterized by *EWS-FLI1* and *EWS-ERG* translocations. A small subset of Ewing Sarcoma/PNET lack canonical translocations and non-canonical translocations such as *CIC-DUX4* and less commonly *FUS-ERG* have been identified. It is unknown whether these truly represent Ewing/PNET and if the current standard therapies are appropriate for these patients. Preclinical models allow such questions to be answered in this and other rare malignancies. In the present study, *FUS-ERG* fusion Ewing sarcoma/PNET (Askin's tumor) harboring a CDKN2A/B loss was implanted in the right chest wall of nude mice to establish a patient-derived orthotopic xenograft (PDOX) model. The aim of the present study was to determine efficacy of conventional chemother-

apy and CDK4/6 and IGF-1R inhibitors on this *FUS-ERG* PDOX model.

Methods: Harvested tumor from the patient's chest wall tumor was microdissected and initially implanted subcutaneously in a nude mouse; after growth, this tumor was subsequently implanted into the right chest wall of the nude mouse corresponding to the patient's tumor location via a microsurgical approach. Tumor sequencing was carried out via Foundation Medicine Sequencing. The PDOX models were randomized into the following groups when tumor volume reached 50 mm^3 : G1: untreated control; G2: treated with doxorubicin (i.p., 3 mg/kg, weekly, 2 weeks); G3: treated with Palbociclib (p.o., 100 mg/kg, daily, 14 days); G4: treated with Linsitinib (p.o., 25 mg/kg, daily, 14 days).

Results: We were able to establish a PDOX model of a rare *FUS-ERG* Ewing Sarcoma/PNET. Tumor growth was significantly suppressed both in G3 (palbociclib) and in G4 (linsitinib) compared to G1 (untreated control) at all measured time points. The model characterized the CDKN2A/B loss as a driver mutation in this patient's tumor and identified palbociclib as a putative treatment for her disease. In contrast, the standard of care DOX did not inhibit tumor growth at any time point. This was in concert with a modest 10% tumor necrosis rate of 2 cycles of neoadjuvant VDC chemotherapy.

Conclusion: The results of the present study demonstrate the power of the PDOX model to model the human disease and to identify effective targeted therapy of a DOX-resistant Ewing sarcoma while incorporating genetic sequencing technologies. The results of this study suggest the potential of PDOX models to individually tailor targeted therapies for molecularly defined rare cancers.

P1 - Poster 026 2553440

DEPENDENCE RECEPTORS INTERFERENCE TO PREVENT OSTEOSARCOMA PROGRESSION AND METASTATIC DISSEMINATION

Morgane Monchanin[1]; Jean Baptiste Langlois[2]; François Leloarer[1]; Clementine Favrot[3]; Perrine Marec-Bérard[1]; Agnes Bernet[3]; Jean-Yves Blay[1]; Aurelie Dutour, PhD[1]
[1]Centre Léon Berard, Lyon, Rhone Alpes, France; [2]CERMEP, Lyon, France; [3]CRCL, Lyon, France

Objective: Despite the intensification of chemotherapy regimen, 5 years survival of patients with metastatic or relapsed osteosarcoma remains of 20 %. The secreted factor netrin 1 (Nt1) is overexpressed in many human cancers as a mechanism to block apoptosis. Recent studies showed that chemotherapies induce Nt1 overexpression in tumors and that blocking Nt1 interaction with its receptors potentiates chemotherapy efficacy. These data suggest that combining chemotherapies with Nt1 interference could be a promising therapeutic approach for resistant tumors like osteosarcoma. Thus we evaluated the antitumoral and antimetastatic effects of anti- Nt1 monoclonal antibody (Anti-Nt1) combined to doxorubicin (Dox) in a rat syngeneic and metastatic osteosarcoma model.

Methods: Dox and Anti-Nt1 were tested as single agent or in combination in rat osteosarcoma model either as as curative treatment or in a primary tumorrelapse model. In both settings, treatments were administered twice a week over a period of 3 to 4 weeks. Tumor progression was monitored throughout treatment by caliper measures and MRI imaging. At the end of the experiments tumors and lung were collected for molecular and immunohistological analyses. To confirm Nt1 induction by chemotherapies, the expression of Nt1 and dependence receptors were analyzed by RT-qPCR. Treatment's effects on osteosarcoma progression, vascularization and immune infiltration were examined by histological stainings.

Results: In progressive tumor model, the combination of Anti-Nt1 and Doxcaused a marked delay in tumor progression, and increased animals survival compared to reference treatment ($p = 0.0183$). Moreover, this combination dramatically slowed down metastatic spreading. At the end of the study 75 % animals treated with Dox had lung metastases ≥5 mm diameter whereas only 17% of the animals treated with Dox and Anti-Nt1 had lung metastases. In the osteosarcoma relapse model, the combination of Dox and Anti-Nt1 caused a delay in tumor relapse and significantly increased animals survival: 19 days after tumor resection in doxorubicin treated group 10% of rats hadn't relapsed whereas 40 % of animals receiving the combination of Dox and Anti Nt1 hadn't relapsed ($p = 0.0159$).

Conclusion: Combination of Dox and Anti-Nt1 showed both antitumor and anti metastatic activities, either in progressive or relapsed tumor models. These data indicate that this combination could be a way to overcome osteosarcoma chemoresistance and delay metastatic spreading.

P1 - Poster 027 2554630

INHIBITION OF BET BROMODOMAIN PROTEINS IN EWING SARCOMA DOWN REGULATES THEIR TRANSCRIPTIONAL PROGRAM AND BLOCKS TUMORIGENICITY AND INVASIVENESS

Fiona A. Becker-Dettling[1]; Tim Hensel[1]; Chiara Giorgi[3]; Oxana Schmidt[1]; Julia Calzada-Wack[2]; Frauke Neff[2]; Beat W. Schäfer[3]; Stefan Burdach[1]; Günther Richter[1]
[1]Klinikum Rechts der Isar, Technische Universität München and Comprehensive Cancer Center Munich (CCCM), Children's Cancer Research Centre and Department of Pediatrics, München, Germany; [2]Helmholtz-Zentrum München, Institute of Pathology, Munich, Germany; [3]University Children's Hospital, Department of Oncology and Children's Research Center, Zurich, Switzerland

Objective: Ewing sarcomas (ES) are highly malignant bone or soft tissue tumors. Genetically, ES are defined by balanced chromosomal EWS/ETS translocations that give rise to chimeric proteins (EWS-ETS), which generate an oncogenic transcriptional program associated with altered epigenetic marks throughout the genome. Here we analyzed the influence of BET bromodomain proteins (BRDs) for tumorigenesis and orchestration of oncogenic transformation by use of different inhibitors (JQ1, i-BET151) specifically targeting the catalytic domain of BRDs. As a result, we strikingly observed a strong down-regulation of the predominant EWS-ETS protein EWS-FLI1 and its associated transcriptional program as well as an impaired growth which could not be mimicked by knock down of individual BRDs.

The purpose of this study was it to shed further light into the mechanisms necessary to establish and maintain the underlying epigenetic and transcriptional landscape utilized by a plethora of different factors in ES.

Methods: The functional role of BRDs was analyzed by application of specific inhibitors, RNA interference (RNAi) and the generation of stable and inducible knock-downs. To analyze resulting changes RT-PCR, western blotting, cell cycle analysis, proliferation and invasion assays as well as whole transcriptome analysis via microarrays were executed.

Results: Observed changes after treatment with JQ1 or i-BET151 was further analyzed by RNAi for BRD2, 3 or 4. However, only knock-down of BRD3 or BRD4 mimicked JQ1 typical expression but not BRD2, indicating that the EWS-FLI1 mediated expression profile is at least in part regulated via such epigenetic readers.

Furthermore, stable knockdown of BRD2,3 or 4 did not recapitulate the degree of inhibition achieved by JQ1 or I-BET151 treatment, but revealed a significant inhibition in contact independent proliferaton, colony formation as well a reduction of *in vitro* invasiveness – mostly driven by BRD4. These findings indicate a possible cross-correlation within the BET bromodomain protein family and an interdependent BRD replacement after individual loss.

Conclusion: Here we show that ES are susceptible to treatment with epigenetic inhibitors such as JQ1 or i-BET151 blocking BET bromodomain activity and the associated pathognomonic EWS-ETS transcriptional program. Moreover, we demonstrate an interdependent use of BET proteins promoting the ES specific expression profile and a possible substitution effect observed after knock-down of individual BRD proteins.

P1 - Poster 028 2537429

OVEREXPRESSION OF C/EBPβ-1 IN EWING SARCOMA CELLS INCREASES TRANSFORMATION AND ENRICHES CHEMOTHERAPY-RESISTANT CANCER STEM CELLS

Jamie Gardiner[1]; Lisa M. Abegglen[1]; Xiaomeng Huang[1]; Bryce Carter[2]; Elizabeth Schackmann[2]; Marcus Stucki[1]; Christian Paxton[3]; Lor Randall[4]; James Amatruda[5]; Angelica Putnam[6]; Heinrich Kovar[7]; Stephen L. Lessnick[8]; Joshua Schiffman[1]
[1]Departments of Pediatrics and Oncological Sciences, Huntsman Cancer Institute, University of Utah, Salt Lake CIty, UT, USA; [2]School of Medicine, University of Utah, Salt Lake City, UT, USA; [3]ARUP Institute for Clinical and Experimental Pathology, Salt Lake City, UT, USA; [4]Sarcoma Services, Department of Orthopaedic Surgery, University of Utah, Salt Lake City, UT, USA; [5]Departments of Pediatrics, Internal Medicine, and Molecular Biology, University of Texas Southwestern, Dallas, TX, USA; [6]Department of Pathology, University of Utah, Salt Lake City, UT, USA; [7]Children's Cancer Research Institute, Vienna, Austria; [8]Center for Childhood Cancer and Blood Disorders, Nationwide Children's Hospital, and the Division of Pediatric Heme/Onc/BMT, The Ohio State University, Columbus, OH, USA

Objective: In a recent analysis of copy number alterations in Ewing sarcoma (ES) tumors, we identified CEBPB copy number gain to be associated with worse clinical outcome compared to patients with normal CEBPB copy number. We functionally validated CEBPB as a target of EWS-FLI1, the causative translocation of ES. C/EBPβ-1, the largest of the 3 C/EBPβ protein isoforms, also acts as an oncogene in ES cells by increasing cellular transformation and chemotherapy resistance when overexpressed. We aimed to identify downstream targets of C/EBPβ that contribute to this oncogenic phenotype.

Methods: C/EBPβ-1 expression was knocked down, overexpressed, and rescued in 4 ES cell lines (A673, CHLA9, CHLA10, and TC252) by viral gene delivery systems. RNA from these cells was extracted and run on the Human Transcriptome Array 2.0 (Affymetrix). Gene expression data was

analyzed to determine genes and pathways affected by C/EBPβ-1 expression. Protein expression was detected by western blotting to support the gene expression changes identified by microarray. Cells overexpressing the C/EBPβ isoforms were subject to the Aldefluor Assay (STEMCELL Technologies) and also treated with doxorubicin for 48 hours prior to measuring cell viability.

Results: The cancer stem cell (CSC) markers ALDH1A1 and PROM1 are regulated by C/EBPβ-1. ALDH1A1 is among the top differentially expressed genes between C/EBPβ-1 knock down and C/EBPβ-1 overexpression cells (Figure 1A). Protein expression of ALDH1A1 and CD133, encoded by PROM1, increase with C/EBPβ-1 overexpression (Figure 1B). ES cells overexpressing C/EBPβ-1 have increased ALDH activity compared to cells overexpressing C/EBPβ-2 or -3 ($p<0.005$, $p<0.01$ respectively) or empty vector transduced cells ($p<0.005$) (Figure 2). Finally, C/EBPβ-1 overexpressing cells had greater resistance to chemotherapy-mediated cell death compared to empty vector transduced cells ($p<0.05$) (Figure 3).

Conclusion: Overexpression of C/EBPβ-1 in ES cells regulates expression of CSC genes and enriches the population of CSC. Further, these cancer stem cells are resistant to chemotherapies. Understanding the role of CSC in ES and the molecular contributions of C/EBPβ to the CSC-like phenotype may lead to the development of novel therapies and improved treatments for ES patients.

Figure 1

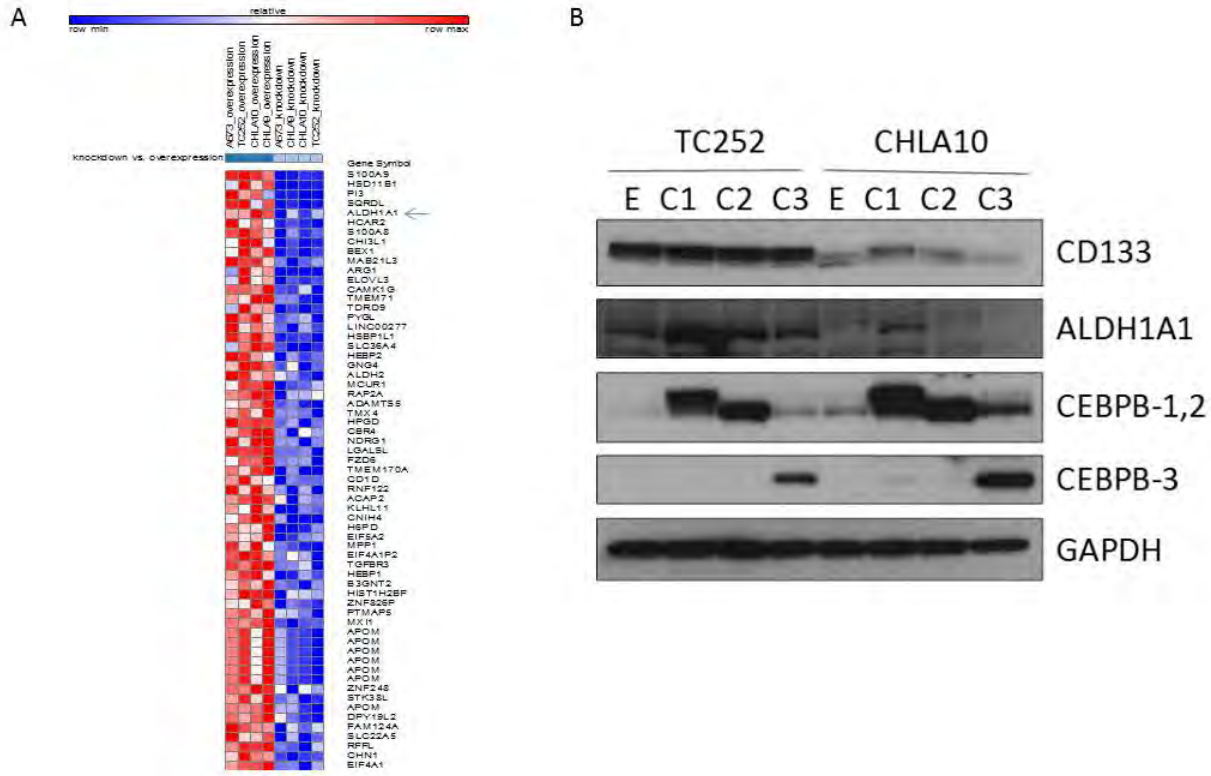


Figure 1. ALDH1A1 and PROM1 are targets of C/EBPβ-1. A, Heat map of differentially expressed genes with C/EBPβ-1 knockdown and C/EBPβ-1 overexpression. Gene list was ranked by average fold-change between knockdown and overexpression. Top 43 genes (fold change >1.25) that positively correlated to C/EBPβ-1 expression are shown on the list. Red represents upregulated genes and blue represents downregulated genes. B, C/EBPβ isoforms were overexpressed in CHLA10 and TC252 cells. Protein lysates were analyzed by Western blot and levels of ALDH1A1, CD133, C/EBPβ, and GAPDH were detected. E=empty vector (control); C1= C/EBPβ-1; C2= C/EBPβ-2; C3= C/EBPβ-3.

Figure 2

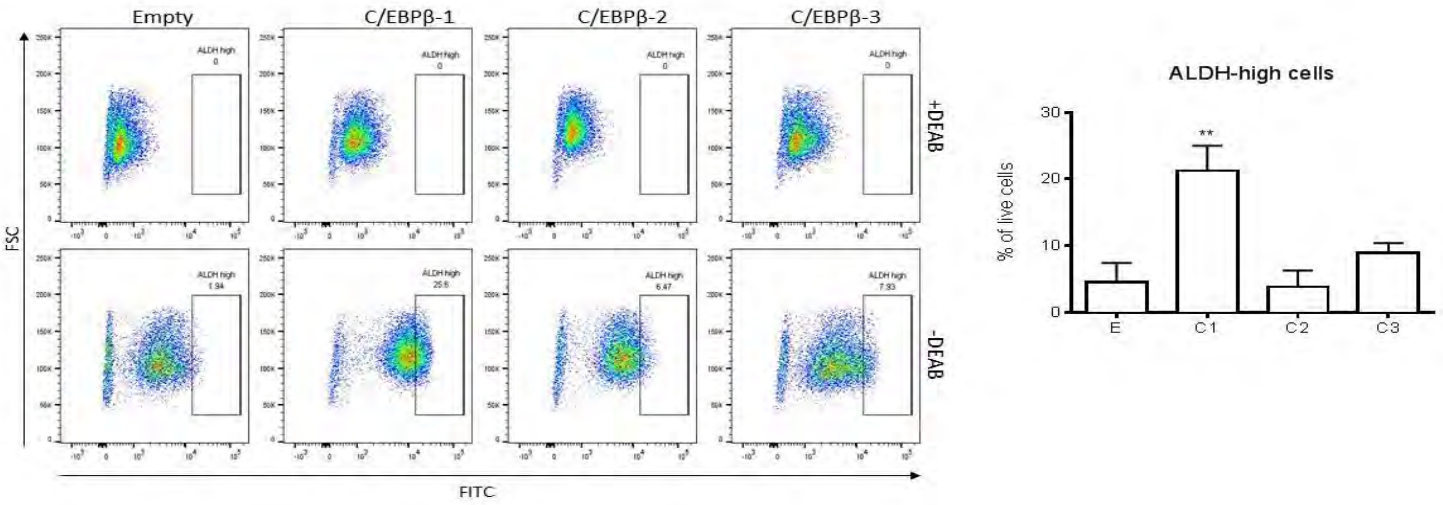


Figure 2. C/EBPβ overexpressing cells have high ALDH activity. A, Representative FACS analysis of TC252 cells subject to the Aldefluor Assay. Percentage of viable cells that are gated as ALDH-high is shown. E=empty vector (control); C1= C/EBPβ-1; C2= C/EBPβ-2; C3= C/EBPβ-3.

Figure 3

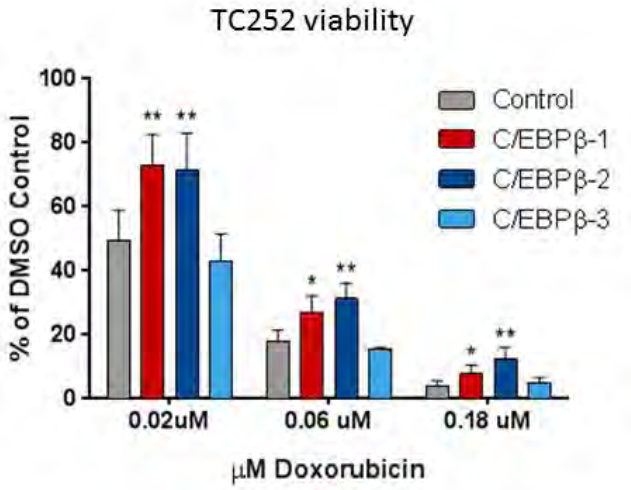


Figure 3. C/EBPβ overexpression leads to chemoresistance in Ewing sarcoma cells. Viability of TC252 cells overexpressing each of the C/EBPβ isoforms after 48 hours of doxorubicin treatment. E=empty vector (control); C1= C/EBPβ-1; C2= C/EBPβ-2; C3= C/EBPβ-3.

P1 - Poster 029 2569795

D-3-PHOSPHOGLYCERATE DEHYDROGENASE (PHGDH) INHIBITION TARGETS SERINE BIOSYNTHESIS IN OSTEOSARCOMA

Richa Rathore; Bethany Prudner; Jeff Kremer; Abigail V. Giles; Brian Van Tine
Medical Oncology, Washington University in St. Louis, University City, MO, USA

Objective: Osteosarcoma is the most common type of primary malignant bone tumor found in both children and adults. Currently, curative regimens involve the use of high-dose methotrexate (HD-MTX). MTX targets the folate pathway in osteosarcoma by inhibiting dihydrofolate reductase, as part of a pathway that converts serine to purines and thymidylate. We have demonstrated that osteosarcoma cell lines have low expression of phospho-PKM2 (pPKM2), and an upregulated serine biosynthesis pathway when compared to soft tissue sarcomas. We hypothesized that inhibition of PHGDH, the first and rate-limiting step in this pathway, with the small molecule inhibitor CBR-5884, would be active for the treatment of osteosarcoma. We suggest that, long term, PHGDH inhibition may replace the use of HD-MTX in osteosarcomas.

Methods: MG63 and NOS1 (osteosarcoma) and SKLMS (leiomyosarcoma) cell lines were treated with CBR-5884, a small molecule PHGDH inhibitor. Cell death was measured using propridium iodide (PI) Fluorescence-Activated Cell Sorting (FACS). Additionally, we utilized PHGDH knockdowns by shRNA to demonstrate specificity. These results were correlated with cell response to methotrexate treatment.

Results: We saw that pPKM2-low, PHGDH-high osteosarcoma cell lines were highly susceptible to treatment with single agent CBR-5884. Knockdown of PHGDH demonstrated that the effects of CBR-5884 were specific and not off-target. Cell lines that were more sensitive to methotrexate were also more sensitive to CBR-5884.

Conclusion: We have found that osteosarcoma cell lines have upregulated serine biosynthesis pathways, making them susceptible to treatment with HD-MTX. We have identified that the rate limiting enzyme of this pathway, PHGDH, is highly upregulated in osteosarcomas, and is an attractive target for the future development of treatments in osteosarcoma, in the hopes that we can replace HD-MTX with PHGDH inhibition.

P1 - Poster 030 2533471

PROTEOMIC APPROACHES REVEAL THE INHIBITATION OF THE IRE1/XPB1 PATHWAY REDUCES TUMOR GROWTH IN EWING'S SARCOMAS

Yu Tanabe[1]; Yoshiyuki Suehara[1]; Shinji Kohsaka[2]; Kenta Mukaihara[1]; Daisuke Kubota[1]; Keisuke Akaike[1]; Midori Ishii[1]; Saiko Kazuno[3]; Reiko Mineki[3]; Kazuo Kaneko[1]; Marc Ladanyi[2]; Tsuyoshi Saito[4]
[1]Department of Orthopedics, Juntendo University, Tokyo, Japan; [2]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [3]Laboratory of Biochemical Analysis, Central Laboratory of Medical Sciences, Juntendo University, Tokyo, Japan; [4]Department of Human Pathology, Juntendo University, Tokyo, Japan

Objective: ThEWS/FLi1 gene fusion is detected in approximately 90% of tumors of the Ewing family and acts as an aberrant transcriptional activator. The protein expression profiles associated with EWS/FLI1 have yet to be elucidated. In this study, to identify the regulated proteins associated with EWS/FLi1, we conducted proteomic studies using both EWS/FLI1 knockdown in Ewing's sarcomas lines and human mesenchymal stem cells (hMSCs) expressing EWS/FLI1. Additionally, to develop novel therapeutic targets, we performed network analyses and functional analyses based on the identified proteins.

Methods: To identify the protein profiles associated with EWS/FLI1 proteins in Ewing's sarcoma, we conducted proteomic analyses to identify the proteins whose expression is regulated by EWS/FLI1. We conducted siRNA assays and i-TRAQ using EWS/FLi1 siRNA and four Ewing's sarcoma cell lines. We also conducted analyses expressing EWS/FLI1and i-TRAQ in three hMSC lines. In order to further understand these biological networks and the novel therapeutic targets, we applied the IPA system using each protein profile. We also conducted cell proliferation assays using siRNA and inhibitors of the targets.

Results: In the EWS/FLI1 siRNA assays, four Ewing's sarcoma cell lines were transfected with either EWS/FLI1 type1 siRNA or type2 siRNA. The expression of EWS/FLI1 in the three hMSC cell lines was induced using a retrovirus for gene transfer. The proteins extracted from the transfected cell lines were analyzed using the i-TRAQ method. The analyses identified approximately 2,000 proteins. In the EWS/FLI1 siRNA cells, we identified 90 consistently regulated proteins that were similarly altered in all 4 cell lines. In the network analyses using the IPA system, we performed network assessments using each silenced protein profile and identified several common pathways that included XPB1, p53, SRF, NFE2L2, SP1 pathways. These pathways play a critical functional role in the setting of Ewing's sarcoma. In the cell proliferation assays using XPB1 siRNA and XPB1-IRE1α inhibitors, silencing the XPB1 and XPB1-IRE1α inhibitors significantly suppressed the cell growth of Ewing's sarcoma cells.

Conclusion: We conducted proteomics analyses of EWS/FLi1 associated with Ewing's sarcoma. Our data suggest that the growth of Ewing's sarcoma cells may be enhanced by the physical association between the identified proteins and EWS/FLi1. We believe that these findings may lead to the development of novel therapeutic strategies for Ewing's sarcoma.

Poster 031 2570670

INDOCYANINE GREEN ANGIOGRAPHY QUANTIFIES PRIMARY AND METASTATIC OSTEOSARCOMA TUMOR BURDEN IN AN IMMUNOCOMPETENT MOUSE MODEL

Mitchell S. Fourman, MD, M.Phil[2]; Adel Mahjoub[1]; Jonathan Mandell[2]; Jared Crasto[2]; Shibing Yu[2]; Jessica Tebbets[2]; Kurt Weiss[2]
[1]School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA; [2]Orthopaedic Surgery, University of Pittsburgh, Pittsburgh, PA, USA

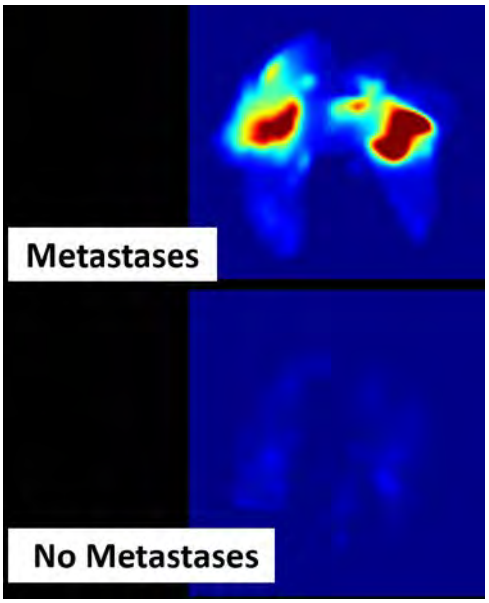
Objective: A challenge in the development of immunocompetent *in vivo* osteosarcoma (OS) models is the quantification of both primary and metastatic tumor burden. Indocyanine green (ICG) is an FDA-approved near-infrared dye that binds tightly to plasma albumin and provides an accurate representation of intravascular flow. In areas of vascular interruption, such as a burn or malignancy, ICG reliably extravasates. No quantitative or prognostic studies of ICG tumor fluorescence have been performed. Here we use ICG Angiography to quantify primary and metastatic tumor burden in an orthotopic mouse OS model.

Methods: Forty 4-6 week-old female Balb/c mice received injections of 0 (control), 100K, 250K, 500K, 750K, and 1 million K7M2 OS cells into their left hindlimbs. Amputations were performed 4 weeks after injection, followed by euthanasia and *ex vivo* lung harvest at 10 weeks. Twenty-four

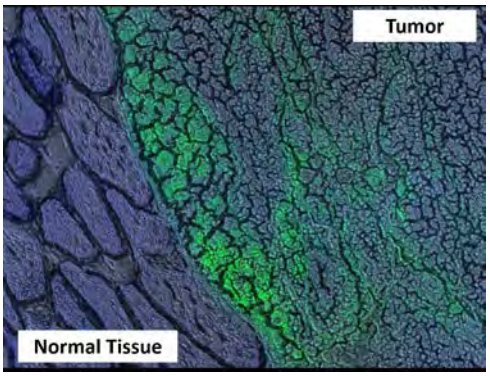
hours after ICG was retro-orbitally injected, fluorescence imaging with SPY-Elite (Novadaq, Bonita Springs, FL, USA) was performed immediately prior to amputation (Figure 1) and euthanasia (Figure 2). Quantification was performed with SPY-Q software (Novadaq) and NIH ImageJ (Bethesda, MD, USA). All tumors were measured using computed tomography (FIDEX, Animage, Pleasanton, CA, USA), and primary and metastatic tumor samples were cryosectioned for near-infrared microscopy. Statistical analysis was performed using Prism 7.0 (GraphPad, LaJolla, CA, USA).

Results: Clinical tumor growth was observed in 30 animals (75% growth rate). Statistically significant ($p < .05$) hindlimb fluorescence was observed in animals injected with 250K, 500K, and 1 Million OS cells. All hindlimbs with clinical tumors had an average normalized hindlimb fluorescence above 1 normalized arbitrary perfusion unit (apu). A linear relationship ($r^2 = .81$) was observed between hindlimb fluorescence and lung fluorescence, which was associated with metastatic burden. This relationship was not observed when computed tomography was analyzed. ICG was histologically localized only to tumor stroma within primary tumor (Figure 3) and lung samples.

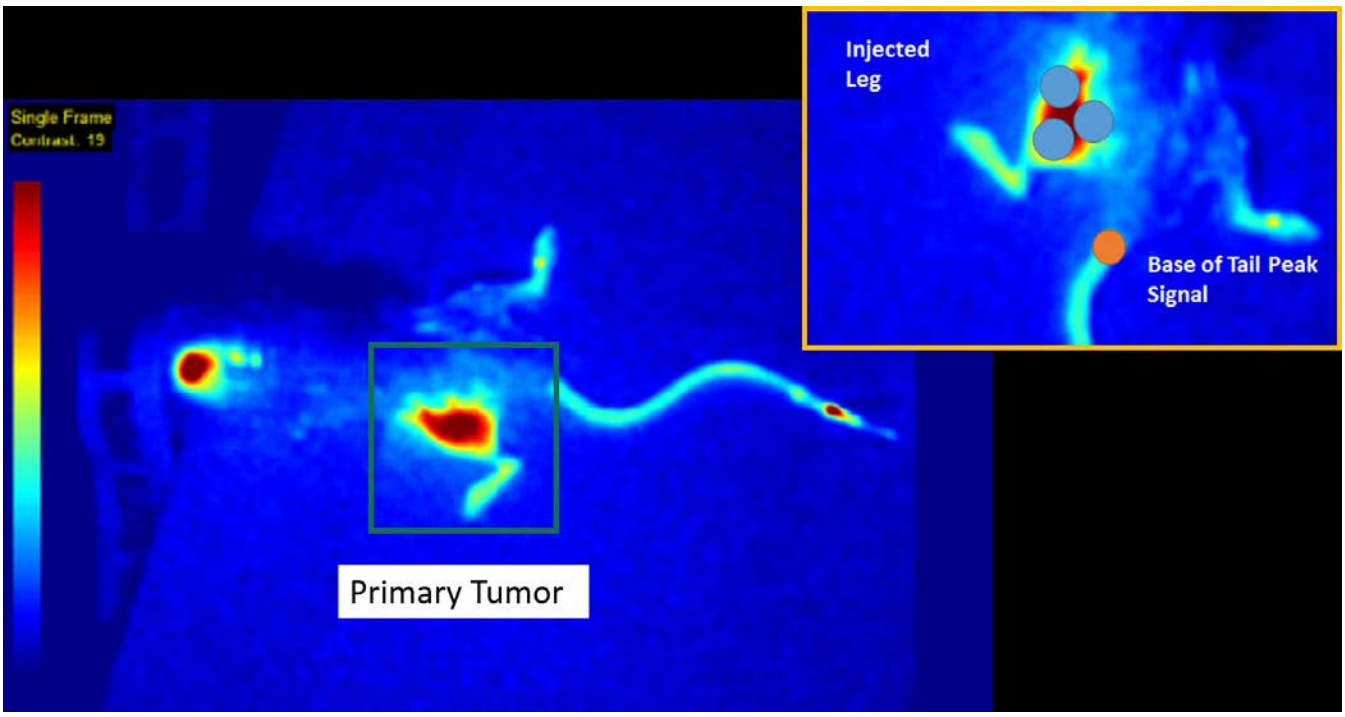
Conclusion: ICG Angiography appears to be a rapid, high resolution technique for characterizing sarcoma. ICG was found to have a high specificity to tumor stroma, a low false positive rate and illustrate a clear relationship between primary and metastatic disease burden not seen using radiographic measurements alone. This model will be used as the basis for our pre-clinical studies.



Lungs demonstrating metastatic (top) and non-metastatic (bottom) disease



ICG (green) localizes only to tumor stroma, while the surrounding muscle demonstrates no fluorescent signal.



Primary tumor fluorescence with quantification and normalization points noted (right)

P1 - Poster 032 2570663

FUNCTIONAL AND MOLECULAR CHARACTERIZATION OF B CELLS AND PLASMOCYTES IN OSTEOSSARCOMA

Sandra Santos, Resident; Ruben Fonseca; João Freitas; Paulo F. Tavares; Jose M. Casanova
Ortopedia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

Objective: The role of B cells in the natural immune response against non-hematologic tumors, in particular osteosarcoma (OS), is largely unknown, with only few studies referring to the presence of $CD19^+$ B cells and plasmocytes in the tissues adjacent to the tumor. Assessing the functional phenotypes of circulating B cell subsets might provide new insights into potential biomarkers for disease progression and response to therapy.

Methods: The functional phenotypes of circulating B cells were determined in 15 patients with diagnosed osteosarcoma and therapy-naïve. The results were compared to those of 14 age-matched healthy controls (HC), analyzed by multicolor flow cytometry. Statistical analysis was performed using the non-parametric Mann-Whitney test (significant for $p<0.05$).

Results: OS patients had significantly more circulating double-negative (IgD-CD27-) memory B cells than HC (OS:6.0%±0.7 vs HC:3.3%±0.4; $p<0.01$). These double-negative cells, considered exhausted memory cells which usually accumulate in the blood of elderly individuals, have poor proliferative capacity and are prone to apoptosis. However, in OS patients these cells –similarly to what was observed in the total B cell pool (MFI CD126: OS=400.5±49.3 vs HC=269.5±58.8; $p<0.05$), have significantly increased expression of the proliferation-linked IL-6R (CD126), which suggests a different functional role than those in seniors. The frequency of B cells expressing apoptosis-related Fas/CD95 was significantly increased in OS patients (OS=19.8%±3.0 vs HC=12.5%±1.8; $p<0.05$), in particular within the memory pool. According to recent studies, activated memory B cells increase CD95-expression, therefore we suggest that in OS patients the memory B cell pool (which comprises the antibody-producing cells) is abnormally activated. Contrasting to this activation of the CD27-expressing memory pool and the augmented proliferative capacity of the double-negative memory pool, OS patients had significantly less circulating regulatory ($CD1d^{hi}IL\text{-}10^{hi}TGFb^+$) B cells (OS:14.1%±6.7 vs HC:28.6%±8.4; $p<0.05$), which was accompanied by a decrease in the expression of the anti-inflammatory cytokine TGFb (MFI TGFb: OS=202.6±35.5 vs HC=488.8±118.8; $p<0.05$).

Conclusion: Overall, our present results indicate major shifts in functional B cell subsets in OS patients, which suggest a direct involvement of these cells in the disease. However, it remains to be determined whether B cell function in OS is aiding tumor growth, or rather having a protective effect.

P1 - Poster 033 2570483

EXPRESSION OF PRAME IN OSTEOSARCOMA TUMOR SPECIMENS

J. Andrew Livingston, MD[1]; Jen-Wei Tsai[2]; Shailesh Advani[3]; Alexander Lazar[4]; Anthony P. Conley[1]; Najat Daw[3]; Wei-Lien Wang[4]
[1]Sarcoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Department of Anatomic Pathology, E-Da Hospital, Kaohsiung City, Taiwan; [3]Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: PRAME (Preferentially Expressed Antigen In Melanoma) is a member of the cancer-testis antigen family and has been shown to have increased expression in solid tumors, including sarcomas. PRAME may serve as prognostic biomarker and potential target for immunotherapy. In this study, we sought to characterize PRAME expression in osteosarcoma specimens obtained from patients at the baseline, at resection following neo-adjuvant chemotherapy, and in metastases.

Methods: A formalin-fixed paraffin-embedded tissue microarray containing 394 osteosarcomas from 265 patients was examined. Immunohistochemistry was performed following antigen retrieval using a mouse anti-PRAME monoclonal antibody (1:150; H10; Santa Cruz). The extent of immunoreactivity was graded according to the percentage of positive tumor cells and the intensity of staining was graded as weak, moderate, or strong. Staining of greater than 50% tumor cells (considered to be diffuse) of at least moderate intensity was regarded as high expression.

Results: The tissue microarray specimens were derived from pediatric and adult patients with osteosarcoma seen at our institution from 1985 - 2012. High PRAME expression was seen in osteosarcoma biopsy (11/60, 18%), resection (77/157, 49%) and metastatic specimens (12/66, 18%). The proportion of specimens with high PRAME expression was significantly greater at resection as compared to biopsy ($p < 0.0001$) or metastases ($p< 0.0001$). When present, PRAME expression was typically moderate to strong and diffuse (>50%). Correlations of PRAME expression with clinical parameters are ongoing and will be presented.

Conclusion: PRAME is expressed in osteosarcomas, found more frequently in treated osteosarcoma, and may be a useful immune therapeutic target. Treatment naïve biopsies also expressed PRAME but to a lesser degree suggesting PRAME expression may be dynamic and increased expression may be elicited by chemotherapy.

P1 - Poster 034 2569655

TARGETING EWING SARCOMA CELLS AND THE TUMOR MICROENVIRONMENT WITH OMTX003 ANTI-ENDOGLIN MONOCLONAL ANTIBODIES

Pilar Puerto-Camacho, Biochemist[1]; Brian A. Menegaz[2]; Ana Teresa Amaral[1]; José Luis Ordóñez[4]; Saioa Domínguez[3]; Carmen Jordán-Pérez[1]; Michele Biscuola[1]; María José Robles[1]; María López-Álvarez[1]; Juan Diaz-Martin[1]; Salah Lamhamedi-Cherradi[2]; Keri Schadler[5]; Myriam Fabre[3]; Joseph A. Ludwig[2]; Enrique de Alava[1]
[1]Department of Molecular Pathology, Institute of Biomedicine of Seville (IBiS), Seville, Spain; [2]Department of Sarcoma Medical Oncology, University of Texas MD Anderson Cancer Center (MDACC), Houston, TX, USA; [3]Oncomatryx Biopharma SL, Derio, Bizkaia, Spain; [4]Cancer Research Center (University of Salamanca-CSIC), Salamanca, Spain; [5]Department of Pediatrics Research, MD Anderson Cancer Center, Houston, TX, USA

Objective: Ewing Sarcoma (ES) is a bone/soft tissue neoplasia affecting mainly children and young adults. ES are heavily angiogenic and present vascular mimicry. Endoglin (ENG), or CD105, is a cell surface receptor, important in the establishment of neo-angiogenesis and vascular mimicry. ENG is shed from the cell surface by Matrix Metalloproteinase 14 (MMP-14) in its soluble form (sEDG) into the extracellular compartment.

Methods: mRNA levels were evaluated by q-RT-PCR in ES cell lines (n=7) and patients (n=24). Protein and subcellular location were studied by western blotting, immunofluorescence and FACS in a set of tumoral/non-tumoral cell lines. sENG, derived from cell line supernatants, was determined by ELISA. Exosomes were isolated from supernatants by ultra-centrifugation. Promoter methylation was evaluated in ES cell lines and mesenchymal stem cells (n=12). Two ES cell lines were xenografted into mice to study *in vivo* tumor binding of the OMTX003 MAbs, targeting human ENG (hENG) or murine ENG (mENG) (n=30). A dose range study (DRS) was performed in healthy mice (n=15) exposed to 3 doses of hENG and mENG.

Results: Whole protein levels correlated with the mRNA levels, and the subcellular location of ENG was primarily at the cell membrane. Only one cell line lacked expression of ENG/MMP14 and, in fact, this was the only cell line with a hyper-methylation pattern in the ENG/MMP14 promoters. sENG levels positively correlated with ENG and MMP14 mRNA levels, consistent with a role of this MMP in the shedding of ENG (n=7) (R=0,6; p=0,031 and R=0,584; p=0,045, respectively). Expression of ENG and MMP14, also positively correlated in a set of ES patients (R=0,44; p=0,02). Interestingly, ENG enrichment was observed in exosomes derived from ES cell lines. Specific *in vivo* binding of hENG OMTX003 was positive in ENG^{++} tumors and negative in ENG^{-} tumors. Impaired tube formation was observed in endothelial cells cultured *in vitro* following exposure to OMTX003. Active internalization of OMTX003 was detected in ES cell lines. Regarding the DRS, histopathological evaluation revealed no significant drug related toxicity after treatment with hENG OMTX003 up to 10mg/Kg and mENG OMTX003 up to 5mg/Kg.
Conclusion: ENG is expressed in ES cells and derived exosomes, suggesting an active role in microenvironmental signaling. *In vivo*, OMTX003 exhibited strong affinity for mENG/hENG and produced no significant toxicity. A therapeutic drug-conjugated OMTX003 antibody is being assessed as a treatment for ES patients.

P1 - Poster 035 2569816

INTERFERON CONSENSUS SEQUENCE-BINDING PROTEIN (ICSBP) REGULATES THE TRANSFORMING GROWTH FACTOR- BETA TYPE I RECEPTOR EXPRESSION IN OSTEOSARCOMA CELLS

Byung-Kiu Park; Jee Young Sung; Kyung-Sil Yoon; Seog Yun Park; June Hyuk Kim; Hyun Guy Kang; Yong-Nyun Kim
National Cancer Center, Goyang, Gyeonggi-do, Korea (the Republic of)

Objective: Previously, we reported that ICSBP expression upregulates TGF-βRI levels and induces EMT-like phenomena (ELP) in osteosarcoma cells. The objective of this study is to test whether TGF-βRI upregulation induced by ICSBP is critical for ELP and tumor growth, and to test the possibility that ICSBP enhances a promoter activity of TGF-βRI gene and thus find putative transcription elements regulated by ICSBP.

Methods: We established stable Mock (vector) and ICSBP cells (ICSBP overexpression) osteosarcoma cell lines. TGF-βRI upregulation was assessed by immunoblotting, RT-PCR, and immunohistochemistry. Enhanced tumorigenicity was examined by soft agar assay and tumor xenografts in mice. ICSBP-dependent TGF-βRI promoter activity was analyzed by luciferase-promoter assay and electrophoretic mobility shift assay (EMSA).

Results: We demonstrate that ICSBP expression up-regulates TGF-βRI and increases epithelial to mesenchymal transition (EMT) like phenotype (ELP) in human osteosarcoma cells. In addition, ICSBP overexpression increased tumorigenicity in mouse xenograft model. To investigate the mechanism of TGF-βRI up-regulation by ICSBP, we tested the possibility that ICSBP enhances a promoter activity of TGF-βRI gene. We analyzed the promoter region of the human TGF-βRI gene in osteosarcoma cells to find putative transcription elements regulated by ICSBP. Analysis of promoter-luciferase reporter assays revealed that ICSBP increases TGF-βRI promoter activity. ICSBP appeared to bind TGF-βRI promoter determined by electrophoretic

mobility shift assay. By serial deletions, truncations and mutations of TGF-βRI promoter region, we identified a putative ICSBP binding site in the TGF-βRI promoter.

Conclusion: Our data suggest that ICSBP induces ELP through TGF-βRI up-regulation, which is induced by ICSBP binding to TGF-βRI promoter, thereby enhancing TGF-βRI gene expression.

P1 - Poster 036 2565736

EGFR-UPAR BISPECIFIC IMMUNOTOXIN SUCCESSFULLY TARGETS PEDIATRIC SARCOMA

Kristy Pilbeam, Doctor of Osteopathy[1]; Rachel Bergerson[2]; Elizabeth Taras[3]; Daniel Vallera[3]; Michael Verneris[4]
[1]Pediatric Hematology Oncology, University of Minnesota, Minneapolis, MN, USA; [2]Pediatrics, University of Minnesota, Minneapolis, MN, USA; [3]Radiation Oncology, University of Minnesota, Minneapolis, MN, USA; [4]Pediatric Bone Marrow Transplant, University of Minnesota, Minneapolis, MN, USA

Objective: Pediatric patients with non-metastatic sarcoma have an overall survival of ~70% when treated with conventional chemotherapy. However, survival for children with relapsed and/or metastatic disease at diagnosis is <30%, with few effective options. The aim of this study is to investigate the activity of a bi-specific toxin targeting epidermal growth factor (EGF) receptor and urokinase receptor (uPAR) against pediatric sarcomas *in vitro* and *in vivo*.

Methods: We confirmed EGFR expression in 3 cell lines: RH30 (Rhabdomyosarcoma), TC-71 (Ewing Sarcoma) and Saos-2 (Osteosarcoma) using flow cytometry.

Each cell line was transfected with a plasmid expressing GFP and Luciferase using the Sleeping Beauty Transposon system.

The bi-specific ligand toxin, EGFATFKDEL, is a de-immunized truncated pseudomonas exotoxin (PE38) linked to 2 tumor specific ligands: EGF and a fragment of urokinase (ATF). *In vitro* killing of each cell line by EGFATFKDEL was measured using a tritiated [^{3}H] leucine proliferation assay. An immune deficient *in vivo* orthotopic sarcoma model was established by injecting 0.5 x10^6 TC-71 cells intraperitoneally into immune deficient (NSG) mice. Five days after establishment of tumors, increasing doses of EGFATFKDEL (5-20 ug/dose injected IP 3-5x/week) are being tested and mice are followed with bioluminescent imaging.

Results: *In vitro* tritiated leucine proliferation assay showed effective killing of each cell line at clinically significant IC50's (TC-71, 0.03-0.4nM; Saos-2, 0.025-0.05nM; RH30, 0.04-0.06nM). *In vivo* studies are ongoing with tumors detectable by bioluminescent imaging prior to treatment. Early results for TC71 bearing mice treated with 10ug of EGFATFKDEL 5 days/week show 6/6 mice with a positive response (1/6 complete response, 4/6 with partial response and 1 stable disease) after 1 week of treatment. In contrast, 3/3 untreated controls show progression.

Conclusion: EGFATFKDEL is a bi-specific ligand toxin that effectively targets and kills TC-71, RH30 and Saos-2 sarcoma cells *in vitro* at sub-nanomolar doses. While our *in vivo* testing of EGFATFKDEL is ongoing, treating animals 5 days/week at 10 ug/dose is well tolerated and shows early promising results, including tumor regression. Experiments with other sarcoma targets and larger animal groups will be presented. In summary, EGFATFKDEL has potential as a new sarcoma directed agent, which could be tested in a phase I/II clinical trial for relapsed and metastatic pediatric sarcomas.

In vitro

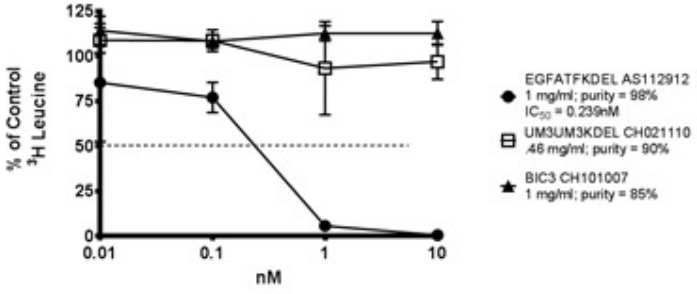


Figure 1a: EGFATFKDEL induces cell death of TC-71 cells *in vitro* at sub-nanomolar concentrations. Shown is the IC50 for EGFATFKDEL (circle) using TC-71 sarcoma cells as a target. Also shown is irrelevant immunotoxins as controls (UM3UM3KDEL/BAC3 targets CD133 [squares] and BIC3 targets CD3 [triangle]).

In vivo

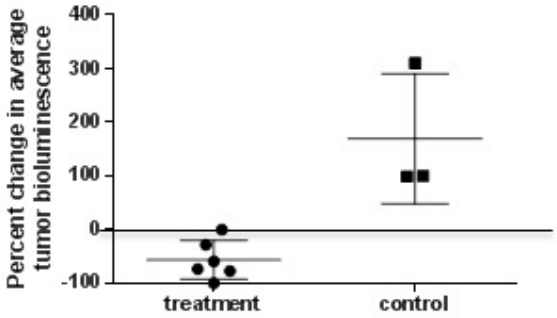


Figure 1b: EGFATFKDEL inhibits sarcoma growth in NGS mice. Shown are the percentage change of bioluminescent tumor growth in mice after one week of treatment (10 mcg/dose; 5 doses/wk, n=6) and controls (PBS treated, n=3). Note: 0% change is stable disease and -100% is complete regression/undetectable disease.

P1 - Poster 037 2570090

NDRG1 INHIBITION SENSITIZES OSTEOSARCOMA CELLS TO COMBRETASTATIN A-4 BY SUPPRESSION OF AUTOPHAGOSOME-LYSOSOME FUSION

Hongsheng Wang; Zhengdong Cai; Yingqi Hua, MD, PhD
Orthopedics, Shanghai General Hospital,
Shanghai Jiao Tong University, Shanghai, China

Objective: Combretastatin A-4 (CA-4), a tubulin depolymerising agent, shows promising anti-tumor efficacy and has been under several clinical trials in solid tumors for ten years. Autophagy plays important pro-survival role in some cancers, thus targeting autophagy may improve the efficacy of anti-tumor agents. N-myc downstream regulated gene 1 (NDRG1) is a significant stress regulatory gene which also mediates cell survival and chemo-resistance. Here we investigate the functional and therapeutic relevance of NDRG1 in the combination treatment of CA-4 and autophagy inhibitor chloroquine (CQ) against human osteosarcoma (OS) cells.

Methods: Cultures of several Osteosarcoma (OS) cell lines, including MG63.2, SJSA, Saos2, and 143B cells, were treated with CA-4 and CQ, or a combination of the two compounds. Cell viability and cell apoptosis were measured and synergy effects assessed by calculation with the combination index. The impact and mechanisms of both CA-4 and CQ on the expression of NDRG1 were investigated. Utilizing short-hair RNA, we performed NDRG1 knockdown experiments and analyzed the cell autophagy and apoptosis in OS cells in culture.

Results: We found that combination treatment of CA-4 and autophagy inhibitor chloroquine (CQ) exerted synergistic cytotoxic effect on human osteosarcoma cells. Meanwhile, CA-4 or CQ could each increase the expression of NDRG1 independently. We further performed mechanistic study to explore how CA-4 and CQ regulate the expression of NDRG1. Using luciferase reporter assay, we found that CA-4 transcriptionally up-regulates NDRG1 expression through activator protein (AP-1). CQ triggered co-localization of NDRG1 and lysosome, which unexpectedly prevented lysosome-dependent degradation of NDRG1. Further, we showed that knockdown of NDRG1 caused reduction of perinuclear lysosomes, which accumulate LC3-positive autophagosomes by decreasing their fusion with lysosomes. Moreover, NDRG1 inhibiton increased apoptosis in response to combination treatment with CA-4 and CQ.

Conclusion: Our study revealed that abrogation of NDRG1 function sensitizes osteosarcoma cells to CA-4 by suppression of autophagosome-lysosome fusion. These results provide clues for developing more effective cancer therapeutic strategies by the concomitant treatment with CA-4 and clinical available autophagy inhibitors.

P1 - Poster 038 2566836

ATRX MUTATION IN CANINE AND HUMAN OSTEOSARCOMA: *IN VITRO* EXPLORATION OF A NOVEL THERAPEUTIC APPROACH

Suzanne Bartholf DeWitt, DVM[1]; Jason Somarelli[2]; Terese Camp[2]; Peng Zhang[1]; Warren Floyd[2]; Samantha Shetler[2]; Rachael Thomas[3]; Matthew Breen[3]; Brian Brigman[1]; Ben Alman[1]; William Eward[1]
[1]Orthopaedic Surgery, Duke University, Durham, NC, USA; [2]Duke University, Durham, NC, USA; [3]College of Veterinary Medicine, NC State University, Raleigh, NC, USA

Objective: The purpose of this study was to assess and manipulate ATRX in canine and human osteosarcoma (OS) cell lines to understand the role of ATRX in OS pathogenesis and to investigate ATR inhibition as a novel therapy for ATRX-mutated OS.

Methods: Three canine OS cell lines (Abrams, Moresco, and D17) and four human OS cell lines (143B, MG63, SAOS2, and U-2 OS) were grown in culture, and ATRX expression was assessed. Knockdowns were performed using two independent siRNAs targeting either human or dog ATRX. Colony forming assays were performed by plating 100 cells per well in 6-well format in triplicate and counting colonies after two weeks. Side population cells were stained with Hoechst and analyzed by flow cytometry.

We obtained the ATR inhibitor, AZD6738, from Astra Zeneca, and tested the cell viability of human 143B cell lines and canine Abrams cell lines with or without siRNA knockdown or CRISPR/Cas9 knockout of ATRX and treatment with AZD6738

Results: ATRX protein was confirmed to be intact in all but the SAOS-2 and U-2OS lines. ATRX knockdown reduced the colony forming capacity of OS cells and the number of side population cells enriched for tumor initiating cells. siRNA-mediated knockdown of ATRX in conjunction with 1μM AZD6738 treatment resulted in a significant reduction of viable cells, supporting our hypothesis. Knockdown of ATRX alone had no effect on Abrams (canine) or 143B (human) OS cells.

Conclusion: ATRX mutation renders OS cells more sensitive to ATR-inhibitors, a therapy that has not been previously investigated in OS. This finding will now be explored in mouse models of OS and xenografts of human and canine OS tumors.

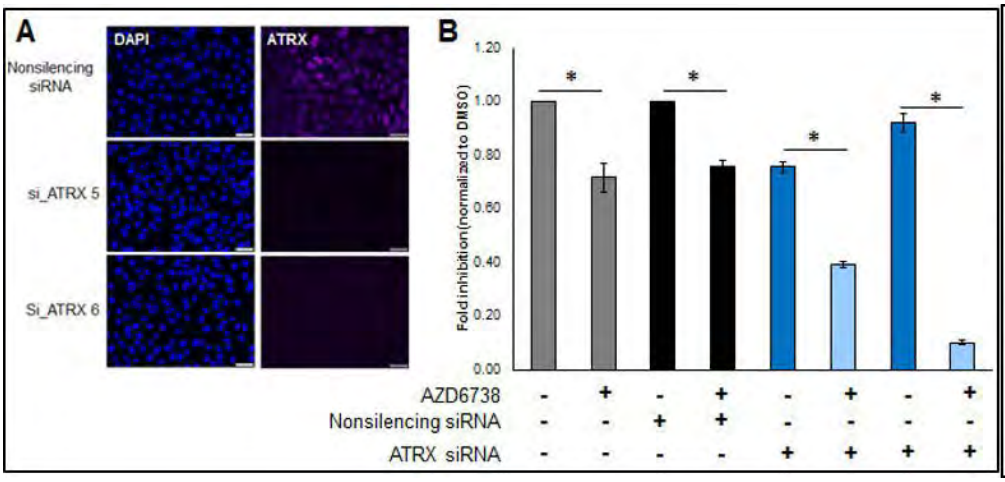


Figure: Loss of ATRX sensitizes OS cells to ATR inhibition. **A.** RNAi-mediated silencing of ATRX protein in human OS 143B cells using two independent siRNAs. **B.** Human OS 143B cells were counted using the Cell Titer Glo assay following siRNA knockdown of ATRX alone or in combination with the novel ATR inhibitor AZD6738. Silencing of ATRX sensitized 143B cells to AZD6738.

P1 - Poster 039 2556924

THE EXTRACELLULAR MATRIX INDUCES EXPRESSION OF INTERLEUKIN 23 P19 IN SARCOMA

Magdalena Jegen; Florian Lenze; Rüdiger von Eisenhart-Rothe; Philipp Mayer-Kuckuk
Orthopedics, Technical University Munich, Munich, Germany

Objective: The survival and growth of tumor cells at both the primary and metastatic sites depends on a permissive tumor microenvironment. Conversely, a microenvironment preventive for tumor growth results in delayed tumor formation, and thus contributes to tumor dormancy. Previous work has shown that loss of interleukin 23 p19 (IL23p19) in the tumor microenvironment prevents effective tumor formation and metastases. This raises the possibility that tumors such as sarcomas express IL23p19 to groom a permissive microenvironment. We hypothesized that IL23p19 is overexpressed in human sarcoma cells. We further speculated that because the extracellular matrix (ECM) is the principle molecular component of the tumor microenvironment, it might serve as a regulator of IL23p19 expression.

Methods: The human osteosarcoma cell lines MG-63 and SaOS-2 were utilized for this study. As normal osteoblasts, primary osteoblasts populations from human bone were used. The ECM was modelled in simple basement membrane extract or gelfoam scaffolds. Gene expression was measured via quantitative real time PCR. The integrin β1 was blocked with an antibody, while intracellular signaling pathways were inhibited pharmacologically with PF573228, LY294002, and UO126.

Results: We observed that IL23p19 expression is elevated by about 3-fold in the osteosarcoma cell lines compared to primary human osteoblasts. Exposure of the osteosarcoma cells to ECM resulted in a further robust increase in IL23p19 expression of approximately 6-fold. This increase was completely blocked if cells were treated with an antibody directed against integrin β1. Further, inhibition of both focal adhesion kinase and PI3K signaling pathways effectively suppressed the ECM-mediated increase in IL23p19 expression. In contrast, suppression of MAPK signaling led to a further increase in IL23p19 expression. Expression of IL23p19 did not result in the extracellular export of IL23 protein. This was due to low expression of the shared IL12p40 subunit despite high expression of IL12p35. We currently assess expression of IL23p19, IL23p40, and IL23p35 in tumor samples from sarcoma.

Conclusion: Our data provides first evidence for a ECM-FAK-PI3K pathway that controls overexpression of IL23p19 in human sarcoma cells.

P1 - Poster 040 2541232

DEFINING THE MECHANISMS OF SENSITIVITY TO HCI-2509: A NOVEL LSD1 INHIBITOR FOR THE TREATMENT OF EWING SARCOMA

Kathleen I. Pishas, PhD[1]; Sunil Sharma[2]; Stephen L. Lessnick[1]
[1]Center for Childhood Cancer and Blood Disorders, Nationwide Children's Hospital, Columbus, OH, USA; [2]Center for Investigational Therapeutics, Huntsman Cancer Institute, Salt Lake City, UT, USA

Objective: The epigenetic effects of LSD1 (lysine-specific demethylase 1) have been implicated in a diverse spectrum of biological processes including cell proliferation, metastasis and regulation of stem cell pluripotency. As LSD1 is highly expressed in Ewing sarcoma tumors and EWS-FLI1 mediated transcriptional repression is facilitated through direct binding of the NuRD-LSD1 complex, this study examined the cytotoxic effects and mechanisms of sensitivity to the novel reversible LSD1 inhibitor HCI-2509.

Methods: The anti-proliferative effects of HCI-2509 was determined through Cell Titre Glo assays following 72 hours of treatment in a comprehensive panel of 17 Ewing

sarcoma cell lines with varying *STAG2*/*TP53* mutational status and basal LSD1 expression levels.

Results: All Ewing sarcoma cell lines were sensitive to the cytotoxic effects of HCI-2509, IC50 range 81-1500nM. In contrast, >200 fold higher concentrations of the irreversible LSD1 inhibitors GSK-LSD1 and tranylcypromine were required to reduce cellular viability by 50%. Importantly, HCI-2509 concentrations required to reduce Ewing sarcoma cell viability were significantly lower than those required for non-malignant cell lines (IMR90 and hMSC) (>2.5μM). Sensitivity to HCI-2509 was not correlated with *TP53* or *STAG2* mutational status (*P=0.267, P=0.602*). In addition, although LSD1 was highly overexpressed (>2 fold) in 14/17 Ewing sarcoma cell lines, basal LSD1 mRNA expression levels were not correlated with HCI-2509 sensitivity (R^2=0.043).

Conclusion: Within our Ewing sarcoma cell line panel innate resistance to HCI-2509 was not observed, highlighting the therapeutic potential of LSD1 inhibition. Further studies are required to elucidate reliable molecular biomarkers which can be used to predict either clinical activity or resistance to LSD1 therapy.

P1 - Poster 041 2565165

IN VITRO EVALUATION OF CB-839 IN COMBINATION WITH METFORMIN IN OSTEOSARCOMA CELL LINES

Ling Ren, PhD; Christine Tran Hoang; Amy K. LeBlanc
Comparative Oncology Program, NIH,
Bethesda, MD, USA

Objective: Osteosarcoma (OS) is a malignant bone tumor that often develops during the period of rapid growth associated with adolescence. Despite constant efforts to identify more effective therapeutics, overall survival in patients remains unchanged over the last 30 years.

Glutamine is one of the key nutrients that fuels the growth of many cancers. A critical step in the utilization of glutamine is its conversion to glutamate by the mitochondrial enzyme glutaminase (GLS). Glutamate and glutamate-derived metabolites support a number of crucial cellular pathways including the tricarboxylic acid (TCA) cycle, redox balance, and amino acid synthesis. CB-839 is a selective glutaminase one (GLS1) inhibitor that has been shown to have antitumor activity across a variety of tumor types, including lymphoma, glioma, breast, pancreatic, non–small cell lung and renal cancers. However, there is sparse literature describing the effect of CB-839 on osteosarcoma.

Metformin is an anti-diabetic drug that regulates glucose homeostasis and reduces insulin resistance. It has also been shown to have antitumor activity in many cancers including OS.

The present study aims to verify whether CB-839 alone or in combination with Metformin has anti-proliferation and apoptosis induction effects on osteosarcoma cell lines.

Methods: We used the highly aggressive and metastatic human (MG63.3 and 143B), murine (K7M2) and canine (MC-KOS) osteosarcoma cell lines. The cells were treated with CB-839 and Metformin both as single agents and in combination.

Results: As single agents, CB-839 inhibited up to 18% of cell growth and Metformin inhibited up to 25% cell growth depending on the cell line. When a combination of the treatments was used, OS cell growth was significantly inhibited. MG63.3 cell growth was inhibited by 94%, 143B by 78%, K7M2 by 47%, and MC-KOS by 60%.

Conclusion: The combination of CB-839 and Metformin in vitro greatly inhibits cell growth in highly aggressive and metastatic osteosarcoma cell lines across several species, supporting further study of the mechanism and the investigation of the combination within in vivo studies.

P1 - Poster 042 2570409

EVALUATION OF ALTERNATIVE IN VIVO SCREENING METHODOLOGY TO IDENTIFY NEW DRUGS FOR TREATING PEDIATRIC CANCER

Peter Houghton, PhD; Raushan T. Kurmasheva
Greehey Children's Cancer Research Institute,
University of Texas Health Science Center,
San Antonio, TX, USA

Objective: Traditional approaches to evaluating antitumor agents using human tumor xenograft models have generally used 8-10 mice in control and treatment groups against a limited panel of tumor models. An alternative approach is to use fewer animals per tumor line, allowing a greater number of models that capture greater molecular/genetic heterogeneity of the cancer type, to be evaluated. Here we retrospectively analyzed 10 years of drug screening results from the Pediatric Preclinical Testing Program (PPTP) to determine whether similar results could be obtained using fewer mice per treatment group.

Methods: We retrospectively analyzed 67 agents evaluated by the Pediatric Preclinical Testing Program (PPTP) to determine whether a single mouse, chosen randomly from each group of a study, predicted the median response for groups of mice using 83 xenograft models. The individual tumor response from one randomly chosen mouse was compared to the group median response using response criteria developed in the PPTP. A total of 2134 comparisons were made.

Results: The single tumor response accurately predicted the group median response in 1604 comparisons (75.16%).

The mean tumor response correct prediction rate for 1,000 single mouse random samples was 78.09%. Models had a range for correct prediction (60%– 87.5%). Allowing for mis-prediction of ± one response category, the overall mean correct single mouse prediction rate was 95.28%, and predicted overall objective response rates for group data in 66 of 67 drug studies. For molecularly targeted agents occasional exceptional responder models were identified and the activity of that agent confirmed in additional models with the same genotype.

Conclusion: Assuming that large treatment effects are targeted, this alternate experimental design has similar predictive value as traditional approaches, allowing for far greater numbers of models to be used that more fully encompass the heterogeneity of disease types.

P1 - Poster 043 2567025

CLINICAL RELEVANCE AND PROGNOSTIC SIGNIFICANCE OF CELLULAR/TISSUE AND CIRCULATING MICRORNA DYSREGULATIONS IN PATIENTS WITH OSTEOSARCOMA

Tomohiro Fujiwara[3]; Toshiyuki Kunisada[3]; Koji Uotani[3]; Aki Yoshida[3]; Takuya Morita[3]; Masaharu Kiyono[3]; Joe Hasei[3]; Yutaka Nezu[2]; Akihiko Yoshida[1]; Eisuke Kobayashi[1]; Takahiro Ochiya[2]; Akira Kawai[1]; Toshifumi Ozaki[3]

[1]National Cancer Center Hospital, Tokyo, Japan; [2]National Cancer Center Research Institute, Tokyo, Japan; [3]Okayama University Hospital, Okayama, Japan

Objective: Although emerging evidence of cellular/tissue microRNA (miRNA) dysregulation in osteosarcoma (OS) has been accumulated, little is know about secretory/circulating miRNA in OS patients. Recent reports have demonstrated that miRNAs are secreted into the circulation from tumor cells and have represented a new diagnostic approach for malignant diseases. We have identified circulating miRNA signature in OS patients and culture media of OS cells, but clinical relevance of cellular/tissue and circulating miRNA dysregulations has been unknown.

Methods: The study protocol was approved by the Institutional Review Board of two referral sarcoma centers of Japan. Tumor specimens (n=45) were collected from OS patients and blood samples (n=36) were collected from OS patients, age-matched non-OS patients, and healthy individuals. qRT-PCR analysis was performed using the extracted RNA and clinicopathological relevance was evaluated by several statistical methods.

Results: Circulating miR-25-3p and miR-17-5p were detected by microarray analysis using serum samples and culture media. These miRNAs were secreted from OS cell lines with exosome fractions and increased with cellular proliferation and tumor growth. Serum miR-25-3p levels before treatment were significantly higher in OS patients compared to controls and revealed higher sensitivity and specificity compared to alkalinephosphatase (ALP). Clinicopathological analysis revealed that high serum miR-25-3p levels at diagnosis was poor prognostic factor (16.7% and 83.3%, respectively; 3-year metastasis-free survival; *P*=0.023), and reflected histopathological response to neoadjuvant chemotherapy in five patients that could be monitored during treatment. Interestingly, we identified that high miR-25-3p levels in biopsy specimens correlated with poor prognosis (47.1% and 91.7%, respectively; 3-year metastasis-free survival, *P*=0.001), indicating that this oncogenic miRNA has not only diagnostic and prognostic significance but also therapeutic potential for OS.

Conclusion: Diagnostic and prognostic significance of circulating miR-25-3p were identified and dysregulation of this miRNA in tumor specimens were also prognostic factor. Although recent investigations have demonstrated the dissimilarity of miRNA profiling between the tumor specimens and circulating blood, the expression levels and prognostic relevance of this oncogenic miRNA are commonly dysregulated, indicating the importance of evaluating serum miRNA as a non-invasive biomarker.

P1 - Poster 044 2568419

IDENTIFICATION OF PHARMACOLOGICALLY TRACTABLE KINASE TARGETS IN OSTEOSARCOMA

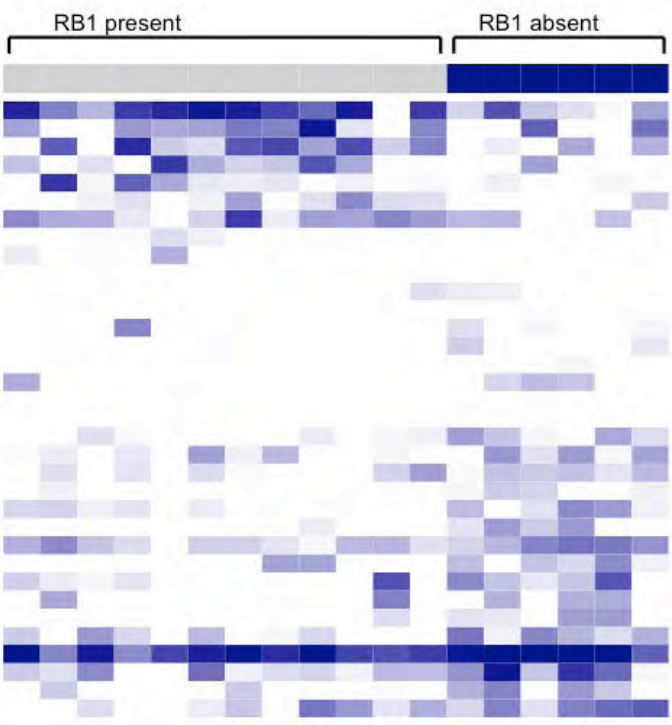
Harriet Holme[3]; Rachel Brough[1]; Helen Pemberton[1]; James Campbell[1]; Colm Ryan[2]; Adrienne Flanagan[3]; Alan Ashworth[4]; Chris Lord[1]; Sandra Strauss[3]

[1]CRUK Gene Function Laboratory and Breast Cancer Now Research Centre, The Institute of Cancer Research, London, United Kingdom; [2]System Biology Ireland, University College Dublin, Dublin, Ireland; [3]UCL Cancer Institute, London, United Kingdom; [4]Helen Diller Family Comprehensive Cancer Centre, San Francisco, CA, USA

Objective: With little improvement in osteosarcoma (OS) outcomes for over a decade, the identification of new therapeutic targets and approaches is critical. Central to designing novel therapeutic strategies is identification of genes that are crucial to survival of tumour cells but play a largely redundant role in normal cells. High throughput RNA interference screens have been employed in other malignancies to identify such genetic dependencies. We performed a series of parallel RNAi screens in a well characterized panel of commonly used OS tumour cell lines and integrated data from these screens with genomic data to identify novel candidate therapeutic targets in genetically defined subsets of OS. We focused on identifying novel targets associated with defects in the *Retinoblastoma* (*RB1,pRb)* tumour suppressor gene.

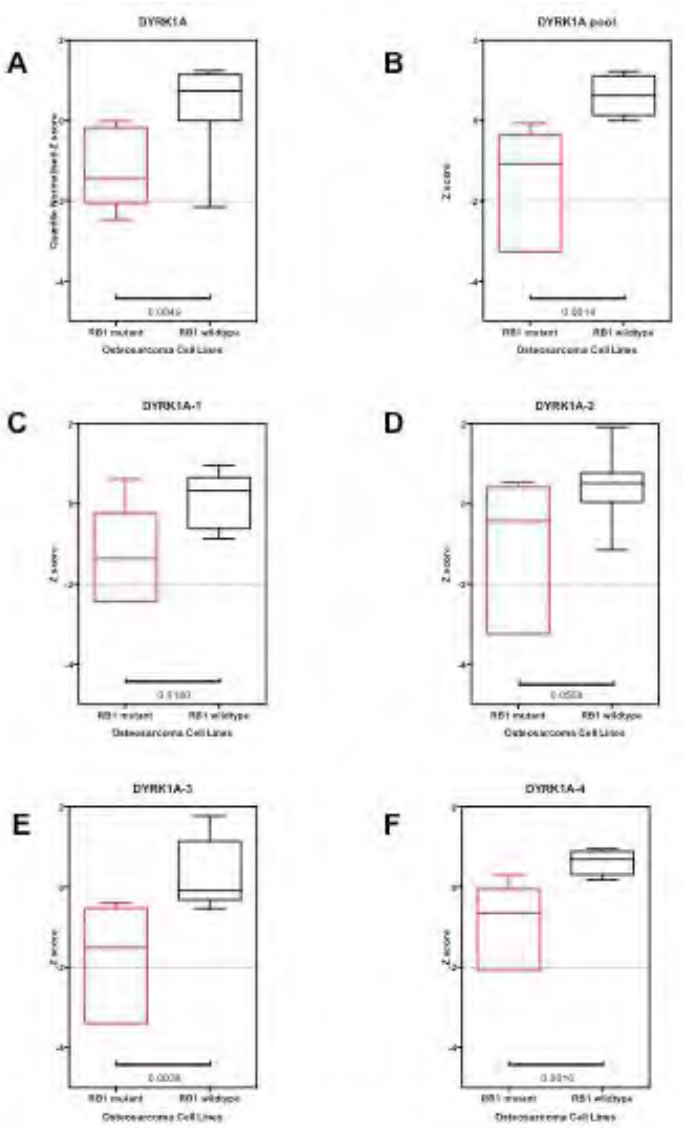
Methods: Using a 384 well plate siRNA library designed to target 886 genes we performed high-throughput RNAi screens in a panel of 18 well-characterized osteosarcoma cell lines representing the different histological subtypes. Five days post siRNA transfection, cell viability was assessed and the effect of each gene siRNA on cell fitness estimated. Alongside these siRNA screens, each OS tumour cell line was exome sequenced. To identify siRNA sensitivity effects that correlated with the presence of driver gene mutations in OS, we used DNA sequencing data and western blot annotation to classify each OS tumour cell line according to the presence or absence of known driver mutations and then used median permutation tests identify siRNA sensitivity effects associated with specific genotypes.

Results: Exome sequencing and western blot analysis of the OS tumour cell line panel identified six models with mutations in RB1 and loss of pRb expression. From the RNAi screen data we identified siRNA targeting the DREAM complex kinase DYRK1A to selectively target pRb defective OS models (Image 1). Using multiple independent siRNA targeting DYRK1A, we confirmed this observation in a panel of OS models (Image 2).



StartFragment
Heatmap of osteosarcoma cell lines demonstrating differences in gene dependency of loss of expression of RB1 and RB1 present osteosarcoma cell lines, by comparison of the Z scores in each group. Only significant ($p<0.05$) genetic dependencies are shown. Each row represents viability effects of knock-down of a target gene, while each column represents a cell line. Dark blue represents loss of viability, whereas white represents no effect on viability.
EndFragment

Conclusion: We have identified that selective silencing of DYRK1A by siRNA in osteosarcoma cell lines with loss of pRb is associated with loss of viability. DYRK1A, a component of the DREAM complex and involved in G1 cell cycle progression, has been previously identified as a protein interaction partner of RB1 and is a pharmacologically tractable kinase. Further work is now underway to mechanistically understand the pRb/DYRK1A synthetic lethality and validate it as a therapeutic target in OS.



DYRK1A revalidation bow and whisker plots. Osteosarcoma cell lines are grouped according to RB1 status and sensitivity to silencing by DYRK1A plotted. (A) Data from the high-throughput screen of osteosarcoma cell using a DYRK1A siRNA smartpool. (B) Low-throughput validation using a DYRK1A smartpool. (C-F) Deconvolution using four different individual siRNAs targeting differing regions of DYRK1A.

P1 - Poster 045 2556367

EWS/FLI HIJACKS CHROMATIN REGULATORY COMPLEXES TO MAINTAIN MALIGNANCY IN EWING SARCOMA CELLS

Emily Theisen, PhD; Stephen L. Lessnick
Childhood Cancer and Blood Disorders, Nationwide Children's Hospital, Columbus, OH, USA

Objective: Ewing sarcoma is an aggressive pediatric tumor characterized by the expression of the oncogenic transcription factor EWS/FLI. EWS/FLI is a fusion protein resulting from a reciprocal chromosomal translocation, t(11;22), involving chromosomes 11 and 22. Apart from this pathognomonic lesion, Ewing sarcoma has one of the lowest mutational rates among cancers. EWS/FLI is a poor candidate for pharmacological blockade due to its intrinsically disordered nature and convex DNA-binding surface. However, EWS/FLI recruits other chromatin regulatory proteins to alter the epigenetic landscape of Ewing sarcoma cells and maintain malignancy, and these factors represent potentially actionable targets. We have identified one such protein, lysine specific demethylase 1, whose depletion and pharmacological inhibition dramatically impair Ewing sarcoma cell viability. However, the mechanistic details of the collaboration between LSD1 and EWS/FLI remain undefined. We aimed to further define the epistatic relationship between EWS/FLI and LSD1.

Methods: In order to test how LSD1 complexes and function might be affected by EWS/FLI we performed co-immunoprecipitations and mass spectrometry to identify how LSD1 protein protein interactions change in the context of EWS/FLI depletion and validated with co-immunoprecipitation and immunoblotting experiments with EWS/FLI depletion and subsequent rescue.

Results: Co-IP to mass spec experiments showed several known interactors of LSD1, including CoREST1 and CoREST3, members of the nucleosome remodeling and deacetylase (NuRD) complex, and BHC80. These experiments identified ZMYM2 as an interactor of of LSD1 in Ewing sarcoma. ZMYM2 interaction with LSD1 was shown to decrease in our mass speci experiments. Upon validation experiments, we further show that EWS/FLI alters the ability of LSD1 to interact with its primary substrate histone H3. This also holds true for ZMYM2. Interestingly, EWS/FLI alters the populationsof LSD1 protein in the nucleus upon knockdown and rescue, suggesting an upstream role for EWS/FLI in the regulation of LSD1 in Ewing sarcoma
.

Conclusion: We conclude the LSD1 complexes remain relatively stable in Ewing sarcoma cells in the context of EWS/FLI depletion. However, EWS/FLI regulates the ability of these complexes to bind to their chromatin substrates. The mechanism by which EWS/FLI causes this remains an area of active study.

P1 - Poster 046 2556450

EWS/FLI REGULATES TRANSCRIPTIONAL ACTIVATION IN EWING SARCOMA VIA LENGTH DEPENDENT GGAA MICROSATELLITES

Kirsten Johnson, BS; Stephen L. Lessnick
Center for Childhood Cancer & Blood Disorders, The Research Institute at Nationwide Children's Hospital, Columbus, OH, USA

Objective: The purpose of this study is to investigate how EWS/FLI transcriptionally activates gene targets via polymorphic GGAA microsatellites. Ewing Sarcoma is a pediatric bone malignancy initiated by a t(11;22) chromosomal translocation that produces the EWS/FLI oncoprotein. EWS/FLI transcriptionally activates and represses its target genes to mediate oncogenic reprogramming. Expression of its up-regulated targets correlates with EWS/FLI binding to associated GGAA microsatellites. These microsatellites show length polymorphisms, suggesting that microsatellite polymorphisms may have critical effects on EWS/FLI-responsiveness of key gene targets. For example, NR0B1 is necessary for EWS/FLI mediated oncogenic transformation, and we found a "sweet-spot" of 20-25 repeat length as optimal for EWS/FLI mediated transcriptional activity at NR0B1. The mechanism underlying this optimal length is unknown.

Methods: We explored the stoichiometry and binding affinity of EWS/FLI for different repeat lengths through biochemical studies, including fluorescence polarization, gel shift binding, and immunoprecipation assays, combined with bioinformatics analysis. Additionally, use of mutant constructs of EWS/FLI has been critical for elucidating particular binding behavior of EWS/FLI at different microsatellite repeat lengths.

Results: Fluorescence anisotropy studies demonstrate that FLI binding affinity is independent of GGAA microsatellite length. In contrast, the stoichiometry of protein to DNA binding increases in specific incremental patterns with increasing microsatellite repeats. Gel shift binding assays elucidate the minimal microsatellite length critical for binding. Our data demonstrate a complex relationship between microsatellite length and transcriptional activity.

Conclusion: Overall our data suggests a model in which the DNA binding domain of multiple monomers of FLI function as independent binding units to facilitate transcriptional activity in a length-dependent fashion. We propose that GGAA microsatellites are necessary and sufficient for EWS/FLI-mediated oncogenic transformation and that repeat length affects optimal DNA binding stoichiometry and transcriptional activity.

P1 - Poster 047 2566620

IDENTIFICATION OF A LONG-NON CODING RNA SIGNATURE ASSOCIATED WITH EWING SARCOMA RESPONSIVENESS TO CHEMOTHERAPY

Katia Scotlandi; Andrea Grilli; Alessandro Parra; Cristina Baricordi; Stefano Ferrari; Piero Picci
Rizzoli Institute, Bologna, Italy

Objective: Treatments of Ewing sarcoma (EWS), the second most common bone tumor in pediatric age, are still firmly confined to conventional chemotherapy. Around 30% of patients do not respond to the therapy and undergo disease progression even during the treatments. Identification of drug resistance mechanisms in EWS has been disapointing and no reliable, validated biomarkers have been selected so far. In this study, we evaluated the genetic landscape of 15 patients with a very different outcome (7 recurring within one year; 8 free of disease after 7 years).

Methods: 250 ng of total RNA extracted by TRIZOL from EWS untreated samples were used for the synthesis of cDNA libraries with TruSeq RNA Sample Prep Kit v2 (Illumina, San Diego, CA), and sequenced by synthesis at 75bp in paired-end mode on HiScanSQ sequencer (Illumina). Reads were aligned with TopHat2/BowTie2 to the reference human genome hg19/GRCh37. Defuse and Chimerascan packages were used to detect chimeric transcripts from RNA-seq data. Raw reads were aligned using TopHat (*version 2.1.0;* to build version hg19 of human genome from UCSC. Counts for UCSC annotated genes were calculated from the aligned reads using HTSeq (version 0.6.0). Normalization and differential analysis were carried out using edgeR package (version 2.12.0) and R (version 3.2.2).

Results: Fusion transcript analysis identified no other translocations than the canonical EWS/ETS, while SNV analysis detected a total of 809 SNVs, of which 87 in at least 2 patients. Analysis of SNV differential expression in good- vs poor-responders identified: 1. missense or nonsense p53 mutations in 4/7 (57%) poor responders vs 0/8 (0%, p=0.02 Fisher's test) 2. Mutations in 5 genes characterize good responders vs poor responders. In particular, we observed mutations in 3/8 (38%) good responders vs 0/7 (0%) poor responders for: NOMO1, NUMP153, OGG1, PIEZO1 and MICB. In addition, we focused our attention to non-coding RNA expression. We found a signature that clearly distinguished good vs poor responders. Differential expression of selected lncRNAs was confirmed by qPCR and functional studies validated their impact on cell chemosensitivity.

Conclusion: Besides confirming the role of p53 mutations as indicator of bad prognosis, our studies actually identifies novel SNVs that appeared to define good responders to chemotherapy. In addition, we found a signature of non-coding RNAs (pseudogenes, miRNA and lncRNA) that define different patient response to chemotherapy.

P1 - Poster 048 2563240

MONOCYTE PHENOTYPE ALTERATIONS ACROSS SPECIES IN OSTEOSARCOMA (OS): A COMPARATIVE ANALYSIS IN MICE, DOGS, AND HUMANS

Joanne Tuohy, DVM[1]; Suzanne Bartholf DeWitt[2]; Brian Brigman[2]; Jason Somarelli[2]; Peng Zhang[2]; Duncan Lascelles[1]; William Eward[2]; Jonathan Fogle[1]
[1]North Carolina State University, Raleigh, NC, USA; [2]Duke University, Durham, NC, USA

Objective: Cancer immunotherapy has seen exciting advances in malignancies such as melanoma and lymphoma, but not in OS. One of the hurdles to immunotherapy development in OS is the paucity of information concerning the composition of peripheral blood monocytes in sarcoma patients, despite observations that monocytes and macrophages are key players in the immune response to OS. Bacterial infection is one form of immunomodulation which can stimulate an anti-OS immune response via monocytes and macrophages, but the exact effects are not well-characterized. The primary purpose of this study was to identify phenotypic differences between monocytes in subjects with OS and in healthy controls.

Methods: Peripheral blood mononuclear cells from mice, dogs, and humans with OS, and normal controls, were incubated with antibodies against a panel of known monocyte and macrophage markers, including CD14, CD62L, CD16, CD11c, CCR2, CX3CR1, CXCR2, and CXCR4 and analyzed by flow cytometry. Dogs and humans with OS were recruited from hospital patient populations. Two murine models were used - a standard syngeneic subcutaneous OS model, and a novel orthotopic OS model induced by Cre-Lox recombination.

Results: In dogs with OS (n=18), monocyte CD16 surface expression was increased, and expression of multiple chemokine receptors (CD62L, CCR2, CCR7, CD43, CX3CR1 and CXCR2) was decreased compared to controls (n=13, $p<0.01$, MWU). In humans with OS (n=8), there was a decrease in monocyte CD163 and CXCR2 expression compared to controls (n=7). In the syngeneic model, mice with OS (n=9) showed an increase in $Ly6c^{hi}$ inflammatory monocytes, and higher monocyte CXCR2, CCR7 expression compared to controls (n=2). In the orthotopic model, mice with OS (n=14) showed a similar increase in $Ly6c^{hi}$ inflammatory monocytes, and higher monocyte CCR2, CCR7 expression, but decreased CXCR2 expression compared to controls (n=8).

Conclusion: The monocyte phenotype profile of OS subjects differs from healthy controls across species. The alteration in chemokine receptor CXCR2 across all three species suggests a conserved mechanism that warrants thorough investigation. Understanding the role of monocytes across species in the immune environment of OS will form a foundation upon which novel immunotherapeutic approaches can be developed against OS.

P1 - Poster 049 2570311

INTERLEUKIN-23 LINKS GLUTAMATE METABOTROPIC RECEPTOR-4 TO OSTEOSARCOMA DEVELOPMENT AND PROGRESSION - IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS FOR OSTEOSARCOMA

Maya Kansara, PhD[1]; Puiyi Pang[2]; Nina Sulkowski[1]; Michele Teng[3]; Mark Smyth[3]; David Thomas[1]
[1]Cancer, Garvan Institute of Medical Research, Sydney, New South Wales, Australia; [2]Sarcoma Genomics and Genetics, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [3]Immunology in Cancer and Infection Laboratory and Cancer Immunoregulation and Immunotherapy Laboratory, QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia

Objective: The 5-year survival rate of patients with metastatic or relapsed osteosarcoma (OS) is less than 25%. OS represent a promising indication for strategies that target the immune system[1]. Here we identify interleukin-23 (IL23), an inflammatory cytokine, as a potential therapeutic target in OS. Our interest in this cytokine as a player in OS is reinforced by the recent genome wide association study, where a polymorphism at the *GRM4* locus (Glutamate metabotropic receptor 4; rs1906953) was the strongest association with genetic susceptibility to OS in man[2]. GRM4 activation in autoimmune diseases is associated with suppression of inflammatory cytokines, including IL23[3], but its role in cancer development is not known.

Methods: We screened a panel of 13 mouse genotypes deficient in immune genes to identify those that modify the development of OS using a radiation model of cancer. IL23 expression was examined in mouse and human OS using *ISH*. We carried out treatment studies in mice using an antagonist of IL23 alone or with doxorubicin. We investigated the role of GRM4 and its association with IL23 and OS using GRM4 knockout mice.

Results: Uniquely amongst all genes tested, IL23 knockout mice were strikingly protected from the development of OS, with 80% of animals tumor-free at 2 years compared to wild type mice (P<0.0001), suggesting an oncogenic role for this cytokine (Fig 1 A). Interestingly, no effect was seen for IL17, a related signalling molecule in the TH17 pathway. In both mouse and human OS IL23 expression was limited to macrophages and dendritic cells. An antagonist to IL23 suppressed tumour growth as a single agent, and the combination of IL23 antagonists with doxorubicin demonstrated marked synergy. Dendritic cells from GRM4 knockout mice have significantly enhanced basal and induced IL23 expression, consistent with a linked role in tumor development (Fig 1B). This finding is confirmed by the use of a GRM4 agonist, which attenuated expression of IL23 in human monocytes.

Conclusion: This is the first study to show a critical role for IL23 in OS, and shows IL23 to be modulated by GRM4. Targeting IL23 mediated inflammation appears a viable therapeutic opportunity, particularly with the emergence of agents targeting IL23 for chronic autoimmune disorders, as well as agonist drugs targeting GRM4.

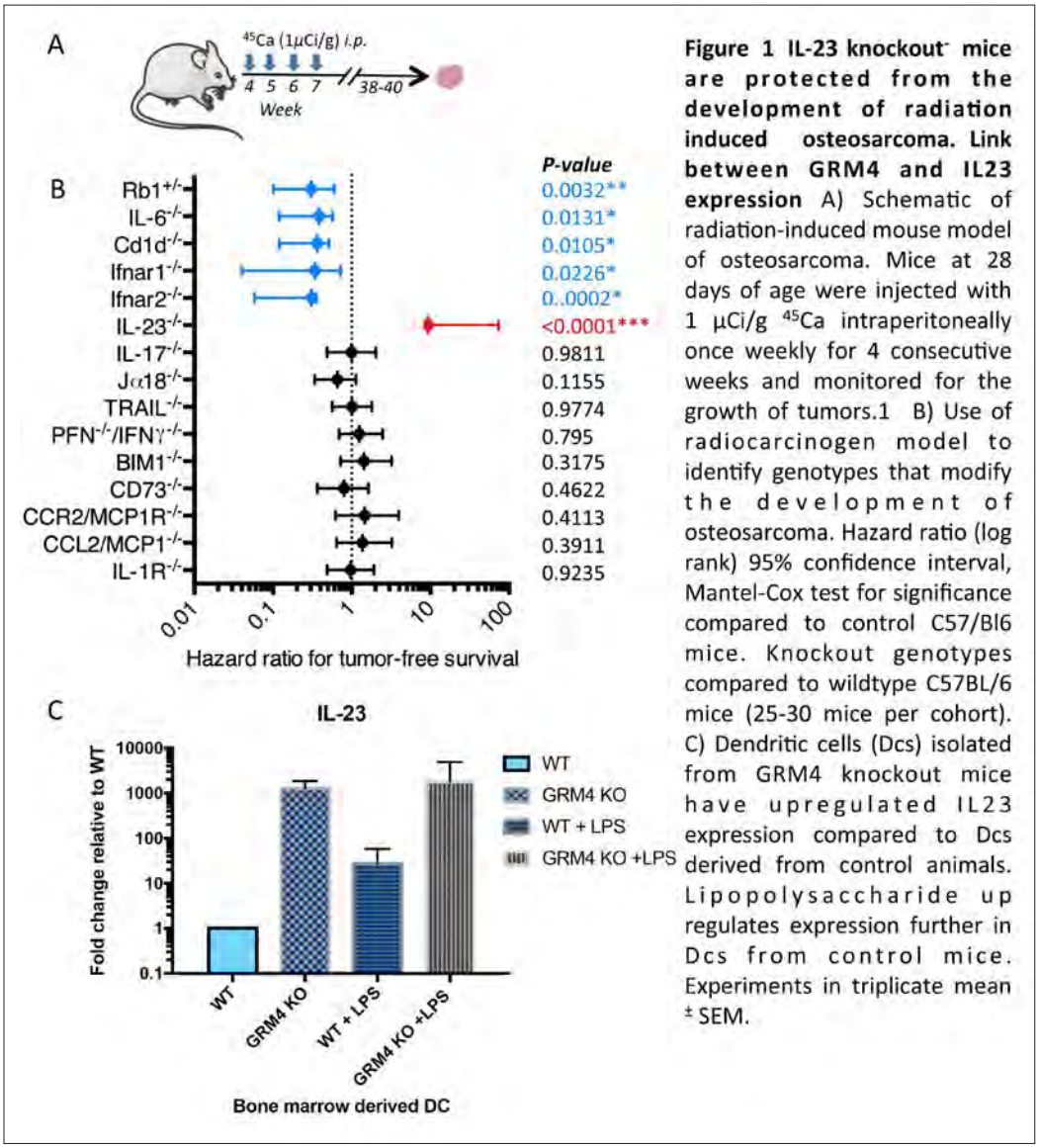


Figure 1 IL-23 knockout mice are protected from the development of radiation induced osteosarcoma. Link between GRM4 and IL23 expression A) Schematic of radiation-induced mouse model of osteosarcoma. Mice at 28 days of age were injected with 1 μCi/g ^{45}Ca intraperitoneally once weekly for 4 consecutive weeks and monitored for the growth of tumors.1 B) Use of radiocarcinogen model to identify genotypes that modify the development of osteosarcoma. Hazard ratio (log rank) 95% confidence interval, Mantel-Cox test for significance compared to control C57/Bl6 mice. Knockout genotypes compared to wildtype C57BL/6 mice (25-30 mice per cohort). C) Dendritic cells (Dcs) isolated from GRM4 knockout mice have upregulated IL23 expression compared to Dcs derived from control animals. Lipopolysaccharide up regulates expression further in Dcs from control mice. Experiments in triplicate mean ± SEM.

P1 - Poster 050 2568493

MICROENVIRONMENT INFLUENCE ON OSTEOSARCOMA'S HISTOLOGICAL RESPONSE TO CHEMOTHERAPY: PRECLINICAL MODELING AND RETROSPECTIVE ANALYSIS

Vincent Crenn[2]; Kevin Biteau[1]; Jérôme Amiaud[1]; Clotilde Dumars[3]; Romain Guiho[1]; Dominique Heymann[1]; Anne Moreau[3]; François Gouin[2]; Françoise Redini[1]
[1]Inserm UMR 957, Nantes, France; [2]Orthopedic Department, Nantes, France; [3]Pathology Department, Nantes, France

Objective: The standard treatment for osteosarcoma is chemotherapy associated with surgery. Chemotherapy effectiveness is assessed by histological analysis rating the surviving degree of tumour cells (Huvos Grading System). However 25% of patients considered good responders by this method will relapse. In our common practice, heterogeneity in the localization of the surviving tumour cell colonies was observed, however, this atypical distribution is not taken into account by the Huvos Score, which is only an averaged count regardless of tissue specificities. Our objective aims at determining whether tumour microenvironment heterogeneity has an impact on histological response to chemotherapy in osteosarcoma.

Methods: Two complementary approaches were conducted: (i) a preclinical study using a syngenic mouse osteosarcoma model in which cells were injected in subcutaneous, para-tibial and intra-osseous microenvironments. These groups were treated with different monotherapies: Ifosfamid, Cisplatin, Doxorubicin versus control group. Tumour growth was assessed during 4 weeks and then necrosis was evaluated in addition to apoptosis rate, vascularisation and proliferation status. (ii) a retrospective analysis was conducted on patients biopsies from osteoblastic osteosarcomas with a Grade III Huvos Score at minimum 5 years follow-up. The localization of surviving tumour cell colonies was determined, and potential correlation with patients' 5 years overall survival was assessed.

Results: Concerning preclinical studies in the syngenic murine model of osteosarcoma, a significant difference of tumour growth was observed between subcutaneous and intra-osseous injection areas ($p = 0.0137$) with a slower growth in the soft tissue group. Histologic analysis is in progress. The response to chemotherapy was also dependent on the microenvironment of the tumor initiation. Concerning analysis on histological human samples, a first set of 10 patients was analyzed as a pilot study for the retrospective study, with complete pathologist review.

Conclusion: Understanding the impact of the heterogeneity of residual tumour cell tissue distribution could improve prognosis accuracy and guide best chemotherapy following surgery. We already identify the importance of microenvironment in the tumour growth between soft tissue and intra-osseous tissue environment in the syngenic murine model we developed.

P1 - Poster 051 2556933

DEREGULATION OF HIPPO TUMOR SUPRESSOR PATHWAY IN EWING SARCOMA

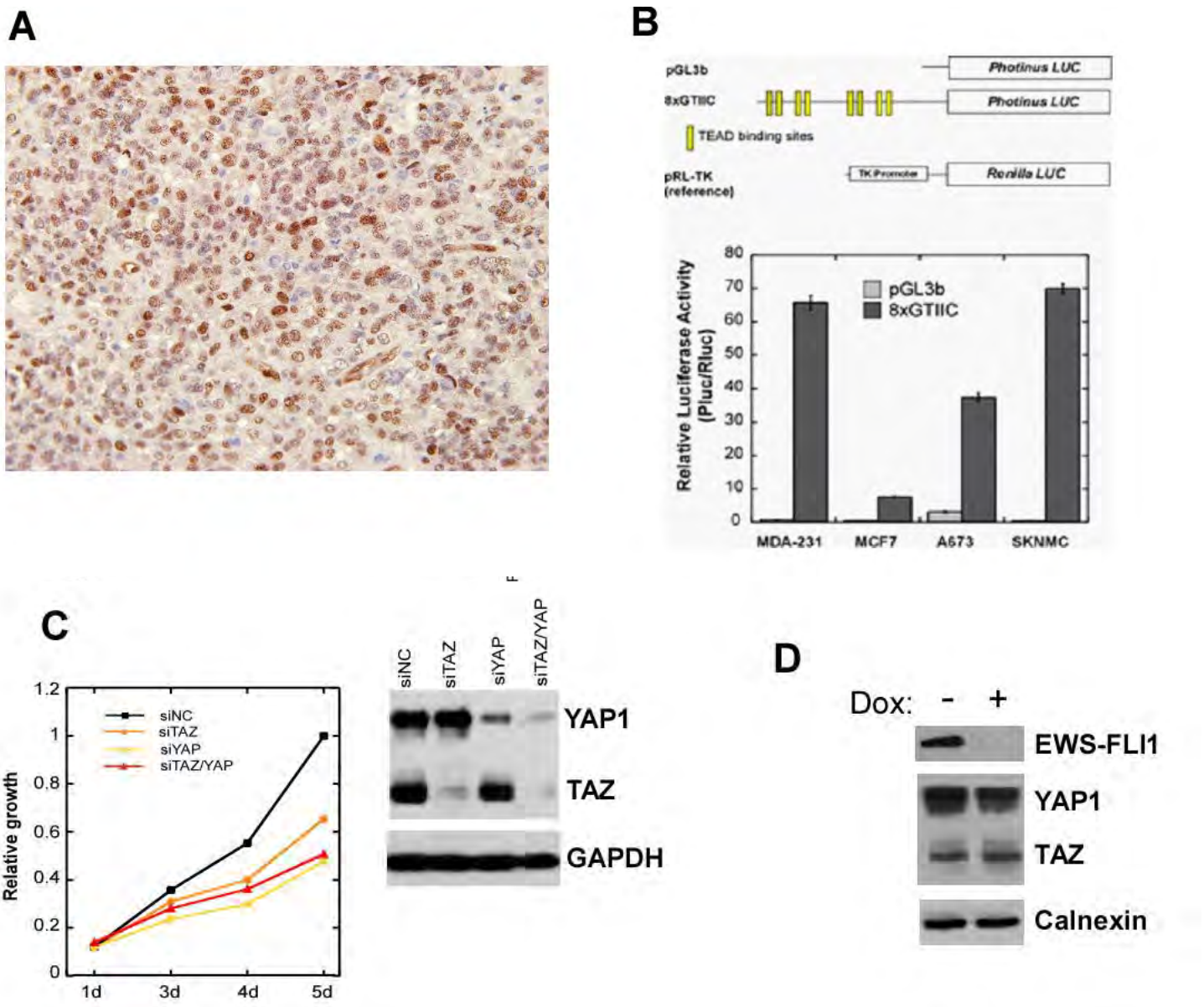
Pablo Rodríguez-Núñez, PhD Student; Laura Romero-Pérez; Rosa García-Mejías; Daniel J. Garcia-Dominguez; Ana Amaral; Lourdes Hontecillas-Prieto; Juan Diaz-Martin; Enrique De Álava *Casado*
Molecular Pathology, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocio/CSIC/ Universidad de Sevilla, Seville, Spain

Objective: The Hippo tumor suppressor pathway plays a critical role in tissue and organ size regulation under homeostatic conditions.The final transducers of this pathway are the oncoproteins TAZ and YAP, transcriptional coactivators of target genes involved in cell proliferation and survival.Deregulation of this pathway leads to TAZ/YAP activation, fostering tumorigenesis in multiple malignant tumor types, including sarcoma.However, mutations in Hippo pathway genes are uncommon.Ewing Sarcoma (ES) and other pediatric fusion-driven cancers exhibit a very low mutation rate, and lack well-established biomarkers to predict poor outcome. Our aim is to elucidate whether Hippo signaling is altered in ES, as well as to unveil its potential contribution to oncogenesis in ES.

Methods: Immunohistochemistry for TAZ/YAP was performed on a series of 41 FFPE ES specimens, and on a panel ofES cell lines. TAZ/YAP transcriptional activity was determined in ES cell lines by using a luciferase-reporter construct bearing TEAD motifs. We used the cell line A673 stably transfected with a doxycicline-inducible shRNA against EWS-FLI1 (Carrillo et al., 2007) to check for TAZ/YAP modulation by the fusion protein. Knock-downof TAZ/YAP were performed using siRNAs or shRNAs for transient and stably silencing of TAZ/YAP respectively.Cell proliferation was assessed bythe ATPlite assay.

Results: We have detected nuclear protein expression of TAZ/YAP in 75% of tumor samples (**A**) and almost all the cell lines analyzed. Moreover, TAZ/YAPtranscriptional activity was observed in ES cell lines (**B**), suggesting that ES transcriptome could be modulated by these factors.In accordance, pharmacologic blockade or TAZ/YAP depletion in ES cell lines induce a decrease in mRNA levels of target genes, accompanied by an inhibitory effect on proliferation (**C**). Knock-down of EWS-FLI1 in the cell line A673 did not affect TAZ/YAP protein levels (**D**), indicating that TAZ/YAP regulation is not dependent on the translocation event. Indeed, we detected high TAZ/YAP protein expression in a mesenchymal stem cell line, proposed as a possible cell of origin in ES.Deregulation of the pathway in ES may be mediated by epigenetic silencing of the tumor suppressor RASFF1A, together with the expression of the protumorigenic isoform RASSF1C.

Conclusion: Deregulation of Hippo signaling leading to TAZ/YAP activation may contribute to the oncogenic properties of ES tumor cells. Hippo-TAZ/YAP axis could be therapeutically actionable in ES.



(A), Representative picture (40X) for TAZ/YAP positive expression in Ewing Sarcoma (D24E4 Rabbit mAb #8418 from Cell Signaling).

(B), Dual-luciferase reporter assays in breast cancer cell lines and ES cell lines. Upper panel: diagrams depicting the constructs used to transfect and monitorize transcriptional promoter activity. Lower panel: transcriptional activity for each construct normalized to the signal of Renilla luciferase.

(C), Left: Growth curve of SK-N-MCcells transfected with control siRNA (siNC), TAZ siRNA (siTAZ), YAP siRNA (siYAP) and double transfected (siTAZ/YAP).Right: Western blot to check for silencing of TAZ and YAP in SK-N-MC cells.

(D), Western blot showing EWS-FLI1 and TAZ/YAP1 expression in the cell line A673 stably transfected with a doxycicline-inducible shRNA against EWS-FLI1.

P1 - Poster 052 2544006

HYPOXIA AND RADIATION INDUCE THE TRANSDIFFERENTIATION OF EWING'S SARCOMA CELLS INTO EWS-FLI-1+ VASCULARE PERCITYES THAT CONTRIBUTE TO TUMOR VASCULARE EXPANSION

Eugenie S. Kleinerman, MD; Zhichao Zhou
Pediatrics, M.D. Anderson Cancer Center, Bellaire, TX, USA

Objective: BM-derived pericytes and DLL4 Notch signaling are critical to Ewing's sarcoma (ES) new vessel formation and for vessel functionality and expansion. Pericytes provide proliferation signals to the endothelial cells. Without pericytes, vessels are leaky and susceptible to regression. Blocking BM cell-differentiation into pericytes inhibited ES tumor growth but did not comletely eradicate vessel pericytes or tumors. Double fluorescent staining revealed a subset of tumor vascular pericytes (Desmin$^+$, NG2$^+$) expressing EWS-FLI-1 in TC-71 *and* patient tumor samples suggesting that these pericytes originated from ES cells. These cells were in hypoxic areas (HIF-1a$^+$) with increased CD133$^+$ stem cells. We determined if hypoxia, or radiation which leads to hypoxia, induced ES cell transdifferentiation in pericytes.

Methods: TC-71 ES cells were irradiated or cultured under hypoxia, then assayed for stem and pericyte marker expression.
To confirm that ES stem cells contributed to the pericyte pool, CD133$^+$ and CD133$^-$ TC-71 cells were isolated after irradiation or hypoxic culture and incubated with 5ug/ml DDL4.
To confirm transdiffereintation into pericytes, TC-71 cells were transduced with a Desmin-driven promoter vector linked to GFP then radiated or cultured under hypoxia.

Results: Radiation *and* hypoxia induced expression of stem cell markers (CD133, Sox-2, Oct 3/4, Nanog) and upregulation of the pericyte markers Desmin, SMA-a and PDGF-BB.
Desmin and NG-2 expression were upregulated in CD133$^+$ but not CD133$^-$ cells. This was blocked by DAPT (GSI).
Culturing TC-71 cells transduced with the GFP-labeled Desmin promoter under hypoxia resulted in GFP expression confirming differentiation into a pericyte lineage.

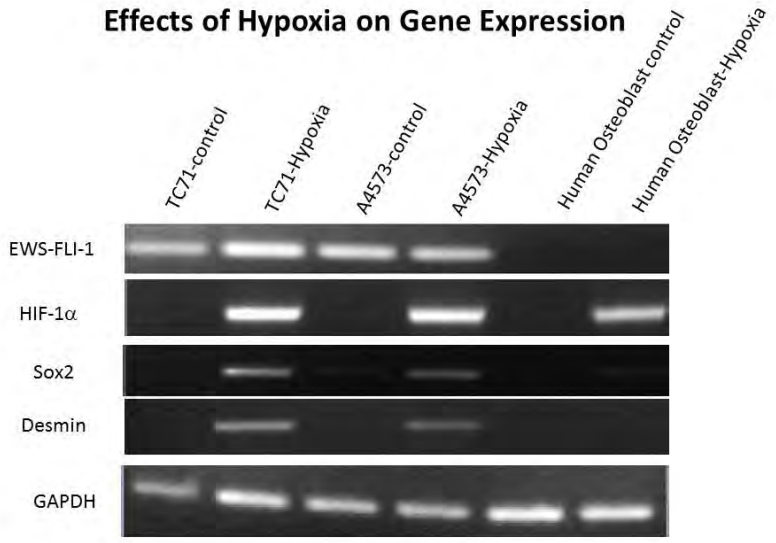


Fig 2. Hypoxia induced the expression Sox2 (stem cell marker) and Desmin (pericyte marker) in TC-71 and A4573 ES cells, but not in normal human osteoblasts. HIF-1a was induced by hypoxia in all 3 cell lines.

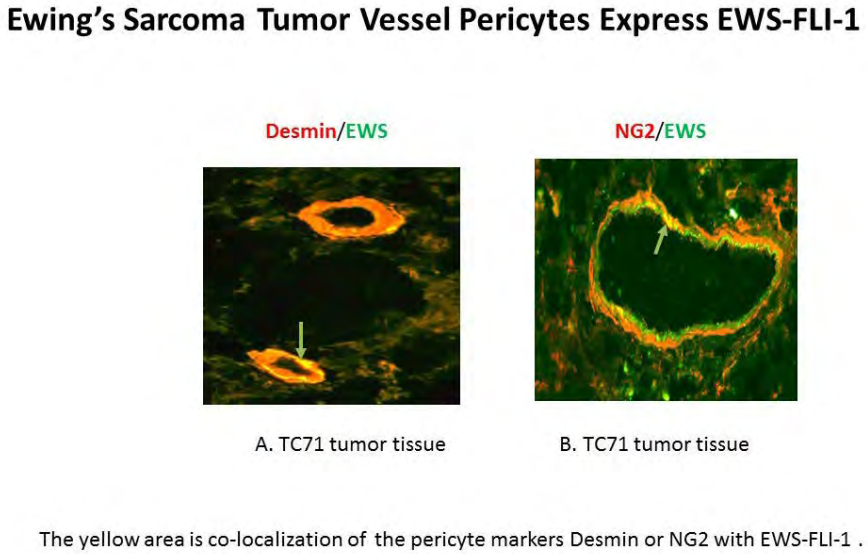


Fig 1. The antibody N-18 recognizes the EWS-FLI-1 fusion protein but not normal EWS. Double flourescent staining identifies cells in the vasculature that express pericyte markers (Desmin or NG2) *and* N-18, indicating that these tumor vessel pericytes are dervied from ES cells. Normal pericytes do not express EWS-FLI-1.

Conclusion: These data show that tumor vessel pericytes are derived not only from BM cells that chemotax into the tumor, but can arise under hypoxic conditions or following radiation from transdifferentiated ES cells themselves. While solid tumors are known to contain subsets of undifferentiated embryonic-like cells with plasticity to serve an endothelial function, this is the first demonstration that radiation and hypoxia can trigger the transdifferentiation of ES cells into pericytes that contribute to tumor vascular formation. This process can assist in maintaining the viability of residual cells following radiation, anti-VEGF and other therapies. Investigations are underway to determine the molecular pathways involved and whether inhibiting ES-pericyte transdifferentiation increases radiation response.

P1 - Poster 053 2557963

TRITHORAX-DEPENDENT REGULATION OF HOXD13 REPRESENTS A THERAPEUTIC VULNERABILITY IN EWING SARCOMA

Laurie Svoboda; Jolanta Grembecka; Tomasz Cierpicki; Rajiv M. Patel; Dafydd G. Thomas; Elizabeth Lawlor
University of Michigan, Ann Arbor, MI, USA

Objective: Normal development is regulated epigenetically by the reciprocal actions of polycomb and trithorax proteins. We recently reported that in Ewing sarcoma posterior HOX genes, in particular *HOXD13*, are abnormally over-expressed and that the promoters of these genes are marked with the activating histone modification H3K4me3, which is mediated by the trithorax protein MLL. In leukemia, MLL and its scaffolding protein menin promote leukemogenesis *via* deregulation of HOXA genes. Based on these data, we investigated whether MLL-dependent activation of HOXD13 is critical for Ewing sarcoma tumorigenesis.

Methods: Ewing sarcoma cell lines were exposed to loss of function studies of HOXD13, MLL and/or menin using shRNA and MI-503, a small molecule inhibitor of the MLL-menin protein-protein interaction. Chromatin immunoprecipitation (ChIP) studies were performed to characterize the chromatin state of the HOXD13 promoter at baseline and following genetic or pharmaologic interventions. *In vivo* xenografts were used to assess the impact of MLL/menin modulation on Ewing sarcoma tumorigenicity.

Results: Genetic loss of function studies led to profound loss of Ewing sarcoma cell survival, proliferation and tumorigenicity, implicating MLL, menin and HOXD13 as tumor promoting oncogenes *in vitro* and *in vivo*. ChIP studies revealed enrichment of the MLL-dependent H3K4me3 mark at the HOXD13 promoter as well as binding of MLL and menin. Exposure of Ewing sarcoma cells to MI-503 led to profound loss of tumorigenicity that was associated with down regulation of *HOXD13* as well as neighboring posterior HOXD genes, *HOXD10* and *HOXD11*. MI-503 also induced loss of MLL and menin protein expression. Treatment with an inactive control compound MI-NC had no effect on tumor phenotype or gene expression.

Conclusion: Together these data demonstrate an essential role for trithorax-dependent activation of HOXD13 in Ewing sarcoma pathogenesis. Inhibitors of the MLL:menin interaction interrupt this critcal oncogenic axis, highlighting a novel opportunity for therapeutic intervention.

P1 - Poster 054 2570456

LIMITED DIAGNOSTIC VALUE OF DMP1 AND SATB2 IMMUNOHISTOCHEMISTRY IN OSTEOSARCOMA

Arjen H. Cleven, MD, PhD[1]; Georgios Agrogiannis[2]; Olaejirinde Olaofe[3]; Inge Briaire-de Bruijn[1]; Judith V. Bovée[1]
[1]Pathology, Leiden University Medical Center, Leiden, Netherlands; [2]Pathology, School of Medicine National and Kapodistrian University of Athens, Athens, Greece; [3]Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University, Ile-Ife, Nigeria

Objective: Diagnosing osteosarcoma can be difficult especially on biopsy material lacking abundant tumor osteoid in which morphology overlaps with other malignant and benign bone tumors. We evaluated the diagnostic value of DMP1 (a non-collagenous matrix protein) and SATB2 (an osteoblastic differentiation marker), which were described to be positive in primary and malignant osteogenic bone tumours.

Methods: Immunohistochemistry was performed for DMP1 and SATB2 on tissue microarrays constructed from 116 osteosarcomas, 15 clear cell chondrosarcomas, 14 mesenchymal chondrosarcomas, 26 dedifferentiated chondrosarcomas, 66 giant cell tumors of bone, 16 chondroblastomas, 14 chondromyxoid fibromas, 6 aneurysmal bone cysts and many soft tissue sarcomas (n=119) including leiomyosarcomas (n=54).

Results: Strikingly, in the majority of osteosarcomas (>99%) DMP1 was negative, including those osteosarcomas that contained abundant tumor osteoid. Since on whole slide section of one osteosarcoma we detected strong but focal expression of DMP1, this finding may reflect lack of representative tumor material for DMP1 in tissue microarrays. In the other tumors, DMP1 expression was exclusively detected in 9% of giant cell tumors of bone, mainly within areas with reactive woven bone or pre-existent bone tissue.

In contrast, SATB2 positive staining was observed in 83% of osteosarcomas, in which the staining was typically strong in a high percentage of tumor cells (>50%). In other bone sarcomas typically moderate staining and a lower percentage of SATB2 positive cells (<50%) was observed, respectively 93% of clear cell chondrosarcomas, 57% of mesenchymal chondrosarcomas and in 28% of dedifferentiated areas in dedifferentiated chondrosarcomas. SATB2 expression was predominantly weak in more than fifty percent of tumor cells in 83% of giant cell tumors of bone, 94% of chondroblastomas, 92% of chondromyxoid fibromas and 100% of aneurysmal bone cysts. In soft tissue sarcomas positive SATB2 staining was detected in rhabdomyosarcoma (67%), desmoid-type fibromatosis (67%), solitary fibrous tumor (50%), synovial sarcoma (33%), gastrointestinal stromaceltumor (33%), liposarcoma (23%) and leiomyosarcoma (5%).

Conclusion: Our results indicate that DMP1 is not a sensitive marker and SATB2 is not a specific marker for osteosarcoma in our series with small tumor material mimicking diagnostic biopsy material. In conclusion, clinical and radiological correlation with histology stays the cornerstone for diagnosing osteosarcoma.

P1 - Poster 055 2570718

ALPHA PARTICLE RADIUM-223 DICHLORIDE (223RACL2) THERAPY AND PERSONALIZED MOLECULAR IMAGING WITH BONE SCINTIGRAPHY, NAF-PET, AND FDG-PET IN HIGH RISK OSTEOSARCOMA

Vivek Subbiah[1]; Pete Anderson[2]; Kalevi Kairemo[3]; Winston Huh[4]; Vinod Ravi[4]; Najat Daw[4]; Neeta Somaiah[4]; Robert S. Benjamin[4]; David S. Hong[1]; Homer Macapinlac[4]; Gregory Ravizzini[4]; Eric Rohren[5]

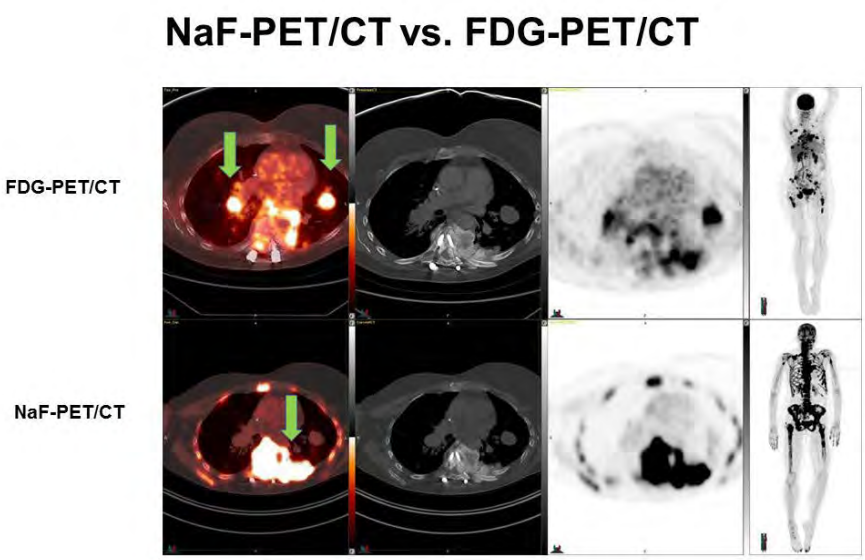
[1]Investigational Cancer Therapeutics, UT MD Anderson Cancer Center, Houston, TX, USA; [2]Cleveland Clinic, Cleveland, OH, USA; [3]Docrates Cancer Center, Helsinki, Finland; [4]MD Anderson Cancer Center, Houston, TX, USA; [5]Baylor College of Medicine, Houston, TX, USA

Objective: Radium-223 dichloride (223RaCl2) is an alpha-emitting radiopharmaceutical and calcimimetic that has intrinsic bone-targeting properties. We hypothesized that 223RaCl2can be safely administered to patients with osteosarcoma (OS) and early signals of response and resistance can be assessed by quantitative and qualitative correlative imaging studies and biomarkers.

Methods: A dose-escalation trial of 223RaCl2 (50, 75, and 100 kBq 223RaCl2/kg) enrolled pts age 15y+ w advanced OS. Molecular imaging with technetium (Tc)-99m bone scan, FDG PET or sodium fluoride-18 (NaF) PET was done at baseline and at restaging.

Results: Overall, 18 pts were enrolled, 15 males, 3 females, age ranging 15-71yrs. Subtypes of OS were osteoblastic in 8 pts, high grade NOS in 3, chondroblastic in 3, fibroblastic in 2, giant cell in 1 and fibrosarcoma in 1. Tumor locations included lesion in the spine (12 pts, 66%), pelvis (10 pts, 55%), ribs (9 pts, 50%), extremity (7 pts, 38%), and skull (2 pts, 11%). Pts received 1–6 cycles of 223RaCl2; cumulative doses varied from 6.84 MBq to 57.81 MBq. G3 thrombocytopenia was seen in 1 pt at dose level 3. NaF-PET identified mets in the in the lung and spine, not avid on FDG PET(Figure 1). One pt had metabolic response in the FDG-PET and NaF PET. Four pts had mixed responses w decreased avidity of bone lesion but increased avidity of surrounding soft tissue lesion. One patient had response in the brain metastasis. The RP2D for using 223RaCl2 for osteosarcoma is 100 kBq/kg monthly. A validated bone pain survey demonstrated a reduction in bone pain.

Conclusion: 223RaCl2 at twice the dose approved for prostate cancer was well tolerated. With the CNS response, we see the first clinical evidence of blood-brain barrier penetration of an alpha particle. Our results indicate that NaF-PET identifies OS lesions in additional sites, which were not avid on FDG PET, highlighting a potential role for NaF PET in OS staging and monitoring response to therapy.



PET showing different areas of active tumor. NAF better defines bone forming component vs FDG PET defines soft tissue component.

P1 - Poster 056 2570092

DO WE NEED BONE SCANS FOR CARTILAGE TUMOURS?

Carola I. Brückmann[1]; Magdalena M. Gilg[1]; Lukas Holzer[1]; Franz Quehenberger[2]; Thomas Schwarz[3]; Andreas Leithner[1]

[1]Orthopedic Surgery, Medical University of Graz, Graz, Styria, Austria; [2]Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz, Graz, Styria, Austria; [3]Department of Radiology, Division of Nuclear Medicine Radiology, Medical University of Graz, Graz, Styria, Austria

Objective: We aimed to identify the diagnostic benefit of bone scans in cartilage tumours.

Methods: We retrospectively analysed 375 patients with a cartilage tumour (321 EC, 54 CS) diagnosed at a mean age of 45.8 years (range, 6 – 84) in whom a Tc99 bone scan (3 phasic) was performed. Bone scan data, x-rays, MRI and histopathological records were evaluated. In cases, in which diagnostic and histopathological workup were inconclusive, the definitive diagnosis was made in

the multidisciplinary team meeting. Diagnostic accuracy of bone scans was assessed with receiver operator characteristic curves (ROC) to evaluate the area under the curve (AUC).

Results: Of 375 patients, 65 (17%) underwent biopsy and 176 (46%) surgery, while in 134 cases (35%) a conservative treatment was chosen. The most common localisation of tumours were the long bones (n=245, 65%), followed by hand/foot (n=99, 26%) and trunk (n=20, 5%). The mean tracer uptake for EC was 3.8 (range 0.5 – 68.0), for CS grade *1* 4.47 (range 0,5 – 12,3), grade *2* 8.2 (range 3,3 – 13,5) and grade *3* 7.5 (range 6,3 – 8,9). The mean tracer uptake of EC was significantly lower than for all CS (p< 0.001), for low- grade CS (p< 0.001) respectively. In 153/321 lesions (48%) the radiologist identified EC correctly, whereas 3/54 CS (6%) were correctly identified with the bone scan compared to the definitive diagnosis. In 145 patients (39%) the bone scan was inconclusive and in 54 (14%) patients a bone scan did not show any pathological finding. On multivariate analysis tracer uptake was significantly increased with pathological fracture (OR 3.9, 95% CI 3-5.2, p<0.001) and peripheral localisation of tumours (OR 2.8, 95% CI 1.5-5-2, p<0.001). The AUC for all cartilage tumours increased from 0.70 (Sp 80%, Sen. 50%) to 0.80 (Sp. 80%, Sen. 64%) when adding bone scan information. The AUC for EC and CS grade *1* increased from 0.67 (Sp 80%, Sens 46%) to 0.73 (Sp 80%, Sen. 52%).

Conclusion: We could see a statistically significant increase of tracer uptake in CS (all CS vs. EC; Grade *1* vs. EC) compared to EC. The presence of pathological fracture and peripheral localisation were significant independent predictors for higher tracer uptake. However, assessment of diagnostic performance showed that bone scans only provide minimal additional information to select between EC and low-grade CS. Taking into account costs and resources to perform a bone scan as well as radiation exposure for patients, its use in the group of cartilage tumours should be reconsidered in the future.

P1 - Poster 057 2556460

OSTEOSARCOMA OF THE SPINE AND PELVIS: 115 PATIENTS OF A SINGLE INSTITUTION

Haotong Wang, MD[1]; Alex Jacobson[1]; Saveli Goldberg[1]; David Harmon[2]; Edwin Choy[2]; Gregory M. Cote[2]; Francis Hornicek[2]; Kevin Raskin[2]; Pateur Nielson[2]; Thomas F. DeLaney[1]; Yen-Lin Chen[1]
[1]Radiation Oncology, MGH, Burlington, MA, USA; [2]MGH, Boston, MA, USA

Objective: Spine and pelvis are uncommon sites of involvement for osteosarcoma that pose unique challenges for treatment. Radiation therapy plays a greater due to the challenge of complete resection in these sites. We reviewed a large series of spine and pelvic osteosarcoma for treatment approach and clinical outcomes.

Methods: Patients with osteosarcoma in their spine or pelvis who presented to our institution from 1964 to 2013 were identified. We retrospectively reviewed of the clinical presentation, treatment, outcome, and patterns of failure. Clinical and pathologic variables were recorded. Kaplan-Meier analysis and Cox proportional hazards regression were used to analyze survival outcomes and prognostic factors.

Results: Of 115 patients out of 128 patients with follow up, the median age was, range 4 – 84. 26 (22.6%) patients presented with metastatic disease, and 89 (77.4%) patients had non-metastatic disease. 17 patients were determined to be potentially radiation associated. The detailed anatomic distribution of the primary tumors include: C spine (5, 4.3%), T spine (12, 10.4%), L spine (13, 11.3%), Sacrum and coccyx (14, 12.1%), Pelvis (71, 61.7%). Histology subtypes include: osteosarcoma, NOS (69, 60.0%), chondroblastic osteosarcoma (35, 30.4%), fibroblastic osteosarcoma (6, 5.2%), small cell osteosarcoma (4, 3.5%), parosteal osteosarcoma (1, 0.9%). 40 (34.8%) patients were treated with surgery without radiation therapy (RT). The median RT dose administered is 56Gy. With the median follow up of 24.6 months, the 3- and 5-year overall survival (OS), and are 70.9% (95%CI: 60.1-79.2) and 61.7% (95%CI: 49.8%-71.5), respectively. Among patients who presented with non-metastatic disease, multi-variate analysis identified Grade 3 (HR=4.3, p=0.014), no chemotherapy received (HR=4.2, p=0.003), and no surgical resection (HR=8.2, p=0.074) as worse prognostic factors for OS. Among patients who have received surgery, positive margins (HR=5.9, p=0.004) are associated with worse survival rate, and treatment without chemotherapy (HR=6.3, p=0.005) is associated with worse prognosis.

Conclusion: Osteosarcoma in spine and pelvis are challenging bone sarcomas for management. For non-metastatic disease, we identified surgery with negative margins and adjuvant chemotherapy are associated with better survival. RT with more than 56Gy as total dose is associated with better local control.

P1 - Poster 058 2565988

CARBON ION RADIOTHERAPY FOR UNRESECTABLE AXIAL OSTEOSARCOMA

Reiko Imai; Tadashi Kamada
National Institute of Radiological Sciences, Chiba, Japan

Objective: The mainstay treatment for osteosarcoma is chemotherapy and complete resection. However, curative surgery is challenging for axial osteosarcomas due to proximity of critical organs. Carbon-ion radiotherapy (CIRT) has precise dose distribution and high biological effectiveness, and may be a promising therapy for sarcoma.

In this study, we evaluated the results of CIRT in patients with unresectable axial osteosarcoma.

Methods: A retrospective analysis of 96 patients with axial osteosarcoma treated with CIRT was performed. Evaluated patients were treated under two protocols between 1996 and 2000 and 2000 and 2014 at a single institution. Radiation-associated osteosarcoma was excluded. The median age was 42 years old ranging from 11 to 83. There were 57 males and 39 females. The maximum tumor diameter was 15 cm and the median tumor volume was 553 cm^3. There were 81 primary tumors, 11 recurrent tumors after surgery, and 4 metastatic tumors. Regarding the location of tumors, 20 were in the spine and paraspine close to the spinal cord, 74 in the pelvis, and 1 in the mediastinum. The most frequently applied dose was 70.4 Gy (RBE) in 16 fractions over 4 weeks.

Results: The median follow-up period was 24 months ranging from 2 to 234. In all patients the 2-year and 5-year local control rates were 72% and 62%, respectively. The 2-year and 5-year overall survival rates were 51% and 33%, respectively. Twenty four patients survived for more than 60 months and 5 patients use wheel chairs in their ordinary lives. According to tumor volume, 2-year and 5-year overall survival rates in patients with <500 cm^3 were 65% and 47% respectively. On the other hand 2-year and 5-year overall survival rates in patients with >500 cm^3 were 39% and 20% respectively. For primary tumors <500 cm^3 and SD/PR after chemotherapy, 5-year overall survival rate was 57%. Grade 3 late skin toxicity was observed in 5 patients.

Conclusion: CIRT was safe and effective for the management of unresectable axial osteosarcoma, providing good local control and offering a survival advantage.

P1 - Poster 059 2570184

PROTON BEAM RADIOTHERAPY FOR INOPERABLE BONE AND SOFT TISSUE SARCOMA

Hirohisa Katagiri, PhD[1]; Shigeyuki Murayama[2]; Tetsuo Nishiumura[2]; Mitsuru Takahashi[1]; Hideki Murata[1]; Junji Wasa[1]; Seiichi Hosaka[1]; Yousuke Honda[1]
[1]Orthopedic Oncology, Shizuoka Cancer Center, Shizuoka, Japan; [2]Radiation and Proton Therapy Center, Shizuoka Cancer Center, Shizuoka, Japan

Objective: The objective of this study was to assess whether proton beam radiotherapy (PBRT) improves local control in the patients with inoperable bone and soft tissue sarcoma and to clarify the effect of concurrent chemotherapy on survival, by analyzing retrospectively the clinical results of radiotherapy for the patients with inoperable bone and soft tissue sarcoma.

Methods: Between 2002 and 2015, 82 patients with unresectable sarcoma underwent radiotherapy were the subjects of this study. There were 43 males and 39 females, with a mean age of 59 years (14-94). Among the subjects, 69 patients received concurrent chemotherapy. Forty-three (43) patients underwent 3D conformal radiotherapy with photons (CRT), whereas, 39 patients received proton beam radiotherapy (PBRT). We evaluated the overall survival rate, local control rate, and complications.

Results: The overall survival rates for all patients at 2 and 5 years were 54% and 33%, respectively, while the local control rates were 68% and 44%, respectively. The total radiation dose averaged 52.6 Gy in the CRT group (40-70) and 69.7 Gy (54-84) in the PBRT group. The 2- and 5-year survival rates were significantly higher in the PBRT group than in the CRT group (73% and 55% vs. 38% and 14%, P<0.0001), as were the 2- and 5-year local control rates (74% and 56% vs. 56% and 24%, P=0.02, Fig1). The median survival was 11 months longer with concurrent chemotherapy; however, the difference was not statistically significant. Major complications developed in 13 patients (16%) and that of GI tract were associated with PBRT.

Conclusion: Eighty-two (82) patients with inoperable sarcoma were treated with definitive radiotherapy. Patients treated with PBRT showed higher survival rate and superior local control compared to the patients with CRT. Although the PBRT group included many large tumors, PBRT enabled the use of a higher dose of radiotherapy, and the local control rate was better. PBRT with a dose of more than 60 Gy is an excellent treatment for inoperable sarcomas.

Table1. Characteristics of all patients

Age (years)		
median (range)	59	(14–94)
Sex		
male	43	
female	39	
Follow up (months)		
median (range)	23.7	(2–141)
Stage		
M0		45
M1		37
Histological diagnosis		
Undifferentiated Pleomorphic Sarcoma		22
Osteosarcoma		12
Leiomyosarcoma		9
Ewing sarcoma family		9
Solitary fibrous tumor		5
Spindle cell sarcoma		5
Other		20

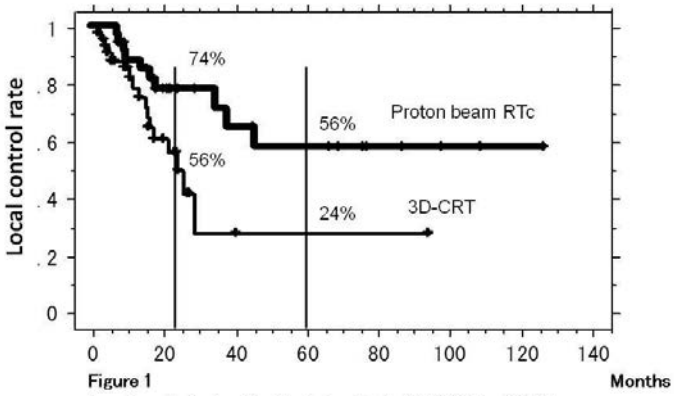


Figure 1
Local control rate of the patients treated with PBRT and CRT

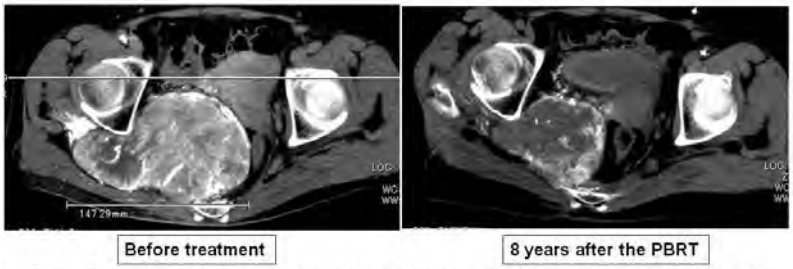


Figure 2. Enhanced CT image of patient with huge malignant SFT treated with 70Gy of PBRT

Figure 2
Enhanced CT image of a patients with huge malignant solitary fibrous tumor treated using PBRT

P1 - Poster 060 2560531

TWO CASES OF PELVIC SARCOMA ORIGINATING IN THE ACETABULUM WITH MORE THAN 10 YEARS OF FOLLOW-UP AFTER CARBON ION RADIOTHERAPY

Katsuhisa Kawanami; Toshihiro Matsuo; Keiji Sato; Masataka Deie
Aichi Medical University, Nagakute City, Japan

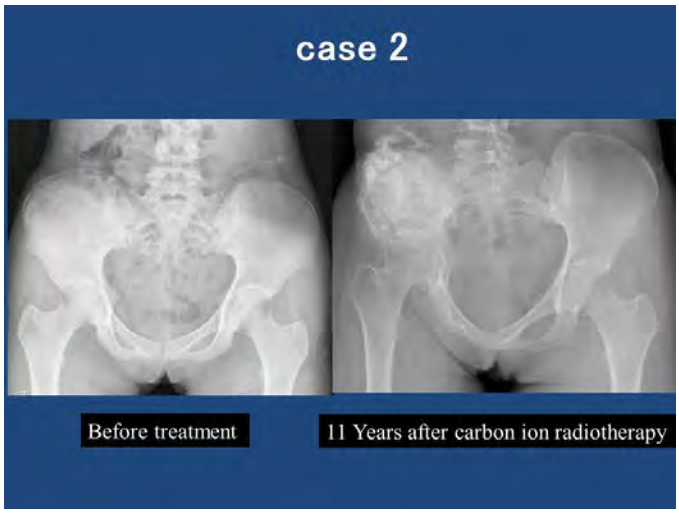
Objective: Carbon ion radiotherapy is thought to cause few complications. However, there is still a great deal of uncertainty regarding functional, long-term prognosis following carbon ion radiotherapy.

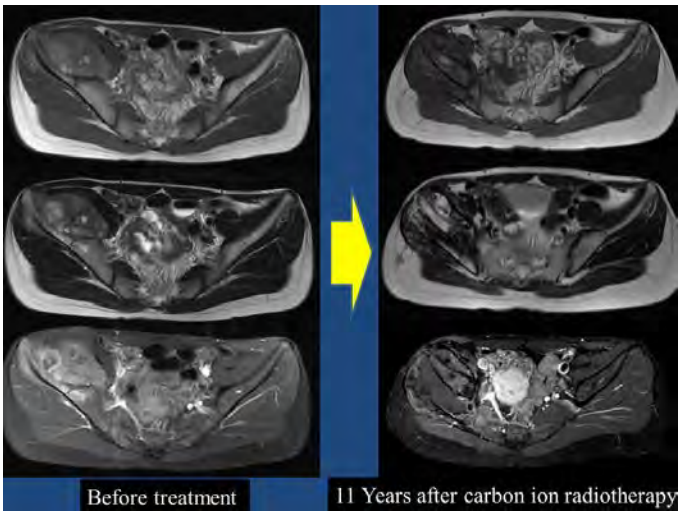
Particularly with tumors originating in the acetabulum where joint loading occurs, a good functional, long-term prognosis is problematic. Here we report two cases from the National Institute of Radiological Sciences (NIRS), Chiba, Japan in which long-term follow-up was possible. The patients received carbon ion radiotherapy against pelvic sarcoma and were followed up for over 10 years.

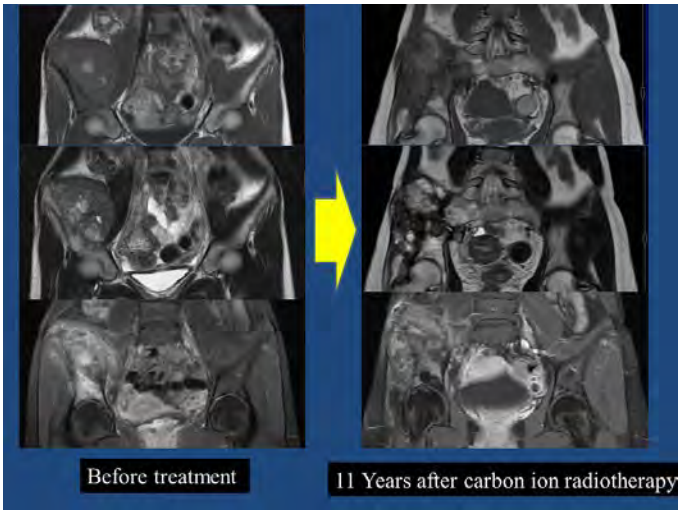
Methods: The study included sarcoma cases diagnosed at our department between 2002 and 2010. With few other therapeutic options available, requests were made to the NIRS to use carbon ion radiotherapy, following which long-term follow-up of over 10 years was possible for two cases.

Results: The patient in case 1 was an 18-year-old woman. The histopathological diagnosis was a telangiectatic osteogenic sarcoma originating from the acetabulum. The patient in case 2 was a 15-year-old girl. The histopathological diagnosis was Ewing sarcoma originating from the iliac acetabulum. In both patients, remarkable antitumor effects of carbon ion radiotherapy were observed, but severe acute reactions (Grade >3) were not observed. There was delayed osteonecrosis accompanied by pathological fracture at 5 and 8 years post-therapy in cases 1 and 2, respectively. Migration of the femoral head began to cause; therefore, patients currently require walking aids (crutches). A few studies have reported the delayed side effects of carbon ion radiotherapy after a long-term follow-up of more than 10 years. A study from 2002 by the NIRS reported only 1 RTOG/EORTC Grade 1 case and 1 RTOG/EORTC Grade 2 case with adverse osteoarticular events out of 60 cases of bone and soft-tissue tumors and no cases of serious adverse osteoarticular events of Grade 3 or higher. The two cases presented here involved Grade 3 reactions and both patients are likely to require surgery in the future. Thus, the percentage of adverse osteoarticular events that emerge must change depending on the duration of follow-up.

Conclusion: While carbon ion radiotherapy has excellent localization control and is an effective therapy against pelvic sarcomas, a treatment that considers the ability of patients to perform activities of daily living in the future is necessary in the long-term management of cases originating in the acetabulum.







P1 - Poster 061 2565856

LIMB-SALVAGE RECONSTRUCTION AFTER ACETABULAR RESSECTION: CLINICAL OUTCOMES

Marta S. Silva; Pedro M. Serrano; Luis Barros; João Esteves; Pedro Neves; Vânia Oliveira; Pedro F. Cardoso
Centro Hospitalar do Porto, Porto, Portugal

Objective: Malignant tumors of the pelvis present challenging oncological and reconstructive problems. Limb-salvage treatment by means of endoprosthetic replacement has become more common but still associated with high complication rates. The authors present 3 acetabular tumors as well as their follow-up.

Methods: Case1: 60 year old male with a grade 2 acetabular condrossarcoma, submited to excision and arthroplasty with a Lumic cup and standard stem. At 3 months of follow up the patient presents no methastization or progression of local disease.

Case2: 32 year old female with a grade 3 acetabular condrossarcoma, submited to excision and arthroplasty with a custom made implant. At 15 months of follow up the patient died because of progression of local and distant disease. Case3: 19 year old female with a Ewing sarcoma, submited to excision and arthroplasty with a Lumic cup and standard stem. At 16 months of follow up the patient presents no methastization or progression of local disease.

Results: All patients begun partial load after 2 weeks, with an average functional score (MSTS) of 18 at 4 weeks and 25 at 4 months. No complications were registered.

Conclusion: Hemipelvic endoprosthetic replacement was developed to restore bone defects, pain relief and hip function but is often associated with a high complication rates. Results in our study were very positive. We believe the hemipelvic arthroplasty is an acceptable reconstructive option that offers advantages of early patient mobilization, stability, flexibility, and durability in tumours requiring pelvic resection.

P1 - Poster 062 2570532

FUNCTIONAL AND ONCOLOGICAL OUTCOME FOLLOWING RESECTION OF MALIGNANT BONE TUMORS OF THE PELVIS AND HIP TRANSPOSITION

Per-Ulf Tunn; Maya Niethard; Carmen Tiedke; Matthias Werner; Peter Reichardt; Jan Mettelsiefen
Sarcomacenter Berlin-Brandenburg, HELIOS Klinikum Berlin, Berlin, Berlin, Germany

Objective: The treatment of primary malignant bone tumors of the pelvis remains a big challenge. Primary therapy goal is to achieve wide margins and a good long-term functional outcome. External hemipelvectomy is currently rarely required. High rates of complications after endoprosthetic replacement led to a preferential treatment with biological reconstructive procedures. The aim of this retrospective study was to evaluate the oncological and functional outcome of patients after a hip transposition.

Methods: Between July 2001 and December 2011 a biological reconstruction with a hip transposition (P2/3 resection n=9, P1-3 resection n=4) because of a primary malignant bone tumor (Ewing`s sarcoma n=6, osteosarcoma n=3, chondrosarcoma n=3 and MFH n=1) was performed in 13 patients. The average tumor size was 104 mm, the mean operation time 235 minutes. The median follow up was 52 months. The analysis was performed using our database, the patient files and the informations of our continuous follow up. The Musculoskeletal Tumor Society (MSTS) scoring system for the lower limb was applied to evaluate the functional outcome.

Results: Three patients died of disease (osteosarcoma n=1, Ewing`s sarcoma n= 2). Ten patients are still alive, six of them with no evidence of disease, 4 patients live with a

metastasized disease. The mean overall survival time of the patients was 52 months (21-88 months). In twelve patients wide margins were achieved, one patient with a chondrosarcoma underwent an intra-lesional resection. This patient received an adjuvant radiotherapy and is actually free of progression and metastasis. Four patients experienced a local recurrence (chondrosarcoma n=1, osteosarcoma n=1, Ewings sarcoma n=2). The postoperative complications included one infected hematoma and one sexual dysfunction. The mean MSTS score was 60% (40-93,3%). Five patients could return to work after completion of therapy (osteosarcoma n=2, Ewing``s sarcoma n=3).

Conclusion: The oncological outcome is comparable to findings in the literature. Complication rates after biological reconstruction with hip transposition are significantly lower compared to replacement with megaprostheses of the pelvis or reimplantation of autoclaved resected bone. Primary instability and long-term rehabilitation finally lead to comparable functional results and in absence of tumor to a long-lasting reconstruction result. Therefore hip transposition should be taken into consideration especially in young patients.

P1 - Poster 063 2570403

ONCOLOGICAL AND FUNCTIONAL RESULTS OF SPINOPELVIC RECONSTRUCTION FOLLOWING THE RESECTION OF MALIGNANT BONE TUMORS INVOLVING IPSILATERAL SACROILIAC JOINT

Takeshi Okamoto[1]; Junya Toguchida[2]
[1]Orthopedic Surgery, Kyoto University, Kyoto, Japan; [2]Tissue Regeneration, Frontier Medical Sciences, Kyoto University, Kyoto City, Japan

Objective: Total resection of the sacroiliac joint for malignant bone tumors and spinopelvic reconstruction still remain surgical challenge. Although several reconstructive procedures have been reported, complications associated with reconstruction are not uncommon. The purpose of this study is to assess the oncological and functional results of the spinopelvic reconstruction following the resection of high-grade malignant bone tumors involving ipsilateral sacroiliac joint.

Methods: Five patients underwent total resection of the ipsilateral sacroiliac joint for high-grade bone sarcomas and spinopelvic reconstruction. The median age of the patients at the index of the treatment was thirty-three years. Two patients were with osteosarcoma, one patient with Ewing sarcoma, one patient with undifferentiated pleomorphic sarcoma, and one with leiomyosarcoma. Resection was performed by combined anterior and posterior approach in all patients. Reconstruction was performed using lumbar pedicle screw and iliac screw instrumentation and autologous bone graft. All patients received neoadjuvant and adjuvant chemotherapy, and two patients were given postoperative radiation. Functional outcome were evaluated using the Musculoskeletal Tumor Society Score (MSTS).

Results: The median follow-up duration was six years and two months. At the time of latest evaluation, four patients were in continuously disease free and one patient was in alive with disease. No patient experienced local recurrence. As postoperative complications, four patients experienced transient L5 nerve root palsy, one patient suffered from late infection. All complications were cured completely. Four patients were ambulatory without any support, and crutches were necessary in one patient. The mean score of MSTS (percent to total full mark) at the latest follow-up was 68%. Bone union was achieved in four patients, and pseudoarthrosis was observed in one patient.

Conclusion: Spinopelvic reconstruction using pedicle screw system instrumentation and autograft following the resection of high-grade malignant bone tumors involving ipsilateral sacroiliac joint could provide good oncological and functional outcome.

P1 - Poster 064 2548727

RESULTS OF THE EN-BLOC VERTEBRECTOMY FOR PRIMITIVE SPINE TUMORS

Alessandro Luzzati, Chief[1]; Giuseppe Perrucchini[1]; Gennaro Scotto[1]; Marco Alloisio[2]; Alessandro Gronchi[3]; Roberto Biagini[4]; Carmine Zoccali[4]
[1]Oncological Orthopaedic Department, Istituto Ortopedico Galeazzi Milan, Milan, Italy; [2]Toracic Surgery, Humanitas, Milano, Italy; [3]Chirurgia dei Sarcomi, Istituto Nazionale dei Tumori, Milano, Italy; [4]Oncological Orthopaedics, Regina Elena National Cancer Institute, Rome, Italy

Objective: The main principle of surgery for malignant muscular-skeletal tumors is obtaining wide margin. This is important for tumors located in the limbs but also in the spine. The aim of presenting paper is to verify the results of wide surgery in primitive spine tumors.

Methods: all patients undergone en-bloc surgery for primitive spine tumors were reviewed. The selected cohort was composed by 77 patients (average age 42,1 years, min 3 – max). The histologies were chordoma (16 cases), osteosarcoma (13 cases, whereof 3 low-grade and one radio-inducted), chondrosarcoma (11 cases), hemangioendothelioma (10 cases), Ewing's sarcoma (8 cases), Malignant Peripheral Nerve Sheath Tumor (8 cases), Malignant Solitary Fibrous Tumor (3 cases), leiomyosarcoma (3 cases), myoepithelial carcinoma (1 case), rhabdomyosarcoma (1 case), spindle cell sarcoma (1 case), synovial sarcoma (1 case), epithelioid sarcoma (1 case). Local recurrence and survival were valued considering the specific histologies as well.

Results: the surgeries were performed by the same sur-

gical team using single or double approach depending on tumor site. Surgeries lasted an average time of 573 minutes (min: 360 - max: 900).

- ***Margin***: In 71 out 77 patients marginal margin was reached but in 8 cases focal contaminations were present; in 5 cases wide margin was reached and in one case intralesional margin was obtained.

- ***Survival***: At 72,5 months of average follow-up (min 12 – max 253), 56 out 77 cases are alive (72,7%). 52 out of 56 patients are free of disease, 3 had a local recurrence where of two underwent a new en-bloc surgery and are free of disease at 74 and 108 months of follow-up; one patient is alive with lung metastasis at 28 months of follow-up. The five years' survival, valued on 52 patients, was 67,3% (the remain part did not reach a sufficient follow-up).
All 21 cases dead with lung metastasis at an average follow-up of 54,9 months from surgeries (min 12 – max 144); 12 out of 21 dead without local recurrence, 9 with local recurrence at 23,9 months (min 4 – max 72) from this.

Conclusion: The principle of surgery in primitive muscular-skeletal tumors in obtain wide margin. This principle is true also in spine, where because of the complex anatomy surgery is technically difficult but, when performed by expert surgeons assure a survival rate not so different from the correspective tumors located in the limbs. More studies with more patients are advisable to better verify our preliminary results.

P1 - Poster 065 2565418
PELVIC RING TUMORS:
RESECTION AND RECONSTRUCTION
João Esteves; Luis Barros; Marta S. Silva;
Pedro Neves; Vânia Oliveira; Pedro F. Cardoso
Orthopaedics, Centro Hospitalar do Porto,
Porto, Portugal

Objective: This study intended to retrospectively evaluate our pratice along 15 years in the treatment of pelvic ring tumors.

Methods: Twenty-five patients underwent pelvic/sacral surgery from 2000 till 2015 in our department. The most common diagnostics were condrosarcoma (n=8), cordoma (n=5), giant cell tumor (n=4), osteosarcoma (n=2) and metastases (n=2). We also had one case of Ewing sarcoma, peripheral nerve sheath sarcoma, condroblastoma and schwannoma.

In the tumors in the zone I (n=6), there was the need for reconstruction with allograft or autograft in 3 cases. In the zone II (n=3) we treated the lesions with aggressive curettage. We didn't need any reconstruction options for the zone III lesions. There was one osteosarcoma involving both the zone I and II, and the patient underwent radical resection and reconstruction with and iliofemoral arthrodesis. There were 5 lesions involving both the zones II and III, and 2 underwent reconstruction with total hip replacement anchored on the remaining ilium. There was one giant cell tumor that invaded both the zone I and IV and was treated with aggressive curettage.
The sacrum, zone IV, was the most involved zone, with 7 cases, in which 3 underwent total sacrectomy with illiolumbar reconstruction.

Results: There were 7 curettages and 18 ressections, 13 with wide margins, 3 marginal and 2 intralesional.
There were 4 infections, all in the sacrectomy patients, 2 resolved and 2 became chronic.
Also neurologic sequels were presented in the 3 total sacrectomy patients. One of the pelvic reconstruction failed and there was the need for revision.
The relapses occurred in 4 condrosarcomas, 3 of which evolved with lung metastases and death, and 1 had the need for pelvic amputation, and the patient is still alive.
There were 3 relapses among the cordomas, and all eventually led to death.
Both cases of osteosarcoma evolved with metastases and death.
The functional score (American Musculoskeletal Tumor Society) of the patients that survived is, in average, 79% in the 9 patients who underwent some form of resection and 94% in the 8 that underwent aggressive curettage.

Conclusion: Pelvic resections carry a high risk of complications. However the challenge for the limb preservation is worth if we take into account the very good functional outcome of the surviving patients.
When it is surgically feasible, the histology allows it and the adjuvants are predictably effective, some less invasive surgical treatment should be chosen to try to reduce the morbidity of the procedure.

P1 - Poster 066 2557898
INTERCALARY ALLOGRAFT AUGMENTED WITH INTRAMEDULLARY CEMENT AND PLATE FIXATION: A RELIABLE SOLUTION AFTER TUMOUR RESECTION
Sanjay Gupta; Lisa Kafchinski; Kenneth R. Gundle;
Anthony Griffin; Jay Wunder; Peter Ferguson
Mount Sinai Hospital, Glasgow, United Kingdom

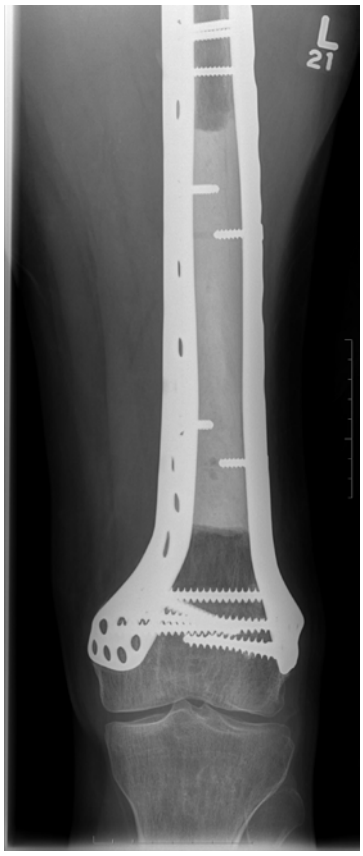
Objective: Biological reconstruction techniques after diaphyseal tumour resection have increased in popularity in recent years. Intercalary allografts have however had high complication and failure rates reported, with recent studies questioning their role in limb-salvage surgery. At our institution we routinely augment large segment allograft with intramedullary cement and use compression plating for fixation.

We evaluate the long-term oncologic outcomes, reconstruction survivorship, complications and functional outcomes of these intercalary reconstructions.

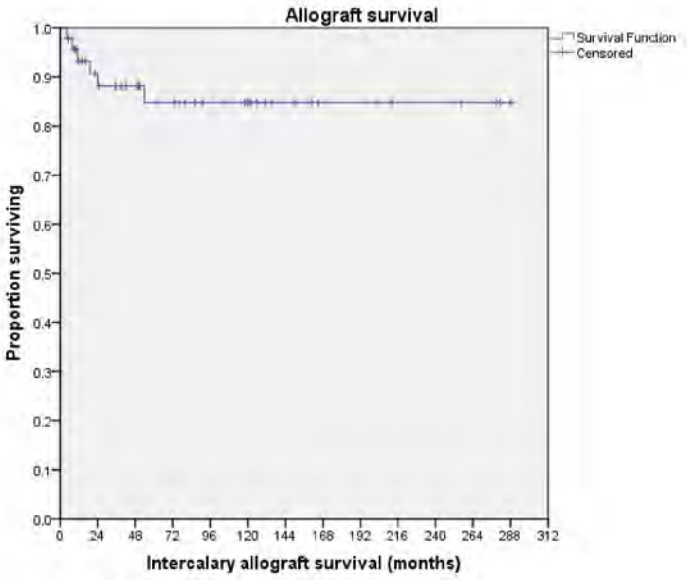
Methods: Forty-six patients who had reconstruction with an intercalary allograft following tumour resection between 1989 and 2014 were identified from our prospectively collected database. Allograft survival, local recurrence-free, disease-free and overall survival were assessed using the Kaplan-Meier method. Patient function was assessed using the Musculoskeletal Tumor Society (MSTS) scoring system and the Toronto Extremity Salvage Score (TESS).

Results: The 26 women and 20 men had a median age of 34 years (14-77). The most common diagnoses were osteosarcoma (n=16) and chondrosarcoma (n=9). There were 21 femur, 16 tibia and 9 humerus reconstructions. At a median follow-up of 92 months (4-288) allograft survival was 84.8%. Fifteen of 46 patients (32.6%) experienced complications: 5 wound healing complications, 4 infections, 3 non-unions, 2 fractures and 1 nerve palsy. Five allografts (11.9%) were revised for complications and 1 (2.4%) for local recurrence. The mean score for MSTS 87 was 29.1 (+/- 4.5), MSTS 93 was 82.2 (+/-15.7) and TESS was 81.2 (+/-16.8).

Conclusion: Intercalary allograft augmented with intramedullary cement and compression plate fixation provides a reliable and durable method of reconstruction after tumour resection, with high levels of patient function and satisfaction.



Distal femur intercalary resection and reconstruction with allograft in situ



Allograft Survival

P1 - Poster 067 2570591

LOWER EXTREMITY LIMB SALVAGE IN PEDIATRIC ONCOLOGY PATIENTS: A RETROSPECTIVE CASE SERIES EXAMINING COMPLICATION RATE AND FUNCTIONAL OUTCOMES AFTER NON-INVASIVE EXTENDIBLE ENDOPROSTHESIS RECONSTRUCTION

Andrea Gale[1]; Wendy Allen-Rhoades, MD[3]; Shiley Aguilar[3]; Hari Sankaran[3]; Lauren Nicholls[2]; Nino Rainusso[3]; Lisa L. Wang[3]; Rex A. Marco[1]
[1]Orthopedics & Sports Medicine, Houston Methodist Hospital, Houston, TX, USA; [2]Pediatrics, University of Arizona, Phoenix, AZ, USA; [3]Pediatrics, Baylor College of Medicine, Houston, TX, USA

Objective: To evaluate the complication rate and functional outcomes of skeletally immature patients who underwent lower extremity limb salvage surgery for primary bone malignancy with a Stanmore noninvasive extendible endoprosthesis (Elstree, United Kingdom)

Methods: This is a retrospective case series of skeletally immature patients with a primary lower extremity bone malignancy who underwent limb salvage surgery with a Stanmore noninvasive extendible endoprosthesis at a single institution between October 2, 2009 and March 3, 2014. Legal guardians gave consent to enroll on study, and patients provided age appropriate assent to participate. All patients completed neoadjuvant and adjuvant chemotherapy as per standard of care under direction of a pediatric oncologist. Demographic and clinical data were extracted from medical records. Patients and/or guardians completed age appropriate Pediatric Outcomes Data Collection Instrument (PODCI) and a Musculoskeletal Tumor Society (MSTS) outcomes instrument to assess functional outcomes.

Results: 13 patients were identified during the study period, and 11 consented to participate in the study. One patient had two endoprostheses; the second was placed after contralateral tumor recurrence for a total of 12 limbs included in this study. Average age of patients at the time of surgery was 8.6 +/- 2.2 years old, and the average follow-up time was 26.5 months. The complication rate was 72%, which included five postoperative flexion contractures of the knee requiring manipulation under anesthesia, two periprosthetic fractures, one popliteal artery vasospasm, one deep infection, one superficial infection, and two revisions for non-infectious reasons. The average MSTS score was 21.3, and the average mean global PODCI was 78.5 in the pediatric group and 88 in the adolescent group. There was an 82% overall survival rate.

Conclusion: In this series, the overall survival at two years was 82% with no local recurrences or need for secondary amputations. This case series differs in two key areas compared to previously published reports. First, the average age at the time of surgery was younger, and there was a higher complication rate when post operative knee manipulations were included. Secondly, the functional outcomes on the sports and physical function domains of the PODCI and MSTS were lower than previously reported. Further investigations are warranted to determine if age contributes to increased complications and inferior functional outcomes in this patient population

P1 - Poster 068 2570269

EXTRAARTICULAR KNEE AND SHOULDER RESECTION FOR SARCOMAS: CLINICAL AND FUNCTIONAL OUTCOME

Eduardo J. Ortiz Cruz, MD, PhD[1]; Manuel Peleteiro-Pensado[2]; Irene Barrientos-Ruiz[2]; Daniel Bernabeu-Taboada[3]; Jose J. Pozo-Kreilinger[4]; Carmen Iglesias[5]

[1]Orthopaedic Oncology, Hospital Universitario La Paz, Hospital Ruber Internacional, Madrid, Madrid, Spain; [2]Orthopaedic Oncology, Hospital Universitario La Paz, Madrid, Madrid, Spain; [3]Musculoskeletal Radiology Department, Hospital Universitario La Paz, Madrid, Madrid, Spain; [4]Pathology Department. Musculoskeletal Pathology, Hospital Universitario La Paz, Madrid, Madrid, Spain; [5]Plastic Surgeon Department, Hospital Universitario La Paz, Madrid, Madrid, Spain

Objective: To find if the extra-articular resection can be an alternative for primary amputation in patients with intra-articular tumor extension.
Limitations: Small group of patients and the sarcomas included are biologically heterogeneous

.

Methods: In a retrospective study between 2011 and 2014, we performed 27 extra-articular tumor resections of the knee, shoulder, pelvis and ankle joints for a bone or soft tissue sarcomas.

We show 21 extra-articular tumor resection and its clinical outcome of the knee and shoulder area. The pelvic tumors and ankle were discarded. The limb was reconstructed using a prosthesis, except two humeral cases with vascularized fibula. The reconstruction around knee the extensor mechanism was preserve partially. Mean age was 22.95 years old (9-47)

The diagnosis were: Osteosarcoma (15/21) was the most common primary malignancy and less frequent were synovial sarcoma (2/21), Ewing Sarcoma (1/21), bone undifferentiated pleomorphic sarcoma (1/21), malignant peripheral nerve sheath tumor (1/21) and mesenchymal chondrosarcoma (1/21).

Staging: 18 /21 were IIB and 3/21 were IIIB at diagnoses. The proximal humerus was the most frequent site (10 /21), distal femur (7/21), scapula 2/21), popliteal fossae (1), intraarticular knee joint (1).

Results: There are 12/21 patients ANED at two years of FU, and DOD 8/21 (38 %) and 1/21 (4.7 %) was dead of leukemia secondary chemotherapy.

All had a wide margin except one, which has a femur pathological fracture; this patient had a local recurrence, infection and multiple pulmonary metastases and DOD.

Deep infection rate was 9.5% (2/21). 2 /21 (9.5%) patients, the primary implanted prosthesis failed during FU. The fail was the polyethylene in knee prostheses. No aseptic loosening, but one patient had a quadriceps tendon rupture.

3/21 (9.52%) patients had local recurrence and they are DOD. One of them are correlated with marginal margins Functional outcome scores according to MSTS from knee surgery 21.11 y from shoulder 22, 8 of survivors for more than 1 year.

Conclusion: The results suggest that extra-articular resection can be an alternative for primary amputation. It is a technical demanding procedure with acceptable local recurrence rates in patients with in general, poor survival

P1 - Poster 069 2565954

BIOLOGICAL DIAPHYSEAL RECONSTRUCTION AFTER EXCISION OF MALIGNANT BONE TUMORS USING A VSCULARISED FIBULAR GRAFT

Yoshikazu Tanzawa, PhD; Eisuke Kobayashi; Makoto Endo; Fumihiko Nakatani; Akira Kawai; Hirokazu Chuman
Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan

Objective: Reconstruction options following segmental resection of malignant bone tumours in the diaphysis include vascularized fibular graft, interposition of an allograft, combination of vascularized fibula and allograft, segmental prosthesis, insertion of a devitalized autograft, and segmental transportation. The aim of the present study was to analyze the operative results, complications, and postoperative function after vascularized fibular graft transfer and the indications for this procedure.

Methods: From 2000 to 2014, we performed VFG on 27 cases to reconstruct the bone defect after resection of a musculoskeletal tumor. There were 13 males and 14 females with a mean age of 32.6 years(3-67) at the time of surgery. Reconstructed bone defects were located in the femur in 12 cases, the tibia in 11 cases, the humerus in 3 cases and the radius in 1 case. Preoperatively, the pathological diagnosis was Ewing sarcoma (n=7), osteosarcoma (n=10), adamantinoma (n=5), chondrosarcoma (n=1), metastatic osteosarcoma (n=1), low grade sarcoma (n=1) and soft tissue sarcoma (n=3). 20 patients were given chemotherapy preoperatively or postoperatively. The mean follow-up period after surgery was 42.5 months (range: 12 to 132). Free vascularized fibula flap was used in 13 patients and ispilateral pedicle vascularized fibula in 5, vascularised fibula and pasteurized bone composite in three cases, and vascularised fibula and frozen autograft composite in 6 cases. The average length of the resected segment was 16.2 cm. We evaluated the success of primary bone union, the period required to achieve bone union, complications, clinical outcome, and the International Symposium of Limb Salvage system (ISOLS) score.

Results: Clinical outcome status was continuous disease free in 17 patients, no evidence of disease in 1, alive with disease in 2, and died of disease in 7. Successful bone union was achieved for 89% of cases. The average period required to achieve bone union was 9.5 months. Nine patients had local complications. Complications included non-union in three, infection in three, fracture in four and local recurrence in one. The mean ISOLS score at final follow-up was 82%.

Conclusion: Long bone reconstruction using a vascularized fibular graft is a reliable technique providing satisfactory functional results. It is possible to prevent postoperative complications by a combined approach with treated bone and/or double barrel fibular grafts.

P1 - Poster 070 2570417

CUSTOM-MADE CERAMIC SPACER FOR CHILDREN WITH OSTEOSARCOMA OF LOWER EXTRIMITIES: A LONG FOLLOW- UP

Fumihiko Nakatani; Takeshi Hirose; Shunichi Toki; Tomoaki Mori; Yoshihiro Araki; Takenori Uehara; Koki Shimizu; Masato Sugawara; Eisuke Kobayashi; Makoto Endo; Yoshikazu Tanzawa; Akira Kawai; Hirokazu Chuman
National Cancer Center Hospital, Tokyo, Japan

Objective: Limb salvage surgery for malignant bone tumors may present difficult problems, especially in cases of skeletally immature patients. The aim of this study was to evaluate our surgical method of reconstruction with custom-made ceramic spacer for the highly skeletally immature patient with osteosarcoma, especially focusing on the major complications of surgery, function of salvaged limbs.

Methods: From 1996 to 2006, six children with osteosarcoma in the lower limbs underwent the limb salvage surgery with custom-made ceramic spacer and followed through January 2016. There were three males and three females, ranged in age from 6 to 11 years (median age: 8 years old) at the time of operation. They were followed up for at least 10 years after the first operation (average, 12.9 years). The location of the tumors were distal femur in one patient, proximal tibia in five. Ceramic spacers were designed about one month in advance to the operation according to the images of plain X-ray and CT scanning. All the spacers were manufactured by KYOCERA Medical Corporation, Osaka, Japan.

Results: In all patients, tumor resections were successfully performed in radical procedure with negative margins. We have reconstructed proximal tibia with ceramic spacer varied from 120 to 150mm in length. Diameters of the stems were varied from 8 to 10mm. As for the distal femur case, we have used the ceramic spacer of 250mm in length and diameter of the stem was 12mm. Three cases were performed revision operations with expandable endoprosthesis because of the substantial limb length discrepancy and/or loosing of the spacer. One femur case was amputated at the site of the above knee, because of early loosening of the spacer followed by late deep infection of the surgical site. There are two cases under observation with soft or hard external prosthesis, waiting to undergo the revision operation with endoprosthesis. All cases are alive with complete disease free status.

Conclusion: With the use of custom-made ceramic spacer, limb salvage surgery was safely performed in the appropriate schedule. However, there are some cases of early loosening of the implant or instability of the suffered joint.

P1 - Poster 071 2570493

TECHNIQUE AND RESULTS IN RETRANSPLANTATION OF RADIOSTERILIZED BONE TUMOURS WITH AND WITHOUT FIBULAR AUGMENTATION

Alexander Klein[1]; Yasmin Bakhshai[1]; Falk Roeder[2]; Andrea Baur-Melnyk[3]; Thomas Knösel[4]; Lars Lindner[5]; Volkmar Jansson[1]; Hans R. Dürr[1]
[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany; [2]Department of Radiotherapy, LMU Munich, Munich, Germany; [3]Institute of Radiology, LMU Munich, Munich, Germany; [4]Institute of Pathology, LMU Munich, Munich, Germany; [5]Medical Clinic III, LMU Munich, Munich, Germany

Objective: After resection of bone tumors, the resulting defect must be reconstructed. Having a mechanical stable tumour resection specimen, particularly suitable in diaphyseal defects, replantation after sterilization with or without fibular augmentation is possible.

Methods: Between 1999 - 2015, this technique was done in 21 patients in 22 locations (one patient simultaneously in femur and tibia). Autoclaving was used just in one case in 21 cases we preferred radiation with 300 Gy. The average age of the 13 men was 41 years (10-83 years) that of the 9 women 47 years (12-79 years). The diagnosis was Ewing sarcoma in 8 cases, metastaatic disease in 6 cases (5 NCC, HCC 1), 5 osteosarcomas, chondrosarcoma, leiomyosarcoma and myxofibrosarcoma each one. The location was in 2 cases epimetapyseal (prox. tibia, dist. tibia), otherwise diaphyseal and metadiaphyseal. In 12 cases the lesion was in the femur, in 7 cases in the tibia in 2 cases in the calcaneus and in one case in the scapula. In 14 cases, a additional fibula was used. At follow-up 5 of the 21 patients (2 NCC, 1 HCC and 2 patients with Ewing sarcoma) had died. The follow-up was on average 52 months (6-129 months), in 3 patients less than one year.

Results: In one case (osteosarcoma after nailing of a pathological fracture before admittance) local recurrence developed outside the graft, we attribute that to fracture hematoma. Of 22 cases, only in 9 no revision for reasons as complications or nonunions had to be carried out. In 5 cases, 1 revison, in 4 cases 2 revisions, each one case 3, 4, 5 and 8 revisions were necessary. In 18 cases a complete healing was achieved, in 2 cases, there is a nonunion and in one case, the implantation of a tumorprosthesis (femur) was necessary. In one patient of a complete calcaneal replantation description of bone healing is technically impossible. Healing was achieved on average in 13 months (4-35 months).

Conclusion: Overall, the course of healing is lengthy but showed good results at the end. Ultimately, the patient must be prepared for a longer period of non or partial weightbearing and (as shown above in 55%) accept sometimes multiple revisions. The technique is safe in terms of tumor recurrence and in younger patients with diaphyseal or metadiaphyseal location now our standard procedure.

P1 - Poster 072 2544310

THE PROPHYLACTIC ANTIBIOTIC REGIMENS IN TUMOR SURGERY (PARITY) MULTICENTER RANDOMIZED CONTROLLED TRIAL: INTERNATIONAL EXPANSION OF THE COLLABORATIVE NETWORK

Michelle Ghert, MD, FRCSC; The PARITY Investigators
Surgery, McMaster University, Hamilton, ON, Canada

Objective: PARITY is an international multi-center randomized controlled trial in which patients with a bone tumor of the lower extremity undergoing endoprosthetic reconstruction are randomized to one of two study arms: 1 day of post-operative antibiotics, or 5 days of postoperative antibiotics. The study opened to pilot phase enrolment in 2013. The following is an update of the trial progress with a focus on enrolment and international expansion.

Methods: PARITY patients are randomized by the pharmacy team at each site through an online randomization program (www.randomize.net). The remaining study participants (patients, surgeons, nurses, study personnel) are blinded to treatment allocation. The primary outcome is surgical site infection and outcomes assessment is adjudicated by the PARITY Adjudication Committee through an online secure platform (Global Adjudicator™). Data is monitored for patient safety by an independent Data Safety and Monitoring Committee. Data quality is screened at regular intervals to maintain high standards of data quality. A total of 37 sites across 7 countries and 5 continents have opened for enrolment in the PARITY trial.

Results: At the time of abstract submission, a total of 156 patients have been randomized across sites in the United States, Canada, Argentina, Brazil, South Africa, Spain and Australia. Sites currently in the active start-up phase (contract negotiations and ethics applications) represent the United States, the Netherlands, Israel, Denmark, Germany, France and India. The PARITY Pilot was published in September 2015 and the Canadian Institutes of Health Research and the Canadian Cancer Society have awarded funding for the definitive phase of PARITY. Data from the pilot study confirms feasibility in enrolment, follow-up and data quality. The regulatory complexities of opening the study in Europe were overcome in early 2016 and the first European patient was enrolled in Spain in February 2016.

Conclusion: Challenges of multi-center collaboration have been overcome by strong investigator and research personnel support at each site in facilitating contract negotiations, trouble-shooting ethics applications, translating study material into different languages, managing variances in available antibiotics and working with national regulatory requirements. Despite the momentum of the PARITY trial, the pace of enrolment indicates that a larger collaborative network will be crucial for reaching the enrolment target of 600 patients.

P1 - Poster 073 2570235

LIGASURE™ SYSTEM IN SARCOMA SURGERY CAN DECREASE INTRAOPERATIVE BLOOD LOSS AND POSTOPERATIVE HOSPITAL LENGTH OF STAY

Yidan H. Zhang[1]; Mikhail Bekarev[1]; Zach H. Jurkowski[1]; David Geller[1]; Hoang H. Bang[1]; Rui Yang[1]; Richard Gorlick[2]; Michael E. Roth[2]; Jonathan B. Gill[2]
[1]Orthopaedic Surgery, Montefiore Medical Center, New York, NY, USA; [2]Pediatrics, Children's Hospital at Montefiore, Bronx, NY, USA

Objective: To investigate the hemostatic efficacy of the LigaSure™ Small Jaw vessel sealing and dividing system and correlate its use with clinical outcomes in sarcoma surgery.

Methods: The charts of 49 consecutive patients who underwent various bone and soft tissue sarcoma surgeries from June 2013 to February 2016 were retrospectively studied. During this time period, the LigaSure™ vessel sealing and dividing system was introduced at our institution and replaced traditional electrocautery as the primary instrument used in deep tissue dissection, resulting in two distinct groups of patients. Patients' demographic data and baseline characteristics were reviewed. Comparisons of hemostasis proxies, such as intraoperative blood loss, intraoperative and postoperative blood transfusion volume, as well as clinical outcomes such as postoperative length of stay, were made between these groups. All adverse effects were reviewed and recorded.

Results: Twenty patients underwent sarcoma surgery without the use of Ligasure™, and 29 patients had LigaSure™ used for deep dissection in their surgeries. Demographic characteristics were not statistically different between the studied groups. Our results showed average intraoperative blood loss, intraoperative blood transfusion volume, and intraoperative pRBC transfusion amount to decrease by 46% (839cc vs 451cc), 75% (1162cc vs 293cc), and 73% (962cc vs 259cc) in LigaSure™ group. The average length of postoperative hospital stay was also found to decrease by 57% (22.1 vs 9.6 days) in LigaSure™ group. There was no difference in the procedure duration between the two groups. No adverse events related specifically to the LigaSure™ system have been identified so far.

Conclusion: The LigaSure™ vessel sealing and dividing system is a safe and effective hemostatic tool for deep dissection in bone and soft tissue sarcoma surgery. Our results suggest that the use of Ligasure™ substantially reduces intraoperative blood loss and blood transfusion requirement without significant increase in case duration. Similarly, our data suggests shorter postoperative hospital stay in patients undergoing sarcoma surgery with the use of Ligasure™.

P1 - Poster 074 2565814

SIMULTANEOUS BILATERAL OPEN THORACOTOMIES FOR PULMONARY METASTASES IN OSTEOSARCOMA TO REDUCE DELAY IN SYSTEMIC THERAPY

Caroline Kelmis; Antonio Logan; Caleb Oh; Graham A. Zolkowski; Michelle March; Paul Kent
Rush University Medical Center, Vernon Hills, IL, USA

Objective: Osteosarcoma (OST) is the most common type of primary bone malignancy in children and young adults. Approximately 10-15% of patients will have primary metastases, and 66% will have recurrence with 90% involving the lungs (JCO 2002; 20(3):776-90, COG Can 2009; 115(22):5339-48). Aggressive surgical resection of all metastatic sites has a known survival advantage (J Ped Surg 2006; 41(1):194-9). Bhattasali et al. surveyed 183 surgical and medical CTOS members on management of metastatic OST. Respondents endorsed thoracotomy for all scenarios (69%-81%) with one exception, an untreated isolated nodule (58%) (Can Med 2015; 4(4):523-31).

Preference for staged versus simultaneous open thoracotomies for bilateral metastases has not yet been studied. Although Chen et al. describes 8 of 12 OST patients with bilateral disease who underwent simultaneous thoracotomies, no data on delays in chemotherapy was available (Eur J Card thor Surg 2008; 34(6):1235-39). In a retrospective analysis of 10 children who underwent simultaneous bilateral thoracotomies, Häcker et al. reported no increased risk (Eur J Ped Surg 2007; 17(2):84-9). Simultaneous bilateral open thoracotomies in pediatrics have not been described in detail. Our goal is to report our experience with simultaneous bilateral open thoracotomies in young OST patients.

Methods: We reviewed all patients with bilateral OST lung metastases at our institution in the last 10 years. Delay time was calculated by subtracting pre-surgery from post-surgery cycle start dates.

Results: Among the 8 patients reviewed, 50% (n= 4) received simultaneous versus staged bilateral thoracotomies. Age ranged from 8-22 years with 5 males and 3 females. Of the patients who underwent simultaneous thoracotomies, 2 had complications resulting in 21, 23-day delays in chemotherapy, and 2 had no complications resulting in 1, 10-day delays (Mean: 13.75 days, Standard Deviation (SD): 10.24). Of the patients who underwent staged thoracotomies, 3 had multiple complications resulting in 62, 75, and 121-day delays. The one patient who underwent staged thoracotomies without complication experienced a 16-day delay (Mean: 68.50 days, SD: 43.19). An independent t-test comparing simultaneous versus staged bilateral thoracotomy was computed (t= 2.47, *p*-value= 0.049).

Conclusion: Simultaneous bilateral open thoracotomies appear to be a safe approach for resection of metastatic

OST lung disease with a potential benefit of decreased delay in chemotherapy in young patients.

P1 - Poster 075 2529558

THREE-DIMENSIONAL FLUOROSCOPIC NAVIGATION-ASSISTED SURGERY FOR TUMORS IN PATIENTS WITH TUMOR- INDUCED OSTEOMALACIA

Hiroshi Kobayashi[1]; Toru Akiyama[3]; Tomotake Okuma[1]; Yusuke Shinoda[1]; Nobuaki Ito[1]; Seiji Fukumoto[1]; Hirotaka Kawano[2]; Sakae Tanaka[1]
[1]The University of Tokyo Hospital, Tokyo, Japan; [2]University of Teikyo, Tokyo, Japan; [3]Saitama Medical Center, Jichi Medical University, Saitama, Japan

Objective: Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome usually caused by phosphaturic mesenchymal tumors (PMTs). Segmental resection has been recommended for these tumors because curettage was found to be associated with a high local recurrence rate. Navigation-assisted surgery provides radiological information to guide the surgeon during surgery. To our knowledge, no previous study has reported the efficacy of navigation-assisted surgery for tumors in patients with TIO. Therefore, the present study aimed to evaluate the efficacy of navigation-assisted surgery for tumors in these patients.

Methods: The study included 7 patients (4 male and 3 female patients) with TIO who were treated between January 2003 and December 2014 at our hospital. All patients underwent surgical treatment with or without the use of a 3-dimensional (3D) fluoroscopy-based navigation system. The location and size of the tumor, laboratory data (serum phosphate, alkaline phosphatase, and fibroblast growth factor 23 levels), and oncological outcomes were evaluated.

Results: The minimum follow-up period was 16 months (range, 16–149 months). The tumors were located at the femur (n = 4), ischium (n = 1), spine (n = 1), and ilium (n = 1), and the mean tumor size was 28.8 mm (range, 5–60 mm). Of the 7 patients, 5 underwent navigation-assisted surgery and 2 underwent surgery without navigation assistance. In the 2 patients who underwent surgery without navigation assistance, a complete cure was not obtained and osteomalacia did not resolve. In these cases, we cannot distinguish the tumor from normal cancellous bone. One of these 2 patients accepted secondary surgery with navigation assistance, which resulted in a complete cure. Of the 5 patients who underwent navigation-assisted surgery, 4 patients achieved complete excision and 1 patient had incomplete resection due to massive invasion of the tumor into the spinal canal. Osteomalacia resolved in the 4 patients, and no recurrence was observed.

Conclusion: Navigation-assisted surgery using a 3D fluoroscopy-based navigation system is effective for tumors in patients with TIO, because it is difficult to distinguish tumors from normal bones during surgery.

P1 - Poster 076 2562584

LONG-TERM (> 15 YEAR) OUTCOMES OF CEMENT IN CEMENT TECHNIQUE FOR REVISION ENDOPROSTHESIS SURGERY

Nicholas Bernthal[1]; Stephen Zoller[1]; Vishal Hegde[1]; Howard Park[1]; Daniel Johansen[1]; Frederick R. Eilber[2]; Frederick C. Eilber[2]; Chandhanarat Chandhanayingyong[2]; Jeffrey Eckardt[1]
[1]Orthopaedics, UCLA, Santa Monica, CA, USA; [2]UCLA, Los Angeles, CA, USA

Objective: Cemented endoprosthetic reconstruction after resection of primary bone sarcomas has been a standard-of-care option for decades. With increased patient survival, the incidence of failed endoprostheses requiring revision has increased. Revision of endoprotheses by cementing into the existing cement mantle is technically demanding. Stress shielding, cement extrusion, and subsequent fixation in previously cemented bone create considerable challenges for revision. This study aims to examine the clinical outcomes of revision cemented endoprostheses using the cement in cement (CiC) technique.

Methods: This is a retrospective review of our database consisting of 512 consecutive cemented endoprosthetic reconstructions performed for oncologic diagnoses between 1980 and 2014. 54 of 512 (10.5%) of these were revised at the cement-implant interface with a CiC technique. Bushing changes, revisions for adjacent joint pathology, revisions to total femur endoprostheses, and planned expansions of growing implants were excluded. Outcomes evaluated were prosthesis survival, further revision surgery categorized according to the Henderson Failure Mode Classification, complications, and functional outcomes. Analyses were repeated for subsequent CiC revisions.

Results: Fifty-four patients (10.5%) underwent initial CiC revision of their primary endoprosthesis (mean 10.2 years post-op) for aseptic loosening (29), structural failures (20), and infection (5). Five-, 10-, and 15-year Kaplan-Meier survival of initial revision implants were 73%, 51%, and 34%, respectively. 15-year survival of initial CiC revision of distal femur replacement was 32%, proximal femur replacement was 62%, and proximal tibia replacement was 0%. Mean MSTS Score was 27 in this cohort. Thirty-four of 54 patients (69%) required a subsequent revision (mean 8.9 years post-op) for aseptic loosening (15), structural failure (15), infection (5), and tumor progression (2). Three of 54 (6%) required amputation. Five-, 10-, and 15-year Kaplan-Meier survival of subsequent revision implants were 65%, 58%, and 44%, respectively.

Conclusion: At long term follow up, endoprostheses re-

vised with the CiC technique showed consistent 15-year survival from initial (34%) to subsequent (44%) revision. Survival rates were influenced by location of replacement. Outcome scores were high in this cohort. Despite a relatively high failure rate, these results are encouraging and demonstrate that this repeatable technique is a reasonable solution to a challenging problem.

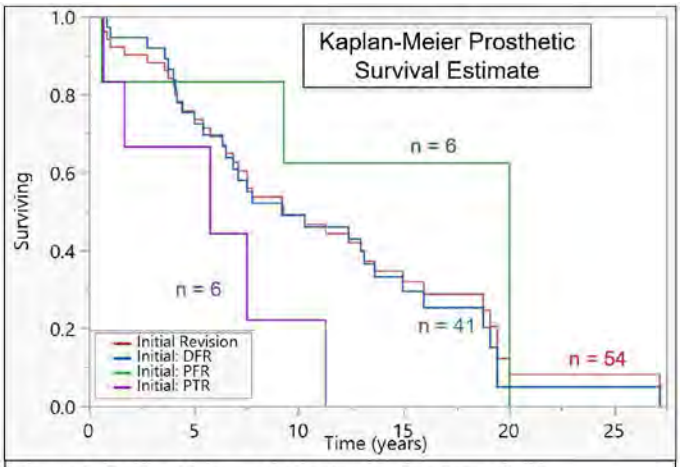


Figure 1. Kaplan-Meier survival estimate of endoprosthetic reconstructions. Initial revision = first revision after index procedure. DFR = distal femur replacement. PFR = proximal femur replacement. PTR = proximal tibia replacement.

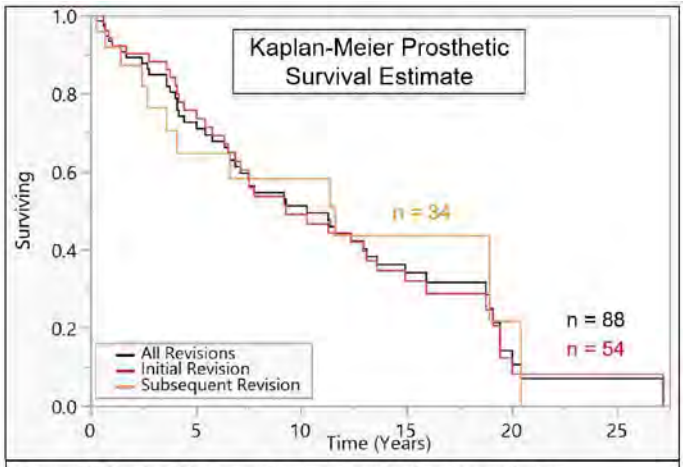


Figure 2. Kaplan-Meier survival estimate of endoprosthetic reconstructions. Initial revision is first revision after index procedure. Subsequent revision is second revision after index procedure.

P1 - Poster 077 2543749

AUTOREGISTRATION IN NAVIGATED BONE TUMOR SURGERY

Prakash R. Nayak, MD[1]; Michelle Arkhangorodsky[2]; Jimmy Qiu[2]; Michael Daly[2]; Harley Chan[2]; Robert Weersink[2]; David Jaffray[2]; Jonathan Irish[2]; Peter Ferguson[1]; Jay Wunder[1]

[1]Musculoskeletal Oncology, Mount Sinai Hospital and Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Guided Therapeutics (GTx) Program, Princess Margaret Cancer Centre, Toronto, ON, Canada

Objective: Registration is the key step in image-guided surgery,but can often be time consuming ,frustrating and hamper workflow.Anatomical points are often unavailable and surface matching forces unnecessary exposure of 'normal' uninvolved bony anatomy.This study presents development and clinical validation of a novel metal-free tool to achieve reliable and consistent automatic registration validated with low fiducial and target registration errors(FRE and TRE).

Methods: Tools made of Ultem(amorphous thermoplastic polyetherimide) with fixed geometry and attached reflective markers were designed.The 'auto-reg' tools were placed on or beside the patient ensuring that both the tumor and tools were visible in the Cone-Beam CT imaging field of view (iCBCT,Zeego, Siemens Healthcare, Germany)(Fig1). The points corresponding to the tool geometry were then accurately identified on the CT image.The spatial coordinates of the auto-reg tools and the tracker (a dynamic reference base fixed to patient's bone anatomy) were also captured at the same instance by an infrared camera (NDI Polaris,Waterloo,Canada)(Fig 2).Registration was then easily achieved as both the image and tracker coordinates of the tools were known.This process involved no surgeon interaction and registration was possible before the surgical incision.The process was validated using FRE and TRE maps.

Results: This technique has been used clinically on 14 patients with extremity tumors as a part of a study to validate a novel surgical navigation platform.The ability to have registration before a surgical incision and with no surgeon interaction to identify bony points was a significant benefit enabling a seamless workflow.The process brought down the mean registration time to less than 2 minutes once CT images were captured (mean time ~7 mins).The absence of metal artifacts and the ability to position the 'auto-reg' tools on or off the patient allowed freedom in optimizing fiducial configurations resulting in registration errors of less than 1 mm:mean TRE=0.90±0.24mm(sd) and mean FRE=0.86mm±0.23(sd)(Fig3).

Conclusion: A novel method for automatic registration has been developed that is anatomy agnostic and free of metal artifact which allows freedom in optimizing fiducial placement.Using this system registration is possible

before making the surgical incision and without surgeon interaction, and demonstrated consistent and reliably low FRE and TRE in a clinical setting for extremity bone tumor navigation using intra-operative cone beam CT imaging.

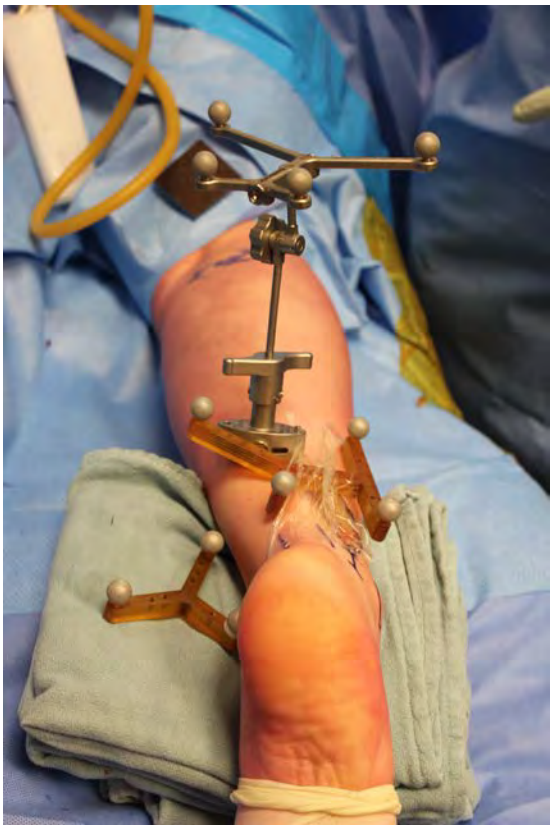


Fig 1: Ultem tools with known fixed geometry and attached reflective spheres

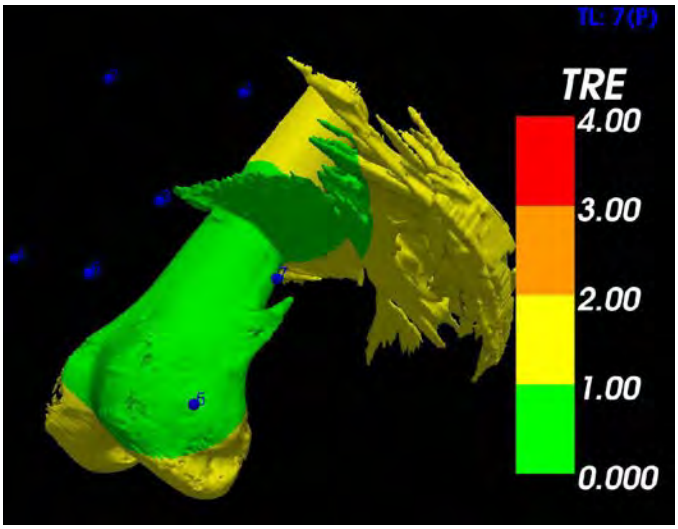


Fig 3:Target registration error (TRE) map showing the green zone with error less than 1mm

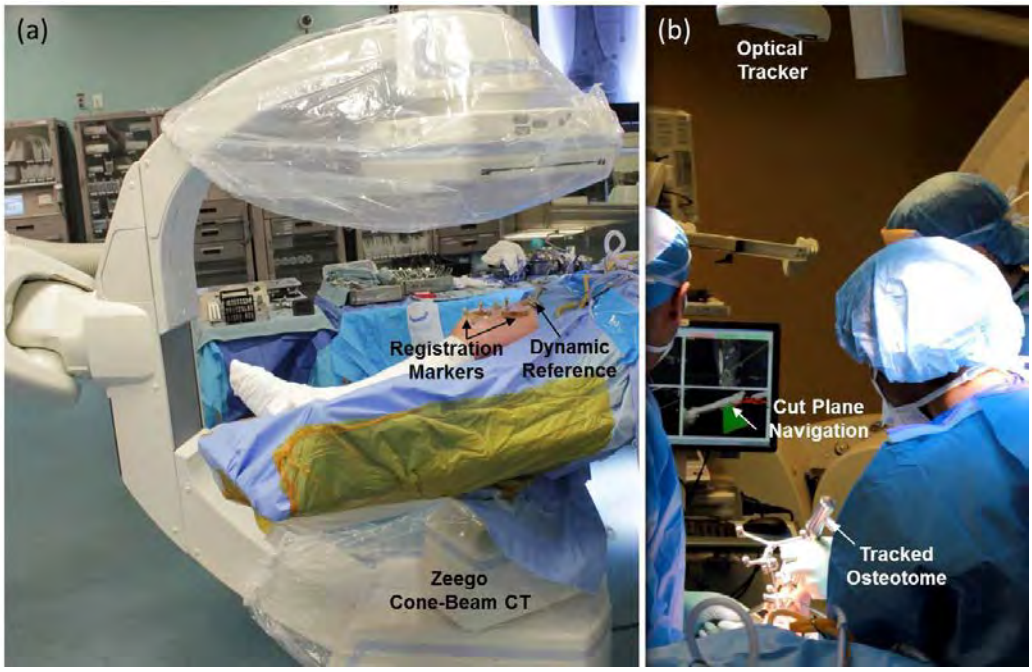


Fig 2: Setup showing the registration tools in the CT field of view with the overhead infrared camera capturing its spatial coordinates

P1 - Poster 078 2571290

RECONSTRUCTION USING STERILISED TUMOUR BONE FOR PRIMARY MALIGNANT TUMOURS OF UPPER LIMB

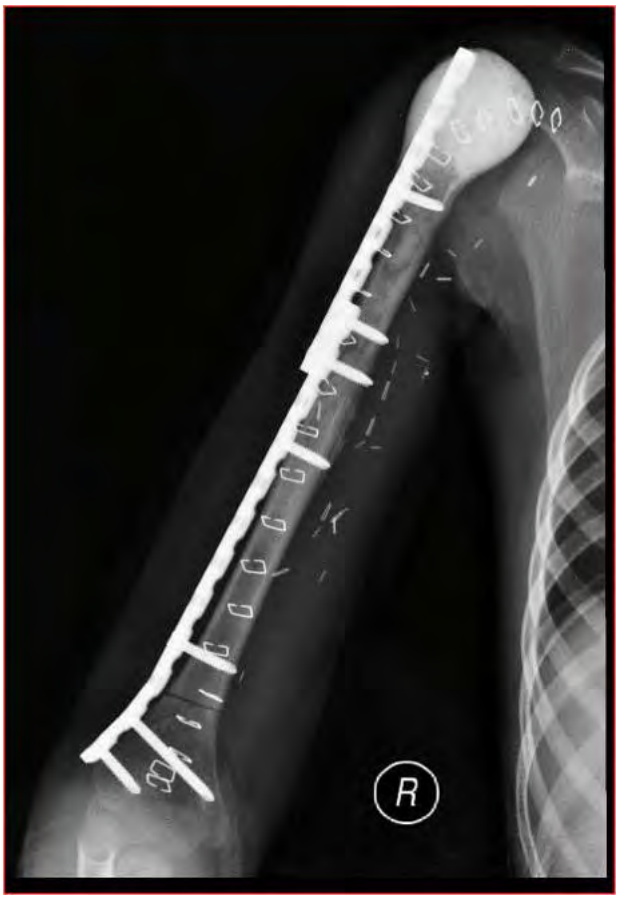
Bhaskar S. Sugath, Fellowship Orthopaedic Oncology Orthopaedics, Aster Medcity, Kochi, India, Trivandrum, Kerala, India

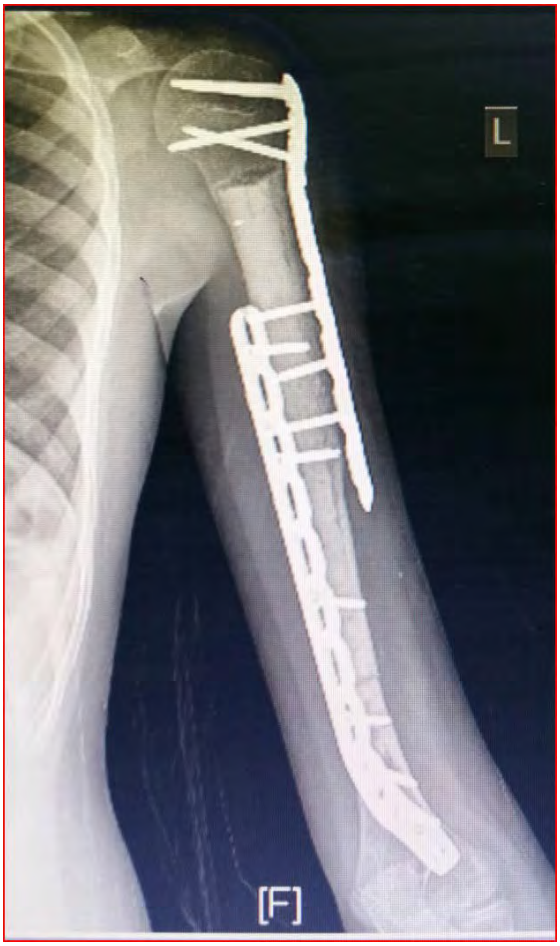
Objective: Delivery of lethal dose radiation to resected tumor bearing bone, and reimplantion of the resultant dead autogenous graft, is a selectively used option for limb preservation. Thoughit has been used as a reconstruction option in lower limb limb salvage procedures it is not commonly used in upper limbs. We report an analysis of 6 patients treated likewise in our institution.

Methods: This is an analysis of 6 patients from a prospectively maintained database from Aster Medcity Kochi & Regional cancer centre, Trivandrum, who underwent extra-corporal radiation therapy between March 2012 and December 2015. After en-block resection, the bone was cleared of tumor, subjected to50Gy single dose radiation and re-implanted. Bone cement was used to fill the medullary canal. Adjuvant, neoadjuvant therapies and follow up were as per institution protocol. Patients were evaluated for surgery related complications, resultant delay in adjuvant therapy, bone union, recurrences, functional outcome using Musculoskeletal Tumor Society (MSTS) scoring system and deaths.

Results: The median age of study patients was 12 years (1-34).There were 4 males and 2 females. 5 had osteosarcoma and one patient had Ewings sarcoma. The involved bone was humerus in in all the cases. Trucut biopsy was used for tissue diagnosis in all patients. all patients received neoadjuvant chemotherapy. The mean length of bone resected was 10.57cm (9-18). Bone and marrow margins were free of tumor in all cases. One patient had surgery related complications, wound hematoma, which required wound wash out. Bone grafting as a second surgery was done in 2 patients Adjuvant chemotherapy was started within 3weeks of surgery in 5(83.83%) patients. There were no local recurrence. One patient developed lung metastasis.. The mean MSTS score of study population was 26.33.

Conclusion: Extracorporeal radiation therapy is an oncologically safe option with satisfactory functional outcome for selected cases of upper limb malignant tumours. It ensures effective tumor kill and spares surrounding tissues of radiation. Careful patient selection, meticulous pre operative planning, implementation of these plans intra operatively and the infrastructure support to back it up is essential for the success of this procedure.





P1 - Poster 079 2556321

CORE NEEDLE BIOPSY IS A SAFE AND EFFECTIVE MODALITY FOR DIAGNOSIS OF ANEURYSMAL BONE CYST

Zachary Burke, MD[1]; Vishal Hegde[1]; Stephen Zoller[1]; Daniel Johansen[2]; Benjamin Kelley[2]; Noah Federman[3]; Leanne Seeger[4]; Scott Nelson[5]; Nicholas Bernthal[1]
[1]Orthopedics, UCLA, Santa Monica, CA, USA; [2]David Geffen School of Medicine, Los Angeles, CA, USA; [3]Mattel Children's Hospital at UCLA, Los Angeles, CA, USA; [4]Radiology, UCLA, Los Angeles, CA, USA; [5]Pathology, UCLA, Los Angeles, CA, USA

Objective: While there is widespread acceptance of core needle biopsy (CNB) for solid tumors, the current standard for diagnosis of aneurysmal bone cysts (ABC) remains open biopsy. There has been a historical reluctance to use CNB for the diagnosis of ABCs due to concerns of safety and reliability when procuring cystic tissue, particularly to rule out malignant diagnoses. We aim to study the safety and efficacy of CNB as an initial diagnostic modality for ABC.

Methods: A retrospective review of our pathology database (1990-2016) was performed using search criteria "aneurysmal bone cyst" or "telangiectatic osteosarcoma". All cases were reviewed for the presence of a core needle biopsy. Core needle biopsy diagnosis, subsequent open biopsy results (if applicable), and resection pathology were reviewed. Core biopsies were defined as "effective" if the core diagnosis matched the final resection diagnosis with respect to malignant potential. Biopsies were defined as "non-diagnostic" if further tissue was needed for histologic characterization. Charts were reviewed for any medical complications resulting from the biopsy.

Results: Seventy-three consecutive CNBs met the above criteria. There were no biopsy complications. Fifty-eight biopsies were read as benign, 53 of which were benign on final diagnosis. Of the remaining five "benign" lesions, four biopsies were read as benign with a recommendation for obtaining further tissue because of areas of concerning histology (3) or discordant, aggressive imaging (1). One patient was taken for definitive surgery with a presumed benign diagnosis that was malignant on final pathology. Seven CNBs were read as malignant, all of which were malignant on final diagnosis. Eight CNBs were non-diagnostic, requiring open biopsy. In total, 82% (60/73) of CNBs were considered "effective."

Table 1: Core needle biopsy and final pathology results.

	Final Pathology		Total
	Benign	Malignant	
Biopsy Pathology			
Benign	53	5	58
Malignant	0	7	7
Non-diagnostic	5	3	8
Total	58	15	73

Conclusion: CNBs were effective in distinguishing between ABCs and TOS. The biopsies led to no medical complications and only one patient (1%) went to surgery with a diagnosis of ABC that later was determined to be a malignant lesion. The validity of CNBs are improved with evaluation by a multidisciplinary tumor board where concerning imaging or atypical, but benign histology can be identified.

P1 - Poster 080 2543237

PRELIMINARY VALIDATION OF SKIN FIDUCIALS FOR NAVIGATION-ASSISTED MUSCULOSKELETAL TUMOR RESECTIONS: A CADAVER STUDY

Rodolfo Zamora Rendich, MD; Claudia Christman-Skieller; Cegniz Yildirim; John Shapton; Jedediah White; Stephanie Punt; Ernest U. Conrad
Orthopaedics and Sports Medicine,
University of Washington, Seattle, WA, USA

Objective: The aims of this study are: first, verify the accuracy of final postoperative margins using skin fiducials in comparison with bone fiducials (gold standard) for navigation registration. Second, compare the accuracy of navigated postoperative margins obtained in long bone resections compared to pelvic/sacrum resections.

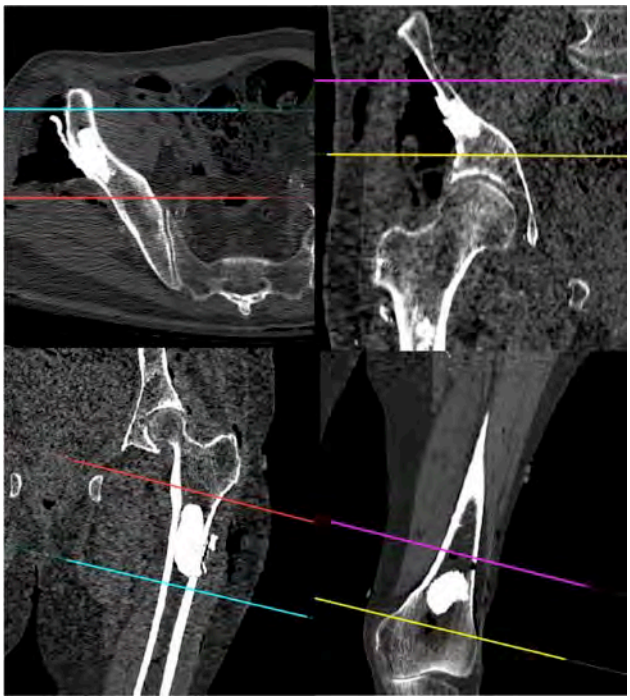
Methods: Osseous resections were carried out in three cadavers with intact pelvic and lower extremity anatomy using navigation guidance. Bone tumors were simulated by placing a 5 cm intraosseous cement mass in the ilium/sacrum (6), proximal/distal femur (12) and proximal/distal tibia (12). Skin fiducials were placed on bony prominences along the skin surface. Bone fiducials were generated through the placement of Kirschner wires. For each cadaver, computer tomography of the pelvis and lower extremities was obtained with simulated bone tumors with fiducials in place. A tumor map and preoperative margins were planned using the Stryker software 3.0 for Oncologic Navigation. Each planned margin was set as 1.0cm for proximal and distal margins in the long bones and anterior, posterior, lateral and medial margins in the pelvis/sacrum. Margin accuracy was separately calculated.

Results: 16 Long bone tumor resections (32 postoperative margins) were performed using skin fiducials and eight long bone tumor resections (16 postperative margins) using bone fiducials. Six pelvic tumor resections (20 postoperative margins) were performed using skin fiducials.
Mean postoperative margin for pelvis/sacrum resections using skin fiducial registration was 11.3 mm (5-17 mm). Skin fiducial registration was comparatively more accurate in the long bones resections than pelvis/sacrum resections, p=0.036 (Figure 1).

Mean margin accuracy obtained was significantly greater for long bone--skin (M=-0.521 mm, SD=1.97) and bone fiducials (M=-1.125 mm, SD=1.63) than pelvis-skin fiducials (M=1.316 mm, SD=3.37). Standard error across the skin and bone fiducial comparisons in the long bone and pelvis were within expected limits.

Conclusion: Osseous tumor margins in the long bones achieved with skin fiducial registration have similar accuracy to margins obtained with bony fiducial registration. Skin fiducial registration in the pelvis resulted in a slightly larger error than in the long bone resection, expected by the complex anatomy of the pelvis and the difficulty to find clear margins.

Skin fiducials for navigation have good accuracy for long bones resections and are acceptable for pelvic/sacrum resections.



Preoperative plan on a CT scan. Tumors were created with bone cement and preoperative margins were pre-plan and set 1 cms from tumor.

Long Bone—Skin Fiducials
M=9.48 (6-15)mm, SD=1.97, SE=1.96

PT 1	DT (Dist)	DT (Prox)	PT (Dist)	PT (Prox)	DF (Dist)	DF (Prox)	PF (Dist)	PF (Prox)
Right	11	10	9	8	6	11	10	12
Left	9	9	11	9	6	15	10	9
PT 2	DT (Dist)	DT (Prox)	PT (Dist)	PT (Prox)	DF (Dist)	DF (Prox)	PF (Dist)	PF (Prox)
Right	13	12	9	9	10	9	13	8
Left	9	13	6	10	9	9	8	8
PT 3	DT (Dist)	DT (Prox)	PT (Dist)	PT (Prox)	DF (Dist)	DF (Prox)	PF (Dist)	PF (Prox)
Right	9	9	7	6	10	7	13	9
Left	9	8	10	11	8	9	10	10

Pelvis—Skin Fiducials
M=11.3 (5-17)mm, SD=3.28, SE=3.21

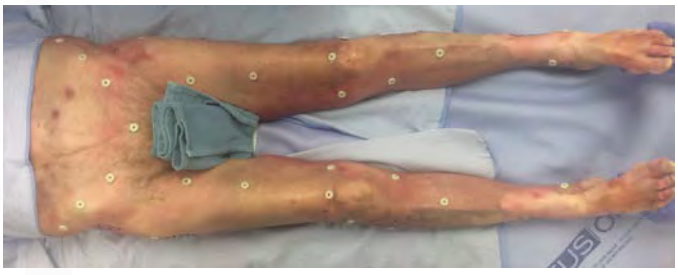
PT 1	S	I	A	P				
Right	-	-	-	-				
Left	11	-	-	-				
PT 2	S	I	A	P				
Right	10	15	14	-				
Left	15	15	16	5				
Sacrum	10	9	10	13				
PT 3	S	I	A	P				
Right	8	7	17	9				
Left	10	12	12	8				

Long Bone—Bone Fiducials
M=8.9 (7-12)mm, SD=1.63, SE=1.81

PT 1	DT (Dist)	DT (Prox)	PT (Dist)	PT (Prox)	DF (Dist)	DF (Prox)	PF (Dist)	PF (Prox)
Right	-	-	-	-	-	-	-	-
Left	-	-	-	-	-	-	-	-
PT 2	DT (Dist)	DT (Prox)	PT (Dist)	PT (Prox)	DF (Dist)	DF (Prox)	PF (Dist)	PF (Prox)
Right	-	-	-	-	-	-	-	-
Left	-	-	-	-	10	9	8	7
PT 3	DT (Dist)	DT (Prox)	PT (Dist)	PT (Prox)	DF (Dist)	DF (Prox)	PF (Dist)	PF (Prox)
Right	10	7	7	7	8	9	10	12
Left	10	7	10	11	-	-	-	-

Postoperative Margin Data and Descriptive Statistics

	# Tumors	# Margins	Average Margin	Standard Deviation	Average Margin Variation	Standard Error
Long Bone-Skin	16	32	9.48 (6-15)	1.97	-0.52	1.98
Pelvis-Skin	6	20	11.3 (5-17)	3.28	1.32	3.21
Long Bone-Bone	8	16	8.9 (7-12)	1.63	-1.13	1.82



Skin Fiducials Position

P1 - Poster 081 2566216

INDOCYANINE GREEN DYE ANGIOGRAPHY PREDICTS RESIDUAL TUMOR GROWTH IN A POST-AMPUTATED IMMUNOCOMPETENT ORTHOTOPIC MOUSE MODEL

Adel Mahjoub, BS; Mitchell S. Fourman; Jonathan Mandell; Shibing Yu; Jessica Tebbets; David Hirsch; Kurt Weiss

Orthopedic Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Objective: Currently, surgery is the primary treatment for soft tissue sarcoma (STS). STS tumors are periodically not completely resected and these positive tumor margins portray a poor prognosis for patients. The ability to identify and remove positive tumor margins would be a powerful surgical tool that can portend a better prognosis for patients. Here, we quantify the ability for indocyanine green dye angiography (ICG) to identify positive tumor margins and predict residual tumor growth in a post-amputated immunocompetent orthotopic osteosarcoma (OS) mouse model.

Methods: 24 hours prior to leg amputation, 30 uL of a 7.5 ug ICG dilution was injected retro-orbitally into eighteen 4-6 week-old female Balb/c mice that had received 500,000 K7M2 mouse OS cells in their left hindlimbs 4 weeks prior. After amputations, 7 mice had negative tumor margins while 11 mice had positive tumor margins detected via fluorescence measurement using SPY-Elite (Novadaq, Bonita Springs, FL). Animals were then examined weekly for post-operative tumor recurrence and compared against initial positive margins, defined as fluorescent signaling greater than one standard deviation above the background signal obtained with fluorescence angiography. Analysis consisted of descriptive statistics.

Results: Using ICG, ten of the eleven animals which exhibited positive tumor margins after hindlimb amputation exhibited reccurent tumor growth at time of sacrifice 6 weeks later. All seven of the animals which exhibted negative tumor margins displayed no reccurent tumor growth 6 weeks later. SPY could accurately predict 94.4% of the time the residual tumor growth based on margins detected or not deteced at time of amputation. ICG displayed 0% false negative rate (tumor there but not detected), 5.56% false positive rate (tumor not there, but detected), 100% sensitivity, 88% specificity, 90.1% positive predictive, and 100% negative predictive value.

Conclusion: ICG demonstrates the ability to visualize positive margins in STS resections, which accurately predicts subsequent residual tumor growth. Due to the limitations of chemotherapeutics in treating sarcoma, surgery remains the most viable choice in most cases. The use of SPY at the time of tumor resection will aid surgeons in visualizing positive margins, thereby preventing local tumor reccurence. Future work aims to increase the power of this study to confirm the efficacy of ICG as a tool to detect positive tumor margins at the time of STS resection.

Summary of Descriptive Statistics

False Negative Rate (FNR)	0%
False Positive Rate (FPR)	5.56%
Negative Predictive Value (NPV)	100%
Positive Predictive Value (PPV)	90.1%
Sensitivity	100%
Specificity	88%

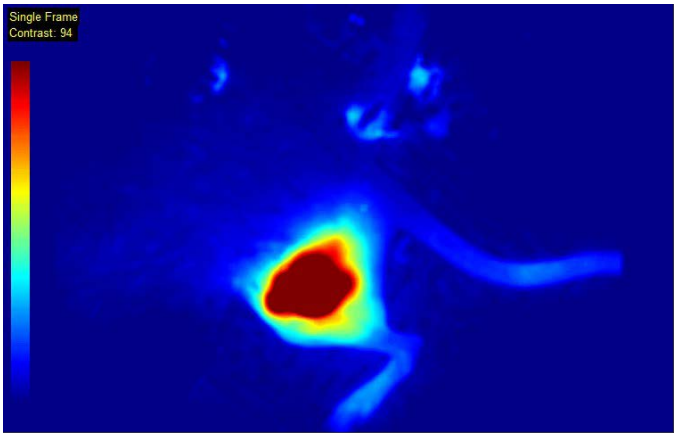


Figure 1- Primary Tumor Fluorescence:
Osteosarcoma in the hind limb of a mouse

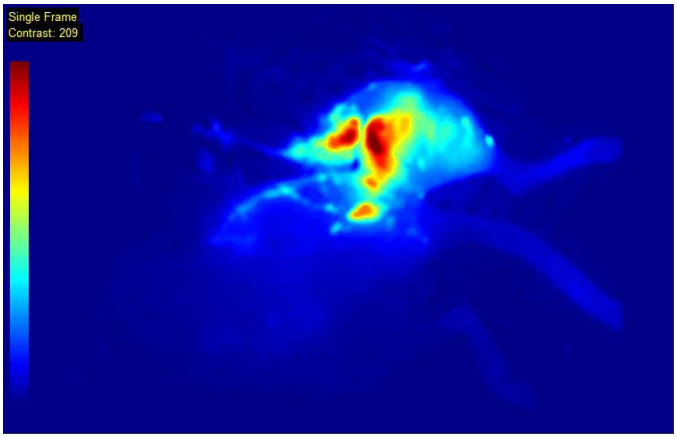


Figure 2- Positive Residual Tumor.
Note the deposits of elevated signal in the residual limb.

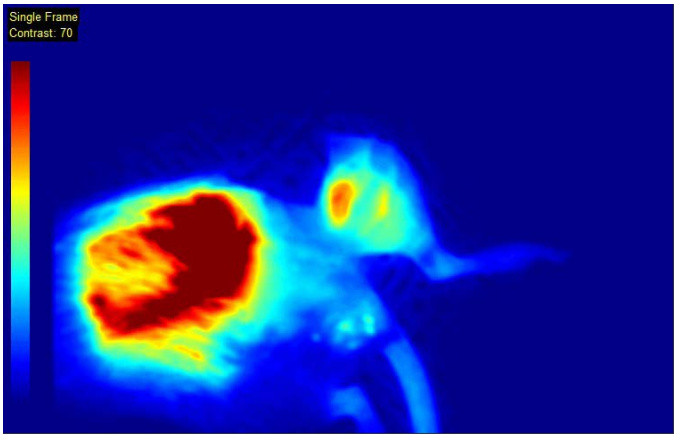


Figure 3- Negative Residual Tumor.
Note the lack of high signal (red) at the residual limb.

P1 - Poster 082 2570227

PRECLINICAL STUDY OF THE COMBINATION OF PEVONEDISTAT WITH DOXORUBICIN, GEMBITABINE OR BMN673 IN EWING SARCOMA

Daniel J. Garcia-Dominguez[1]; Lourdes Hontecillas-Prieto[1]; Pablo Rodríguez-Núñez[1]; Rosa García-Mejías[1]; Angel Montero Carcaboso[2]; Guillem Pascual-Pastó[2]; Juan Diaz-Martin[1]; Laura Romero-Pérez[1]; Enrique De Álava *Casado[1]*

[1]Molecular Pathology, Instituto de Biomedicina de Sevilla (IBiS)/Hospital Virgen del Rocio/CSIC/Universidad de Sevilla, Seville, Spain; [2]Developmental Tumor Biology Laboratory, Fundacio Sant Joan de Deu, Department of Pediatric Hematology and Oncology, Hospital Sant Joan de Deu, Barcelona, Spain

Objective: Ewing sarcoma (ES) is an aggressive tumor that arises from the bone or soft tissue of children and young adults. In a previous genomic study we identified CDT2, a component of cullin-RING ubiquitin ligase (CRL) complexes, as a potential therapeutic target. We have conducted an in-depth preclinical evaluation of Pevonedistat and we confirmed that ES tumors exhibited high sensitivity to CRL complex inhibition. However, several drug candidates successfully tested in preclinical studies fail in clinical trials. Therefore, we wanted to explore the effects of combination of Pevonedistat with DNA damaging agents (doxorubicin and gemcitabine) and DNA repair inhibitors (BMN673) to complete its the preclinical study. We performed *in vitro* assays to demonstrate synergistic effects, and we are carrying out *in vivo* assays with patient-derived xenograft models to detect potential side effects as well as markers of response to treatment.

Methods: Every drug combination was tested at different times and concentrations on a wide panel of ES cell lines. ATP-lite was used to evaluate cell viability and sensitivity. We evaluated cell-cycle alterations and apoptosis by flow cytometry using propidium iodide and Caspase3. To study directional cell migration we carried out a wound healing assay, and we used soft-agar culture for clonogenic capacity. Western blot were used to study the modulation of CRL complexes and specific targets in treated cell lines. Finally, PDXs studies with ES patients tumors were used to assess the drug combinations *in vivo.*

Results: The studies of cellular viability and proliferation confirmed the existence of synergistic effect in combinations with Doxorubicin and Gemcitabine (combination indexes ranged between 0.559-0.279). However, combinations involving BMN673 were synergistic or antagonistic depending on the cell line tested. In those cell lines with antagonistic response, we confirmed that synergism with BMN673 was observed when Pevonedistat was administered in a concentration high enough to cause DNA damage. We observed a statistically significant increase in the percentage of apoptosis in all the combinations compared to monotherapy. Finally, we demonstrated the synergistic effect in clonogenic capacity (but not in migration) in ES cell lines.

Conclusion: Simultaneous pharmacological blockade of CRL complex and DNA-damaging agents, or PARP1 inhibition, have synergistic effects in ES. Our preclinical studies warrant the design of clinical trials using Pevonedistat in ES patients

P1 - Poster 083 2570372

RESULTS OF METHOTREXATE-ETOPOSIDE-IFOSFAMIDE BASED REGIMEN IN OSTEOSARCOMA PATIENTS INCLUDED IN THE FRENCH OS/SARCOME-09 STUDY

Laurence Brugieres[1]; Bob Valery Occean[2]; Hélène Pacquement[3]; Cyril Lervat[4]; Perrine Marec-Bérard[5]; Jean Claude Gentet[6]; Nadège Corradini[7]; Natacha Entz Werle[8]; Marie Dominique Tabone[9]; Laure Saumet[7]; Nathalie Gaspar[1]; Emmanuelle Bompas[10]; Marta Jimenez[10]; Sophie Piperno-Neumann[3]; Marie-Cecile De Leley[2]

[1]Children and Adolescent Oncology, Gustave Roussy, Villejuif, France; [2]Gustave Roussy, Villejuif, France; [3]Institut Curie, Paris, France; [4]Centre Oscar Lambret, Lille, France; [5]CHU, Lyon, France; [6]AP-HM, Marseille, France; [7]CHU, Nantes, France; [8]CHU Hautes Pierres, Starsbourg, France; [9]APHP Trousseau, Paris, France; [10]Unicancer, Paris, France

Objective: In most countries, the standard chemotherapy for osteosarcoma combines high-dose methotrexate (M) and doxorubicin-cisplatin (AP). Based on the randomized OS94-trial, the French reference pre-operative chemotherapy for children and adolescents with osteosarcoma combines M and etoposide-ifosfamide (EI). We describe here the outcome of the 409 patients less than 25y, with either localized or metastatic osteosarcoma, included in the French OS2006-trial between 2007 and 2014 and treated with M-EI

Methods: Pre-operative chemotherapy combined 7 M-courses (12g/m^2) and 2 EI-courses (E=75 mg/m^{2}x4, I=3 g/m^{2}x4). Post-operatively, patients with good histologic response (<10% viable cells) and no metastases received 12 M-courses, 3 EI-courses whereas patients with poor histologic response or initial metastases or unresectable primary received 5 M-courses and 5 AP-courses (A=37,5 mg/m^{2}X2, P=120 mg/m^2). In addition 249 patients were randomized to receive(n=125) or not (n=24) 10 monthly perfusions of Zoledronate.

Results: Median age was 14.3 years (4.7-24.5). Primary tumor was located on a limb in 383 (94%) axial in 26 (6%) cases, and associated with distant metastases in 67 (16%). Median duration of chemotherapy was 37.4 weeks (34.7

; 39.9). Overall, 391 patients underwent surgery, conservative in 359 (88%); among them, 258 (65%) had a good histologic response.

Toxicity is only evaluable in patients included in the zoledronate randomized trial: most patients experienced at least one episode of severe toxicities (grade-4 hematological or grade-3/4 extra-hematological) without any difference between groups including neutropenia (97%), transaminase elevation (92%), febrile neutropenia (83%), thrombocytopenia (45%), metabolic toxicity (39%), infection without neutropenia (39%), mucositis (34%), and other gastrointestinal toxicity (34%).

With a median follow-up of 4.8 years, an event was reported in 168 patients. Five-year event-free (EFS) and overall (OS) survivals were 56% (95%CI, 51-62%) and 72% (66-78%) respectively for the whole cohort, and 24% (15-36%) and 40% (28-53%) respectively for patients with definite metastases. Five-year EFS was 68% (62-74%) and 39% (30-49%) for good and poor responders respectively.

Conclusion: MTX-Etoposide-ifosfamide proved feasible and efficient leading to survival rates similar to MAP regimen, while sparing 30% of the patients from long-term toxicity of cisplatinum and doxorubicin

P1 - Poster 084 2566193

COMPARISON OF METHOTREXATE-ETOPOSIDE-IFOSFAMIDE AND API-AI BASED REGIMEN IN 18-25 YR OSTEOSARCOMA PATIENTS INCLUDED IN THE FRENCH OS2006/SARCOME-09 STUDY

Valerie Laurence[1]; Laurence Brugieres[2]; Bob-Valery Occean[3]; Nathalie Gaspar[2]; Emmanuelle Bompas[4]; Jean Yves Blay[5]; Didier Cupissol[6]; Nicolas Penel[7]; Cyril Lervat[8]; Patrice Kerbrat[9]; Antoine Italiano[10]; Celine Mahier[11]; Marie-Cecile Le Deley[3]; Sophie Piperno-Neumann[1]; Perrine Marec-Berard[12]
[1]Institut Curie, Paris, France; [2]Children and Adolescent Oncology, Gustave Roussy, Villejuif, France; [3]Biostatistics, Gustave Roussy, Villejuif, France; [4]Medical Oncology, Centre René Gauducheau, Nantes, France; [5]Medical Oncology, Centre Leon Berard, Lyon, France; [6]Centre Val Aurelle, France, France; [7]Medical Oncology, Centre Oscar Lambret, Lille, France; [8]Pediatric Oncology, Centre Oscar Lambret, Lille, France; [9]Medical Oncology, Centre Eugene Marquis, Rennes, France; [10]Medical Oncology, Institut Bergonie, Bordeaux, France; [11]Unicancer, Paris, France; [12]Pediatric Oncology Department, Centre Leon Berard, Lyon, France

Objective: Based on the randomized OS94 pediatric trial and a phase 2 study in adult osteosarcoma, the French reference chemotherapy (CT) for osteosarcoma combines Methotrexate (M) and etoposide-ifosfamide (EI) in children and adolescents, and API-AI (doxorubicin-cisplatin-ifosfamide) in adults. In the French OS2006 trial, patients (pts) aged 18-25 could receive either HD-MTX or API-AI according to a predetermined center policy. We describe the outcome of all pts aged 18-25 at diagnosis included in this trial between 2007 and 2014.

Methods: In the HD-MTX regimen, pts received 7 M and 2 EI courses pre-operatively; post-operative CT was adapted to risk factors: M-EI in standard risk pts (SR: good histological response, no metastasis) and 5 cycles of M-AP (doxorubicin/cisplatin) in high risk pts (HR: poor histological response, initial metastases and/or unresectable primary). In the API-AI regimen, pre-operative CT combined 3 API and 2 AI courses, and post-operative CT 2 AI and 2 PI courses in SR, and 5 EI courses in HR. Planned duration of treatment varied from 37 weeks to 38 weeks in HD-MTX and from 31 weeks to 34 in API-AI.

Results: 95 pts, median age 20.1 (IQR 19.0-21.3) were included, 55 treated with HD-MTX and 40 with API-AI. Initial characteristics are similar in both groups, except a non-significant excess of metastases at diagnosis in the API-AI group (Table 1). Overall, 66 pts (69%) received the planned pre-operative CT without any modification, 35 (64%) and 31 (78%) in HD-MTX and API-AI group respectively. Ninety pts (95%) underwent surgery, conservative in 76 (80%). Good histological response was observed in 59% and 41% evaluable pts in HD-MTX and API-AI groups respectively (p=0,13). Most pts experienced at least 1 episode of severe toxicity, with a significant excess of anemia with API-AI and transaminase elevation with HD-MTX. Median follow-up is 5.0 years. Overall, 5-year EFS was 50% (95%CI, 39-60) (Table 2). Hazard ratio of event associated with API-AI compared to HD-MTX, adjusted for metastases at diagnosis, histological response and age was HR=1.10 (95%CI, 0.59-2.08, p=0.74).

Table 1 : Baseline characteristics

Patient and tumor characteristics	Overall N=95	HD-MTX N=55	API-AI N=40	p
Median age	20.1	20.0	20.5	0.20
Adult oncology center	71 (75%)	39 (71%)	32 (80%)	0.31
Axial primary	8 (8%)	4 (7%)	4 (10%)	0.72
Definite metastases	20 (21%)	8 (15%)	12 (30%)	0.07
Non randomized	36 (38%)	19 (35%)	17 (43%)	0.42
Randomized without zoledronate	30 (32%)	18 (33%)	11 (28%)	
Randomized with zoledronate	29 (31%)	18 (33%)	12 (30%)	

Conclusion: In these French young adults with osteosarcoma, no major difference was observed in terms of survival and acute toxicities between HDMTX containing and non-containing regimen. However, survival outcomes in this age group appear disappointing as compared to younger patients. Whether it is linked to treatment or to biological factors remains to be explored.

Table 2 : Patient treatment and outcome

Outcome	Overall N=95	HD-MTX N=55	API-AI N=40	p
Surgery	90 (95%)	51 (93%)	39 (98%)	0.39
Good histological response (not evaluable in 2 pts with initial surgery)	45/88 (51%)	24/49 (59%)	16/39 (41%)	0.09
Median time between surgery and start of postoperative chemotherapy, weeks (IQR)	3.3 (2.7-4.1)	3.0 (2.4-3.8)	3.8 (2.9-4.9)	0.77
Number of progressions/ relapses	44	23	21	
Local progression/relapse	6	5	1	
Metastatic progression / relapse	37	17	20	
Local and metastatic	1	1	0	
Second malignancy	1	0	1	
5-year EFS (95%CI)	50% (39-60)	53% (40-66)	45% (30-61)	
HR of event (95%CI)		1	1.11 (0.59-2.08)	0.74
Number of deaths	31	16	15	
5-year OS (95%CI)	65% (54-74)	70% (56-82)	57% (40-72)	0.43
HR of death (95%CI)		1	1.06 (0.47-2.4)	0.89

P1 - Poster 085 2523557

DOSE-INTENSITY RELATION TO EVENT-FREE SURVIVAL IN OSTEOSARCOMA PATIENTS: A NEW ANALYTIC APPROACH

Jakob Anninga[1]; Carlo Lancia, PhD[2]; Cristian Spitoni[3]; Jeremy Whelan[4]; Matthew Sydes[5]; Gordana Jovic[5]; Hans Gelderblom[6]; Pancras Hogendoorn[7]; Henk van den Berg[8]; Marta Fiocco[2]

[1]Oncology, Radboud University Medical Center, Nijmegen, Netherlands; [2]Medical Statistics and Bioinformatics, Leiden University Medical Center, Leiden, Netherlands; [3]Epidemiology, University Medical Center Utrecht, Utrecht, Netherlands; [4]Oncology, University College London Hospital, London, United Kingdom; [5]Clinical Trials Unit, Medical Research Council, London, United Kingdom; [6]Oncology, Leiden University Medical Center, Leiden, Netherlands; [7]Pathology, Leiden University Medical Center, Leiden, Netherlands; [8]Oncology, Emma Children Hospital, Academic Medical Centre, Amsterdam, Netherlands

Objective: The impact of Received Dose Intensity (RDI) in treatment regimens for osteosarcoma on survival outcome is unclear. Estimates of survival rate through standard Cox regression models are biased by the so-called *treatment-adjustment effect*: toxic side-effects of treatment and RDI are both risk factors for mortality, and the former predicts the latter – i.e. toxicity is a *time-dependent confounder*.

Methods: This abstract presents an analytical model for the effect of RDI on Event-Free Survival (EFS), defined as time from the end of therapy until the first event (local recurrence, evidence of new or progressive metastatic disease, second malignancy, death or a combination of those events) or censoring at last contact. The model is developed on a sample of 217 patients enrolled in the control arms of European Osteosarcoma Intergroup randomized controlled trials MRC BO03 and BO06 (EORTC 80861 and 80931). The sample contains only patients that completed 6 courses of 3-weekly Doxorubicin (75 mg/m^2) and Cisplatin (100 mg/m^2).

Kaplan-Meier (KM) curves (Fig. 1) suggest that Histological Response (HRe) might change the effect of High/Low RDI regimens (cut-off level 80%) on EFS. Following this insight, a Marginal Structural Cox Model (MSCM) was fitted to assess the joint effect on EFS of RDI (<60%, 60-80%, or >80%) and HRe (good/poor). MSCMs are a practical methodology that corrects the treatment-adjustment bias by creating a pseudo-population where toxicities no longer predict RDI modifications. This mimics a randomised trial where treatment-intensity is randomly assigned to patients.

Results: The MSCM confirms the trend in EFS of the KM curves (Fig. 1). With respect to the reference category, i.e. Poor Responders (PRs) and RDI >80%, there was some evidence of that a reduced RDI regimen improved survival

(RDI <60%**:** HR 0.80, 95%CI [0.32, 2.02]; RDI 60%-80%: HR 0.82, 95%CI [0.55, 1.23]). Conversely, among Good Responders (GRs) an increase of RDI yields a better survival (RDI <60%: HR 0.85, 95%CI [0.26, 2.85]; RDI 60-80%: HR 0.34 [0.14, 0.80]; RDI >80%: HR 0.29, 95%CI [0.15, 0.54]). Fig. 2 graphically outlines these results.

Conclusion: The present study suggests that a strong interplay might exist between RDI and HRe. The proposed model correctly captures the effect of increased RDI on GRs, the results on PRs are however difficult to interpret. For this reason, it is desirable that the proposed model be validated on larger datasets and different therapeutic regimens.

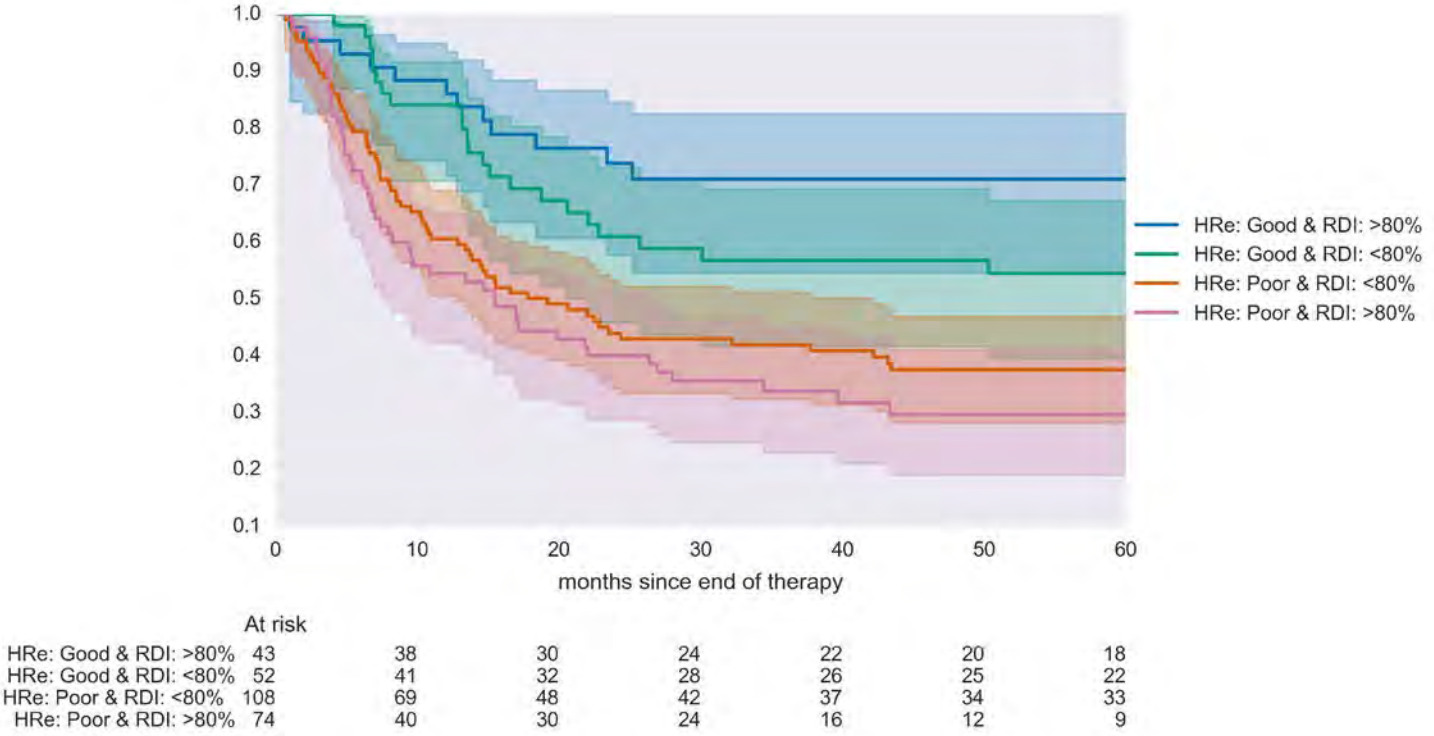


Fig. 1
Kaplan-Meier curves for EFS from completion of the last course, conditioned on Good or Poor HRe and RDI <80% or >80%.

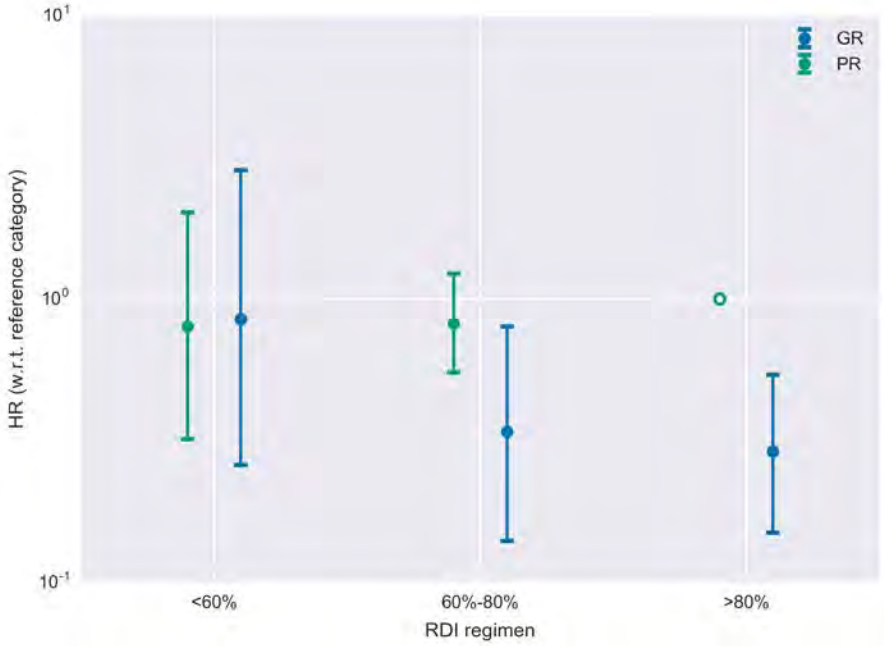


Fig. 2
Hazard Ratios for different RDI regimens and HRe produced by the Marginal Structural Cox Model. The reference category is represented by a hollow marker.

P1 - Poster 086 2554306

PHASE 1 STUDY OF SIROLIMUS IN COMBINATION WITH ORAL CYCLOPHOSPHAMIDE AND TOPOTECAN IN CHILDREN AND YOUNG ADULTS WITH RELAPSED AND REFRACTORY SARCOMA AND OTHER SOLID TUMORS

Kieuhoa T. Vo, MD, MAS[1]; Erin E. Karski[1]; Nicole M. Nasholm[1]; Shelly Allen[1]; Fabienne Hollinger[1]; W. Clay Gustafson[1]; Janel R. Long-Boyle[2]; Stephen Shiboski[3]; Katherine K. Matthay[1]; Steven G. DuBois[1]

[1]Pediatric Hematology/Oncology, UCSF Benioff Children's Hospital, University of California, San Francisco School of Medicine, San Francisco, CA, USA; [2]Clinical Pharmacy, University of California, San Francisco School of Medicine, San Francisco, CA, USA; [3]Epidemiology and Biostatistics, University of California, San Francisco School of Medicine, San Francisco, CA, USA

Objective: The combination of the mammalian target of rapamycin (mTOR) inhibitor, sirolimus, and chemotherapy inhibits growth of pediatric solid tumor models through pro-apoptotic and antiangiogenic mechanisms. The purpose of this study was to determine the maximum tolerated dose (MTD), toxicities, and pharmacodynamics effects of sirolimus combined with oral metronomic topotecan and cyclophosphamide in a pediatric population.

Methods: Patients who were 1 to 30 years of age with relapsed/refractory solid tumors were eligible. Patients received daily oral sirolimus and cyclophosphamide (25-50 mg/m^2/dose) on days 1-21 and oral topotecan (0.8 mg/m^2/dose) on days 1-14 in 28-day cycles. Sirolimus steady-state plasma trough concentrations of 3-7.9 ng/mL and 8-12.0 ng/mL were evaluated, with dose escalation based on a 3+3 phase 1 design. Biomarkers of angiogenesis were also evaluated.

Results: Twenty-one patients were treated (median age 18 years, range 9-30; 17 with sarcoma histologies). Dose-limiting toxicities included myelosuppression, ALT elevation, stomatitis, and hypertriglyceridemia. The MTD was sirolimus with trough goal of 8-12.0 ng/mL; cyclophosphamide 25 mg/m^2/dose; and topotecan 0.8 mg/m^2/dose. No objective responses were observed. Four patients with sarcoma had prolonged stable disease $\geq$ 4 cycles, including patients with alveolar soft part sarcoma (12 cycles), desmoplastic small round cell tumor (11 cycles), osteosarcoma (6 cycles), and Ewing sarcoma (4 cycles). Correlative biomarker analyses demonstrated reductions in thrombospondin-1 and soluble vascular endothelial growth factor receptor-2 plasma concentrations at 21 days compared to baseline (Figure 1).

Conclusion: The combination of oral sirolimus, topotecan, and cyclophosphamide was well tolerated and biomarker studies demonstrated modulation of angiogenic pathways with this regimen. The convenience associated with oral administration and findings of several patients with sarcoma subtypes with prolonged stable disease suggest this regimen may be an attractive option for salvage therapy in this population.

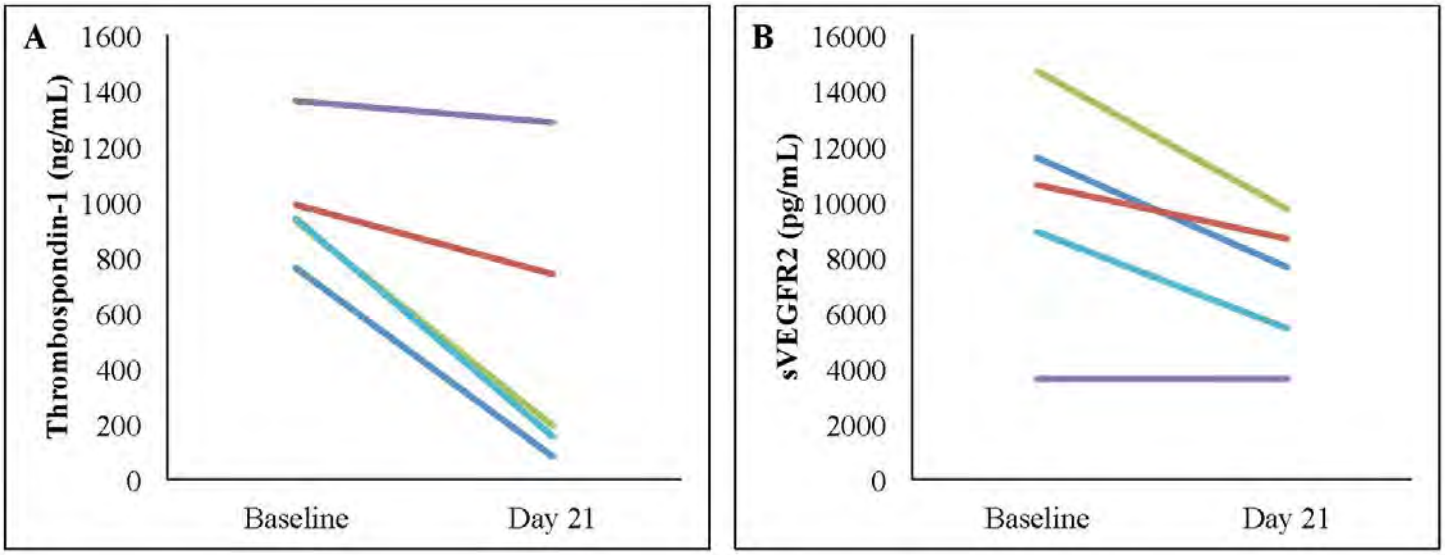


Figure 1. Changes in plasma (A) thrombospondin-1 and (B) soluble vascular endothelial growth factor receptor-2 (sVEGFR2) concentrations from baseline to day 21 ± 2 of cycle 1 in five patients with paired samples.

P1 - Poster 087 2544843

AEROSOL GEMCITIBINE ADMINISTRATION FOLLOWING AMPUTATION ERADICATES OSTEOSARCOMA LUNG METASTASES WITHOUT INTERFERING WITH WOUND HEALING IN THE BONE OR SKIN

Eugenie S. Kleinerman, MD[1]; Ling Yu[1]; Andrea Hayes-Jordan[2]; Nancy Gordon[1]
[1]Pediatrics, M.D. Anderson Cancer Center, Houston, TX, USA; [2]Surgical Oncology, M.D. Anderson Cancer Center, Houston, TX, USA

Objective: The survival rate for osteosarcom (OS) has not improved for 30 years, particularly for patients with a poor response to induction chemotherapy. Complicating this is the 3-4 week delay in starting post-operative chemotherapy due to its interference with wound healing. This delay allows lung micrometastases to grow. Identifying a "bridge therapy" that targets lung tumors without inhibiting wound healing may prevent relapse. Aerosol Gemcitibine (GCB) at 1/10th the systemic dose eradicated OS lung metastases. We investigated whether aerosol GCB affected healing following amputation and primary tumor removal, and its effect on dorsal cutaneous and tail would healing.

Methods: Mice were injected with K7M3 OS cells into the tibia. Primary tumor (1.5 cm) and lung metastases were present at 3 weeks. Amputation above the knee was perfomed. 24-hrs later, full-thickness exicisional wounds on each side of the midline and tail wounds down to the fascia (10mm x 3mm) were made. Aerosol PBS or aerosol GCB (0.5mg/kg) given 3 times/wk for 3 wks was started 48 hrs after amputation. Wounds were measured on days 1,3,5,7,9 &11. Wound sections (bone, tail and dorsal) were examined by H&E and IHC for Ki-67, mast cells, M1/M2 macrophage ratios, CD31, VEGF, IL-10, FGF2.

Results: Aerosol GCB inhibited lung metastases but did ***not*** affect wound healing following amputation or the healing of the dorsal and tail skin wounds. Time to closer was the same as the control mice. Fibroblast proliferation (Ki-67), number of mast cells and macrophages, M1/M2 ratios and CD31 were similar to control mice. IL-10, bFGF, & VEGF (factors important in wound healing) were not inhibited by aerosol GCB compared to mice treated with aerosol PBS.

Conclusion: Wound healing involves 3 phrases: a) recruitment of mast cells & macrophages (M1 & M2) which promote cell proliferation and tissue repair; b) migration and proliferation of fibroblasts and endothelial cells; c) tissue remodeling requiring IL-10, VEGF & bFGF. Aerosol GCB initiated 48 hrs after amputation of the limb with the primary OS tumor eradicated microscopic lung metastases, but had no effect on the 3 phases of wound healing in the dorsal skin, tail or bone. These data support the use of aerosol GCB following primary tumor resection to prevent and kill OS lung metastases during the 2-4 weeks prior to initiation of systemic neoadjuvant chemotherapy. This approach may prevent early relapse and improve Event-Free and Overall survival. A phase I/II trial aerosol GCB trial is underway.

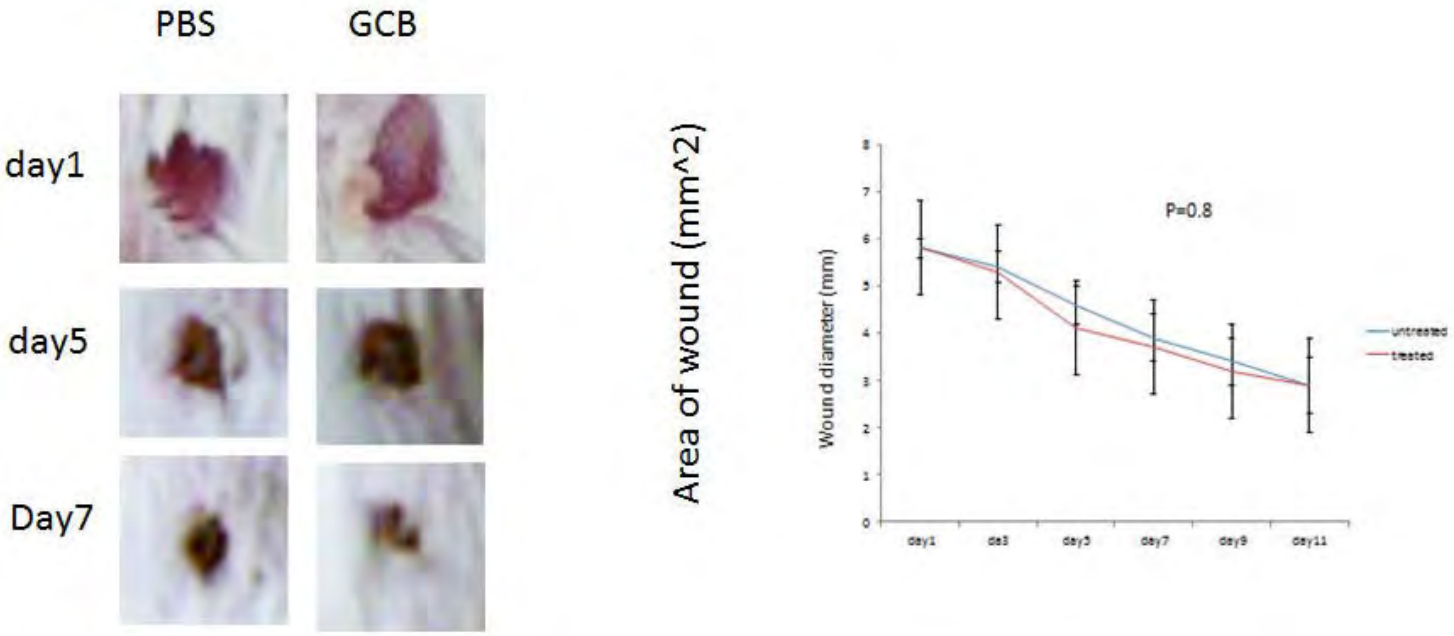


Fig 1. Aerosol GCB had no effect on would healing.
The open area of the cutaneoous dorsal skin wound was measured on days 1,3,5,9,&11 to assess the effect of aerosol GCB on macroscopic healing. There was no dealy in healing in mice treated with aerosol GCB.

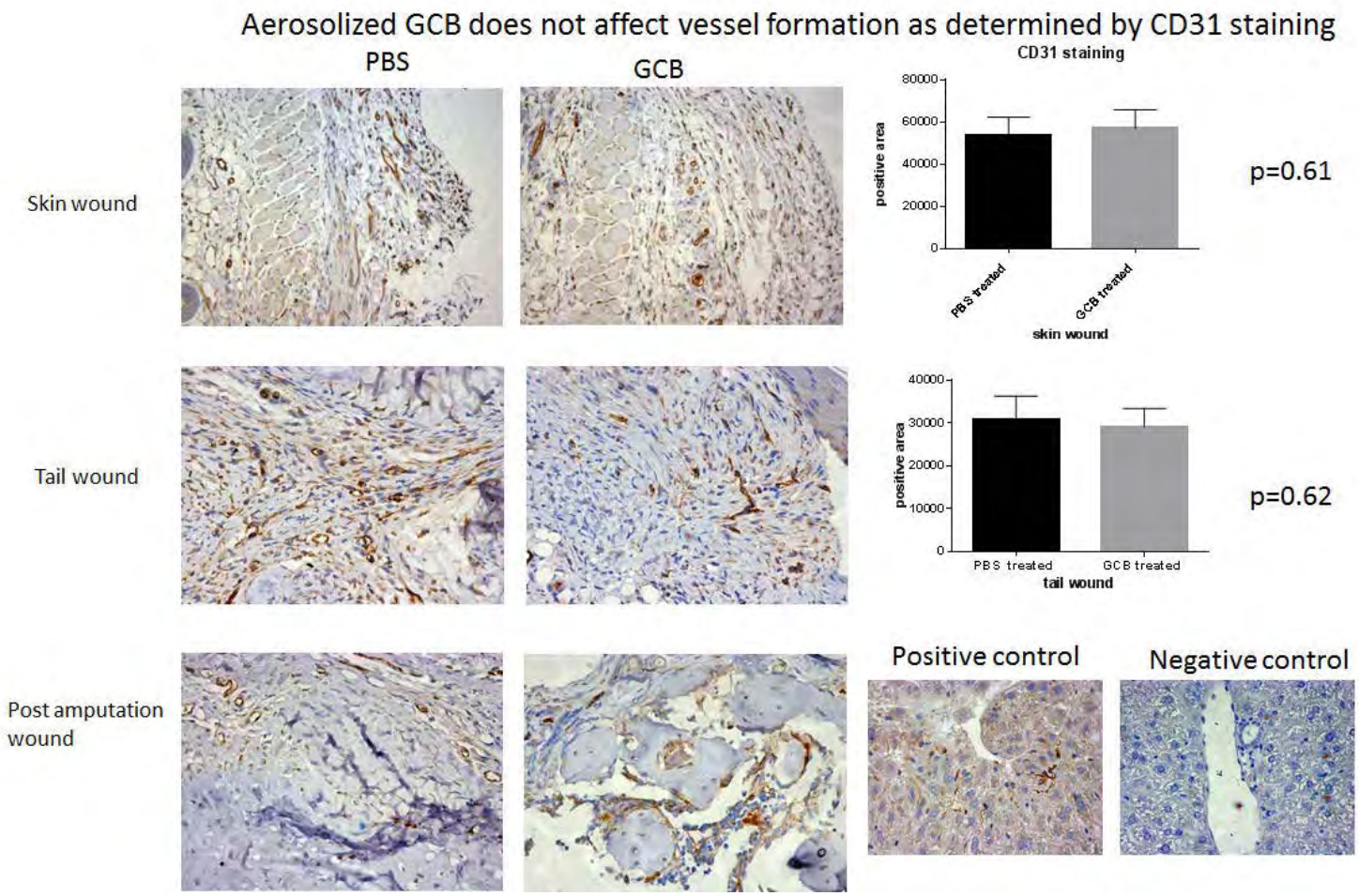


Fig 2. Effect of aerosol GCB on new vessel formation.
Tissue sections of the skin, tail, and amputation wounds from mice treated with aerosol PBS or aerosol GCB were evaluated for vessel formation by quantifying CD31 expression using IHC. There was no difference between control and aerosol GCB-treated mice.

P1 - Poster 088 2569866

RESULS OF API-AI BASED REGIMEN IN OSTEOSARCOMA PATIENTS (PTS) INCLUDED IN THE FRENCH OS2006/SARCOMA-09 STUDY

Sophie Piperno-Neumann, MD[1]; Bob-Valery Occean[2]; Jean-Yves Blay[3]; Didier Cupissol[4]; Nicolas Penel[5]; Perrine Marec-Berard[6]; Antoine Italiano[7]; Emmanuelle Bompas[8]; Olivier Collard[9]; Axel Le Cesne[10]; Maria Rios[11]; Patrice Kerbrat[12]; Marta Jimenez[13]; Laurence Brugieres[14]; Marie-Cecile Le Deley[2]
[1]Medical Oncology, Institut Curie, Paris, France; [2]Biostatistics, Gustave Roussy, Villejuif, France; [3]Medical Oncology, Centre Léon- Bérard, Lyon, France; [4]Medical Oncology, Institut de Cancérologie, Montpellier, France; [5]Medical Oncology, Centre Oscar-Lambret, Lille, France; [6]Pediatric Oncology Department, Centre Léon- Bérard, Lyon, France; [7]Medical Oncology, Institut Bergonié, Bordeaux, France; [8]Medical Oncology, ICO, Nantes, France; [9]Medical Oncology, ICL, Saint-Priest, France; [10]Medical Oncology, Gustave Roussy, Villejuif, France; [11]Medical Oncology, Institut de Cancérologie de Lorraine, Nancy, France; [12]Medical Oncology, Centre Eugène Marquis, Rennes, France; [13]Unicancer, Paris, France; [14]Children and Adolescent Oncology Department, Gustave Roussy, Villejuif, France

Objective: In the OS2006 study, the chemotherapy regimen was stratified according to age: pts <18 received a methotrexate-based regimen while pts >25 were treated with a doxorubicin-cisplatin-ifosfamide–based regimen (API-AI) and pts aged 18-25 with either regimen according to the predetermined decision of the center. We describe the outcome of pts enrolled between 2007 and 2014 and treated with API-AI.

Methods: Pre-operative chemotherapy combined 3 API courses (doxorubicin 60 mg/m2, ifosfamide 6g/m2, cisplatin 100 mg/m2) and 2 AI courses (doxorubicin 60 mg/m2, ifosfamide 6g/m2). Post-operative chemotherapy consisted in 2 courses of AI alternating with 2 courses of PI (cisplatin 100 mg/m2, ifosfamide 6g/m2) in pts with good histological response and no metastasis, and 5 cycles of EI (etoposide

300 mg/m2, ifosfamide 12g/m2) in pts with poor histological response, metastases and/or unresectable primary. Planned duration of treatment varied from 31 to 34 weeks according to post-operative regimen.

Results: 106 pts with a median age of 30 years (IQR 21-37) were enrolled in 20 centers. Tumor was axial in 29 (27%) pts, and associated with metastases in 24 (23%). Treatment started with a median interval of 28 days after the biopsy (range 7-87), and pre-operative chemotherapy was given as planned in 100 pts (94%). Overall, 96 pts underwent surgery, conservative in 82 (85%); 36/95 evaluable pts (38%) had a good histological response (less than 10% viable cells).

Most pts experienced at least one episode of severe toxicity (Gr-4 hematological or Gr-3/4 extra-hematological): anemia (82%) neutropenia (88%), febrile neutropenia (63%), and thrombocytopenia (75%). Gr 3-4 cardiotoxicity, renal toxicity and ototoxicity were seen in 3, 3 and 2 pts, respectively. With a median follow-up of 4.7 years (IQR 3.2-5.8), an event was reported in 54 pts: 53 progressions/relapses (4 local, 41 metastatic, 8 combined), 1 secondary malignancy. A death was reported in 39 pts, all after a progression/relapse. Five-year event-free (EFS) and overall survival (OS) were 46% (95%CI, 36-56%) and 57% (95%CI, 46-67%) for the whole cohort. In pts with localized disease, 5-year EFS and 5-year OS were 53% (95%CI, 42-65%) and 69% (95%CI, 57 -79%) respectively, with no difference between good and poor responders.

Conclusion: In this trial, API-AI proved feasible with no excess of acute toxicity. Survival was poor in metastatic pts, and results remain insufficient in all subgroups compared to younger pts treated with a methotrexate-based regimen.

Outcome according to subgroups	N	5-year EFS (95% CI)	5-year OS (95% CI)
Age ≤ 25 years	40	45% (30 - 61)	57% (40 - 72)
Age > 25 years	66	46% (33 - 59)	57% (44 - 70)
Limb primary	77	44% (32 - 56)	57% (45 - 69)
Axial primary	29	51% (33 - 68)	56% (37 - 73)
Localized disease	82	53% (42 - 65)	69% (57 - 79)
Definite metastases	24	21% (9-40)	15% (5-38)
Good histological response (<10% viable cells)	26	51% (34 - 68)	67% (48 - 81)
Poor histological response	59	44% (31 - 58)	55% (41 -69)

P1 - Poster 089 2570644

TEN-YEAR SURVIVAL OF PATIENTS WITH LOCALIZED RESECTABLE OSTEOSARCOMA TREATED WITHOUT METHOTREXATE

Michael W. Bishop[1]; Milena Villarroel[2]; Mariela Fuenzalida[2]; Juan Quintana[2]; Shenghua Mao[1]; Jianrong Wu[1]; Valerie McPherson[1]; Jesse Jenkins[1]; Bhaskar Rao[1]; Michael Neel[1]; Victor Santana[1]; Fariba Navid[1]; Najat Daw[3]
[1]St. Jude Children's Research Hospital, Memphis, TN, USA; [2]Hospital Luis Calvo Mackenna, Santiago, Chile; [3]University of Texas MD Anderson Cancer Center, Houston, TX, USA

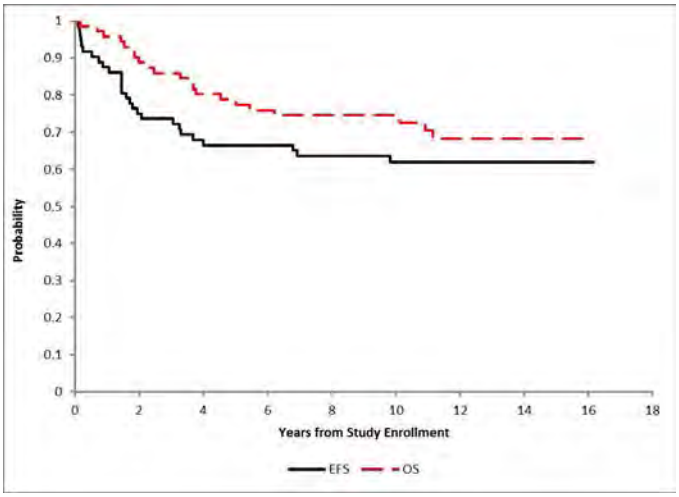
Objective: We previously reported results of our multi-institutional trial (OS99) evaluating the efficacy of carboplatin, ifosfamide, and doxorubicin without high-dose methotrexate (HDMTX) for the treatment of patients with localized resectable osteosarcoma. Here, we report the updated 10-year survival of patients treated on OS99, and compare their outcomes to patients treated on a prior institutional trial utilizing the same agents in combination with HDMTX (OS91).

Methods: OS99 patients received 12 cycles of chemotherapy over 35 weeks including 3 cycles of carboplatin (targeted to area under concentration-time curve of 8 mg/mL*min) and ifosfamide (2.65 g/m^2 daily for 3 days) and one cycle of doxorubicin (25 mg/m^2 daily for 3 days) before tumor resection, followed by 2 additional cycles of carboplatin/ifosfamide and 3 cycles each of doxorubicin (25 mg/m^2 daily for 2 days) combined with ifosfamide or carboplatin. Kaplan-Meier methods were used to estimate event-free survival (EFS) and overall survival (OS). Log-rank test was used to compare survival of patients treated on OS99 vs. to those treated on OS91, and to evaluate associations of clinical and treatment parameters with EFS and OS.

Results: Seventy-two patients (57% male) were enrolled on OS99 between May 1999 and May 2006; median age at diagnosis was 13.7 years (range 3.2-23.0 years). Median time to last follow-up for survivors was 12.0 years (1.5-16.2 years). For patients with an event (relapse, progression, second malignancy or death), median time to event was 1.5 years (0.1-9.8 years). Five patients (6.9%) developed a second malignancy (acute myeloid leukemia/myelodysplastic syndrome (n=3), rhabdomyosarcoma (n=1), renal cell carcinoma (n=1)). Estimated 10-year EFS was 62.0%±6.4% for OS99, and 63.8%±6.5% for OS91. Estimated 10-year OS was 74.5%±5.7% for OS99, and 70.2%±6.5% for OS91. No significant difference was observed between studies for either EFS or OS (p>0.95). Histologic response to preoperative chemotherapy on OS99 (≥90% tumor necrosis) was significantly associated with both EFS (77.9%±7.5% vs. 43.5%±9.4%, p=0.0015) and OS (87.5%±6.0% vs. 58.3%±9.7%, p=0.0057).

Conclusion: Treatment on OS99 yielded durable long-

term survival outcomes that are comparable to those achieved with standard therapeutic regimens containing cisplatin and/or HDMTX. The OS99 regimen remains a viable alternative for patients intolerant to HDMTX or for institutions unable to provide pharmacokinetic monitoring for methotrexate.



Kaplan-Meier curve demonstrates event-free and overall survival for patients with localized resectable osteosarcoma treated on OS99.

P1 - Poster 090 2570633

NEW USES FOR OLD DRUGS: ARSENIC TRIOXIDE AS TREATMENT OPTION FOR PEDIATRIC SMALL ROUND BLUE CELL TUMORS

Frank Traub, MD, PhD[1]; Sabine Schleicher[2]; Rosa Riester[1]; Rupert Handgretinger[2]; Karen Boehme[1]
[1]Department of Orthopaedic Surgery, University Hospital Tuebingen, Tuebingen, Germany; [2]Department of Paediatric Hematology and Oncology, Children's Hospital of the University of Tuebingen, Tuebingen, Germany

Objective: Rhabdo-myosarcoma (RMS) and Ewing sarcoma (ES), small round blue cell tumors of childhood share a similar appearance in routine histology. Although, tumors of both groups differ in their source, predicted cells of origin and the occurrence of specific gene fusions, they share an aberrant activation of the Hedgehog (Hh) pathway. The activation of the Hh pathway has been implicated in the development of cancers and additionally in chemo-resistance and dissemination. Actually, there is an urgent need for new therapeutic options suitable for treatment of drug-resistant, recurrent and metastatic RMS and ES. In this context, the Hh pathway seems to be an attractive target for therapeutic intervention. The glioma-associated oncogene (GLI) transcription factors are downstream mediators of Hh pathway, which can be targeted by arsenic trioxide (ATO). The aim of this study was to determine the effect of ATO on RMS and ES cells.

Methods: Different RMS and ES cell lines were investigated and primary skeletal muscle cells (SKMC) as well as mesenchymal stem cells (MSC) as control. To investigate the effects of ATO on cell viability (MTS assay), proliferation (colony formation, 3D spheroid assay) and induction of apoptotic cell death (western blot, flow cytometry, caspase assay) cells were incubated with different concentrations of ATO. Moreover, ATO was combined with another Hh antagonist - the Smoothened inhibitor itraconazole or lithium chloride for treatment of RMS cell lines. ES cell lines were cultivated with combinations of ATO, etoposide and doxorubicin.

Results: RMS and ES cell lines showed a time- and dose-dependent decrease of proliferation and induction of apoptosis using ATO. Combination of ATO with other drugs resulted in significantly improved viability and proliferation inhibition as well as cell death induction, using concentrations that were only partially effective as single agent. Moreover, ATO has been shown to reduce GLI1 and GLI2 mRNA abundance in RMS cell lines. SKMC and MSC control cells were scarcely affected by drug concentrations which generate a maximal response in RMS and ES cells.

Conclusion: These data indicate that the use of ATO in combination with other drugs may be a promising strategy for the treatment of RMS and ES.

P1 - Poster 091 2569609

REDUCING TOXICITY OF HIGH DOSE METHOTREXATE (MTX) IN OSTEOSARCOMA WITH GLUCARPIDASE (GLU) – RESULTS OF A RANDOMISED CROSSOVER STUDY, GLU-1 (EUDRACT 2006-003203-40)

Rachael Windsor; Martha Perisoglou; Menelaos Pavlou; Beatrice Seddon; Sandra Strauss; Maria Michelagnoli; Palma Dileo; Julie Barber; Jeremy Whelan
The London Sarcoma Service, University College Hospitals NHS Foundation Trust, London, United Kingdom

Objective: High dose methotrexate is an essential component of standard curative chemotherapy regimens for osteosarcoma. Its use is associated with significant toxicity, mostly mucositis, myelosuppression and nephrotoxicity despite routine use of leucovorin rescue (LR). This can lead to premature discontinuation of MTX and delays in delivery of other cytotoxics. Glucarpidase (GLU) offers an alternative route to MTX elimination by cleaving extracellular MTX to inactive metabolites. It has an established role in treatment of acute MTX toxicity. GLU-1 was designed to test the safety and efficacy of GLU when added to standard LR after high dose MTX for bone sarcoma.

Methods: A prospective, randomised, cross-over, phase II study was undertaken to investigate the efficacy and safety

of GLU. Patients received four consecutive MTX courses, two with LR and two with both LR and GLU. One treatment cycle comprised two MTX courses. The primary end point was fitness to receive chemotherapy on day 15 of each cycle. Secondary outcomes included incidence of significant mucositis, renal toxicity and neutropenia, anti-GLU IgG antibody response and quality of life assessment.

Results: 34 patients entered the study, median age 16yrs (range 10-48). 114 MTX courses were administered; 60 (58%) with LR alone and 54 courses (42%) with both LR and GLU. Ten patients did not complete all four treatment courses. There were no adverse events related to GLU. Reasons for failure to meet Day 15 fitness criteria included impaired renal function, delayed methotrexate elimination, myelosuppression and mucositis. Day 15 fitness and toxicity data will be presented.

Conclusion: Improved rescue after MTX may allow better outcomes and improved patient experience. This study aims to determine the value of routine administration of GLU in conjunction with LV to ameliorate MTX toxicity and improve timely delivery of chemotherapy for patients with bone sarcoma.

P1 - Poster 092 2571005

OUTCOMES IN NON-METASTATIC OSTEOSARCOMA PATIENTS WITH PLATINUM-BASED COMBINATION CHEMOTHERAPY WITHOUT HIGH-DOSE METHOTREXATE

Vikas T. Talreja, MBBS, MD (Medicine), DM (Medical Oncology 1st Year); Jyoti Bajpai; Arun Chandrasekharan Medical Oncology, Tata Memorial Hospital, Mumbai, Maharashtra, India

Objective: To determine prognostic significance of various factors in relation to efficacy & safety in non metastatic osteosarcoma patients treated with intensive multidrug, chemotherapy regimen.

1) Demographic variables: age, gender & socioeconomic status.
2) Tumour site.
3) Tumour burden indicators: LDH, SAP,& tumour volume.
4) Other factors like Hb, WBC, vitamin b12, folate, transferrin saturation, ferritin, albumin & BMI.

Methods: A consecutive series of patients were prospectively treated on an institutional regimen (called OGS-12) comprising of total 8 sequential doublet courses(with hematopoietic growth factor support) of two of the following drugs: doxorubicin, cisplatin and ifosfamide.Four courses each, were planned in the neoadjuvant (NACT) and adjuvant settings. Data was prospectively collected on baseline characteristics, histological response to neoadjuvant chemotherapy, disease-free (DFS) and overall survival (OS) and toxicity.

Results: Between 2011 and 2014, 333 patients with osteosarcoma were seen, of whom 250 [75%] were non-metastatic. The median age was 17 [6-56]years,174[69.6%] were males, mean tumor size was 11 (4-34 cm cm, serum LDH was elevated in 202 (83%), body mass index was<18 in 120(48%), iron deficiency was present in 131 (54%) and vitamin B12 deficiency was present in 112(46%) patients, respectively.

Of the 250 non-metastatic patients, 30 (11.9%) were lost to follow-up and 220 (88%)were analyzable for outcome. Of the latter, 227(91%) underwent neoadjuvant chemotherapy, of whom 190 (76%) were able to undergo surgery. Necrosis of >90%in the surgical specimen was seen in 130(59%) patients undergoing NACT. At a median follow-up of 25[1-51]months, the 3-year OS andDFS were 87% and 68%, respectively. All 250 patients who received at least one cycle of chemotherapy were analyzed for toxicity. The most common grade III/IV toxicities were febrile neutropenia(27%), thrombocytopenia (24%)and anaemia (48%). Two patients (0.8%)died due to regimen related toxicity.

Conclusion: Treatment with platinum based sequential doubletsin patients with non-metastatic osteosarcoma resulted in outcomes that were comparable to those achieved using HDMTX based regimens. Non-HDMTX regimens can be considered an acceptable standard of care in this patient population.

P1 - Poster 093 2544677

THE RESPONSE EVALUATION CRITERIA IN SOLID TUMORS (RECIST) IS A POOR SURROGATE ENDPOINT FOR SURVIVAL IN OSTEOSARCOMA

Lillian M. Guenther, MD[1]; R. Grant Rowe[1]; Patricia Chang[2]; David W. Swenson[2]; Stephanie C. Meyer[1]; Catherine Clinton[1]; Dongjing Guo[1]; Madhumitha Sridharan[1]; Wendy B. London[1]; Holcombe E. Grier[1]; Kirsten Ecklund[2]; Katherine A. Janeway[1]
[1]Pediatric Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [2]Radiology, Boston Children's Hospital, Boston, MA, USA

Objective: In osteosarcoma, ten-year overall survival (OS) is approximately 60% and has not changed in over 30 years. Nor has there has been reduction in treatment-related toxicity. Consequently, it is imperative to conduct phase II trials evaluating novel agents for activity in this disease. We hypothesized that, because of the calcified matrix, RECIST may not be the ideal primary endpoint for phase II trials in osteosarcoma. We investigated whether RECIST was an adequate surrogate marker of outcome in osteosarcoma by assessing RECIST response in newly diagnosed patients who received neoadjuvant chemotherapy proven to be of benefit.

Methods: Patients treated at our institution for newly diagnosed localized or metastatic osteosarcoma who had paired tumor imaging before and after adequate neoadjuvant chemotherapy were included in this retrospective study. Two radiologists blinded to date and point in treatment performed RECIST measurements from diagnosis and post-neoadjuvant chemotherapy CT or MRI. RECIST measurements in paired chest CT from patients with pulmonary nodules 1 cm or greater were assessed in the same manner. From these measurements, RECIST response was calculated and categorized as complete response (CR) ,partial response (PR), stable disease (SD) or progressive disease (PD). Correlation between RECIST response and histological necrosis and OS was assessed.

Results: 74 patients met criteria for inclusion in this analysis. 15% of the patients had metastatic disease at diagnosis and the most common primary site of disease was the distal femur. 5-year OS and event-free survival were 77%±7% and 61%±8%, respectively. No patient had a CR or PR. 64 (86%) patients had SD, and 10 (14%) had PD after receiving neo-adjuvant chemotherapy. We found no significant association between poor histological necrosis and PD. The 5-year OS in patients with SD was 77%±7% compared to 74%±27% in patients with PD. 3 patients had metastatic disease with pulmonary nodules ≥ 1.0 cm. 2/3 had a PR in the target lung lesion while the primary site had SD.

Conclusion: RECIST is a poor surrogate endpoint in osteosarcoma and alternative endpoints for phase II clinical trials in osteosarcoma are necessary. Further study of pulmonary metastatic disease including the incidence of pulmonary nodules 1 cm or greater and RECIST response to neoadjuvant chemotherapy is needed.

Demographic factors		n (%)	Median (Range)
Age at diagnosis (years)		74	13.5(6.4, 23.9)
Sex	Female	34 (46%)	
	Male	40 (54%)	
Metastatic	Yes	11 (15%)	
	No	63 (85%)	
Necrosis	Poor (<90%)	47 (64%)	
	Good (≥90%)	26 (36%)	
	Missing	1	
RECIST	Response	0 (0%)	
	Stable	64 (86%)	95% CI: 86 (77, 93)
	Progressive	10 (14%)	95% CI: 14 (7,23)
Primary tumor measurement (mm)		74	105.5 (42, 380)
Days from pre-neoadjuvant to post-neoadjuvant imaging		74	85.5 (62, 192)

P1 - Poster 094 2570615

COPPER IMPROVES TUMORICIAL EFFECTS OF DISULFIRAM IN BOTH MURINE AND HUMAN SARCOMA CELLS

Jonathan Mandell; Mitchell S. Fourman; Adel Mahjoub; Jessica Tebbets; Shibing Yu; Kurt Weiss
University of Pittsburgh, Gibsonia, PA, USA

Objective: Disulfiram is a FDA approved anti-alcoholism drug which acts as an aldehyde dehydrogenase (ALDH) inhibitor. Metastatic cell lines have been shown to have elevated amounts of ALDH, which elevate cancer stem cell characteristics such as resistance to oxidative stress and increased activity of multidrug efflux pumps. Disulfiram cytotoxicity of cancer cells has been shown to be copper dependent in glioblastoma, breast, and colon cancers. We examined use of copper in disulfiram treatment of both metastatic murine and human sarcoma cell lines in vitro.

Methods: K7M2, a metastatic murine osteosarcoma cell line, and a primary human metastatic high grade myxoid sarcoma cell population (MS3) were used for experiments. Cells received checkerboard dosing of copper sulfate (0, .001, .01, .1, 1, 10um) and disulfiram (0, .01, .1, 1, 10, 100um). 24 hours after dosing pictures were obtained with a Leica DM IRB Microscope using QCapture software. Cells were lifted and counted using an Invitrogen Countess Automated Cell Counter (ThermoFisher Scientific). Cells were also treated for 24 hours and stained with an Invitrogen LIVE/DEAD Viability/Cytotoxicity Kit (ThermoFisher Scientific); plates were read using a BioTek Synergy HT fluorescence reader.

Results: In both K7M2 and MS3 checkerboard dosing of disulfiram and copper revealed copper alone shows no cytotoxic effect even at highest dose of 10um, while disulfiram alone shows cytotoxicity at 10um. Comparable cytotoxicity is observed with synergistic dose of .1um disulfiram and 1um copper, a 100 fold decrease in effective disulfiram dose. Viable cell counts showed statistically decreased viability in .1um disulfiram and 1um copper group compared to control, .1um disulfiram alone, and 1um copper alone groups. LIVE/DEAD readings showed combined treatments yield statistically significant lower LIVE/DEAD ratios compared to control and single treatments.

Conclusion: We have shown the need for copper co-treatment with disulfiram to see the full cytotoxicity the ALDH inhibitor can achieve in metastatic sarcoma cells in vitro. Our recent in vitro and in vivo murine model data have displayed that disulfiram is only slightly effective at killing K7M2, and also seems to inhibit the actions of another other chemo agent, doxorubicin, when given together. Next our group will work on copper and disulfiram treatment of our mice to show increased cytotoxicity of disulfiram and create synergistic activity between disulfiram and doxorubicin.

P1 - Poster 095 2536216

A COMPARATIVE ONCOLOGY STUDY OF THE IMPACT OF SIROLIMUS ON METASTATIC PROGRESSION IN CANINE OSTEOSARCOMA AS A MODEL FOR THE PEDIATRIC DISEASE

Amy K. LeBlanc, DVM[1]; Christina Mazcko[1]; Laura E. Selmic[2]; Timothy M. Fan[2]
[1]Comparative Oncology Program, NIH/National Cancer Institute, Bethesda, MD, USA; [2]Department of Veterinary Clinical Medicine, University of Illinois at Urbana-Champaign, Urbana, IL, USA

Objective: Osteosarcoma (OS) is an aggressive malignancy of bone affecting ~1000 pediatric/adolescent patients and ~ 10,000 dogs yearly in the US. Canine OS shares many important biologic features with pediatric OS, such as comparative histology, genomic profiling, and clinical behavior. Inhibition of mTOR signaling has been shown to delay metastatic progression in mouse OS models, and both canine and human OS cell lines are responsive to mTOR pathway inhibition. The study of naturally-occurring canine OS provides a framework for conception, design and execution of clinical trials of novel agents to define the impact of drug exposure on tumor metastasis, which is the leading cause of death in both canine and human OS patients. Herein we describe a randomized prospective Phase III clinical trial carried out in pet dogs with OS where the mTOR inhibitor sirolimus is added to standard of care therapy in the minimal residual disease setting to define its impact on metastatic progression.

Methods: This study is led by the intramural NCI Comparative Oncology Program's Clinical Trials Consortium (COTC). Dogs are randomized to either standard of care (SOC) alone or followed by sirolimus (SOC + S), where 4 28-day cycles of sirolimus, using daily oral dosing of 0.1 mg/kg on a 4-day on/3-day off schedule, are added sequentially to the SOC backbone (amputation of the affected limb followed by 4 cycles of carboplatin chemotherapy). Dogs are followed until detection of metastasis, with disease-free interval (DFI) as the primary endpoint. The study is powered to detect a 50% increase in the DFI within the SOC + S arm compared to SOC alone.

Results: To date, 118 dogs (target recruitment of 180) have enrolled at 18 participating COTC institutions since the trial opened in November 2015. 60 dogs have enrolled to SOC. 58 dogs have enrolled to SOC + S, of which 14 dogs have completed a median of two 4-week cycles of sirolimus treatment, with no significant adverse events. 32 dogs have been removed from study; 16 dogs due to disease progression, 6 were deemed not eligible ex post facto, 7 were removed due to post-operative complications, development of secondary malignancies, or other non-disease related reasons. 3 dogs died in the immediate post-operative period. Data maturation is expected in mid-2017.

Conclusion: The pet dog with naturally-occurring OS provides a novel approach to define the impact of novel therapeutic strategies on metastatic progression via a facile, centrally-managed clinical trial mechanism.

P1 - Poster 096 2557811

A PHASE II STUDY OF HUMANIZED MONOCLONCAL ANTIBODY 3F8 (HU3F8) WITH GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR (GM-CSF) IN THE TREATMENT OF RECURRENT OSTEOSARCOMA

Alexander Chou, MD; Stephen Roberts; Heather Magnan; Srikanth Ambati; Emily Slotkin; Leonard Wexler; Paul Meyers; Yi Feng; Hoa Tran; Dara Schwam; Elizabeth Chamberlain; Irene Cheung; Nai-Kong V. Cheung
Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: GD2 is expressed in a majority of osteosarcoma (OS) patient samples. Anti-GD2 therapy is effective in neuroblastoma. Data from phase I studies show anti-GD2 therapy is safe in OS and may be effective in the minimal residual disease (MRD) setting. This is a single institution phase II clinical trial assessing the efficacy of anti-GD2 immunotherapy using the monoclonal antibody hu3F8 combined with GM-CSF in patients with recurrent OS.

Methods: Relapsed OS patients in second or greater complete remission are eligible for protocol therapy. Protocol therapy consist of a 30 minute IV infusion of hu3F8 at a dose of 2.4mg/kg/dose for 3 days (day 1, 3, and 5) along with subcutaneous (sc) GM-CSF on days -4 through +5. Therapy is administered in the outpatient setting and cycles are repeated at 2-4 week intervals between first days of hu3F8. A maximum of 5 cycles are administered on protocol.

Results: 8 patients have been enrolled on study. Grade 3/4 toxicities included: respiratory distress (gr. 3, n=1), fever (gr. 3, n=2), anaphylaxis (gr. 3, n=1), hypertension (gr. 3, n=1), hypotension (gr. 4; n=1), urticaria (gr. 3n=1), and nausea/vomiting (gr. 3, n=1). 1 Patient was removed from study due to expected but unacceptable toxicities (respiratory

distress gr. 3, hypotension gr. 4). 2 patients progressed after 2 cycles. 5 patients remain without recurrent disease: 4 patients remain on active therapy and 1 patient completed all planned therapy. 3 of 8 patients developed human anti-human antibody (HAHA) despite no prior anti-GD2 therapy. This study is ongoing.

Conclusion: Hu3F8+GMCSF can be safely given in the outpatient setting and is well-tolerated in relapsed OS patients with MRD. Development of HAHA is seen in a subset of patients but the clinical significance of this remains uncertain. Combination hu3F8+GMCSF warrants further study in OS in the setting of MRD.

P1 - Poster 097 2565832

OFF-LABEL USE OF PAZOPANIB FOR METASTATIC BONE SARCOMAS

Ninna Aggerholm-Pedersen, MSc, MD, PhD; Philip Rossen; Hanne Rose; Akmal Safwat
Aarhus University Hospital, Aarhus, Denmark

Objective: Few treatment options are available for patients with metastatic bone sarcomas and the outcome is usually poor. Since 2011, the Department of Oncology at Aarhus University Hospital has routinely given pazopanib to patients with metastatic bone sarcomas (osteosarcoma, chondrosarcoma and spindle cell sarcoma of bones) that failed or were too sick to receive standard therapy. Treatment was always preceded by an acceptance from the Second Opinion Committee of the Danish medical Authority. This abstract report the results of all 10 consecutive patients treated since 2011.

Methods: This is a retrospective analysis of all patients with metastatic bone sarcomas treated with pazopanib between October 1st 2011 and July 1st 2015. All patients had documented progression at the time they started treatment with pazopanib. Demographics, treatment and survival outcomes were collected from medical records. Overall survival (OS) and progression free survival (PFS) were calculated from the time pazopanib treatment was initiated.. Radiological response was evaluated using RECIST criteria.

Results: Ten patients with refractory relapsed bone sarcoma were identified with a median age of 38 years (range 18-62). Five patients (50%) had osteosarcoma. Nine out of 10 patients (90%) had either disease stabilisation or partial response as best radiological response. The median OS was 15 months while median PFS was 6.3 months. The toxicity profile in our cohort was in line with the PALETTE study and no toxic deaths occurred.

Conclusion: Pazopanib may have some promising activity in metastatic bone sarcoma and it was generally well tolerated. We suggest that pazopanib for metastatic bone sarcoma should be tested in a proper clinical trial.

P1 - Poster 098 2566916

A CASE REPORT OF STABLE DISEASE WITH PAZOPANIB AND EVEROLIMUS IN A PATIENT WITH EWING'S VARIANT SARCOMA

James Chen
Department of Biomedical Informatics and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA

Objective: Ewing's variant sarcoma is an uncommon malignancy for which there is no standard systemic treatment. We report a case of durable disease control with oral pazopanib and everolimus in a 58-year-old man with malignant, extraosseous Ewing's variant sarcoma.

Methods: In June 2013, the patient was admitted for investigation of blood in the stool. Upper and lower endoscopy revealed constriction in the transverse colon. CT-guided biopsy with pathology identified a high-grade tumor, with a small round-cell component. PET/CT revealed a large hypermetabolic mass in the left upper quadrant invading the stomach and adjacent colon. Immunohistochemistry showed diffuse CD99-expression with positive staining for cytokeratins AE1/3, vimentin, and Sox-9. DNA sequencing revealed *EWSR1-NFATC2* gene fusion, consistent with a diagnosis of Ewing's variant sarcoma.

Results: Following distal pancreatectomy, with splenectomy, partial colectomy, and gastrectomy to remove the tumor mass, PET/CT revealed multiple persistent hypermetabolic foci, indicating residual disease. In September 2013, the patient initiated treatment with 4 cycles of chemotherapy (vincristine + doxorubicin + cyclophosphamide followed by ifosfamide + etoposide). After chemotherapy, PET/CT in March 2014 showed no hypermetabolic activity in the left upper quadrant and no other hypermetabolic metastases or lymphadenopathy. Subsequent PET/CT (May 2014) showed mild hypermetabolic activity in the nodular soft tissue density anterior to the left kidney, indicating potential progression. The patient started once-daily 400 mg pazopanib. Following initial disease stability for 4 months, subsequent CT showed slowly progressive disease. The patient then received 2 cycles of irinotecan with concurrent pazopanib. However, PET/CT demonstrated continued progression in the abdomen and pelvis, and, in February/March 2015, the decision was made to stop irinotecan and initiate daily 5 mg everolimus in addition to the pazopanib regimen. PET/CT in April 2015 showed similar distribution of hypermetabolic soft tissue abdominal nodules to the previous scan. Most recent follow-up CT showed ongoing stable disease for 6 months.

Conclusion: The case data suggest that combined inhibition of angiogenesis and mTOR signaling may be a viable oral option for disease control in patients with Ewing's variant sarcoma harboring *EWSR1-NFATC2* gene fusion.

P1 - Poster 099 2526097

IMMUNE CHECKPOINT INHIBITOR EXPRESSION OF HUMAN AND CANINE OSTEOSARCOMA

Matthew Cascio, DO[1]; Rowan Milner[2]; Lung-Ji Chang[3]
[1]Pediatric Hematology/Oncology, University of Florida, Gainesville, FL, USA; [2]Veterinarian Medicine, University of Florida, Gainesville, FL, USA; [3]Molecular Genetics and Microbiology, University of Florida, Gainesville, FL, USA

Objective: Identify regulatory immune checkpoints on osteosarcoma (OS) cells, and compare these differences across canine and human primary and metastatic tumors.

Methods: Under IACUC and IRB approvals fresh OS biopsy specimens are dissected and processed for cell culture. Single cells are collected by physical pressing with a glass rod to release cells and digested with collagenase, hyaluronidase, and DNase to dissociate connective tissues. The single cell suspension is then collected for immediate culture or frozen for later use. Tumor cells are cultured in DMEM with 12% FBS and processed with EDTA. Cells are then stained with anti-checkpoint inhibitor ligand (CIL) (ie. anti-PDL1, anti-B7H3, anti-HVEM, B7) antibodies and analyzed by flow cytometry. Purchased cell lines are also cultured and processed according to manufacturer details, and stained synonymous to biopsy collected samples. For further comparison, cell cultures are placed into chamber slides and cultured until confluent. Cells in chamber slides are then washed and then incubated with respective CIL IHC antibodies and analyzed against unstained controls.

Results: There is very high positive expression of PDL1 and B7H3 checkpoint inhibitor ligands, and moderate HVEM expression in all of the two commercially available human cell lines and three patient tumor samples studied (primary, metastatic, and relapsed) using flow cytometry. All three canine cell lines also produced positive expression of B7H3 and HVEM. PDL1 failed to show expression in canine OS cultures on flow cytometric analysis most likely secondary to species-specific antibody limitations. However, IHC staining of canine cell lines revealed positive PDL1 expression comparable to that of human. IHC staining for B7H3 and HVEM also resulted positive on both species' cell lines, complimentary to flow cytometry data.

Conclusion: Both canine and human osteosarcoma cell lines express a variety of checkpoint inhibitor ligands, specifically PDL1, B7H3, and HVEM. Furthermore, immune checkpoint inhibitor ligands appear to be expressed across patient primary, metastatic, and relapsed tumor samples. Canines serve as an effective immunotherapy model for immune checkpoint inhibitor targets in human osteosarcoma.

P1 - Poster 100 2561834

INVESTIGATING THE IMMUNE MICROENVIRONMENT IN BONE AND SOFT-TISSUE SARCOMA

Nalan Gokgoz, PhD[1]; Junghyun Nam[1]; Beatrice Lau[2]; Brendan C. Dickson[2]; Jay Wunder[1]; Irene L. Andrulis[1]
[1]Lunenfeld-Tanenbaum Research Institute, Sinai Health System, Toronto, ON, Canada; [2]Department of Pathology and Laboratory Medicine, Sinai Health System, Toronto, ON, Canada

Objective: The importance of immune checkpoint proteins - such as programmed death-ligand 1 (PD-L1) on tumor cells, and the corresponding programmed death receptor 1 (PD-1) on tumor infiltrating lymphocytes (TILs)- has been illustrated in several cancers; however, their role in bone and soft tissue sarcoma (B/STS) remains unclear. Examining the more common, and therapeutically relevant, types of B/STS the aim of this study is to:1) characterize PD-L1 gene expression profiles, and 2) determine whether a subset of B/STS harbour a significant TIL population.

Methods: RT-qPCR was utilized to quantify the relative level of PD-L1 expression in RNA extracted from frozen specimens including 70 cases of primary osteosarcoma (OS), 22 cases of undifferentiated pleomorphic sarcoma (UPS) and 32 cases of myxofibrosarcoma. The presence of TILs and immune checkpoint proteins was characterized by immunohistochemistry (IHC) in 25 cases of UPS, 25 cases of myxofibrosarcoma, 25 cases of liposarcoma and 25 cases of leiomyosarcoma using standard techniques, and antibodies included: CD3, CD4, CD8, CD20, PDL1 and PD1.

Results: Preliminary RT-qPCR results from 70 OS (Figure1) and 54 UPS/myxofibrosarcoma cases demonstrate PD-L1 expression varies among each sarcoma subtype. For OS a 50 fold difference in PD-L1 expression was observed between the highest and lowest quartile. A significant, positive correlation of the PD-L1 expressions was found between the RT-PCR and RNA-sequencing generated from the RNA of 11 OS (r_s=0.855, p=0.001) and 14 UPS (r_s=0.952, p<0.001). Previously generated mRNA microarray data for OS was utilized to classify genes that are differentially expressed between PD-L1 high and low groups. SAM moderated t-tests and network analysis using IPA were performed in order to compare the expression between PD-L1 high and low groups. Several important biological pathways were identified including EIF2 signaling. IHC staining and biostatistical analysis is in progress.

Conclusion: OS and STS express various levels of PD-L1 mRNA with some tumors expressing very high levels detected by RT-PCR. In OS, several important biological pathways distinguish PD-L1 high and low groups. It is necessary to determine which cells express PD-L1 and whether TILs are present; this is being examined by IHC. The stratification of patients with B/STS with respect to potential immune therapies may be improved through the

investigation of the presence or absence of TILs, and the expression pattern of immune markers and checkpoint proteins.

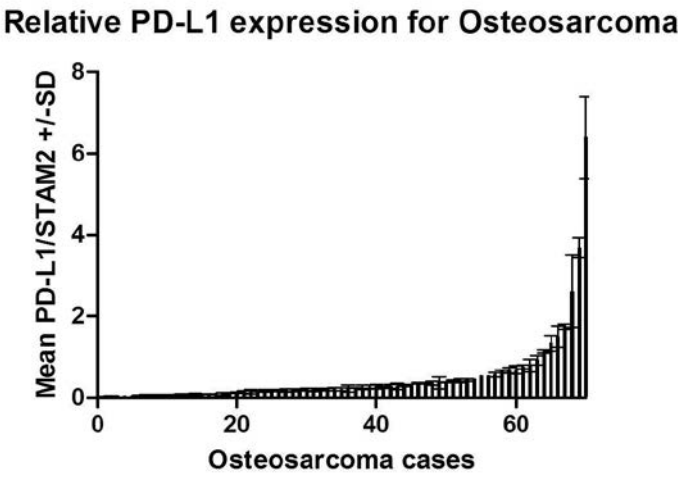


Figure 1: Relative Expression of PD-L1 in Osteosarcoma tumors by RT-qPCR

P1 - Poster 101 2567963

RETROPERITONEAL EWING SARCOMA (ES): AN ITALIAN SARCOMA GROUP (ISG) AND ROYAL MARSDEN HOSPITAL (RMH) JOINT STUDY

Emanuela Palmerini[1]; Robin Jones[2]; Dario Callegaro[3]; Giovanni Grignani[4]; Piero Picci[1]; Luca Cevolani[1]; Davide Donati[1]; Michela Libertini[1]; Emanuela Marchesi[1]; Martina Piccioni Leopardi[1]; Michela Pierini[1]; Lorenzo D'Ambrosio[4]; Charlotte Benson[2]; Alessandro Gronchi[3]; Stefano Ferrari[1]
[1]Istituto Ortopedico Rizzoli, Bologna, BO, Italy;
[2]Royal Marsden Hospital, London, United Kingdom;
[3]Istituto Nazionale Tumori, Milan, Italy;
[4]IRCC Candiolo, Torino, Italy

Objective: Retroperitoneal Ewing sarcoma (ES) are extremely rare tumors, representing less than 10% of extraskeletal ES and < 1% of retroperitoneal sarcomas. Case reports are described but there is no consensus on optimal management.

Methods: An ISG – RMH combined study on clinical features, treatment and outcome of patients (pts) with retroperitoneal ES is reported.

Results: A total of 40 patients with extraskeletal ES treated between Oct 1971 – Dec 2012 were identified. Median age 31 years (range 17-69 years), 16 F/ 24 M. LDH (in 24 pts): 11 normal; 13 high; ECOG (in 27 pts): 0 in 16, 1 in 8, 2 in 3 pts. Synchronous metastases were reported in 14 patients, while 26 patients were localized at first diagnosis. All patients received different chemotherapy regimens based on the acive drugs against ES (vincristin, adrymicin, ifosfamide, etoposide, cyclophosfamide, dactinomycin) according to the institutional practice. Five patients did not receive local treatment, 30 patients underwent surgery (in 14 cases combined with adjuvant radiotherapy), 5 patients received radiotherapy only.

In 33 patients the response to primary chemotherapy was available: the objective response rate (ORR) was 88%: 1 CR (3%) + 28 PR (85%), with SD in 4 (12%) cases.

With a median observation time of 32 months (2-159), 25 patients have died and 15 are alive. The median survival was 38 months (4-159) for localized patients and 18 months (2-86) in patients with metastases.

The 5-year OS was 38 % (95%CI 25-57): 15% (95%CI 0-35) in metastatic patients, 50% (95%CI 30-70) in localized patients (p=0.001).

In 21 localized patients who received local treatment and achieved complete remission, the 5-EFS was 48% (95%CI 26-70): 50% in patients who underwent surgery (12 pts), 44% in case of surgery and radiotherapy (9 pts), and 0% for radiotherapy only (2 pts). The 5-year EFS was 61% in case of CR/PR and 25% in case of SD.

Grade 3-4 neutropenia was 66%, with febrile neutropenia in 46%, anemia 20% and thrombocytopenia 22%. 2 patients had kidney toxicity (1 hemodialysis), 2 had cardiac toxicity, 1 CSN toxicity. 58% of patients required dose reduction or treatment delay or both in, and permanent discontinuation life threatening infection 1 case.

Conclusion: Extraskeletal abdominal ES showed a high response rate to standard chemotherapy. Surgery combined with standard chemotherapy should be recommended. The use of adjuvant radiotherapy must be better defined.

P1 - Poster 102 2562359

EXTRASKELETAL EWING SARCOMA: A RETROSPECTIVE ANALYSIS FROM A SINGLE INSTITUTION SERIES OF PEDIATRIC AND ADULT PATIENTS

Michela Libertini[3]; Robin Jones[1]; Edward Armstrong[1]; Cyril Fisher[1]; Khin Twhay[1]; Aisha Miah[1]; Ian Judson[1]; Winette Van der Graaf[1]; Julia Chisholm[2]; Shane Zaidi[1]; Charlotte Benson[1]

[1]Sarcoma Unit, Royal Marsden Hospital, London, United Kingdom; [2]Children and Young People's Unit, Royal Marsden Hospital, Sutton, London, United Kingdom; [3]ESO Clinical Training Centres Fellow 2016, Sarcoma Unit, Royal Marsden Hospital, London, United Kingdom

Objective: The Ewing sarcoma family of tumours includes tumours arising from bone and soft tissue. Extra-skeletal Ewing sarcoma is rare, and the use of chemotherapy schedules in localized disease has been extrapolated from data in skeletal Ewing sarcoma. There are few published data documenting the treatment and outcome of patients with extra-skeletal Ewing sarcoma. The aim of this study was to document the management and outcome of patients with extraskeletal Ewing sarcoma treated at a single referral centre.

Methods: We retrospectively reviewed a prospectively collected database of 109 consecutive patients diagnosed with extra-skeletal Ewing sarcoma (EES) treated at the Royal Marsden Hospital (RMH) between 1995 and 2015. Overall survival (OS) and Disease-free survival (DFS) were assessed using the Kaplan-Meier method; statistical analysis regarding prognostic factors is ongoing.

Results: One hundred and nine patients had data available for analysis [Male:Female = 60 (55%) vs 49 (45%), median age at diagnosis 31 years (range 7-84 yrs]. Median tumour size was 8 cm (range 1,3-25). Demographics, tumour localization, and treatment are summarised in table 1. Forty-three out of 109 had molecular confirmation by the presence of *EWSR1* translocation or *EWSR/FL1* transcription. Sixty-six were diagnosed on morphology and immunohistochemistry alone. Thirty-three (30%) had metastatic disease at diagnosis. Among 76 patients with localised disease, 63/76 (83%) underwent surgery [38 (59%) after induction therapy, 26 (41%) at diagnosis], 10 (13%) had primary radiotherapy (median 54 Gy/30#), 3 (4%) did not receive any local treatment. Seventy-three of 76 patients (96%) received a 4 drug schedule (median 8 cycles: range 3-15). The 5 and 10 yrs OS was 67% and 50% respectively, DFS after 1, 2 and 5 yrs was 68%, 66% and 60% respectively. The 5-yrs OS for the whole group (metastatic and localised disease) was 50%.

Conclusion: The outcome for patients with EES treated similarly to skeletal ES does not differ substantially from the skeletal Ewing sarcoma. Detailed analysis of prognostic factors is ongoing.

Tab.1 Localised disease, Patients' characteristics (n=76)

Site	# (%)
Head and neck	10 (13)
Extremities	13 (17)
Thorax	22 (29)
Abdomen (intra-abdominal/pelvis)	13 (17)
Retroperitoneum	10 (13)
Paraspinal	8 (11)
Age	.
<15	7 (9)
15-30	32 (42)
>30-84	37 (48)
Drugs	.
Anthracycline	45 (59)
Ifosfamide	51 (67)
Cyclophosphamide	29 (38)
Actinomycin	43 (56)
Etoposide	32 (42)
Vincristine	65 (85)
Other	4 (5)
High dose chemotherapy with autologous stem cell transplantation	2 (3)
Worst Toxicity	.
Sepsis	33 (43)
Renal failure	1 (1)
Treatment related death	1 (1)
Primary radiotherapy	10 (13)
Head and neck	3 (30)
Extremities	1 (10)
Thorax	2 (20)
Abdomen	2 (20)
Paraspinal	2 (20)

P1 - Poster 103 2569888

EWING SARCOMA OF THE HEAD AND NECK (HN ES): LOCAL TREATMENT EVALUATION OF THE FRENCH POPULATION

Jebrane Bouaoud[2]; Stéphanie Bolle[1]; Stéphane Temam[1]; Kahina Belhous[2]; Louise Galmiche[2]; Frédéric Kolb[1]; Quentin Quassemyar[1]; François Bidault[1]; Vincent Couloigner[2]; Nathalie Cozic[1]; Marie-Cecile De Leley[1]; Natacha Kadlub[2]; Nathalie Gaspar[1]

[1]Gustave Roussy, Villejuif, France; [2]APHP Necker, Paris, France

Objective: To describe the characteristics, local relapses, survival, long-term outcome, according to the choice of local control modalities.

Methods: We analyzed prospectively collected data of the French HN ES patients registered in the Euro-Ewing 99 (EE 99) trial from 1999 to 2014 and retrospectively reviewed their charts to refine some items on local treatment and sequels. EFS and OS were calculated with the Kaplan

Meyer method.

Results: Overall 47 pts presented HN ES, confirmed by FISH or RT-PCR. Median age was 13 years [1-32]. Primary tumors were mainly osseous (90%) with small initial volume (<200ml; 91%), mainly located in skull (n=26), mandible (n=10) and maxilla (n=5), and with regional lynph node (26%) and metastatic extension (9%). After neoadjuvant chemotherapy (VIDEx6 for 20 weeks [18-32 weeks]), local treatment consisted on combined surgery/radiotherapy (RT) (n=26, 55%), surgery alone (n=13, 28%) or exclusive RT (n=8, 17%). Good histological response was observed in 85% of patients operated after induction CT. The median follow up was 9.2 years. Seven and 4 patients had local and metastatic recurrences (median time, 22 and 33 months, respectively). The 3-years EFS and OS were respectively 76% and 88%. Local relapses occurred after exclusive radiotherapy (n=3/8 pts) or surgery alone (n=4/13 pats). None was observed with the 26 pts who received combined surgery/RT, whatever the quality of surgical margin. Pathological reports were review using the classification adopted for the Euro-Ewing 2012 trial. Surgical margin EE99-R0 margins were reclassified as EE2012-R1a margin (margin within post-chemotherapy necrotic tumor or reactive fibrosis) in 11/18 localized HN ES. The 4 local relapses in localized HN ES with EE99-R0 margin, occurred in tumor reclassified as R1a that did not received post-operative RT, while no relapse occurred in R1 HN ES who received post-operative RT. Long term sequels of local treatment were observed in 75% of the pts, especially when combined local therapy was used, and depended on the primary tumor site and pt age.

Conclusion: French HN ES as describe on the literature had good survival rate, partially due to favorable clinical characteristic but a source of functional-esthetic problems in survivors. HN ES local relapse remains of poor prognosis. Optimizing the local treatment might avoid-minimized these two problems. It requires an expert surgeon to get R0 margin and appropriate reconstruction and a good evaluation of the surgical margin, to avoid RT.

P1 - Poster 104 2529965

CIC-REARRANGED SARCOMAS: CLINICAL FEATURES AND TREATMENT OUTCOME

Makoto Endo, MD, PhD; Akihiko Yoshida; Eisuke Kobayashi; Shunichi Toki; Takeshi Hirose; Takenori Uehara; Masato Sugawara; Tomoaki Mori; Koki Shimizu; Yoshikazu Tanzawa; Fumihiko Nakatani; Hirokazu Chuman; Akira Kawai
National Cancer Center, Tokyo, Japan

Objective: Recent molecular genetic analyses have disclosed that a subset of “Ewing sarcoma-like” small round cell sarcomas harbor a rearrangement of the CIC gene that is located at 19q13. The rearrangement results in CIC-DUX4 or CIC-FOXO4 fusion gene in their tumor cells. The objective of this study is to clarify the clinical characteristics and treatment outcome of CIC-rearranged sarcomas because little is known about this newly-established soft tissue sarcoma.

Methods: We retrieved 17 patients with CIC-arranged sarcoma diagnosed at our hospital. The clinical information was collected from the medical charts.

Results: The patients were 12 males and 5 females whose ages at the initial visit ranged from 15 to 73 years (median 22 years). The tumors were located in soft tissue of the extremities in 8 cases, and in the trunk in 9 cases. They situated in the superficial soft tissue in 4 cases, and in the deep tissue in 13 cases. The most frequent symptom was local pain, observed in 10 patients. The largest tumor size ranged from 1.7 to 31 cm (mean 10.9 cm). On images, all 17 cases presented lobular pattern, and 15 of the 17 cases showed heterogeneous and ring-like enhancement. Four patients received PET examination, which revealed that SUVmax ranged from 8.4 to 11.5 (mean 10.3). At the initial visit, 12 patients had distant metastasis to lung (n=10), lymph node (n=4), bone (n=3), pleura (n=3), and brain (n=3); metastasis was overlapped in some patients. Surgery was performed at 4 of the 5 patients without distant metastasis, resulting in no local recurrence. Chemotherapy was performed at all of the 12 patients with distant metastasis, using VDC/I(E) (n=5), VAC (n=3), AI (n=2), or doxorubicin alone (n=2) as the first-line regimen. Best overall response was CR (n=1), PR (n=2), SD (n=3), and PD (n=6). Median overall survival was 10 months, and the clinical outcome was CDF (n=3), NED (n=1), AWD (n=1), and DOD (n=12). All patients with CDF or NED shared the common clinical feature that the tumor existed in the superficial soft tissue.

Conclusion: CIC-rearranged sarcomas are likely to occur in young adults, and frequently accompanied by local pain at presentation. The prognosis of CIC-rearranged sarcoma is extremely poor although a patient with superficial one has a potential for long-term survival.

P1 - Poster 105 2526665

CLINICOPATHOLOGICAL FINDINGS AND TREATMENT RESULTS OF BCOR-CCNB3 SARCOMA

Masato Sugawara, MD, PhD[1]; Makoto Endo[2]; Akihiko Yoshida[3]; Eisuke Kobayashi[2]; Yoshikazu Tanzawa[2]; Fumihiko Nakatani[2]; Michiaki Takagi[1]; Hirokazu Chuman[2]; Akira Kawai[2]

[1]Orthopaedic Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan; [2]Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [3]Pathology, National Cancer Center Hospital, Tokyo, Japan

Objective: BCOR (BCL6 co-repressor)-CCNB3 (testis-specific cyclin B3) sarcoma is harboring a novel recurrent paracentric inversion on chromosome X resulting in a BCOR-CCNB3 fusion gene. Although BCOR-CCNB3 sarcoma is one of Ewing-like sarcomas as having a similar morphology, the clinical feature and treatment results of this tumor is not well recognized. We investigated the clinicopathological findings, treatment and outcome of patients with BCOR-CCNB3 sarcoma.

Methods: We selected patients of bone or soft tissue sarcoma with BCOR-CCNB3 fusion that confirmed by fluorescence in-situ hybridization. The clinical information including age, sex, tumor site, size, initial pathological diagnosis, treatment and outcome was obtained from medical records.

Results: The clinical data of all 7 patients with BCOR-CCNB3 sarcoma was summarized in Table 1. All 7 patients were males diagnosed in a median age of 12 years (range, 4-16 years). Five of 7 tumors had arisen in the bone (pelvis 2, rib 1, facial bone 1, big toe 1), and two of 7 tumors were soft tissue origin (pelvic cavity 1, thigh 1). A median of the largest tumor diameter was 9.6 cm (range, 2.5-18 cm). All 7 patients had no metastasis at the time of diagnosis. The initial pathological diagnoses were as follows: Ewing sarcoma 2, round cell liposarcoma 1, mesenchymal chondrosarcoma 1, BCOR-CCNB3 sarcoma 1, unclassified sarcoma 2. Six patients received neoadjuvant and/or adjuvant chemotherapy such as VDC-IE, AI and VAC. Pathological necrosis in surgical specimens after chemotherapy were 2 of Grade 2, and 1 of Grade 4 (Grade 1: necrosis of less 50 % of the tumor, Grade 2: 50-90 %, Grade 3: 90-99 %, Grade 4: 100 %). Surgical resection was performed in 6 patients, five were wide resection (R0), and one was a gross margin positive resection (R2). Postoperative radiotherapy was given to 3 patients. One patient received carbon ion radiotherapy to primary site as a local treatment. At a median follow-up of 64 months (range, 7-194 months), oncological outcomes were CDF in 6, and AWD in 1.

Conclusion: Our study showed that BCOR-CCNB3 sarcoma was predominantly seen in male children, and had a trend for good outcome as previous reports described. Although complete resection seems to be necessary for a good outcome, definitive result for what chemotherapy should be done was not obtained. In the future, we expect to analyze what kind of regimen is appropriate for treatment of BCOR-CCNB3 sarcoma after accumulating more patients.

Table 1

Case	Age/Sex	Site (B/ST)*	Size** (cm)	Initial pathologocal diagnosis	Chemotherapy (neoadjuvant/ adjuvant)	Protocol	Radiotherapy	Surgery	Margin	Pathological necrosis	Local recurrence	Metastasis (site)	Outcome (months of FU)***
1	4/M	Thigh (ST)	10	Round cell liposarcoma	+/+	VAC+AI×5	None	Wide resection	R0	−	−	−	CDF (64)
2	16/M	Pelvic cavity (ST)	18	Ewing sarcoma	+/+	VDC/IE	Postoperative radiotherapy 55.8Gy	Wide resection	R0	Grade 3	−	−	CDF (87)
3	7/M	10th rib (B)	7	Ewing sarcoma	+/+	VDCI×2+ VDCIE×4	None	Wide resection	R0	Grade 1	−	−	CDF (164)
4	11/M	Proximal phalanx of great toe (B)	2.5	Unclassified sarcoma	None	−	None	Wide resection (amputation)	R0	−	−	−	CDF (48)
5	16/M	Pelvis (B)	13	BCOR-CCNB3 sarcoma	+/−	AI×6+VCIE×2	Carbon ion radiotherapy 70.4GyE	None	−	−	−	−	CDF (7)
6	16/M	Facial bone (B)	7	Mesenchymal chondrosarcoma	−/+	AI×2	Postoperative CyberKnife	Intralesional resection	R2	−	+	+ (Bone, Lymph node)	AWD (38)
7	14/M	Pelvis (B)	10	Unclassified sarcoma	+/+	VDCI×2+ VDCIE×4	Postoperative radiotherapy 40Gy	Wide resection	R0	Grade 1	−	−	CDF (194)

* B; bone, ST; soft tissue, **The laegest diameter, *** FU; follow-up, CDF; continuous disease free, AWD; alive with disease

P1 - Poster 106 2556527

CUMULATIVE BURDEN OF CHRONIC HEALTH CONDITIONS IN ADULT SURVIVORS OF CHILDHOOD BONE SARCOMAS: A REPORT FROM THE ST. JUDE LIFETIME (SJLIFE) COHORT STUDY

Michael W. Bishop; Kiri Ness; Chenghong Li; Wei Liu; Kumar Srivastava; Nickhill Bhakta; Yutaka Yasui; Alberto Pappo; Les Robison; Melissa Hudson; Daniel Mulrooney
St. Jude Children's Research Hospital, Memphis, TN, USA

Objective: Adult survivors of malignant bone tumors are at risk for adverse health outcomes but comprehensive assessments are lacking. We evaluated the burden of chronic health conditions among adult survivors of osteosarcoma and Ewing sarcoma.

Methods: Among 299 survivors of osteosarcoma and Ewing sarcoma treated at St. Jude Children's Research Hospital, surviving ≥10 years and ≥18 years old, 208 returned for a comprehensive clinical assessment. A modified version of the Common Terminology Criteria for Adverse Events was used to grade 168 chronic health conditions. Multiple imputations, based on demographic and treatment exposures, were used to construct grades for 91 eligible for SJLIFE with only retrospective data. Cumulative burden was estimated by calculating mean cumulative count of chronic conditions with age as the time variable. Associations with treatment for prevalence of conditions ≥grade 2 were estimated using logistic regression. Among on-campus participants, physical function, adjusted for age and gender, was measured and compared to 272 community-controls.

Results: Survivors (56% male), median age 14 years (range 1.7-24.8) at diagnosis and 35 years (20-64) at evaluation, were a median of 22 years (10-47) from diagnosis. Exposures (mean ±SD) included: anthracyclines (358.5 mg/m^2±75.5), alkylators (13943.6 mg/m^2±8617.6), and cisplatin (370.7 mg/m^2±85.8). At 35 years of age, survivors averaged 10.2 (95% CI, 8.9-11.5) grade 1-5 (mild to fatal) and 3.9 (3.3-4.5) grade 3-5 (severe to fatal) chronic health conditions per survivor, compared to 0.9 (0.7-1.1) and 0.03 (0.01-0.05), respectively, among controls. On average, one in three survivors (0.3, 0.2-0.4) experienced a grade 3-5 cardiovascular condition. Among participants screened on-campus, prevalent conditions (≥grade 2) included cardiomyopathy (24.5% vs. controls 0.7%), hypertension (25.5% vs. 16.5%), myocardial infarction (7.7% vs. 0.7%), pulmonary diffusion deficit (23.1% vs. 0.4%), hearing loss (10.1% vs. 1.1%), and chronic kidney disease (6.3% vs. 1.1%). Significant treatment associations are shown in the table. Survivors exhibited worse flexibility, isometric knee strength, and six minute walk test than controls (all p<0.0001). Amputees had superior flexibility but poorer mobility testing compared to survivors with a limb (p<0.01).

Conclusion: By age 35 years, survivors of childhood bone sarcomas experience a significant burden of chronic disease, particularly cardiovascular, as well as significant functional deficits.

Multivariable Analysis of Prevalence of Chronic Health Conditions (≥Grade 2) by Treatment Exposures

Condition	Exposure	Odds Ratio Estimate (95% CI)	p-value
Cardiovascular			
Cardiomyopathy	Anthracycline (per 100mg)	1.9 (1.3-2.9)	<0.01
Myocardial Infarction	Anthracycline (per 100mg)	2.0 (0.9-4.2)	0.07
Pulmonary			
Diffusion Deficit	Thoracotomy Chest Radiation Bleomycin (per 100mg)	4.4 (2.0-9.4) 4.4 (1.7-11.0) 2.7 (1.0-7.3)	<0.01 <0.01 0.05
Obstructive Deficit	Thoracotomy Chest Radiation Bleomycin (per 100mg)	6.0 (2.1-17.4) 7.2 (2.3-22.9) 3.0 (0.9-10.2)	<0.01 <0.01 0.07
Restriction Deficit	Thoracotomy Chest Radiation Bleomycin (per 100mg)	5.5 (1.6-18.7) 10.2 (2.8-37.3) 3.2 (0.8-12.8)	<0.01 <0.01 0.10
Auditory			
Hearing Loss	Platinum (Any)	54.6 (6.0-496.3)	<0.01
Renal			
Chronic Kidney Disease	Platinum (Any)	3.9 (1.1-14.1)	0.04

P1 - Poster 107 2570711

PROGNOSTIC NOMOGRAMS FOR PREDICTING THE 10-YEAR PROBABILITY OF LOCAL-CONTROL FAILURE, RECURRENCE, AND DEATH IN BONE OSTEOSARCOMA

Ruoyu Miao, MD; Haotong Wang; Alex Jacobson; Saveli Goldberg; Yen-Lin Chen
Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA

Objective: In this retrospective study, we reviewed the clinical characteristics and outcomes of patients treated for nonmetastatic bone osteosarcoma in our institution, and developed nomograms to predict the 10-year probability of local-control failure, recurrence (including both local recurrence and distant metastasis), and death.

Methods: We reviewed 340 osteosarcoma patients treated from 1996 to 2013. Patients with limited follow up were excluded, resulting in 259 cases for analysis. Clinical and pathologic variables were recorded. Predictor variables included age at diagnosis, gender, radiation history, tumor size (<= 8, > 8 cm, or discontinuous), histologic grade (low, intermediate, or high), histologic subtype (fibroblastic, chondroblastic, NOS, or other), and site (head or neck, extremity, spine or pelvis, or other). The multivariate Cox proportional hazards regression was used to analyze survival outcomes and risk variables.

Results: At 10 years, the local-control survival was 80.0% (95% confidence interval, 74.0% to 86.0%), recurrence-free survival was 63.9% (56.8% to 71.1%), and overall survival was 70.1% (63.4% to 76.7%). Multivariate Cox model identified radiation history (p=0.027 and p=0.048, respectively), tumor size (p=0.010 and p<0.001, respectively), and site (p=0.023 and p=0.049, respectively) were correlated with both local-control and recurrence-free survival, whereas patient age at diagnosis (p<0.001), tumor size (p=0.015), histologic grade (p=0.023), and histologic subtype (p=0.014) were associated with overall survival. The nomograms were drawn on the basis of the Cox regression model and were internally validated using bootstrapping.

Conclusion: We identified significant prognostic factors for patients with nonmetastatic bone osteosarcoma and developed nomograms to predict the 10-year local-control failure, recurrence and death. We suggest that this tool may be useful for individualized risk evaluation, patient counseling, and making clinical decisions.

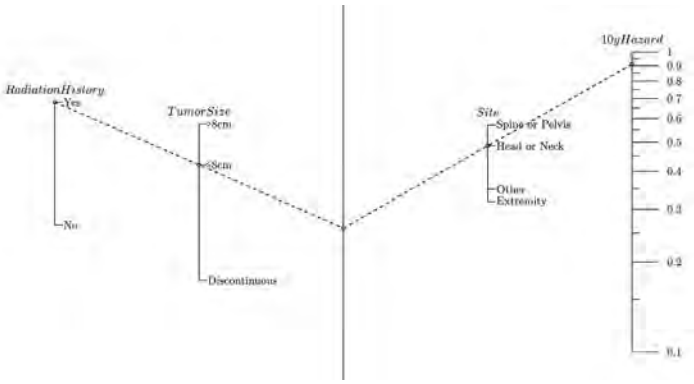


Fig 1. Prognostic nomogram for 10-year local-control failure. The dash lines show an example of a patient with radiation history, tumor size of <= 8 cm, and head or neck tumor who has a predicted 10-year local-control failure hazard of 91.0%.

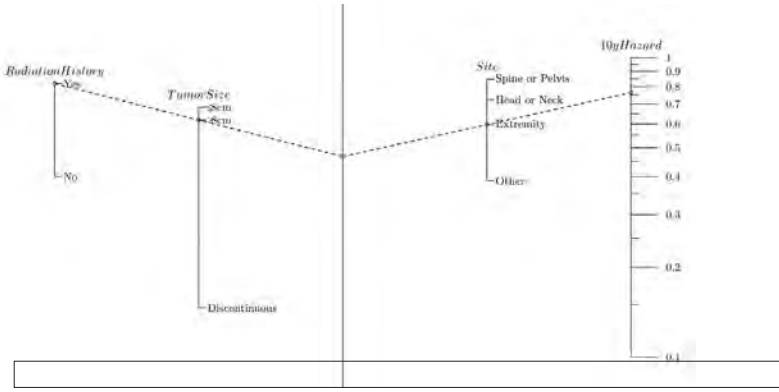


Fig 2. Prognostic nomogram for 10-year recurrence. The dash lines show an example of a patient with radiation history, tumor size of > 8 cm, and extremity tumor who has a predicted 10-year recurrence hazard of 76.4%.

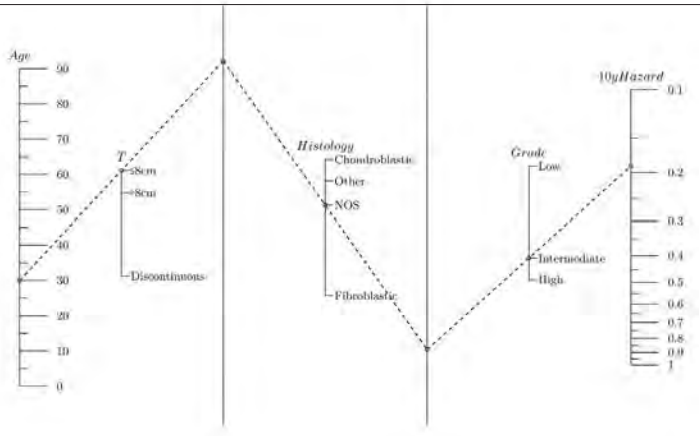


Fig 3. Prognostic nomogram for 10-year mortality. The dash lines show an example of a 30-year old patient with tumor size of <= 8 cm, histologic subtype of NOS, and intermediate grade who has a predicted 10-year mortality hazard of 19.0%.

P1 - Poster 108 2570656

BONE LESIONS AT DIAGNOSIS: EXPERIENCE OF THE OS2006 STUDY

Cyril Lervat[1]; Laurence Brugieres[3]; Bob-Valery Occean[3]; Perrine Marec-Bérard[5]; Nadege Corradini[5]; Natacha Entz Werle[4]; Jean- Claude Gentet[7]; Ludovic Mansuy[8]; Hélène Pacquement[6]; Marie-Dominique Tabone[2]; Sophie Piperno-Neumann[6]; Marie-Cécile Le Deley[3]
[1]Pediatrics, Centre Oscar Lambret, Lille, France; [2]Trousseau, Paris, France; [3]Gustave Roussy, Villejuif, France; [4]Hôpital Hautepierre, Strasbourg, France; [5]Ihope, Lyon, France; [6]Curie, Paris, France; [7]La Timone, Marseille, France; [8]CHU Nancy, Nancy, France

Objective: We aimed to describe the clinical characteristics and outcome of patients with osteosarcoma and several bone lesions.

Methods: Description of all patients prospectively enrolled in the French OS2006 study between April-2007 and March-2014, for a newly diagnosed high-grade osteosarcoma with at least one synchronous distant or regional bone lesion in addition to the primary. MRI of the primary site and technetium bone scintigraphy (TBS) were mandatory at diagnosis, Positron Emission Tomography (PET) was optional.

Results: From the 518 study patients, 21 patients (median age=13.7; range, 5.7-37) had several bone lesions: 10 with a unique lesion in addition to the primary, and 11 with multifocal lesions. Bone metastases were localised in a bone contiguous to the primary tumour in 6 patients. Pulmonary metastases were associated in 10/21 patients. TBS and PET were both performed in 11/21 patients: secondary bone lesions identified on TBS were associated with a strong PET signal in 6 and a weak signal in 2, whereas both tests were negative in 2 patients and PET signal was weak in 1 patient with bone lesions diagnosed on MRI. A complete remission was obtained in 12 patients after polychemotherapy combined with local treatment of primary site and metastatic lesions. Only 5 patients (4 with a unique lesion and 1 with 2 regional lesions) are alive free of event with more than 2 years of follow-up, leading to a 2-year EFS of 24% (95%CI, 11%-45%), not significantly different from that of patients with lung metastases only (p=0.52). Overall survival was 36% (95%CI, 19%-56%).

Conclusion: Multiple bone lesions are rare in osteosarcoma and not always evidenced by PET. The prognosis of these patients remains poor, but in our study it was no worse than that of patients with lung metastases only. Number and sites of bone lesions may influence patient outcome.

P1 - Poster 109 2559702

PRIMARY OSTEOSARCOMA OF THE BONE WITH RHABDOID FEATURES: A RARE, PREVIOUSLY UNDESCRIBED PRIMARY MALIGNANT TUMOR OF BONE

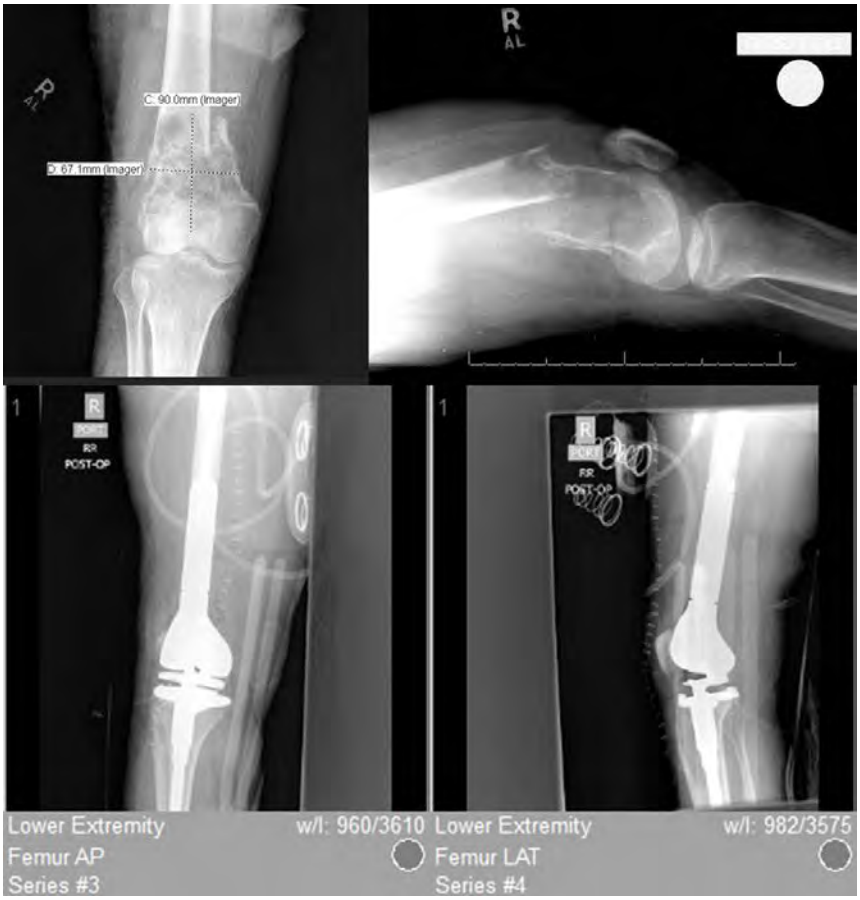
Max Seiter, MD[1]; Motasem Al Maaieh[1]; Rosenberg Andrew[2]; Sheila Conway[1]
[1]Orthopaedic Surgery, University of Miami/Jackson Memorial Hospital, Miami, FL, USA;
[2]Pathology, University of Miami Hospital, Miami, FL, USA

Objective: This case report presents a novel finding; the first case of primary osteosarcoma of bone with rhabdoid features reported in the literature, verified via histopathology and tissue-specific staining.

Methods: Rhabdoid tumors have been identified in nearly every anatomical site in the body, and previously extraskeletal rhabdoid osteosarcomas have been twice presented in the literature, however primary osteosarcoma of bone has not yet been described. We present here a case-report of a 69 year-old female, who presented with a pathological fracture of the right femur and ultimately underwent distal femur radical resection and reconstruction with endoprosthesis; on final histopathology she was found to have osteosarcoma with rhabdoid features.

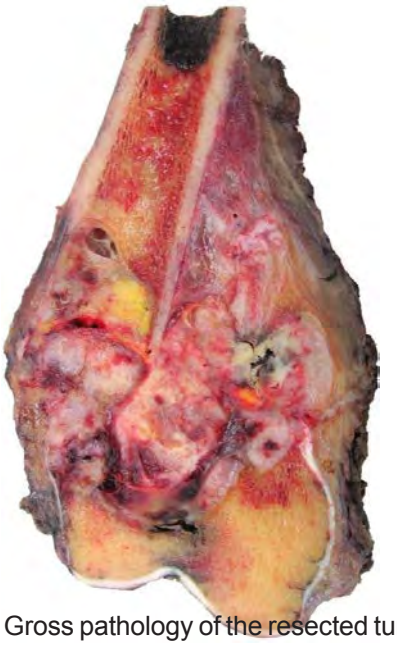
Results: Plain radiography showed a markedly expansile, aggressive, geographic, lytic, and poorly-defined lesion measuring 9x6.7cm in the distal aspect of the femur with lateral cortical destruction and associated pathological fracture at the proximal extent of the lesion. CT chest/abdomen/pelvis and PET scan revealed no primary lesions. Pathology from needle biopsy featured rhabdoid cells with no osteoid noted. Differential Diagnosis at the time included metastatic carcinoma of unknown origin with rhabdoid features vs. rhabdoid sarcoma. Histopathology obtained after right distal femur radical resection revealed osteoid, consistent with primary osteosarcoma with prominent rhabdoid cells. Staining for special AT-rich sequence-binding protein 2 (SATB2) was positive.

Conclusion: This case report presents the first case of primary osteosarcoma of bone with rhabdoid features in the literature, verified via histopathology and tissue-specific staining. Rhabdoid tumors have been previously identified in nearly every anatomical site in the body, and extraskeletal rhabdoid osteosarcomas have been twice presented in the literature; however this represents the first description of primary osteosarcoma of bone with rhabdoid features.

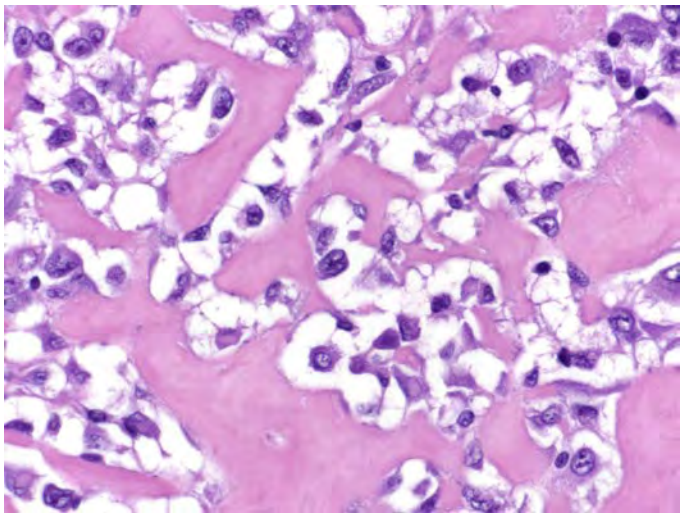


Pre-operative AP/Lateral radiographs showing an expansile, aggressive-appearing, lytic lesion of the distal femur with associated extra-articular pathologic fracture

Post-operative AP/Lateral radiographs status-post wide resection of the lesion and replacement with distal femoral endoprosthesis



Gross pathology of the resected tumor showing an aggressive lesion with expansion beyond the cortices of the distal femur and into the soft tissue, and new bone formation within the lesion



High resolution histopathology slide prominently featuring rhabdoid-appearing cells and the presence of osteoid-pathognomic for osteosarcoma.

P1 - Poster 110 2554640

IDENTIFICATION OF PATIENTS WITH LOCALIZED EWING SARCOMA AT HIGHER RISK FOR LOCAL FAILURE: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP

Safia K. Ahmed, MD[1]; William Harmsen[2]; Steven G. DuBois[4]; Mark Krailo[3]; Karen Marcus[7]; Katherine A. Janeway[4]; David Geller[10]; Joel Sorger[5]; Richard B. Womer[8]; Linda Granowetter[11]; Holcombe E. Grier[4]; Lor Randall[9]; Richard Gorlick[6]; Nadia N. Laack[1]

[1]Radiation Oncology, Mayo Clinic, Rochester, MN, USA; [2]Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA; [3]Preventative Medicine, University Of Southern California, Los Angeles, CA, USA; [4]Pediatrics, Dana-Farber/Boston Children's Cancer and Blood Disorders Center and Harvard Medical School, Boston, MA, USA; [5]Pediatrics, Cincinnati Children's Hospital, Cincinnati, OH, USA; [6]Pediatric Hematology and Oncology, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, USA; [7]Radiation Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center and Harvard Medical School, Boston, MA, USA; [8]Pediatrics, University of Pennsylvania Perelman School of Medicine and Children's Hospital of Philadelphia, Philadelphia, PA, USA; [9]Orthopedics, Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA; [10]Pediatrics and Orthopedic Surgery, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, USA; [11]Pediatrics, New York University (NYU) Medical School and NYU Langone Medical Center, New York, NY, USA

Objective: Reported local failure rates in modern Ewing sarcoma series range from 5%-25%. The variables associated with local failure (LF), particularly association between site and local control modality, are unclear. The purpose of this study is to identify clinical and treatment variables associated with higher risk of LF in patients treated on recent Children's Oncology Group protocols.

Methods: Localized, osseous Ewing sarcoma patients treated with ifosfamide and etoposide-based chemotherapy on Children's Oncology Group protocols from 1988-2005 with complete local control and relapse data were analyzed. Local control modalities [defined as surgery, radiotherapy only (RT), or surgery +RT] were assessed considering other events as competing risks, and variable associations assessed using method of Fine and Gray. Event-free survival (EFS) from the time of local control was estimated using Kaplan-Meier and variable associations assessed using the Cox model.

Results: The cohort included 956 patients, with a median age of 13 years and median follow-up of 77.4 months. Five-year EFS was 70.1% (95% CI, 67.2-73.1) and cumulative incidence of LF was 7.3% (95%, CI 5.6-8.9) for all patients. The five-year cumulative incidence of LF by local control modality was 15.3% for RT, 3.9% for surgery, and 6.7% for surgery+RT (Table 1). Significant univariate associations with an increased risk of LF included pelvic primary, age ≥18 years, and use of RT (compared to surgery+RT) (Table 1). Age ≥18 years and RT for local control remained significant on multiple variable analysis (Table 1). For patients treated with definitive surgery, age ≥18 years was associated with an increased risk of LF (HR 2.81; 95% CI 1.0-7.7). For patients treated with definitive RT, pelvic tumors were associated with a higher risk of LF (HR 2.1, 95% CI 1.1-4.0), with a five-year LF cumulative incidence of 16.3% (95% CI 10.0-30.7) compared to 10.9% (95% CI 5.6-16.0) for non-pelvic tumors. No clinical variables were associated with increased risk of LF in the surgery+RT subset. Tumor size (</≥12cm) was available in 383 patients (40.1%) and correlated with EFS but not local control for any modality.

Conclusion: Our analysis demonstrates older age, pelvic tumors, and use of definitive RT comprise the highest risk cohort for LF. Further efforts should focus on improving outcomes for these patients. Additional clinical and molecular variables are needed to help further identify subgroups requiring intensification of local therapy.

Table 1.
Five-year cumulative risk of local failure (LF), univariate analysis, and multivariate analysis of clinical and treatment variables associated with increased risk of LF.

Variable	Cumulative Risk of LF	Univariate Analysis		Multivariate Analysis	
	5-year (95% CI)	HR (95% CI)	p	HR (95% CI)	p
Age ≥18 years	11.9% (5.6-17.8)	1.97 (1.1-3.5)	0.02	1.86 (1.0-3.4)	0.04
RT only	15.3% (10.4-19.9)	2.43 (1.3-4.5)	<0.01	2.41 (1.3-4.4)	<0.01
Pelvis primary	13.2% (8.0-18.0)	2.23 (1.4-3.7)	<0.01	--	
Surgery	3.9% (2.2-5.7)	--		--	
Surgery + RT	6.7% (3.3-9.9)	--		--	

P1 - Poster 111 2554555

OUTCOME OF 114 OSTEOSARCOMA PATIENTS OLDER THAN 50 YEARS: A RETROSPECTIVE STUDY FROM THE FRENCH GROUP SARCOMA (GSF-GETO)

Pascaline Boudou-Rouquette[1]; David Blau[2]; Jean-Yves Blay[3]; Antoine Italiano[4]; François Gouin[5]; Olivier Mir[6]; Nicolas Penel[7]; Florence Duffaud[8]; Nelly Firmin[11]; Christine Chevreau[12]; Jean-Emmanuel Kurtz[13]; Sophie Piperno-Neumann[10]; François Goldwasser[1]; Frédérique Larousserie[9]; Philippe Anract[2]

[1]Medical Oncology, Cochin Hospital, Assistance Publique-Hôpitaux de Paris, Université Paris Descartes, Sorbonne Paris Cité, Paris, France; [2]Orthopedic surgery, Cochin Hospital, Assistance Publique-Hôpitaux de Paris, Université Paris Descartes, Sorbonne Paris Cité, Paris, France; [3]Medical Oncology, Centre Leon Bérard, Lyon, France; [4]Early Phase Trials and Sarcoma Units, Institut Bergonié, Bordeaux, France; [5]Orthopedic surgery, CHU Nantes, Nantes, France; [6]Medical Oncology, Gustave Roussy Institute, Paris, France; [7]Medical Oncology, Centre Oscar Lambret, Paris, France; [8]Medical Oncology, Hopital Universitaire La Timone, Aix Marseille University, Paris, France; [9]Pathology, Cochin Hospital, Assistance Publique-Hôpitaux de Paris, Université Paris Descartes, Sorbonne Paris Cité, Paris, France; [10]Medical Oncology, Curie Institute, Paris, France; [11]Medical Oncology, Institut du Cancer, Montpellier, France; [12]Medical Oncology, Institut Universitaire du Cancer Toulouse - Oncopole, Paris, France; [13]Medical Oncology, CHRU Strasbourg, Paris, France

Objective: To study the characteristics and outcome of osteosarcoma (OS) patients (pts) over 50 years-old. The optimal management and the benefit of neoadjuvant chemotherapy (CT) in OS pts older than 50 years are poorly documented.

Methods: Retrospective study from the French sarcoma network (RESOS and NetSarc) covering January 2000 to May 2015. Inclusion criteria were central pathological review of OS, high-grade, age over 50 years old at diagnosis. Out of 191 OS pts>50 years, 74 were excluded for missing data or low-grade OS (3).

Results: A total of 114 pts, from 19 sarcoma centers, were included. Median age was 63 years (range: 51.2 to 84.3), 52.6% male, 63% with Performance Status (PS) 0-1. Conventional OS was the most frequent (78 pts). Secondary OS represented 27%, mostly after irradiation. The most common primary tumor locations were limbs (38%), skull/face (18%) and pelvis (14%). At diagnosis, 9 pts (8%) had a pathologic fracture, 20% synchronous metastasis and 21% an unplanned initial surgical treatment. Eighty-six pts (75%) underwent surgery (72% had a limb salvage). Half of the pts (51%) received neoadjuvant CT. In this group, pts were younger ($p<0.0001$), had less unplanned initial treatment ($p<0.0001$). During neo-adjuvant CT, 13 pts (26.5%) had a good histological response to CT (≥ 90% tumor necrosis) and 32 pts (65.3%) a poor response, despite CT was not suboptimal. In the neo-adjuvant CT group, R0 resection was more frequent (71% of pts, $p<0.0001$). At last review, 61 patients had died, after a median follow-up of 17 months (Q1-Q3: 6-32). The overall survival (OS) probability rates at 2 and 5 years were 55% and 36%, respectively. The metastasis-free survival rates at 2 and 5 years were 50% and 46%, respectively. The local recurrence-free survival rates at 2 and 5 years were 70% and 62%, respectively. Parameters negatively influencing survival in univariate analysis were older age ($p<0.0001$), PS>2 ($p<0.0001$) and metastasis at diagnosis ($p=0.0026$). Pts who received both surgery and CT, regardless the order of the sequence, showed better OS ($p=0.00042$). In multivariate analysis, PS> 2 ($p=0.0089$) and metastasis at presentation ($p=0.095$) were the most important predictors of OS.

Conclusion: Pts older than 50 years with high-grade OS had a poor clinical outcome. This older age group is characterized by more axial skeleton and craniofacial bones primary site and a poor histological response to chemotherapy. The main predictors of OS were age, PS, metastasis at diagnosis and treatment received.

Table 1. Characteristics of the patients at presentation.

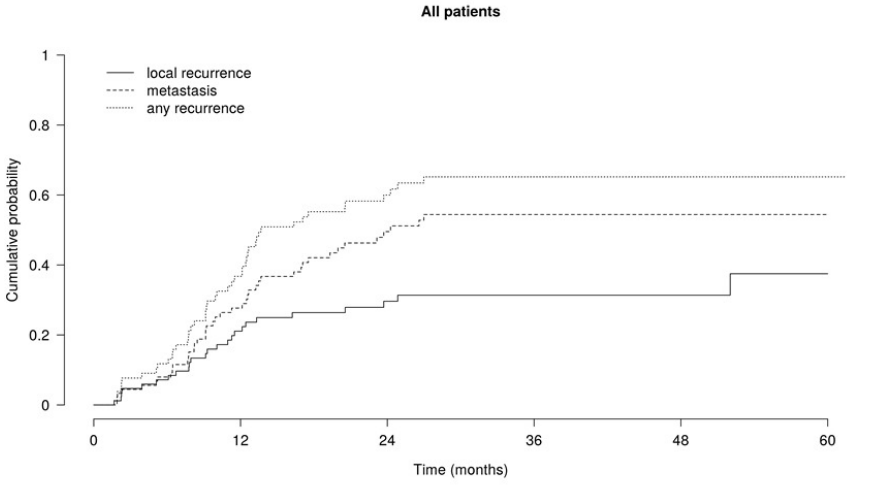
Characteristic	All patients (n=114)	Without neo-adjuvant chemotherapy group (n=56)	Neo-adjuvant chemotherapy group (n=58)	P*
Age, median (Q1-Q3)	63 (58 to 72)	69 (62 to 77)	60 (55 to 65)	<0.0001
Sex				0,2
female male	54 (47.4) 60 (52.6)	23 (41) 33 (59)	31 (53) 27 (47)	
BMI, median (Q1-Q3)	25 (23 to 28)	25 (22 to 27)	25 (23 to 30)	0,37
Performance status				
0 1 2 3 4	20 (18) 49 (45) 25 (23) 14 (13) 2 (2)	6 (11) 22 (41) 14 (26) 10 (19) 2 (4)	14 (25) 27 (48) 11 (20) 4 (7) 0 (0)	
Previous bone pathology				0,26
none irradiation Paget other	61 (54) 25 (22) 6 (5) 22 (19)	26 (46) 13 (23) 5 (9) 12 (21)	35 (60) 12 (21) 1 (2) 10 (17)	
Previous cancer				0,55
yes no	39 (34) 75 (66)	21 (38) 35 (62)	18 (31) 40 (69)	
Main symptom				0,22
pain mass fracture imaging	72 (63) 30 (26) 9 (8) 3 (3)	36 (64) 12 (21) 7 (12) 1 (2)	36 (62) 18 (31) 2 (3) 2 (3)	
Days from symptoms to diagnosis, median (Q1-Q3)	88 (30 to 212)	93 (29 to 202)	82 (32 to 212)	0,88
Days from diagnosis to treatment, median (Q1-Q3)	27 (14 to 49)	25 (10 to 45)	28 (16 to 54)	0,87
Days from symptoms to treatment, median (Q1-Q3)	126 (69 to 242)	122 (44 to 247)	129 (79 to 239)	0,82
Affected bone				0,39
skull/face humerus spine/sacrum pelvis femur tibia other	21 (18) 7 (6) 8 (7) 16 (14) 26 (23) 10 (9) 26 (23)	9 (16) 3 (5) 7 (12) 9 (16) 13 (23) 4 (7) 11 (20)	12 (21) 4 (7) 1 (2) 7 (12) 13 (22) 6 (10) 15 (26)	
Tumor histology				0,63
conventional OSA surface OSA other OSA	78 (68) 7 (6) 29 (25)	41 (73) 3 (5) 12 (21)	37 (64) 4 (7) 17 (29)	
Tumor size, median (Q1-Q3)	8 (6 to 11)	8 (5 to 11)	8 (6 to 11)	0,57
Soft-tissue invasion				>0.99
no yes	11 (10) 97 (90)	5 (10) 46 (90)	6 (11) 51 (89)	
Metastasis				<0.0001
no lungs \& other other	91 (80) 21 (18) 2 (2)	33 (61) 21 (36) 2 (4)	58 (100) 0 (0) 0 (0)	
Radiographic appearance				
blastic lytic mixed	12 (13) 60 (65) 21 (23)	6 (14) 28 (65) 9 (21)	6 (12) 32 (64) 12 (24)	
Adequate care				0,01
yes no*	89 (79) 23 (21)	38 (69) 17 (31)	51 (89) 6 (11)	

Continuous data are presented with mean and first to third quartile values (Q1-Q3); count data are presented with proportion and percentage. P-values refer to the comparison of patients “without neo-adjuvant chemotherapy” and “neo-adjuvant chemotherapy” groups, with Student’s t test for continuous data and Fisher’s exact test for count data. Adequate care: no* referred to patients who were misdiagnosed and received unplanned surgery.

Table 2. Characteristics of the treatments received.

Characteristic	All patients (n=114)	Without neo-adjuvant chemotherapy (n=56)	Neo-adjuvant chemotherapy group (n=58)	P*
Neoadj. chemotherapy*	58 (51)	0 (0)	58 (100)	
Doxorubicin Cisplatin Ifosfamide Etoposide Other	54 (96) 51 (91) 44 (79) 3 (5) 5 (9)		54 (96) 51 (91) 44 (79) 3 (5) 5 (9)	
Toxicity neoadj. chemo.*				
hospitalisation treatment modification other none	20 (36) 7 (12) 4 (7) 25 (45)		20 (36) 7 (12) 4 (7) 25 (45)	
Adjuvant chemotherapy*	41 (36)	15 (27)	26 (45)	0,053
Doxorubicin Cisplatin Ifosfamide Etoposide Other	21 (54) 10 (26) 31 (79) 18 (46) 4 (11)	13 (93) 5 (36) 11 (79) - 3 (25)	8 (32) 5 (20) 20 (80) 18 (72) 1 (4)	
Toxicity adj. chemo.*				
hospitalisation treatment modification other none	9 (23) 8 (21) 1 (3) 21 (54)	2 (14) 3 (21) 0 (0) 9 (64)	7 (28) 5 (20) 1 (4) 12 (48)	
Palliative chemotherapy*	12 (11)	12 (21)	0 (0)	
Doxorubicin Cisplatin Ifosfamide Etoposide Other	10 (83) 8 (67) 6 (50) 2 (17) 4 (33)	10 (83) 8 (67) 6 (50) 2 (17) 4 (33)		
Toxicity palliative chemo.*				
hospitalisation treatment modification none	4 (36) 4 (36) 3 (27)	4 (36) 4 (36) 3 (27)		
Surgery**	86 (75)	37 (66)	49 (84)	
primary limb-salvage	76 (89) 62 (72)	29 (81) 25 (68)	47 (96) 37 (76)	0,033 0,47
articular invasion	17 (24)	10 (34)	7 (17)	0,16
R0 R1 R2	50 (60) 23 (27) 11 (13)	15 (43) 9 (26) 11 (31)	35 (71) 14 (29) 0 (0)	<0.0001
Response to neoadj. chemo***				
poor good	32 (71) 13 (29)		32 (71) 13 (29)	
Radiotherapy for primary tumor	19 (17)	8 (14)	11 (19)	0,62
Adjuvant XRT Exclusive XRT Palliative XRT	11 (58) 6 (32) 2 (11)	4 (50) 2 (25) 2 (25)	7 (64) 4 (36) -	
Treatments				<0.0001
chemo. only surgery only xrt only surgery+chemo. chemo.+xrt surgery+xrt chemo.+surgery+xrt no treatment	15 (13) 18 (16) 3 (3) 56 (49) 4 (4) 2 (2) 10 (9) 6 (5)	10 (18) 18 (32) 3 (5) 14 (25) 0 (0) 2 (4) 3 (5) 6 (11)	5 (9) 0 (0) 0 (0) 42 (75) 4 (7) 0 (0) 7 (12) 0 (0)	

* indicates that proportion in subgroups are for patients who received chemotherapy.
** indicates that proportion are for patients who had surgery.
*** indicates that proportion are for patients who had surgery and neoadjuvant chemotherapy



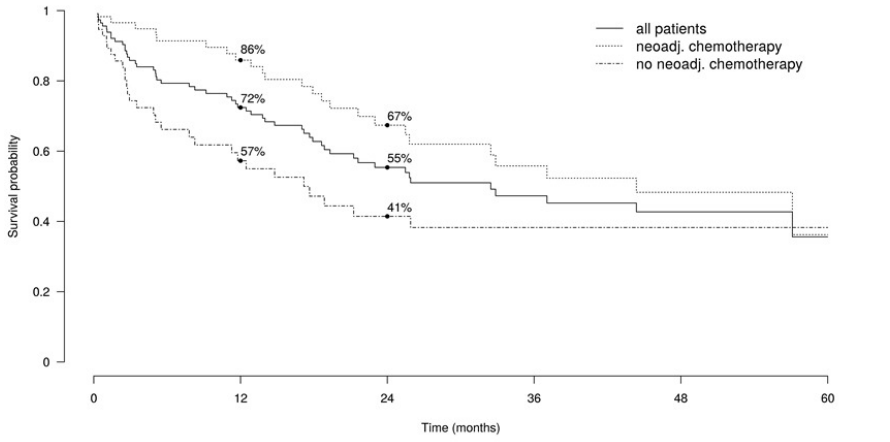


Figure 2: Univariable and multivariable regression models for overall survival. Estimates presented are cause-specific hazard ratio. P value are from log-rank and score tests

Variables	Hazard ratio	P values	Hazard ratio	P values
Age (in decades)	1.85 (1.36-2.52)	**<0.0001**	1.19 (0.78-1.8)	0,42
Performance status (>2)	2.97 (1.69-5.2)	**<0.0001**	2.49 (1.26-4.93)	0,0089
Previous bone pathology (irradiation/paget)	1.68 (0.94-2.99)	0,074	1.27 (0.62-2.61)	0,51
History of previous cancer (yes)	1.68 (0.97-2.9)	0,061	1.4 (0.7-2.83)	0,34
Affected bone (appendicular)	0.75 (0.43-1.3)	0,3	-	-
Tumor size (in cm.)	1.03 (0.98-1.09)	0,19	-	-
Time from symptom to treatment (in months)	1.01 (0.98-1.04)	0,49	-	-
Type of osteosarcoma (conventional OSA)	1.09 (0.61-1.95)	0,77	-	-
Metastasis at diagnosis (yes)	2.46 (1.34-4.49)	**0,0026**	1.83 (0.9-3.74)	0,095
Adequate care (yes)	0.79 (0.42-1.52)	0,49	-	-
Treatment (surgery and chemo.)	0.39 (0.22-0.67)	**0,00042**	0.89 (0.42-1.87)	0,76

P1 - Poster 112 2565259

INITIAL REPORTS OF EURO EWING 2012 AND REECUR - INTERNATIONAL RANDOMISED CONTROLLED TRIALS OF CHEMOTHERAPY FOR NEWLY DIAGNOSED AND RECURRENT/ REFRACTORY EWING SARCOMAS (ES)

Bernadette Brennan, MBChB MD[1]; Martin Mccabe[2]; Veronica Moroz[3]; Uta T. Dirksen[4]; Nathalie Gaspar[5]; Perrine Marec-Bérard[6]; Javier Martín[7]; Kirsten Sundby Hall[8]; Jukka Jukka Kanerva[9]; Hans Gelderblom[10]; Stefano Ferrari[11]; Sandra Strauss[12]; Jeremy Whelan[12]; Keith Wheatley[3]

[1]Paediatric Oncology, Royal Manchester Children's Hospital, Manchester, United Kingdom; [2]University of Manchester, Manchester, United Kingdom; [3]Cancer Research UK Clinical Trials Unit, Birmingham, United Kingdom; [4]Gesellschaft für Pädiatrische Onkologie und Hämatologie, Muenster, Germany; [5]Société Française de Lutte contre les Cancers et Leucémies de l'Enfant et de l'Adolescent, Paris, France; [6]Centre Léon Bérard, Lyon, France; [7]Grupo Español de Investigación en Sarcomas, Madrid, Spain; [8]Scandinavian Sarcoma Group, Oslo, Norway; [9]Helsinki University Central Hospital and University of Helsinki, Helsiniki, Finland; [10]European Organisation for Research and Treatment of Cancer, Brussels, Luxembourg; [11]Italian Sarcoma Group, Bologna, Italy; [12]University College Hospital london, London, United Kingdom

Objective: The Euro Ewing Consortium (EEC) programme supports two international clinical trials; Euro Ewing 2012 which aims to improve the outcomes for all newly diagnosed Ewing sarcomas by comparing VIDE versus VDC/IE induction chemotherapy strategy, and testing the role of the addition of zoledronic acid after induction chemotherapy, and the rEECur trial for recurrent and refractory ES which aims to identify the optimum chemotherapy regimen by comparing Topotecan/Cyclophosphamide (TC) and Irinotecan/Temozolomide (IT) and Gem-

citabine/Docetaxel (GD) and High dose Ifosfamide (IFOS). Here we report the initial recruitment, clinical variables, patient screening log for trial acceptability and reportable outcomes just under half way through the trial.

Methods: The data for each trial on eligibility screening, patient characteristics and treatment received was obtained from the study databases at a cut-off point of June 2016. Trial enrolment began in March 2014 for Euro Ewing 2012 and January 2015 for rEECur.

Results: EE2012 trial: 166 patients (83 in each arm) have been randomised to R1 and 50 to R2 (25 in each arm), from 4 European countries. For the R1 randomisation, the median age was 15 years (range 2 to 49), 55% male. Lung and/or pleural metastases were present in 18% (30 patients), tumour volume was < 200ml for 55%. 26% of patients were of pre-pubertal status. For the R2 randomisation, the proportion of male patients was slightly higher at 54% (27 patients). Lung and/or pleural metastases were present in 24% (12 patients) and 34% (17 patients) were localised disease poor risk patients. rEECur;65 patients (19 in TC, 17 in IT, 20 in GD and 9 in IFOS arm) have been randomised from 7 European countries. The median age was 20 years (range 5 to 49), 65% male. There were 22% (n=14) of primary refractory, 58% (n=38) with first recurrences and 20% (n=13) with second or subsequent recurrences. Sites of recurrence at trial inclusion were local only (n=14, 22%), pleuropulmonary (n=16, 25%), other metastatic (n=35, 53%).Majority of patients had measurable disease (n=59, 91%).

Conclusion: Despite the difficulties opening trials across multiple European countries, these data demonstrate that it is possible and importantly acceptable to patients, especially in the relapsed setting. These trial structures also allow further adaptation to add other therapeutic interventions and new agents as they become available, imperative to improve the outcomes in Ewing sarcoma.

P1 - Poster 113 2561930

TIMELINES ASSOCIATED WITH OPENING TWO CLINICAL TRIALS (EURO EWING 2012 AND REECUR) FOR EWING SARCOMA (ES) PATIENTS ACROSS EUROPE

Bernadette Brennan, MBChB MD[1]; Martin Mccabe[2]; Jennifer Anderton[3]; Perrine Marec-Bérard[4]; Uta T. Dirksen[5]; Javier Martín[6]; Kirsten Sundby Hall[7]; Jukka Jukka Kanerva[8]; Stefano Ferrari[9]; Hans Gelderblom[10]; Veronica Moroz[3]; Nicola Fenwick[3]; Sandra Strauss[11]; Jeremy Whelan[11]; Keith Wheatley[3]
[1]Paediatric Oncology, Royal Manchester Children's Hospital, Manchester, United Kingdom; [2]University of Manchester, Manchester, United Kingdom; [3]Cancer Research UK Clinical Trials Unit, Birmingham, United Kingdom; [4]Centre Léon Bérard, Lyon, France; [5]Gesellschaft für Pädiatrische Onkologie und Hämatologie, Muenster, Germany; [6]Grupo Español de Investigación en Sarcomas, Madrid, Spain; [7]Oslo University Hospital, Oslo, Norway; [8]Helsinki University Central Hospital and University of Helsinki, Helsiniki, Finland; [9]Italian Sarcoma Group, Bologna, Italy; [10]European Organisation for Research and Treatment of Cancer, Brussels, Luxembourg; [11]University Hospital College London, London, United Kingdom

Objective: The Euro Ewing Consortium (EEC) programme supports two international clinical trials; Euro Ewing 2012 first line trial in newly diagnosed Ewing sarcoma, and the rEECur trial for recurrent and refractory ES. Activating large international trials can be a complex process, so we assessed the timelines for trial setup and first patient recruited in 8 European countries participating in one or both trials.

Methods: The following trial set-up milestones were assessed: time taken to obtain the final signature on the National Coordinating Centre (NCC) and Sponsor agreement, date of submission to gaining regulatory approval, from regulatory approval to first patient randomised, and overall time from EEC project start to the first patient randomised in each country. These data were collected from all countries participating in one, or both, trials and which had recruited at least one patient (Czech Republic, Denmark, France, Hungary, Norway, Italy, Spain and UK). The Sponsor for both trials is the University of Birmingham, UK, and as such, a contract is not applicable for the UK.

Results: EE2012 opened for recruitment in December 2013. The time taken to obtain the final signature on the NCC and Sponsor agreement took a median of 237 days (range 99-247), from submission date to regulatory approval a median of 122 days (range 87-145), and from regulatory approval to first patient randomised a median of 233 days (range 98-414) in each country. This equated to a median of 661 days (range 519-960) from the EEC project start date to first patient randomised. rEECur

opened for recruitment in December 2014. The NCC and Sponsor agreements took a median of 102 days (range 92-203) to finalise, regulatory approval a median of 62 days (range 57-83) and from regulatory approval to first patient randomised a median of 163 days (range 73-368) in each country. This gave an overall median of 840 days (range 485-955) from the EEC project start date to first patient randomised.

Conclusion: This data shows that for trials working in accordance with the EU Clinical Trials Directive 2004, activating large European phase III trials remains a lengthy and complicated process and indicates that further streamlining would be beneficial and may lead to increased trial entry in a timely manner for patients with ES. Experience, however, from EE2012 setup shortened the process for the regulatory setup for rEECur.

P1 - Poster 114 2567959

CAN DENOSUMAB CHANGE THE TREATMENT PARADIGM FOR ANEURYSMAL BONE CYSTS (ABC)?

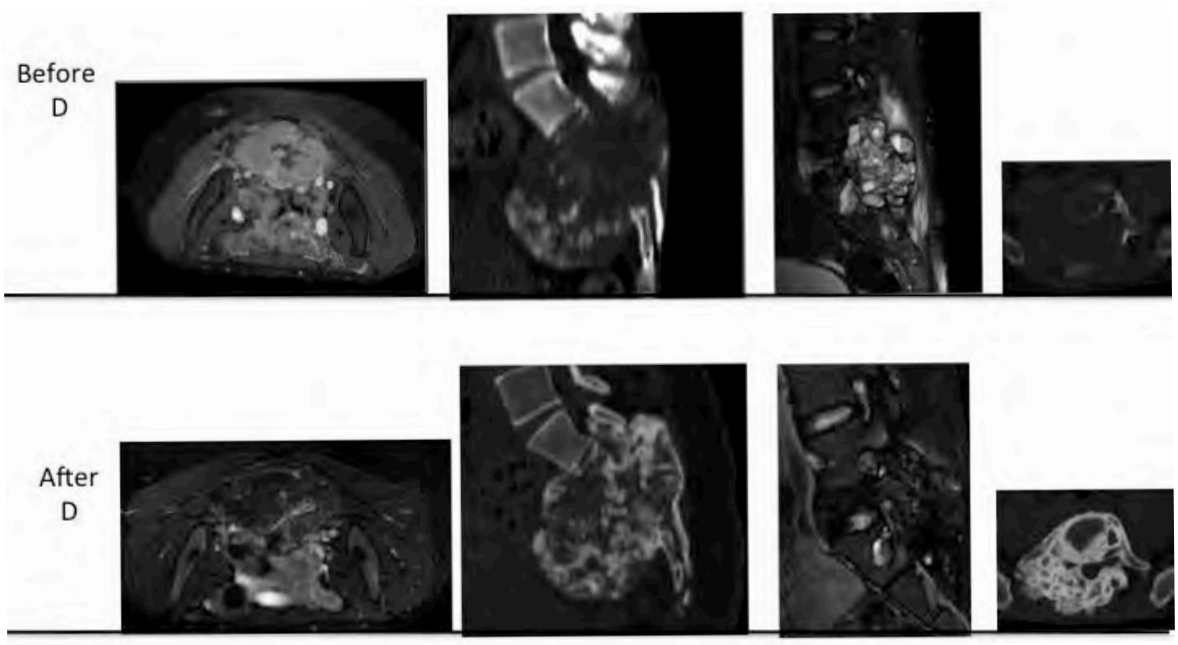
Emanuela Palmerini[1]; Stefano Boriani[1]; Pietro Ruggieri[2]; Domenico Campanacci[3]; Giuseppe M. Milano[4]; Marilena Cesari[1]; Anna Paioli[1]; Alessandra Longhi[1]; Massimo E. Abate[1]; Guido Scoccianti[3]; Silvia Terzi[1]; Giulia Trovarelli[1]; Piero Picci[1]; Stefano Ferrari[1]
[1]Istituto Ortopedico Rizzoli, Bologna, BO, Italy; [2]Università di Padova, Padova, Italy; [3]Florence University, Florence, Italy; [4]Ospedale Pediatrico Bambin Gesù, Rome, Italy

Objective: Aneurysmal bone cysts (ABCs) are rare skeletal tumors that most commonly occur in the first two decades of life. Treatment of ABCs involves surgery, curettage, selective arterial embolization, injection of fibrosing agents, or megavoltage radiotherapy. Treatment for spinal ABCs is associated with high risk of morbidity. Denosumab is a human monoclonal antibody that binds the receptor activator of nuclear factor-kappa B (NFKB) ligand (RANKL), and is approved for the treatment of osteoporosis, skeletal metastases, and giant cell tumor of bone (GCT). Due to immunohistochemical and clinical similarity and relationship between GCTs and ABCs, we hypothesized that denosumab was active in ABC.

Methods: We performed a retrospective analysis of ABC patients (pts) treated with denosumab, 120 mg sc on days 1, 8, 15, 29, and every 4-weeks thereafter. CT scan and/or MRI disease assessment was performed at 3, 6, 9 and 12 months for all pts, and all images were reviewed. We collected information on pain, symptoms and adverse events associated with denosumab.

Results: From October 2012 to July 2015, 7 pts were identified, 4/3 male/female, median age 16 years (range: 14-42 years). Primary site: spine-pelvis in 4 cases, 1 ulna, 1 tibia, 1 humerus. 2 pts received preoperative denosumab. With a median follow up of 12 months (range 10-44), the median number of demosumab administrations was 14 (range 10-50). Outcome: 4/4 pts had pain decrease on the 11-point scale. 1 pt had paresthesia improvement. Responses were observed after 3 to 6 months of denosumab: 1) radiological evidence of bone formation at CT scan was demonstrated in 6/6 evaluable pts; 2) MRI gadolinium contrast media decrease was showed in 4/5 pts. Sustained tumor control was demonstrated in all pts (RECIST does not apply, due to disease site within bone and massive denosumab-induced calcification) (Figure 1). Side effects: Vomiting Gr in 1 pts. None of the pts developed osteonecrosis of jaw (ONJ), nor were abnormal laboratory findings seen such as hypocalcemia.

Conclusion: Denosumab has substantial activity in ABCs, with favorable toxicity profile. We propose a prospective trial to confirm the activity we have noted here.



Denosumab induced bone calcification (CT scan) and contrast medium decrease (MRI) in four aneurismal bone cyst (ABC) patients: baseline images (Before D) and radiologic assesment at 3 months (After D)

P1 - Poster 115 2559023

DENOSUMAB-INDUCED RANK-RANKL PATHWAY CHANGES IN RESECTABLE GCT

Maria Serena Benassi, PhD; Irene Quattrini; Laura Pazzaglia; Laura Campanacci; Piero Picci; Stefano Ferrari; Emanuela Palmerini
Oncology, Istituto Ortopedico Rizzoli, Bologna, Italy

Objective: Giant cell tumor of bone (GCT) is an osteolytic lesion with mononuclear proliferating cells that produce membrane and soluble RANKL. RANKL binds RANK expressed on osteoclast precursors inducing osteoclast differentiation and bone matrix degradation. RANK-RANKL axis has an indirect effect on bone tumor development through a vicious circle controlled by growth factors, cytokines and proteolytic enzymes. Aim of this study is to evaluate if the use of Denosumab, an antibody targeting RANK-RANKL pathway, may reduce the expression of downstream molecules involved in tumor cell - bone matrix interaction and proliferative activity.

Methods: Protein expression was evaluated by immunohistochemistry on Tissue Microarray sections of 15 GCT patients before and after Denosumab treatment. The proteins analysed were RANK (SANTA CRUTZ, sc-9072), RANKL (ABCAM, 12A668), TRAF6, NFIB, TGFβ, IL-1a, IL-6, CAII, BGLAP, FN, c-FOS, MMP-2, MMP-9 following the manufacturer's protocol. Positive controls were included for each antibody and negative controls were prepared omitting the primary antibody.
Staining was scored by intensity (1=weak to moderate expression; 2=strong expression) and by percentage of positive cells (0=less than 10%; 1=10–25%; 2=26–50%; 3= more than 50%). The sum of scores resulted as 1–3 for weak positivity, while 4–5 for moderate to strong positivity was considered as protein overexpression.

Results: Our results demonstrated a moderate to strong expression (score 4-5) of the studied proteins in all GCT patients before treatment. After treatment, the complete disappearance of osteoclast-like cells was accompanied by loss of RANK expression and reduction of TGFβ, IL-1a, NF1B and NF-KB positivity (score 1-3). RANKL expression showed an inter-patient variability. In addition, concomitant negative immunoreactivity of proteolytic enzymes MMP-2 and CAII was observed in the majority of post-Denosumab GCT patients.

Conclusion: Our preliminary results indicate that pre-Denosumab GCT patients present a high expression of molecules involved in tumor cell–bone matrix interaction, also affecting cell proliferative activity.
By targeting the RANK-RANKL axis with Denosumab, the expression of some of these molecules significantly decreased revealing new interconnection end-points between bone remodelling and tumor cell activity useful for further biological studies.

P1 - Poster 116 2569562

PROTEIN EXPRESSION PROFILES CORRESPONDING TO HISTOLOGICAL CHANGES WITH DENOSUMAB TREATMENT IN GIANT CELL TUMORS OF BONE

Yoshiyuki Suehara[1]; Kenta Mukaihara[1]; Yu Tanabe[1]; Shinji Kohsaka[2]; Saiko Kazuno[3]; Midori Ishii[1]; Keisuke Akaike[1]; Daisuke Kubota[1]; Kazuo Kaneko[1]; Tsuyoshi Saito[4]
[1]Department of Orthopedic Surgery, Juntendo University School of Medicine, Tokyo, Japan; [2]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [3]Laboratory of Biochemical Analysis, Central Laboratory of Medical Sciences, Juntendo University School of Medicine, Tokyo, Japan; [4]Department of Human Pathology, Juntendo University School of Medicine, Tokyo, Japan

Objective: Giant cell tumors of bone (GCTB) are locally aggressive osteolytic bone tumors. Recently, some clinical trials have shown that denosumab is a novel and effective therapeutic option for aggressive and recurrent GCTB. Histologically, the post-denosumab-treated samples were characterized by two lesions: the residual stromal cell lesion with a few multinucleated giant cells (SL-lesion), and a fibro-osseous lesion (FO-lesion). Our recent study determined the protein expression profiles of clinical samples obtained both pre- and post-treatment with denosumab in GCTB (Mukaihara K et al. *PLOS ONE*). In that study, we examined only the SL-lesion samples obtained post-treatment with denosumab; as such, the protein expression profiles and functional networks of the FO-lesions have yet to be evaluated. In the present study, to clarify the differences in the protein expression between the SL-lesion and FO-lesion in GCTB treated with denosumab, we conducted comparative proteomic studies using both lesions.

Methods: We collected 10 pairs of pre- and post-denosumab treatment samples from 4 patients to determine the protein profiles of GCTB associated with denosumab treatment. Histologically, we found that 8 out of 10 post-treatment samples consisted of the SL-lesions, while 2 post-treatment samples consisted of FO-lesions. We used i-TRAQ and applied the Ingenuity Pathways Analysis (IPA) system to identified protein profile and critical pathways.

Results: The proteins extracted from the pairs were analyzed using the i-TRAQ method. The analyses identified approximately 2000 proteins in each sample. In the SL-lesions, we found 32 consistently regulated proteins among the 8 pairs of profiles. In the FO-lesions, we identified 37 consistently regulated proteins in the 2 pairs of profiles. As common proteins between the SL-lesion and FO-lesion profiles, we found 8 consistently upregulated and 16 consistently downregulated proteins. In the network analyses using the IPA system, we identified several key proteins whose upstream regulators play a critical functional role in the RANKL pathway.

Conclusion: We conducted proteomic analyses of GCTB treated with denosumab and successfully identified several proteins based on the characteristic histological changes in post-treatment with denosumab. We believe that the identified proteins and the results of the network analysis will help to clarify the effects of denosumab treatment on GCTB.

P1 - Poster 117 2562256

GIANT CELL TUMOR OF THE PROXIMAL FEMUR HAS A HIGHER LOCAL RECURRENCE RATE COMPARED TO OTHER SITES AFTER CURETTAGE AND PACKING THE BONE CAVITY WITH CEMENT OR BONE ALLOGRAFTS

Costantino Errani, MD, PhD; Giulio Leone; Luca Cevolani; Alberto Righi; Marco Gambarotti; Davide Donati
Musculoskeletal Oncology, Istituto Ortopedico Rizzoli, Bologna, Italy

Objective: The purpose of our study was to identify possible risk factors of patients with GCT of the long bones after curettage and packing the bone cavity with bone cement or bone allografts.

Methods: We retrospectively reviewed the records of 249 patients with GCT of the limbs treated at Musculoskeletal Oncology Department of our institution between 1990 and 2013, confirmed histologically and recorded in the Bone Tumor Registry. We reviewed 219 cases located in the lower limb and 30 of the upper limb. This series includes 135 females and 114 males, with mean age 32 years (ranging 5 to 80 yrs). According to Campanacci's grading system, 190 cases were stage 2, 48 cases stage 3, and 11 cases stage 1. Treatment was curettage (intralesional surgery). Local adjuvants, such as phenol and cement, were used in 185 cases; whereas in the remaining 64 cases the residual cavity was filled with allografts or autografts only.

Results: Oncological outcome shows 203 patients alive and continuously disease-free (CDF), 41 patients NED1 after treatment of local recurrence (LR), 2 patients NED1 after treatment of lung metastases, 2 AWD with lung metastases. One patient died of unrelated causes (DOD).
LR rate was 15.3% (38 pts). Lung metastases rate was 1.6% (4 pts). In patients treated by curettage and cement (185 cases) LR was 12% (22 pts). Conversely, in patients treated curettage and bone allografts it was higher (16/64 cases), with an incidence of 25% of cases (p=0.004). Oncological complications seemed to be related with site, more frequently occurring in the proximal femur (p=0.037). LR occurred only in stage 2 or 3 tumors without statistical significance (p>0.05). The mean interval between the first surgical treatment and LR was 22 months (range: 3-89 mos). However, in the multivariate analysis no significant statistical effect on local recurrence rate could be identified for gender, patient's age, Campanacci's grading, or cement vs allografts. The only independent risk factor related to the local recurrence was the site, with a statistical significance higher risk for patients with GCT of the proximal femur (p= 0.008).

Conclusion: Our observation on the correlation of tumor location and risk of local recurrence is new. Therefore, special attention must be given to GCTs in the proximal femur. In fact, primary benign bone tumors in the proximal femur are difficult to treat due to the risk of secondary osteonecrosis of the femoral head or pathologic fracture.

P1 - Poster 118 2570264

DENOSUMAB AS STAND-ALONE TREATMENT IN GIANT CELL TUMOR OF BONE

Sandra Santos, Resident; Ruben Fonseca; João Freitas; Paulo F. Tavares; Jose M. Casanova
Ortopedia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

Objective: Giant cell tumor (GCT) of bone is a common benign skeletal tumor. It is locally aggressive, and the mainstay of treatment has been surgery, often associated with significant recurrence rates and/or morbidity. Denosumab, a monoclonal antibody that targets the osteoclastic activity of GCT, has been in use as a potential adjuvant therapy. However, there is few data available on its use as a stand-alone treatment, as well as on the necessary treatment duration.

Methods: We reviewed clinical data and outcomes regarding patients with histological diagnosis of GCT treated with denosumab at our institution. Denosumab was administered at monthly intervals (120 mg subcutaneously), with additional doses on days 8 and 15 during the first month of therapy only; all patients were prescribed calcium and vitamin D supplementation. Disease status and clinical benefit were assessed based on monthly physical examination, patient reporting and periodic imaging assessment.

Results: A total of 10 patients were identified, 6 female (60%). Median age was 39 (25–81) years. Only 4 patients presented with appendicular skeleton lesions; the remaining had GCT located to the spine and pelvis. The majority (70%) of patients presented with primary GCT, and 30 % had recurrent tumor following previous curative intent procedures. Primary complaint at presentation was pain. 70% of patients had a Campannaci classification III tumor, and all patients had a grade 3 Enneking staging tumor. Patients were treated with denosumab for a median duration of 38 (19–72) months. Only one patient in this group had surgery with curative intent, due to recurrent pain and functional limitation; follow-up showed no recurrence and good function. The remaining patients had significant pain relief and functional improvement. In all cases, there was

radiological evidence (serial radiographs and CT scans) of denosumab efficacy.

Conclusion: Only one patient in our group underwent surgical treatment, with good results and no recurrence to date. The remaining patients, most presenting with tumor locations in which surgery would lead to significant morbidity, are presently symptom free, with no local disease progression. These results support the notion that denosumab therapy may represent an important option for patients with resectable GCT, to control disease and achieve equivalent outcomes with less morbid procedures or even no surgery, and in unresectable tumors, to allow for disease control and symptomatic relief.

P1 - Poster 119 2567761

BONE TURNOVER MARKERS IN A PHASE II STUDY OF DENOSUMAB IN GIANT CELL TUMORS OF BONE (GCTB): CAN WE USE IT BETTER?

Emanuela Palmerini; Loredana Pratelli; Maria Serena Benassi; Annalisa Nobile; Emanuela Marchesi; Laura Campanacci; Eric Staals; Davide Donati; Piero Picci; Stefano Ferrari
Istituto Ortopedico Rizzoli, Bologna, BO, Italy

Objective: Giant cell tumors of bone (GCTB's) are RANK-ligand (RANK-L) positive, aggressive osteolytic tumors. Denosumab, a RANK-L inhibitor, was FDA-approved for adults and skeletally mature adolescents with GCTBs that is unresectable or where surgical resection is likely to result in severe morbidity. Data on serum bone turnover markers (BTM) changes on long-term "denosumab monthly "GCTB's-schedule" (120 mg per 12/year, 1440 mg total dose/year) are lacking. We present a 6-year phase II correlative study, conducted in 1 referral center.

Methods: Methods: All GCTB's patients receiving denosumab, 120 mg on days 1, 8, 15, 29, and every 4-weeks thereafter, from 2006 to 2015, were prospectively assessed for serum level of carboxyterminal crosslinked telopeptide of type I collagen (s-CTX), alkaline phosphatase (ALP), bone alkaline phosphatase (bALP), parathyroid hormone (sPTH), and osteocalcin (OCN). Serum sample were taken at the baseline and repeated at 3 months intervals. Serum BTM changes and progression free survival (PFS) were analyzed.

Results: Fifty-four cases identified (3 case with lung only disease were excluded), male/female 24/30, median age 37 years (range: 17-76 years), 37/54 resectable; primary tumor sites: radium 15/54, sacrum + pelvis 11/54, tibia 13/54, femur 7/54, other sites: 8/54. Serum markers are displayed in the table below (Table 1).

With a median follow-up of 39 months (range 15-84), the 3 years progression free survival (PFS) was 67% (%CI 55-80), with significant worse outcome for patients with *high* (≥ 500 UI/ml) s-CTX at baseline, as compared to *low* s-CTX (< 500 UI/ml) (3-year PFS for *high* CTX was 50% (95%CI 29-73) vs 75% (95%CI 59-91) for low s-CTX. No difference in 3-year PFS according to ALP, bALP, sPTH, OCN was demonstrated.

Conclusion: The use of denosumab in patients with GCTB's induces a generalized reduction in bALP, ALP, OCN and s-CTX with a concomitant increase of sPTH. High baseline s-CTX, a marker of bone resorbtion, identifies a group of patients at higher risk of progression of the disease.

Table 1. Bone turnover markers @baseline, 3, 6, 9, and 12 months of denosumab in GTB

	Baseline median UI/ml (range)	3 months median	6 months median	9 months median	12 months median
s-CTX (pg/ml)	458 (23-1692)	43 (10-189)	49 (10-141)	51 (10-106)	54 (12-87)
ALP (U/l)	82 (43-411)	55 (25-168)	51 (24-149)	49 (24-70)	55 (22-94)
bALP (µg/l)	13 (5-49)	7 (4-17)	6 (1-26)	7 (3-16)	6 (3-10)
sPTH (pg/ml)	30 (7-101)	41 (11-107)	44 (20-92)	37 (10-138)	47 (8-118)
OCN (ng/ml)	23 (3-47)	11 (3-26)	10 (1-20)	10 (4-16)	9 (5-16)

serum carboxyterminal crosslinked telopeptide of type I collagen (s-CTX), alkaline phosphatase (ALP), bone alkaline phosphatase (bALP), parathyroid hormone (sPTH),and osteocalcin (OCN)

P1 - Poster 120 2570499

PIGMENTED VILLONODULAR SYNOVITIS (GIANT-CELL TUMOR OF TENDON SHEATH) RESULTS OF SURGICAL AND ADJUVANT THERAPY

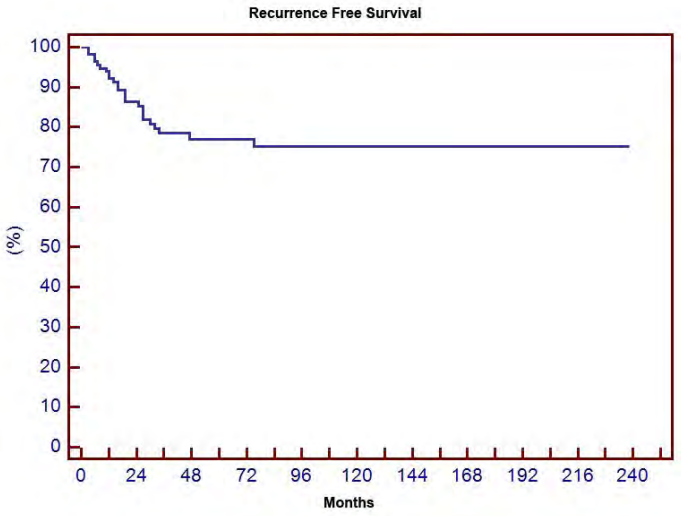
Carl F. Capellen[1]; Reinhold Tiling[2]; Alexander Klein[1]; Andrea Baur-Melnyk[3]; Thomas Knösel[4]; Volkmar Jansson[1]; Hans R. Dürr[1]
[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany; [2]Department of Nuclear Medicine, LMU Munich, Munich, Germany; [3]Institute of Radiology, LMU Munich, Munich, Germany; [4]Institute of Pathology, LMU Munich, Munich, Macao

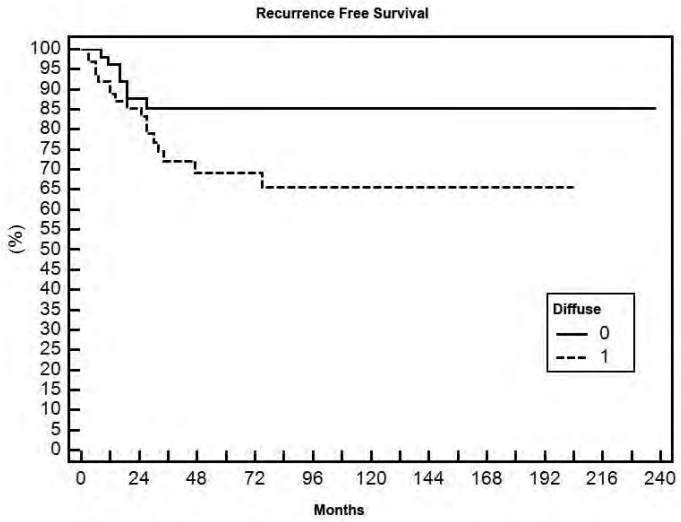
Objective: Pigmented Villonodular Synovitis (PVS) is a rare proliferative lesion of the synovium, affecting mainly younger patients. The standard therapy is resection or synovectomy. Local recurrence is common. Aim of this study is to describe symptoms, surgery and the impact of adjuvant therapy on outcome in a single centre study.

Methods: Between 1996-2014 114 resections in 97 patients had been done. The mean age of 64 women and 59 men was 39,9 years (13-77 years). The most common site was the knee in 60 cases, followed by the foot in 17, hand in 13 and ankle in 9 cases. Each 4 cases were located in the elbow and hip joint, individual cases in other sites. 62 cases had a diffuse, 52 cases a nodular lesion. The mean follow-up time was 68,7 months (13 – 238 months).

Results: The symptoms were pain in 54%, swelling in 40%, effusion in 12%, restriction of movement in 3% and findings by follow-up in 22 %. 24 cases (21%) developed local recurrence. Of the 97 patients currently 92 are free of recurrence (94.8%). For that 78 of these patients needed 1 surgery, 11 2 surgeries, 2 3 surgeries and one patient had 5 surgeries. 5 patients currently have a relapse and have so far received no further surgery/therapy. Despite 2 recurrences all occurred in the first 3 years (Fig. 1). Diffuse forms showed a significantly increased recurrence rate (Fig. 2), (27% vs 13%). In 28 cases we performed adjuvant radiosynoviorthesis, 24 of them at the knee joint. In a total of 33 cases with diffuse knee involvement RSO was performed in 24 cases. The risk of local recurrence with RSO was 25%, without RSO 33% (n.s.).

Conclusion: Overall, the treatment of nodular PVS shows a good result, if recurrences occurred, then preferably at tendon regions as in hand or foot. The diffuse form had with 27% a significantly increased risk of recurrence. RSO decreased that risk (studied at the knee), but this was not significant. A low dose percutaneous radiotherapy was performed only in one case achieving stable disease over years. In 95% of the cases local recurrence was not evident at follow up, but that needed up to 5 surgeries.





P1 - Poster 121 2544543

THE SURGICAL COMPLICATIONS OF THE TENOSYNOVIAL GIANT CELL TUMOUR OF THE FINGER

Michihito Miyagi, MD, PhD[2]; Yoji Shido[2]; Kaori Sugiura[1]; Ryosuke Furuhashi[1]; Takao Omura[2]; Hiroaki Ogihara[1]
[1]Orthopedics Surgery, Hamamatsu Red Cross Hospital, Hamamatsu, Shizuoka, Japan; [2]Orthopaedics Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan

Objective: The tenosynovial giant cell tumor (TsGCT) is the benign tumor which occurs predominantly in the hand. The tumor is known the recurrence rate is high, but the postoperative complications are unknown.We retrospectively analyzed the postoperative complications and recurrence rate of TsGCT of the finger**.**

Methods: Twenty five patients with TsGCT who underwent resection 2002 and 2015 were included in this study. There were nine males and sixteen females with a mean age of

48 years (range, 8-77). The average follow-up period was 41 months (range, 12-115). We retrospectively analyzed the clinical data for each patient, including the tumor share to the diameter around the finger, the recurrence rate, the finger nerve disorder, and functional results.

Results: The tumors less than half around the finger are 11 cases, more than half around finger are 14. The 4 had the finger nerve disorders in more than half around the finger (36%). There were no finger nerve disorders in less than half (p=0.04). There were 4 local recurrence during follow-up (16%), the three cases in more than half around the finger. The limitation of range of motion (ROM) of the affected joint progressed from preoperative in 4 cases (16%).

Conclusion: When the tumor share to the diameter around the finger becomes more than 1/2, the possibility of the finger nerve damage become high and the finger nerve disorder remains in the high rate. The recurrence rate and the tumor share to the diameter around the finger didn't have relation. There is ROM limitation aggravated, so we needs a long-range follow-up.

P1 - Poster 122 2570766

CLINICAL AND HISTOLOGIC RISK FACTORS FOR LOCAL RECURRENCE AND SURVIVAL IN CHORDOMA

Kamil M. Amer, BS (MD in progress)[1]; Bryan Hozack[4]; Stacey Mardekian[2]; Atrayee BasuMallick[3]; Mitchell Maltenfort[4]; Wei Jiang[2]; John A. Abraham[4]
[1]Temple University Lewis Katz School of Medicine, Philadelphia, PA, USA; [2]Pathology, Thomas Jefferson University Hospital, Philadelphia, PA, USA; [3]Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, PA, USA; [4]Orthopedic Surgery, Thomas Jefferson University Hospital, Philadelphia, PA, USA

Objective: Chordoma is a rare locally aggressive malignant spinal neoplasm derived from notochordal tissue. Local recurrence rate of chordoma is very high. The purpose of this study is to identify and analyze both patient clinical and tumor histological variables and determine if they are associated with the increased risk of recurrence or decreased survival from a clinicopathologic series of chordoma patients.

Methods: We retrospectively analyzed the records of 60 patients diagnosed with chordoma with a total of 94 available pathology specimens between 1990 and 2014, who underwent treatment at our institution. Clinical variables, pathology variables, and outcome parameters used are shown in Table 1. These variables were analyzed using Log-rank tests to identify factors affecting survival paramaters.

Results: There were 60 patients with an average follow-up time period of 62.5 months (1-237 months). All patient demographic, clinical, tumor, and survival outcome data can be found in Table 2. There were 2 out of 3 patients that had local recurrences prior to developing metastases. Of the patients with resection surgery, 1 out of 10 patients (10%) had a local recurrence with a disease free interval of 57.1 months. Of the patients presenting with primary disease with local recurrence, 1/9 (11.1%) had wide margin resection at the time of original treatment and 8/9 (88.9%) had intra-lesional margin resection (p=0.01). Using the log rank model, the only two variables that approached significance with respect to increased local recurrence were No radiation therapy (p=0.12) and tumor heterogeneity (p=0.11). Disease specific survival was 49.8 months (2-149) The overall survival was 52.7 months (1-252 months).

Conclusion: The main difficulty in treating chordoma is the high rate of local recurrence. Identifying the risk factors associated with recurrence of chordoma is critical in guiding both the management and surveillance in these patients. This study represents the largest clinicopathologic series on chordoma in the current literature. In our study, local recurrence had a significant negative impact on overall survival, and patients with wide margins had better survival. Our findings also suggest a trend toward significance of use of radiation therapy decreasing local recurrence, and tumor heterogeneity is associated with increased local recurrence. Further study will be needed to confirm these results. Limitations include small sample size, retrospective, and large percentage of intra-lesional procedures.

Table 1

Clinical Variables	Pathology Variables	Outcome Parameters
Age	Tumor Size	Rate of Recurrence
Gender	Histological Sub-type	Rate of Metastasis
Race	Tumor Heterogeneity	Overall Survival (OS)
Anatomical Site	Nuclear Atypia	Disease Free Survival (DFS)
Radiation Therapy Use	Mitotic Activity	Disease Specific Survival (DSS)
Chemotherapy Use	Cellularity	
Resection Margins	Necrosis	

Table 2.

Clinical Variables		
Age (years)		56.4 (19-83)
Gender (M : F)		1.3 : 1
Race	Caucasian	50 (83.3 %)
	African American	4 (6.7 %)
	Other	6 (10 %)
Anatomical Site	Clivus/Skull	25 (41.7 %)
	Cervical Spine	8 (13.3 %)
	Thoracic and Lumbar Spine	15 (25.0 %)
	Sacrococcygeal	12 (20.0 %)
Neo-adjuvant Therapy		
Radiation Therapy		31 (51.7 %)
Tumor Data		
Tumor Size (cm)		5.2 (1.6 - 15.0)
Histological Sub-type	Classic	81 (86 %)
	Chondroid	11 (12 %)
	De-differentiated	2 (2 %)
Pathologic Variables	Tumor Heterogeneity	18 (19 %)
	Nuclear Atypia	18 (19 %)
	Cellularity	53 (56 %)
	Mitotic Activity	53 (56 %)
	Necrosis	24 (26 %)
	Giant Cells	46 (49 %)
Surgical Outcomes		
Resection Margins	Wide	8 (20 %)
	Marginal	2 (5 %)
	Intra-Lesional	30 (75 %)
No Surgical Data		20
Biopsy Only		5

Figure 1. Histologic features of chordoma.

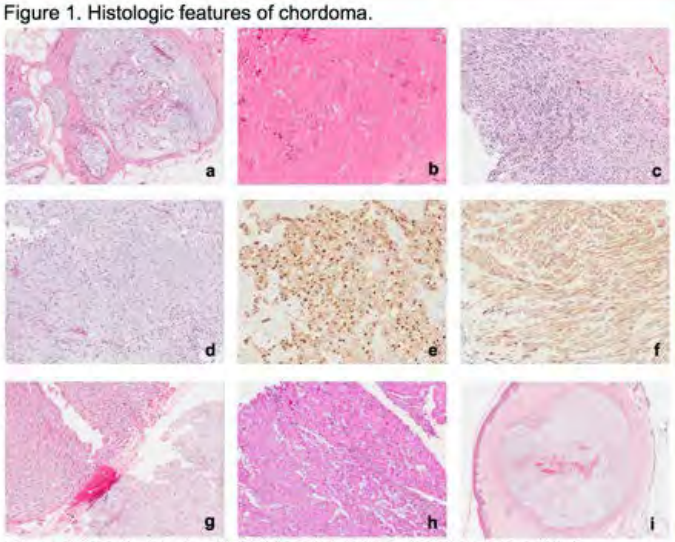
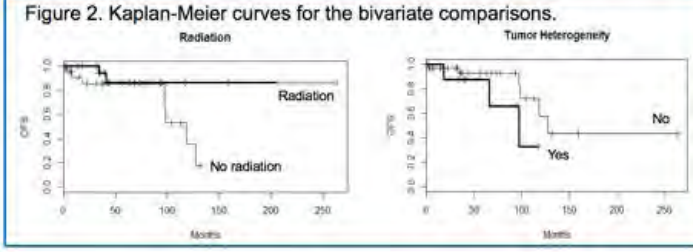


Figure 1. Classic (a), chondroid (b), and de-differentiated chordoma (c). In de-differentiated chordoma, the brachyury nuclear staining is lost (f), whereas the well-differentiated component (d) maintains the staining (e). Heterogeneity defined as significant difference in histologic type, cellularity (g), and/or cytologic atypia (h). Metastatic chordoma to skin dermis (i).

Figure 2. Kaplan-Meier curves for the bivariate comparisons.



	Bivariate log rank	Full Cox
Gender	0.103	0.219
Age	0.742	0.325
Race (non-white)	0.497	0.228
Tumor size	0.149	0.485
Anatomic site	0.680	0.758
Radiation	0.117	0.227
Tumor type	0.440	0.958
Tumor heterogeneity	0.109	0.660
Cellularity	0.921	0.561
Nuclear atypia	0.455	0.214
Mitotic activity	0.173	0.985
Necrosis	0.211	0.938

P1 - Poster 123 2555566

RESPONSE TO CHECKPOINT INHIBITION IN A PEDIATRIC PATIENT WITH METASTATIC REFRACTORY CHORDOMA

Steven J. Jonas, MD, PhD[1]; Caroline J. Gross[1]; Mitchell Kamrava[2]; Arun S. Singh[3]; Jeffrey Goldstein[4]; Nicholas Bernthal[5]; Frederick C. Eilber[6]; Erlinda M. Gordon[7]; Sant P. Chawla[7]; Noah Federman[1]
[1]Pediatric Hematology/Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [2]Radiation Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [3]Medicine, Hematology & Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [4]Pathology and Laboratory Medicine, University of California, Los Angeles, Los Angeles, CA, USA; [5]Orthopaedic Surgery, University of California, Los Angeles, Los Angeles, CA, USA; [6]Surgical Oncology, University of California, Los Angeles, Los Angeles, CA, USA; [7]Sarcoma Oncology, Cancer Center of Southern California, Santa Monica, CA, USA

Objective: This case describes the first reported use of the anti-programmed cell death-1 antibody (PD-1) immune checkpoint inhibitor Nivolumab in an 11 year old male with history of recurrent, refractory chordoma of the clivus with metastatic spread to the scalp, chest wall, and right lung. The patient's primary lesion was treated initially via surgical resection and proton beam radiation with subsequent disease recurrence and progression treated with surgical resection and adjuvant sirolimus and imatinib. PD-1 expression of the tumor was identified by molecular profiling (Caris Life Sciences, TX), which suggested the potential role for novel checkpoint inhibitor agents to achieve disease control.

Methods: Nivolumab was provided through a patient access program (Bristol Meyers Squibb, NY). Nivolumab was administered via infusions at 3 mg/kg in 14 day cycles. Metastatic disease burden was monitored by PET-CT after 7 cycles of therapy. Response to treatment was evaluated by Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 and Immune-Related Response Criteria (irRC) through comparison of pre- and post-treatment imaging.

Results: Interval reduction in size was observed in index metastatic lesions located at the right lower lobe and along the patient's right chest wall upon initiation of nivolumab. The right lower lobe mass, which measured 30x27 mm initially, was noted to decrease to 20x20 mm after 14 weeks, indicating a partial response. In addition, two palpable lesions traversing the right chest wall were found to have a complete response noticeable within the first 4 weeks. The lesions all displayed persistent FDG avidity that we hypothesize represents immune infiltration at the tumor. A third mass at the right superior chest wall demonstrated stable disease.

Conclusion: To our knowledge this case report represents the first demonstration of immune checkpoint inhibitors to treat recurrent, refractory metastatic chordoma, which emphasizes the potential benefit to further clinical investigation of these novel agents in this rare sarcoma.

P1 - Poster 124 2569944

TRENTO PROTON THERAPY CENTRE INITIAL EXPERIENCE FOR SPINE CHORDOMA, CHONDROSARCOMA AND OTHER SARCOMAS

Irene Giacomelli; Daniele Scartone; Marco Cianchetti; Francesco Dionisi; Dante Amelio; Barbara Rombi; Sabina Vennarini; Francesco Fracchiolla; Marco Schwarz; Maurizio Amichetti
Centro Protonterapia Trento, Trento, Italy

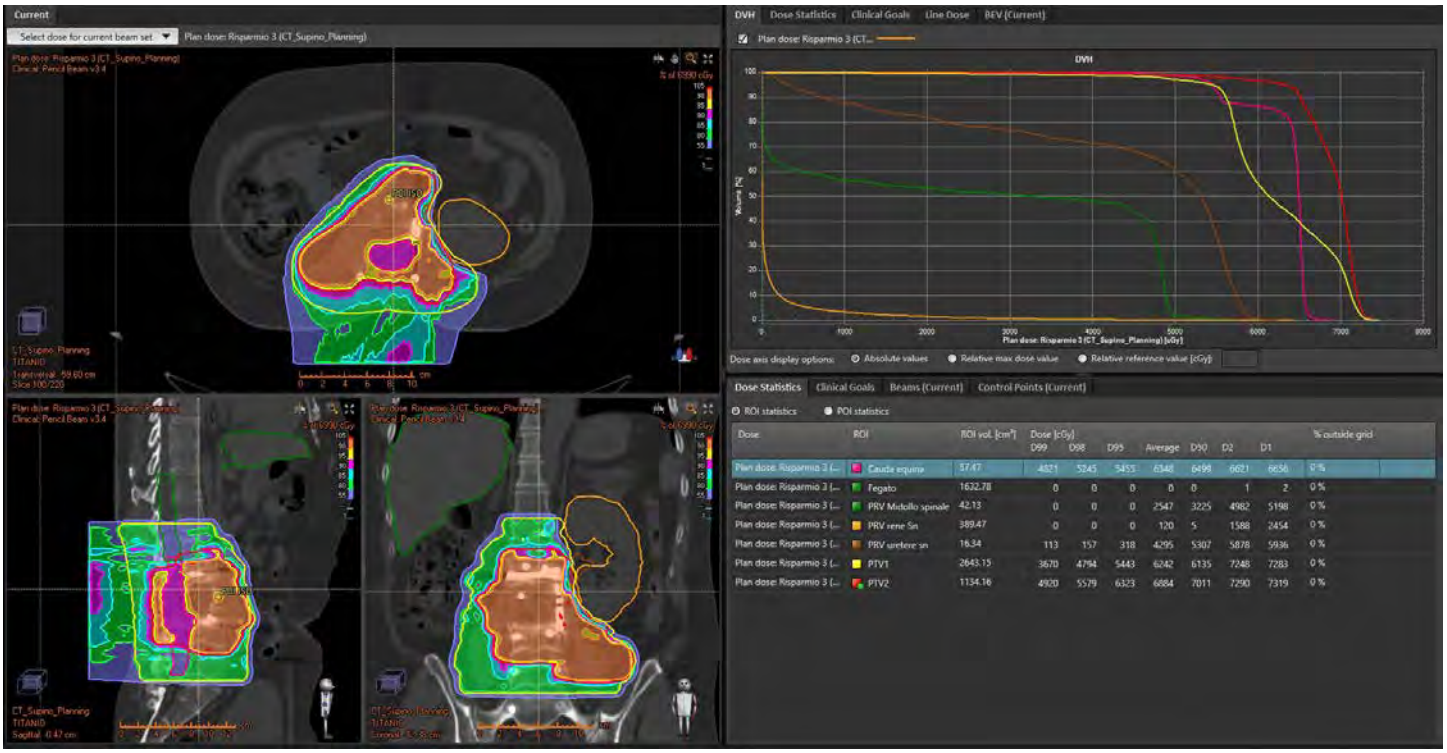
Objective: To report the initial clinical experience of Trento Proton Therapy Centre in treating chordomas (C), chondrosarcomas (CS) and other sarcomas (S) with protontherapy (PT) in terms of safety and feasibility.

Methods: From December 2014 to April 2016 eighteen patients (pts) were irradiated with protontherapy (PT). Median age was 62.8 years (range, 17.8-84.1); median KPS was 90 (range, 80-100); there were 12 C, 4 CS, 1 Osteoblastoma and 1 Giant Cell Tumor; located in sacrococcyx: 9, lumbar spine: 4, cervical spine: 2, iliac bone: 2 and dorsal spine: 1. Eight pts showed spinal canal involvement; sixteen pts had received ≥ 1 surgical treatment and two pts biopsy only before PT. Thirteen pts had gross residual disease at the beginning of PT and received radical treatment (median diameter 64.9 mm; range, 33–110); three pts had adjuvant PT; one patient with macroscopical disease had previously received radiotherapy at a dose of 54 Gy and one, with pulmonary metastases, was treated at a palliative dose. Toxicity was scored according to the CTCAE 4.0.

Results: Median follow-up was 5.2 months (range, 1-14.3). PT was well tolerated and was completed by all pts without breaks related to acute side effects. A conventional fractionation technique was used for 14 pts, 4 pts were irradiated with a Simultaneous Integrated Boost technique. All pts were treated with active beam scanning PT. Median GTV volume was 163.35 cc (range, 3.03–621); median high-risk (HR) PTV volume was 613.12 cc (range, 81.5-2157.6); median low-risk (LR) PTV volume was 1411.88 cc (range, 326-2781.1). Median prescribed total dose was 70 GyRBE (range: 50-74 GyRBE) for HR PTV and 54 GyRBE (range, 50.4-54 GyRBE) for LR PTV. Artificial and biological reconstruction devices were present in 6 pts, all of them were inside the HR PTV. Three pts experienced acute G3 cutaneous toxicity. No other ≥ G3 acute or late ≥G3 side effects were reported (see table). Of the 13 pts treated with radical intent, 11 have locally controlled disease (LCD), 2 local progression and 2 have died of other causes. Three pts treated with adjuvant intent are free of disease. The patient with widespread disease died of cerebral metastases and the patient previously irradiated is alive with LCD.

Acute and late side effects

Acute Toxicity	Grade 1	Grade 2	Grade 3	Grade 4
Cutaneous	8 (44.4%)	2 (11.1%)	3 (16.7%)	-
Pain	-	6 (33.3%)	-	-
Fatigue	-	3 (16.7%)	-	-
Neurologic	1 (5.5%)	-	-	-
Gastro-Enteric	4 (22.2%)	1 (5.5%)	-	-
Late Toxicity	Grade 1	Grade 2	Grade 3	Grade 4
Cutaneous	8 (44.4%)	-	-	-
Pain	1 (5.5%)	-	-	-
Fatigue	1 (5.5%)	-	-	-



Conclusion: Our preliminary data confirm that PT for spine sarcomas is a feasible irradiation modality associated with an excellent tolerance and compliance. A longer follow-up is needed to gain more robust data regarding late toxicity and long term disease control.

P1 - Poster 125 2570211

POSTOPERATIVE OUTCOME AND PATHOLOGICAL INFILTRATIVE FEATURE OF SACRAL CHORDOMAS: A RETROSPECTIVE ANALYSIS OF 46 CASES

Toru Akiyama, MD, PhD[1]; Koichi Ogura[2]; Tabu Gokita[3]; Satoshi Tsukushi[4]; Shintaro Iwata[5]; Tomoki Nakamura[6]; Akihiko Matsumine[6]; Tsukasa Yonemoto[5]; Yoshihiro Nishida[7]; Kazuo Saita[1]; Akira Kawai[2]; Seiichi Matsumoto[3]; Takehiko Yamaguchi[8]

[1]Departments of Orthopaedic Surgery, Saitama Medical Center, Jichi Medical University, Saitama, Japan; [2]Department of Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [3]Department of Orthopedic Surgery, Cancer Institute Hospital, Tokyo, Japan; [4]Department of Orthopedic Surgery, Aichi Cancer Center Hospital, Nagoya, Japan; [5]Division of Orthopaedic Surgery, Chiba Cancer Center, Chiba, Japan; [6]Department of Orthopaedic Surgery, Mie University Hospital, Tsu, Japan; [7]Nagoya University Graduate School and School of Medicine, Nagoya, Japan; [8]Department of Pathology, Dokkyo Medical University Koshigaya Hospital, Koshigaya, Japan

Objective: A chordoma is very rare primary malignant bone tumor known to arise mainly from the sacrum. Chordomas have a high rate of recurrence (30-75%). Our research group discovered the pathological unique infiltration pattern of chordomas, which looks like a skip metastatic lesion in the normal tissue, isolated from the main lesion. We named these lesions “skip-like lesions.” The lesion was a tiny nodule of tumor cells. The aim of our study was to examine the correlation between the existence of skip-like lesions and the occurrence of local recurrence, as well as their relationship with clinical outcome.

Methods: We analyzed the histopathological and clinical data of patients with sacral chordomas treated with en bloc resection from 1991 through 2014 by members of our study group. The following data were obtained and used as patient parameters: Age, sex, tumor size, surgical procedure, adjuvant therapy, site of local recurrence, duration from primary surgery to local recurrence, site of metastasis, length of time from surgery to metastasis, duration of follow up and survival outcome, surgical margin and skip-like lesions.

Kaplan–Meier survival analysis with log-rank tests was performed for overall survival, time from onset to metastasis, and time from onset to local recurrence.

Results: We retrospectively reviewed 46 patients of sacral chordoma treated with en bloc resection. The mean follow-up period was 87 months (range 3-297). Local recurrence rate was 41.3%. The site of predilection for recurrence was the surrounding muscle, especially the gluteus maximus. The disease-specific survival was 70.0% at 10 years. The overall local recurrence-free survival was 47.2% at 10 years. The overall distant metastasis-free survival was 56.0% at 10 years. Skip-like lesions were observed in 19 patients (41.3%). The existence of skip -like lesions were significantly associated with poorer local recurrence-free survival (p=0.048) but not with overall survival and distant metastasis-free survival. The local recurrence-free survival of patients without skip-like lesions was 68.3% at 10 years, but the survival of patients with skip-like lesions was 25.7% at 10 years. A higher “greatest distance from the main lesion to the skip-like lesion” was associated with a higher local recurrence rate (p=0.03). A larger primary tumor size increased the risk of poor overall survival and distant metastasis.

Conclusion: The existence of skip-like lesions was statistically associated with a higher rate of local recurrence.

P1 - Poster 126 2570749

TREATMENT OUTCOMES OF PATIENTS WITH PRIMARY CHORDOMAS TREATED WITH PREOPERATIVE RADIATION (ALONE) FOLLOWED BY SURGERY

Karen De Amorim Bernstein, MD[1]; Saveli Goldberg[1]; Norbert Liebsch[1]; Joseph Schwab[2]; Francis Hornicek[2]; Gregory M. Cote[3]; Edwin Choy[3]; Alex Haynes[4]; John T. Mullen[4]; Yen-Lin Chen[1]; Thomas F. DeLaney[1]

[1]Radiation Oncology, MassachusettGeneral Hospital, Boston, MA, USA; [2]Orthopedic Surgery, Massachusetts General Hospital, Boston, MA, USA; [3]Hematology/ Oncology, Massachusetts General Hospital, Boston, MA, USA; [4]General Surgery, Massachusetts General Hospital, Boston, MA, USA

Objective: To study the clinical outcomes of chordoma patients who only received preoperative RT because complications precluded them from receiving postoperative RT.

Methods: This retrospective analysis includes 17 patients with primary chordomas who underwent treatment with preoperative radiation therapy alone followed by surgery at Massachusetts General Hospital. There were 11 males and 7 females in this cohort, 13 patients had sacrococcygeal chordomas, 3 patients had lumbar chordomas and 1 patient had thoracic chordoma. The median age at diagnosis was 57 (Age range: 26-84). Kaplan-Meier procedure and Cox proportional hazards regression were used to analyze survival outcomes.

Results: With a median follow up of 22.3 months after surgery, 10 patients were locally controlled and 7 patients developed local recurrence. The median total dose delivered was 50 Gy (range 19.8-57.4 Gy). For the patients who were not locally controlled, at 3 years overall survival was 64.3% (95%CI: 15.1-90.2) and distant control was 35.7% (95%CI: 1.4-78.0). For the patients who were locally controlled, at 3 years overall survival was 80% (95% CI:20.4-96.9) and nobody developed distant failure. The

patients who experienced local failure had larger tumors compared to patients who did not experience local failure (mean tumor size 14.6 cm versus 7.3 cm respectively).

Conclusion: Chordomas are usually treated with a combination of surgery and radiation therapy. Traditionally at our institution we have treated patients with a course of preoperative and postoperative radiation therapy. This treatment algorithm has led to high local control rates. The cohort of patients described in this abstract received preoperative RT alone, as in the vast majority of cases wound complications prevented the use of postoperative RT. The results indicate suboptimal local control rates in this cohort compared to patients who receive preoperative and postoperative RT.

P1 - Poster 127 2553038

MULTIDISCIPLINARY APROACH TO SACRAL CHORDOMA

José Manuel Asencio[2]; Maitane Orue-Echebarria González[2]; Pablo Lozano[2]; Julien Ariel[2]; Felipe Calvo[1]; Javier Serrano[1]; José Antonio Calvo Haro[3]; Ana Alvarez[1]; Miguel Cuervo[3]
[1]Radiotherapy, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [2]General Surgery, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [3]Orthopaedic Surgery, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Objective: Sacral chordoma is a rare entity with high local recurrence rates when complete resection is not achieved. Our goal is to report the experience of our Centre in the management of sacral chordoma combining radical resection with both external (EBRT) and intraoperative radiotherapy (IORT). Techinal aspects of sacrectomy will de discussed.

Methods: We retrospectively revised the records of all the patients with sacral chordoma resected in our centre from 1998 to December 2015. Overall survival (OS), Disease free survival, local and distant recurrence were calculated. Comparisons between patients treated with and without IORT were performed.

Results: A total of 12 patients were identified: 6 males and 6 females. Median age was 58 years (range 28-77). Eight patients received IORT and four were treated with surgical resection without IORT. In 10 patients we performed the treatment of the primary tumour and in 2 patients we performed the treatment of recurrence disease. The posterior approach was used in 4 patients. Wide surgical margins (R0) were achieved in 5 patients, marginal margins (R1) in 7 patients and there were not any patient with intralesional (R2) margins. At a median follow up of 38 months (range 11-209 months), two patients died in the group without IORT, 4 patient developed local recurrence and 2 patients distal recurrence whereas 6 patients are alive without disease. The median survival of patients treated with IORT was 91 months versus 56 months for patients treated without IORT (p = 0.60). High sacrectomy treated patients had a median survival of 56 months versus 38 months in low sacrectomy treated patients (p = 0.45). Patients with gluteus spread of the tumor had a median survival of 38 months versus 91 months in patients without spread (p= 0,97). Patients with R0 resection had a median survival of 92 months whereas patients with R1 resection had 38 (p=0.40).

Conclusion: Multidisciplinary management of sacral chordoma seems to improve local control. The use of IORT, in our experience, is associated with an increase in overall survival. The level of resection, gluteal spread and second resection seems to affect survival. The posterior approach is useful in selected cases. Multicenter studies should be performed in order to confirm the utility of IORT.

P1 - Poster 128 2570460

THERAPY AND PROGNOSIS IN CHONDROSARCOMA

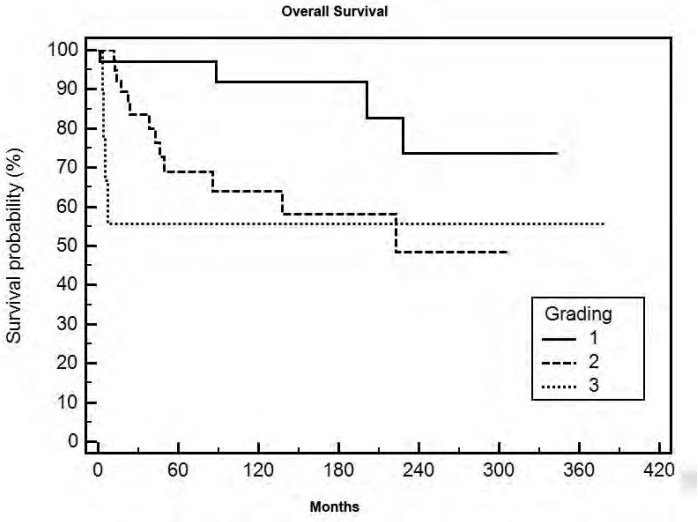
Julian Fromm[1]; Alexander Klein[1]; Andrea Baur-Melnyk[2]; Thomas Knösel[3]; Volkmar Jansson[1]; Hans R. Dürr[1]
[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany; [2]Institute of Radiology, LMU Munich, Munich, Germany; [3]Institute of Pathology, LMU Munich, Munich, Germany

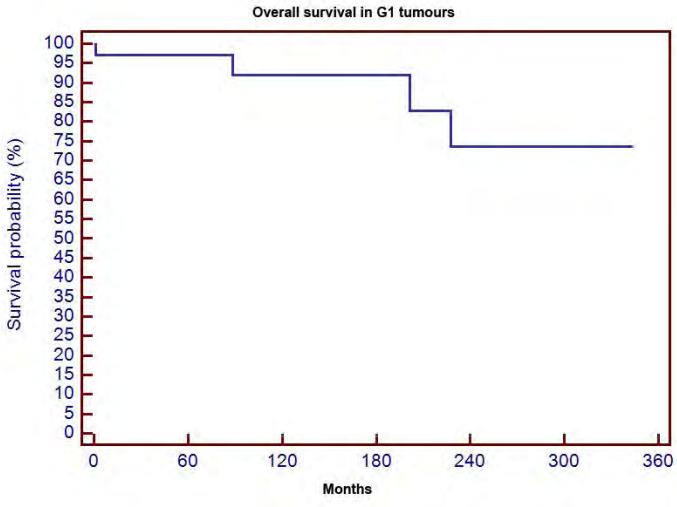
Objective: Chondrosarcomas are a heterogeneous group of tumours , the major prognostic criterion being the grading. The aim of our study was to have a closer look particularly to low-grade lesions, which are increasingly treated intralesionaly.

Methods: Between 1982-2014 a total of 116 resection were performed in 108 patients.The average age of the 73 men was 49 years (15-77 years) that of the 43 female 51 years (15-88 years). The diagnosis was central chondrosarcoma in 87 cases, periosteal chondrosarcoma in 7 cases, clear cell chondrosarcoma in 5 cases, dedifferentiated chondrosarcoma in 4 cases, mesenchymal chondrosarcoma in 3 cases, myxoid chondrosarcoma in 10 cases. 31 patients died in follow-up. The follow-up of surviving patients was on average 110 (12-379) months).
Between 1982-2014 a total of 116 resection were performed in 108 patients. Those 116 cases are described. The average age of the 73 men was 49 years (15-77 years) that of the 43 female 51 years (15-88 years). The diagnosis was central chondrosarcoma in 87 cases, periosteal chondrosarcoma in 7 cases, clear cell chondrosarcoma in 5 cases, dedifferentiated chondrosarcoma in 4 cases, mesenchymal chondrosarcoma in 3 cases, myxoid chondrosarcoma in 10 cases. 31 patients died in follow-up, in 4 cases follow-up was not possible. The follow-up of surviving patients was on average 110 (12-379) months).

Results: In conventional chondrosarcoma overall survival was strongly depending to grading (Fig. 1, p=0.0067). But if we consider only G2 and G3 lesions, there was no difference. In dedifferentiated chondrosarcoma 3 of 4 patients died in the first 9 months after surgery, only one patient lived for 24 months. In chondrosarcoma 54 patients had a R0-, 31 a R1- , and 2 patients a R2-resection. Between R0 and R1 resected patients was no survival difference. This was independent (pelvis vs. other locations) to localization. Pelvic tumours per se had a highly significant worse prognosis. What was surprising was the overall survival of patients with G1 tumors (92% after 10 years, 74% after 20 years). Of these patients (n=36), one patient had metastasized initial, 4 patients metastatized in follow-up (total 5/36, 14%).

Conclusion: Overall no advantage in overall survival was seen between R0 and R1 resected conventional chondrosarcoma. A high rate of metastasis (5/36) in central G1 chondrosarcoma was seen. Pelvic lesions are prognostically significantly less favorable, patients with dedifferentiated chondrosarcomas showed despite one case a fatal course.





P1 - Poster 129 2563640

CLEAR CELL CHONDROSARCOMA MIMICKING BENIGN BONE TUMORS

Chang-Bae Kong; Seung Yong Lee; Won Seok Song; Wan Hyeong Cho; Jae Soo Koh; Dae-Geun Jeon
KCCH, Seoul, Korea (the Republic of)

Objective: The aim of our study was to document the doctor-associated diagnostic errors in patients with clear cell chondrosarcoma and oncologic outcome of those lesions which were misdiagnosed as benign bone tumors.

Methods: From our Orthopaedic Oncology Unit database, we identified 10 patients who were diagnosed and treated for clear cell chondrosarcoma between January 1996 and December 2014. One patient was excluded because of insufficient clinical data. We examined surgeons' and pathologists' errors with respect to patient and tumor characteristics. We also analyzed treatment delay, time to local recurrence and/or metastasis, follow up duration and the patients' oncological outcome.

Results: Initial presumptive diagnosis based on MR imagings for the all 9 patients was benign bone tumors (Fig. 1). Giant cell tumor was the most common clinical impression followed by chondroblastoma, enchondroma, aneurysmal bone cyst. Only 1 patient underwent incisional biopsy. Curettage was performed as initial treatment in 6 cases. For the remaining 2 patients, one received bipolar hemiarthroplasty for pathologic fracture in proximal femur and the other internal fixation with multiple pin. Initially, pain was main symptom in 7 and palpable mass in 2 patients. Three patients were diagnosed because of pathologic fracture. The location of tumor was proximal femur in 3, distal femur in 2, proximal humerus in 2, scapula and distal ulna in 1. Among 8 patients who undergone inappropriate procedure, half of them were diagnosed as clear cell chondrosarcoma immediately after the curettage and then referred to our institute (Fig. 2). For the remaining 4 patients, the surgeon responsible did not send tissue samples to a pathologist for a definite diagnosis (3 patients), and pathologists made an incorrect diagnosis (1 patients). All the referred patients underwent proper surgery with wide surgical margin by us. Average treatment delay were 27 months (range, 0-127) and the average follow up duration was 65 months (range, 13-164). One patient had local recurrence after 12 months. Metastatic disease developed in 2 patients with a median time to definitive treatment of 24 months (12-37).

Conclusion: Even experienced orthopaedic oncologists can misdiagnose clear cell chondrosarcoma as a benign bone tumor and might perform a definite curative surgery without any biopsy procedure. Proper subsequent surgery is mandatory for the patients with clear cell chondrosarcoma who received inadvertent curettage.

Table 1. Patient Demographics

Case No.	Gender/ Age	Tumor location	Symptom	Symptom duration (months)	Presumptive diagnosis	Treatment
1	M/37	Distal femur	Pain	12	GCT	Curettage
2	M/57	Femur head & neck	Pain	Fractured	GCT	Bipolar hemiarthroplasty
3	M/32	Distal ulna	Pain	12	GCT	Curettage
4	F/19	Femur head & neck	Pain	10	GCT	IF with multiple pin d/t pathologic fracture
5	M/58	Distal femur	Pain	Fractured	GCT	Incisional biopsy
6	F/44	Femur head & neck	Pain	2	GCT	Curettage
7	F/8	Scapula	Mass	7	Chondroblastoma	Curettage
8	M/45	Proximal humerus	Pain	Fractured	Enchondroma	Curettage & BC
9	M/31	Proximal humerus	Mass	30	ABC	Curettage

GCT=giant cell tumor, ABC=aneurysmal bone cyst, BC=bone cementing

Table 2. Clinical Courses & Oncologic Outcomes

Case No.	Treatment delay (months)	Initial pathologic diagnosis	Local recurrence (months)	Metastasis site	Metastasis (months)	Follow up (months)	Final status
1	1	CCC				164	CDF
2	16	None	12	spine, rib, lung	37	46	DOD
3	1	CCC				13	CDF
4	10	None				14	CDF
5	Biopsy	CCC				19	CDF
6	1	CCC				119	CDF
7	1	CCC				79	CDF
8	127	CMF				55	CDF
9	60	None		spine, rib, lung	12	76	DOD

CCC; clear cell chondrosarcoma, CMF; chondromyxoid fibroma, CDF; continuous disease free, DOD; died of disease,

P1 - Poster 130 2565811

EFFICIENCY OF TC-99 M MDP AND THALLIUM-201 SCINTIGRAPHY IN THE DIFFERENTIAL DIAGNOSIS OF CHONDROSARCOMA AND CHONDROBLASTIC OSTEOSARCOMA

Yuta Taniguchi; Norio Yamamoto; Katsuhiro Hayashi; Akihiko Takeuchi; Takashi Kato; Takashi Higuchi; Kensaku Abe; Hisaki Aiba; Hiroyuki Tsuchiya
Orthopeadics, Kanazawa University Hospital, Kanazawa, Ishikawa, Japan

Objective: Chondroblastic osteosarcoma (COS) is similar to chondrosarcoma (CS) radiologically and histologically because COS produces a rich cartilage matrix. Therefore, the risk of misdiagnosis between CS and COS exists. This study aims to investigate the efficiency of Tc-99 m MDP and Thallium-201 scintigraphy in the differential diagnosis of CS and COS.

Methods: 25 patients with CS and 17 patients with COS from 1992 to 2015 were enrolled. We examined 12 patients with CS (grade1, 7 cases; grade2, 3 cases; extraskeletal myxoid type, 2 cases) and 9 patients with COS who underwent scintigraphy before an invasive examination (Table 1) . The ratio of Tc-99 m MDP and Thallium-201 uptake at the tumor site/normal site was calculated (Figure 1) . Student t test was used for statistical analysis. Receiver operating characteristic (ROC) curve was plotted.

Results: The ratio of Tc-99 m MDP uptake at the tumor site/normal site was an average of 2.50 (min 0.75, max 4.69) in CS cases and an average of 3.41 (min 2.17, max 4.19) in COS cases. Furthermore, there was an elevated uptake in COS cases (P = 0.066). In patients with grade 1 CS, the ratio was an average of 2.41 (min 1.08, max 4.43). On comparing grade 1 CS with COS, a significant difference was observed (P = 0.049). The ratio of Thallium-201 uptake at the tumor site/normal site was an average of 1.67 (min 0.67; max 2.95) in CS cases and an average of 1.65 (min 0.92, max 2.56) in COS cases. There was no significant difference between CS and COS (P = 0.97). In patients with grade 1 CS, the ratio was an average of 1.72 (min 0.92; max 2.95). No significant difference was observed between grade 1 CS and COS (P = 0.89) (Figure 2). In ROC curve analysis of Tc-99 m MDP uptake between CS and COS, the area under curve (AUC) was 0.75. With a cutoff uptake ratio of 2.18, the sensitivity was 58.3% and the specificity was 100%. In the case of grade1 CS and COS, AUC was 0.78. With a cut-off uptake ratio of 2.37, the sensitivity was 71.4% and the specificity was 88.9% (Figure 3).

Conclusion: Our findings indicate that Tc-99 m MDP scintigraphy is useful for the differential diagnosis of chondrosarcoma and chondroblastic osteosarcoma.

Table 1 Patient characteristics

Patient	CS	COS
Number	12	9
Gender		
Male	8	5
Female	4	4
Age		
Median, years (range)	57.8 (27-81)	23.3 (14-35)
Site		
Upper extremity	3	1
Lower extremity	3	2
Trunk	6	6
Scintigraphy		
Both Tc-99 m MDP and Thallium-201	8	6
Tc-99 m MDP only	4	3
Thallium-201 only	1	0
Grade		
G1	7	
G2	3	
Extraskeltal myxioid	2	

Figure 1 Calculation of the ratio of uptake

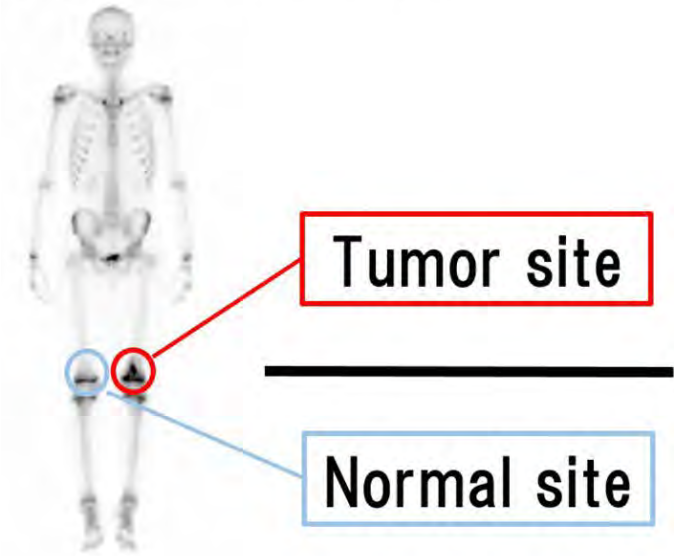


Figure 2 Statistical analysis of uptake ratio

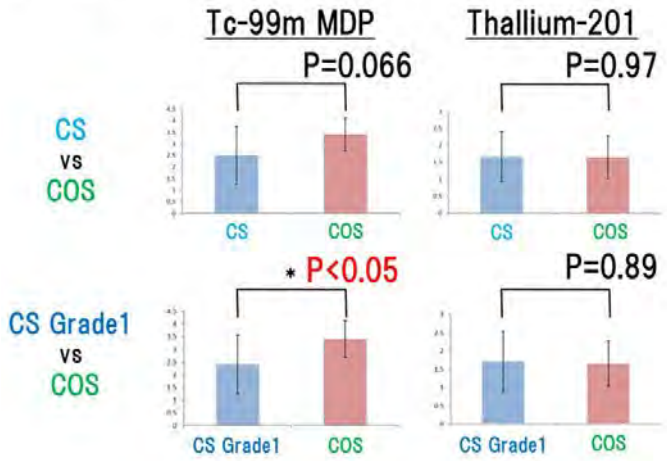
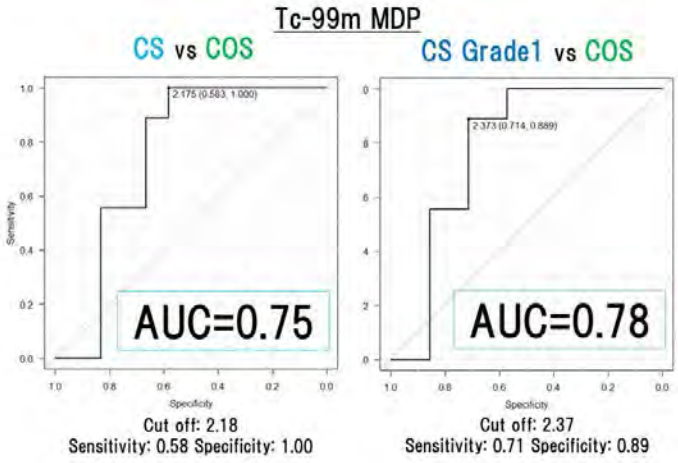


Figure 3 ROC curve in Tc-99 m MDP scintigraphy



P1 - Poster 131 2530300

EFFECT OF CYTOSTATIC PRP-1 ON TUMOR SUPPRESSORS OF INFLAMMATORY PATHWAY AND IL6 MEDIATED SIGNALING IN CHONDROSARCOMA

Karina Galoian, PhD[1]; Shihua Luo[1]; Amir Qureshi[1]; Parthik Patel[1]; Rachel Price[1]; Ashlyn Morse[1]; H.T. Temple[2]

[1]Orthopaedic Surgery, University of Miami, Miller School of Medicine, Miami, FL, USA; [2]Translational Research and Economic Development, Nova Southeastern University, Davie, FL, USA

Objective: Cytokines produced in the tumour microenvironment have an important role in cancer pathogenesis. Understanding their involvement in the failed differentiation programs leading to cancer or lost tumor suppressive functions is undoubtedly one of the challenges on modern molecular oncology.Metastatic chondrosarcoma is the cancer of cartilage .The signaling events resulting in mesenchymal cell transformation to sarcoma are not known. This study pursued characterization of cytokine expression profile in JJ012 chondrosarcoma cell line compared to control C28 chondrocytes ,as well as the effect of proline rich polypeptide 1,PRP-1 on the expression of cytokines ,tumor suppressors of inflammatory related pathways in JJ012 cell line.

Methods: Tissue culture;human inflammatory cytokines ELISA array kit was used to detect panel of 12 cytokines PAGE, western blot.

Results: The IL6 expression was downregulated in human chondrosarcoma JJ012 and fibrosarcoma HT1080 cell lines. In JJ012 line it was 86 fold lower than in C 28 chondrocytes, 52 fold lower than in mesenchymal adult cells based on ELISA results.We have demonstrated 52 fold downregulation of IL6 expression in coculture of chondrosarcoma cells and C28 chondrocytes compared to C28 chondrocytes and 49 fold downregulation of IL6 expression in coculture of mesenchymal stem cells and JJ012 in comparison with its expression in mesenchymal cells. PRP-1 did not affect the levels of IL6 (Fig1).Western blot indicated downregulation of suppressor of cytokine signaling (SOCS3) levels in chondrosarcoma . Addition of PRP-1 restored the expression of SOCS3 in dose response manner(Fig2). TGFβ was much more expressed in C28 cells.It is known that H3K9 methylathion is erased from the promoters of the inflammation genes. H3K9me3 demethylase transcriptionally represses tumor suppressor genes.PRP-1 inhibited H3K9 demethylase activity with IC 50 of 3.72 µg/ml in JJ012 cells (Fig3).

Conclusion: The upregulation of SOCS3 expression by PRP-1 proves once again the ability of this peptide to upregulate tumor suppressor genes in general. SOCS3 can act unrelated to STAT activation. We did not observe STAT3 or SMAD 2 differences. Reduced expression of interleukin 6 was reported by others in advanced stage and undifferentiated tumors and was linked to the compromised differentiation program.The downregulation of IL6 expression in tumor cell line is indicating the presence of a factor or a program in the tumor with the ability to usurp IL6 expression.

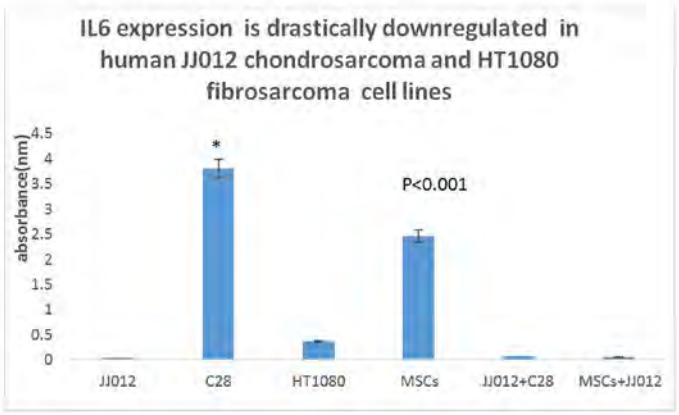


Figure 1. Comparison of IL6 expression between JJ012, HT1080 tumor cell lines with C28 chondrocyte cells, adult mesenchymal stem cells and in cocultures.

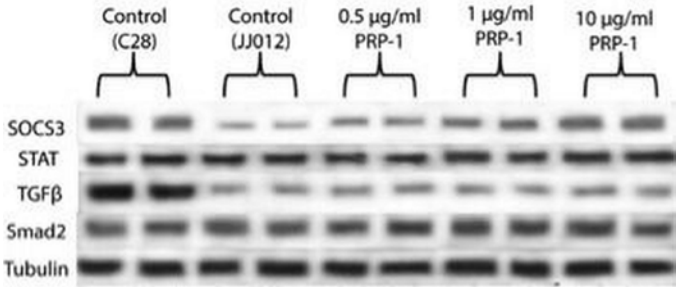


Figure 2.PRP-1 upregulated expression of SOCS3 in human chondrosracoma JJ012 cells in dose response manner

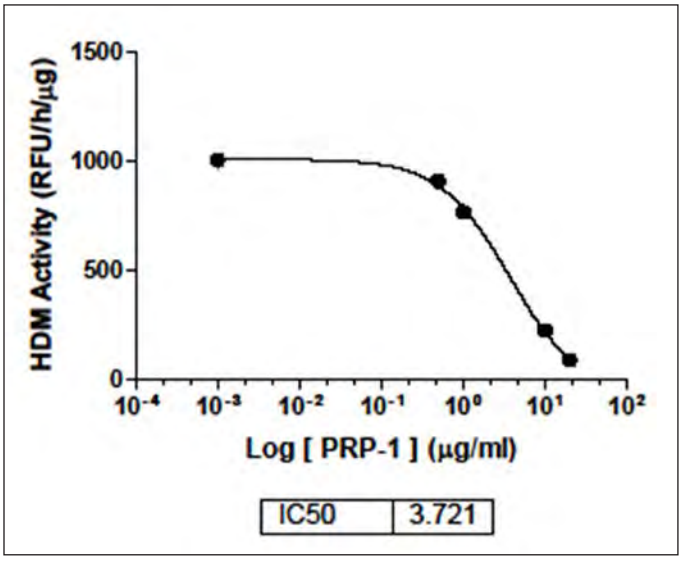


Figure 3. H3K9 demethylase activity inhibition with PRP-1 in human JJ012 chondrosarcoma cell line.

P1 - Poster 132 2570109

EPIDEMIOLOGICAL AND SURVIVAL ANALYSIS OF DEDIFFERENTIATED CHONDROSARCOMA: RESULTS FROM EVALUATION OF SEER DATABASE

Kamil M. Amer, BS (MD in progress)[1]; John A. Abraham[2]; Barry Kenneally[2]; Mitchell Maltenfort[2]; Atrayee BasuMallick[3]

[1]Temple University Lewis Katz School of Medicine, Philadelphia, PA, USA; [2]Orthopedic Surgery, Thomas Jefferson University Hospital, Philadelphia, PA, USA; [3]Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, PA, USA

Objective: Dedifferentiated chondrosarcoma (DCS) is a rare malignant high-grade sub-type of chondrosarcoma with an incidence of about 10% of all cases of chondrosarcoma. Investigation of DCS has been limited because of its rarity. Our objectives were to use a national population-based resource 1) to evaluate patient demographics, clinical behavior, incidence, and survival for DCS, 2) to determine if there was a difference in the 5-year survival for several variables including age, gender, race, grade of tumor, use of radiation, tumor size, or anatomical location.

Methods: The National Cancer Institute's Surveillance, Epidemiology, and End Results database was used to search for patients diagnosed with Dedifferentiated Chondrosarcoma between 1973 and 2015. Patient demographics, tumor characteristics, incidence and survival trends were all analyzed. Logistical regression model was implemented to determine if any of the clinical variables were associated with poor survival. Differences in the 5-year survival and incidence of many variables were also analyzed using Chi-squared analysis and Quasi-Poisson regression model.

Results: All patient demographic, clinical, tumor, incidence, and survival data can be found in Table 1. Using a logistical regression analysis, it was found that increased age was associated with poor survival ($p < 0.05$). The only other variable that approached statistical significance was race (Caucasian) ($p = 0.09$). The regression analysis results for several variables effects on survival is shown in Table 2. The majority of the cases (74.8 %) tend to present with Grade III disease, with distant metastasis noted in approximately one in 6 cases at diagnosis. There was no significant difference in the incidence between genders, however there is a significant difference in the incidence between race, with the highest being in the Caucasian population ($p < 0.05$).

Conclusion: This study evaluated the epidemiological, clinical, and tumor data on DCS from a large population database. The study demonstrated that DCS has an overall low incidence, a predilection for Caucasians, but does not demonstrate any gender predominance. The SEER database does not provide data on specific use of chemotherapy for these tumors, thus we cannot conclude about the effects of chemotherapy. Median survival is 11 months. The results of this study can be used to help provide information regarding the epidemiology and prognosis for this rare disease.

Table 1.

Clinical Variables		
Age (Years)		65.2 (12-100)
Gender	Males	120 (54.1 %)
	Females	102 (45.9 %)
Race	Caucasian	202 (91.9 %)
	African American	8 (3.6 %)
	Asian	11 (5.0 %)
	N/A	1 (0.5 %)
Anatomical Site	Bones	204 (91.9 %)
	Soft Tissues	15 (6.8 %)
	Head	3 (1.5 %)
	Other	1 (1.9 %)
Neo-adjuvant Therapy		
Radiation Therapy		44 (19.8 %)
No Radiation Therapy		171 (77.0 %)
N/A		7 (3.2 %)
Tumor Data		
Size (cms)		10.8
Tumor Grade	Grade I	10 (4.5 %)
	Grade II	13 (5.9 %)
	Grade III	166 (74.8 %)
	N/A	33 (14.9 %)
Metastasis (At Diagnosis)		38 (17.1 %)
Incidence (per 100,000)		0.009
Survival	5-year Survival (months)	22.9
	Median Survival (month)	11

This table demonstrates patient demographic, clinical, tumor, incidence and survival data.

Table 2

Factor	Chi-Squared	p value
Age	16.06	0.0001
Gender	1.38	0.239
Race	4.89	0.087
Anatomical Site	0.01	0.956
Radiation	0.28	0.595
Grade	1.01	0.276
Tumor Size	0.89	0.321

This table demonstrates the regression analysis results for the association of several variables on their effects on survival.

P1 - Poster 133 2570625

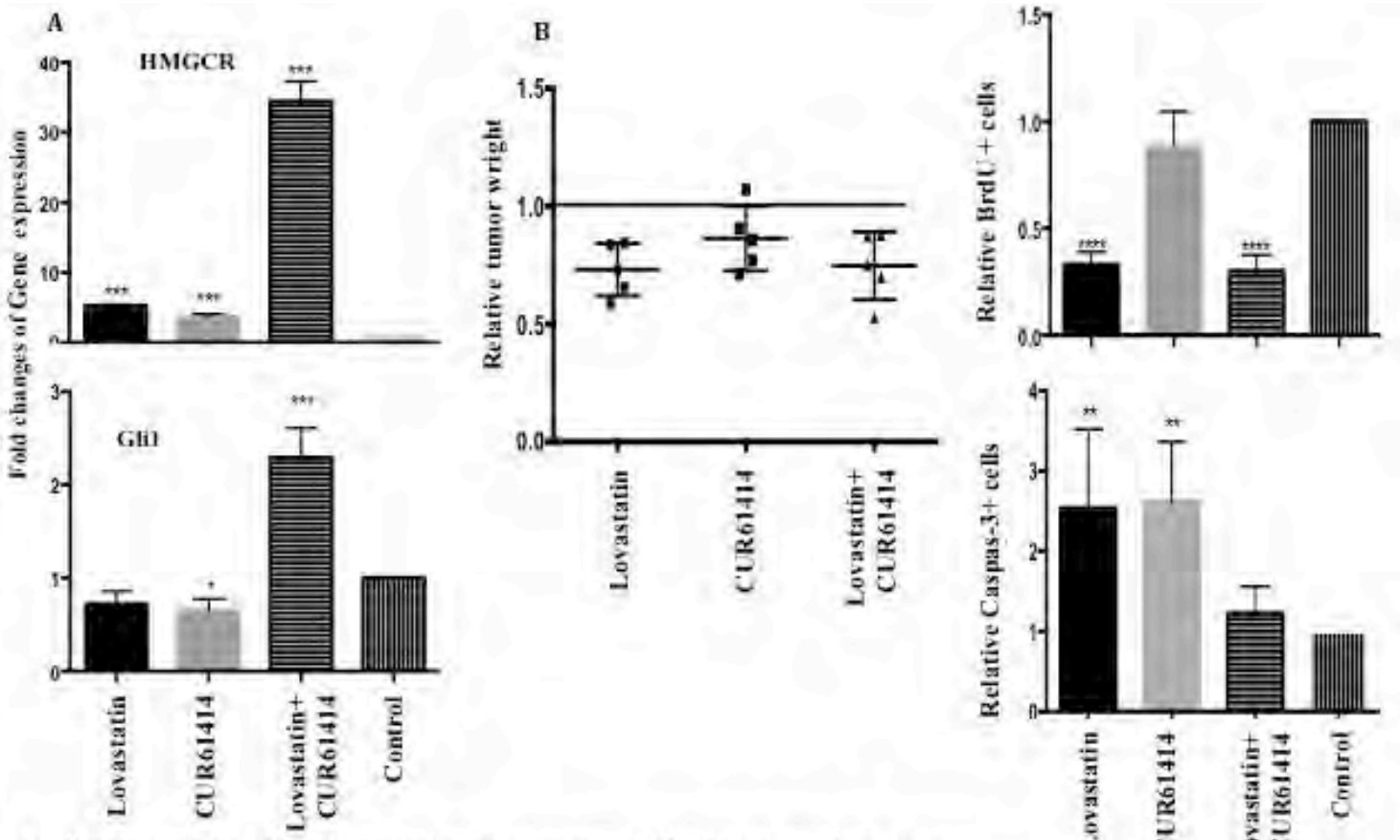
CHOLESTEROL ACTS DOWNSTREAM OF HEDGEHOG (HH) SIGNALING IN CHONDROSARCOMA: IMPLICATION FOR THERAPY

Qingxia Wei[1]; Eyal Ramu[1]; Robert Turcotte[2]; Ben Alman[1]; Jay Wunder[3]
[1]The Hospital for Sick Children, Toronto, ON, Canada;
[2]McGill University, Montreal, QC, Canada;
[3]University of Toronto, Toronto, ON, Canada

Objective: To determine how targeting cholesterol, Hedgehog (Hh) signalling, or targeting both together alters the CSA phenotype.

Methods: Human chondrosarcoma tumor samples were obtained fresh from surgery. For *in vitro* study, chondrosarcoma explants of 2mmx2mm x2 mm cubic in size were established as organ cultures. For *in vivo* study, one million chondrosarcoma cells were subcutaneously injected into interleukin-2 receptor gamma chain (gamma)-null NOD/SCID (NSG) mice. Cells from Five CSAs were treated both *in vitro* and *in vivo* with a hedgehog inhibitor, N-[(3S,5S)-1-(1,3-Benzodioxol-5-ylmethyl)-5-(1-piperazinylcarbonyl)-3-pyrrolidinyl]-N-[(3-methoxyphenyl)methyl]-3,3-dimethyl-benzamide (CUR61414), a cholesterol inhibitor, Lovastatin, or both. For *in vitro* study, chondrosarcoma explants were treated for 48 hours. For *in vivo* study, mice were treated for 4 weeks. At the end of treatment, the explants or xenografts were harvested and processed for further analysis. RT-PCR was used to measure the expression of Hh and cholesterol target genes. Tumor weight measurement, Brdu and Caspas-3 staining were performed for xenografts after drug treatments.

Results: Blockade of Hh signaling significantly decreased Gli1 gene expression, and increased 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) expression indicating decreased intracellular cholesterol (P<0.05). Treatment with the cholesterol inhibitor Lovastatin significantly increased expression of HMGCR (P<0.001). The combination of Hh and cholesterol blockage resulted in an even greater increase in expression of HMGCR (P<0.001, **Fig A**). Analysis of CSA xenografts *in vivo* demonstrated a significant decrease in tumor size with Lovastatin, reduction of Brdu positive cells, and increase in Caspas-3 positive cells(**Fig B**,P<0.001) Treatment with Hedgeog blockage CUR61414 slightly reduced the tumor growth with no significant reduction of Brdu positive cells but an increase of Caspas-3 positive cells. The combination treatment of lovastatin and CUR61414 on xenografts resulted in a decrease in tumor size to the same level as seen with Lovastatin alone.



A: qPCR on primary CSA cells treated with Lovastatin, CUR61414 or both for 48 hours *in vitro* at 20 μm(n=5).
B: Relative weight, BrdU+ cells and Caspas-3 + cells of CSA xenografts treated with 4.5 mg/kg/day of Lovastatin, Cur61414 or both for 4 wks (n=5)

Conclusion: This data suggests that cholesterol functions downstream of the Hh signaling pathway in CSA. The effective reduction in CSA tumor growth with cholesterol inhibition, compared to Hh blockade, without further effect from targeting both together, suggests cholesterol blockade an effective therapeutic approach.

P1 - Poster 134 2566497

ROLE OF MIRNA-143/5 CLUSTER IN CHONDROSARCOMA PROGRESSION

Joaquin Urdinez, MS; Aleksandar Boro; Ana Gvozdenovic; Bruno Fuchs
Orthopedics, Balgrist, Zurich, Zurich, Switzerland

Objective: Chondrosarcoma (CHS) is the second most frequent bone sarcoma with a poor patient prognosis when it metastasizes (5-year survival rate <25%). Due to the insufficient understanding of the genetic drivers that contribute to CHS formation, molecules that could be targeted therapeutically are still missing. Hence, there is an urgent need for novel CHS biomarkers. In addition to this, deregulated miRNAs are known to play a pivotal role in cancer, including CHS, and determining the genes that they regulate is a valuable approach for target discovery. Thus, our objective is to identify deregulated miRNAs in CHS for the subsequent identification of biomarkers of therapeutic value.

Methods: miRNA quantification by qRT-PCR from chondrogenic tumor samples: 17 benign, 8 low grade and 13 high grade, and in CHS established cell lines (JJ012, SW1353, 105KC). Genetic manipulation of miRNA levels by lentiviral transduction and study of transduced cells for phenotypic changes (proliferation, migration, colony formation). Study of direct genetic miRNA targets by qRT-PCR and WB.

Results: We did a meta-analysis of global-miRNA studies in CHS and selected those miRNAs which showed to be consistently deregulated, for validation by qRT-PCR in tumor samples and established cell lines. From the selected miRNAs, we found that miRNA levels of the cluster miR-143/5 inversely correlate with tumor grade, suggesting that these miRNAs are relevant for CHS progression. Thus, we generated CHS cell lines over-expressing miR-145 to test the *in vitro* effect of this miRNA by performing functional assays. miR-145 over-expression does not affect the proliferative/migratory capacity of cells. However, we found a significant reduction of the ability of miRNA-145 over-expressing cells to grow colonies, which agrees with the known tumor suppressor role of miR-145 in other cancer types. Lastly, western blot studies suggest that Fascin-1 (a protein that is linked with metastasis development) is a target of miR-145 in CHS, and could contribute to the malignant phenotype of CHS.

Conclusion: We identified miR-143/5 to be down-regulated in CHS tissue samples and cell lines. When miR-145 levels are through genetic manipulation increased in CHS established cell lines, these show a reduced ability to form colonies and decreased Fascin-1 protein levels. This shows that miRNA-143/5 are relevant in CHS and further studies of miR-143 and miR-143/5 together could elucidate their role in this malignancy and provide new therapeutic targets.

P1 - Poster 135 2555190

EPIDEMIOLOGICAL AND SURVIVAL ANALYSIS OF MESENCHYMAL CHONDROSARCOMA: RESULTS FROM EVALUATION OF SEER DATABASE

Kamil M. Amer, BS (MD in progress)[1]; Atrayee BasuMallick[3]; Mitchell Maltenfort[2]; Barry Kenneally[2]; John A. Abraham[2]
[1]Temple University Lewis Katz School of Medicine, Philadelphia, PA, USA; [2]Orthopedic Surgery, Thomas Jefferson University Hospital, Philadelphia, PA, USA; [3]Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, PA, USA

Objective: Mesenchymal chondrosarcoma (MCS) is a rare malignant high-grade sub-type of chondrosarcoma with an incidence of about 2-5% of all cases of chondrosarcoma. Investigation of MCS has been limited because of its rarity. Our objectives were to use a national population-based resource to 1) evaluate patient demographics, clinical behavior, incidence, and survival for MCS and 2) to determine if there was a difference in the 5-year survival and incidence for several variables including age, gender, race, grade of tumor, use of radiation, tumor size, or anatomical location.

Methods: The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database was used to search for patients diagnosed with MCS between 1973 and 2015. Patient demographics, tumor characteristics, incidence, and survival trends were all analyzed. Logistical regression model was implemented to determine if any of the clinical variables were associated with poor survival. Differences in the 5-year survival and incidence of many variables were also analyzed using Chi-squared analysis and Quasi-Poisson regression analysis.

Results: All patient demographic, clinical, tumor, incidence, and survival data can be found in Table 1. Using a logistical regression analysis, it was found that increased age was associated with poor survival ($p < 0.05$). The only other variables that approached statistical significance were tumor location (bones) ($p=0.12$) and gender (Males) ($p=0.11$). Median Survival was 34 months. Of availble patient data, the majority of the cases (35.8 %) tends to present with Grade III disease, with distant metastasis noted in approximately one in 10 cases at diagnosis. The regression analysis results for several variables effects on survival is shown in Table 2. There was no significant difference in the

incidence between genders, however there is a significant difference in the incidence between race, with the highest being in the Caucasian population ($p < 0.05$).

Conclusion: This study evaluated the epidemiological, clinical, and tumor data on MCS from a large population database. The study demonstrated that MCS has an overall low incidence, a predilection for Caucasians, but does not demonstrate any gender predominance. The SEER database does not provide data on specific use of chemotherapy for these tumors, thus we cannot conclude about the effects of chemotherapy. The results of this study can be used to help provide information regarding the epidemiology and prognosis for this rare disease.

Table 1.

Clinical Variables		
Age (years)		38.0 (2-88)
Gender	Males	123 (54.4 %)
	Females	103 (45.6 %)
Race	Caucausian	166 (73.5 %)
	African American	37 (16.4 %)
	Asian	21 (9.3 %)
	N/A	2 (0.9 %)
Anatomical Site	Joints and Bones	85 (37.6 %)
	Soft Tissues	101 (44.7 %)
	Head	26 (11.6 %)
	Other	14 (6.1 %)
Neo-adjuvant Therapy		
Radiation Therapy		90 (39.8 %)
No Radiation Therapy		133 (58.8 %)
N/A		3 (1.4 %)
Tumor Data		
Size (cm)		8.3 (0.3 - 33.0)
Tumor Grade	Grade I	4 (1.8 %)
	Grade II	14 (16.2 %)
	Grade III	80 (35.4 %)
	N/A	128 (56.6 %)
Metastasis (at Diagnosis)		24 (10.6 %)
Incidence (per 100,000)		0.013
Survival	5-year Survival (months)	74.5
	Median Survival (months)	34 (0 - 451)

Table 1: This table demonstrates patient demographic, clinical, tumor, incidence and survival data.

Table 2.

Factor	Chi-squared	p value
Age	11.78	0.0006
Gender	2.62	0.105
Race	0.31	0.858
Anatomical Site	2.45	0.117
Radiation	0.02	0.876
Grade	0.43	0.654
Tumor Size	0.65	0.421

This table demonstrates the regression analysis results for the association of several variables on their effects on survival.

P1 - Poster 136 2564876

EXPLORATION OF CANDIDATE GENES TO INDUCE CARTILAGE TUMORS WITH MUTANT IDH1 GENE USING IPSC

Takeshi Kamakura[1]; Yonghui Jin[1]; Kazuhito Matsunaga[3]; Makoto Watanabe[4]; Sakura Tamaki[1]; Takeshi Okamoto[2]; Hiroyuki Yoshitomi[1]; Junya Toguchida[1]
[1]Tissue Regeneration, Institute for Frontier Medical Sciences, Kyoto University, Kyoto, Kyoto, Japan; [2]Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan; [3]Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine, Yamaguchi University, Ube, Yamaguchi, Japan; [4]Cell Growth and Differentiation, Center for iPS Cell Research and Application, Kyoto University, Kyoto, Kyoto, Japan

Objective: Mutation of IDH1/2 genes are frequently found in cartilage tumors, but the precise oncogenic roles are not yet known. We have found that the introduction of mutant IDH dysregulated the differentiation of mesenchymal stem cells (MSCs) in association with gene-specific histone modification of bone- and cartilage-related genes. These cells, however, failed to show property as transformed cells, suggesting that additional events are required to become neoplastic. Here, we demonstrate our strategy to explore candidate genes contributing cartilage tumor formation in association with the mutant IDH1 gene using human iPSCs.

Methods: We transfected the mutant IDH1 gene into human iPSCs using piggyBac transposon vector, containing doxycycline-inducible mutant IDH1 gene, and single cell-derived clones were isolated. Then we induced the differentiation toward MSCs via the lateral plate mesoderm (LPM). As the first step, primitive streak was induced by Activin and WNT signal, and then LPM was induced by BMP and WNT signal in sphere culture. Finally, MSCs were induced as outgrowing cells from the sphere attached to plastic dish. After the induction of mutant IDH1 gene by doxycycline, the shRNA library is transfected to MSCs,

and transformed cells are selected by the anchorage independent growth. Selected clones are transplanted into the bone marrow of NOD-SCID mice and the tumorigenic property of them is examined. Finally, the transfected shRNA is identified by tag-based sequence.

We also plan to use the "candidate gene" approach. Based on the current genome analyses, the knock –out of COL2A1 gene, and/or p16 gene will be a rational candidate. Introduction of dominant negative p53 gene will be used to develop highly malignant phenotype.

Results: We have established iPSCs containing the doxycycline-inducible mutant IDH1 gene and induced MSCs via LPM. Property as MSCs of these cells were confirmed by the standard methods for osteo-, chondro- or adipogenic differentiation. Production of 2HG were also confirmed after the treatment with doxycycline. We are now conducting the shRNA transfection. We also plan to knock out the COL2A1 gene by CRSPR/Cas9 system of these clones.

Conclusion: These in vitro experiments will give us the information for precise oncogenic process of cartilage forming tumors.

P1 - Poster 137 2564829

MUTANT IDH1 DYSREGULATES THE DIFFERENTIATION OF MESENCHYMAL STEM CELLS IN ASSOCIATION WITH GENE- SPECIFIC HISTONE MODIFICATIONS TO CARTILAGE - AND BONE-RELATED GENES

Yonghui Jin, PhD[1]; Makoto Watanabe[2]; Sakura Tamaki[1]; Takeshi Okamoto[3]; Junya Toguchida[1]
[1]Institute for Frontier Medical Sciences, Kyoto University, Kyoto, Japan; [2]Department of Cell Growth and Differentiation, Center for IPS Cell Research and Application, Kyoto University, Kyoto, Japan; [3]Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Objective: Somatic mutations of IDH1/2 genes were prevalent in cartilaginous tumors, whereas they have rarely been found in other mesenchymal tumors such as osteosarcomas. To address this unique tumor specificity, we examined the effects of mutant IDH1 (mutIDH1) on the differentiation properties of human mesenchymal stem cells (hMSCs).

Methods: Mutation spectrum of IDH1/2 genes in bone tumors of Japanese patients was analyzed with direct DNA sequencing. After lentiviral infection of Wild type IDH1 or mutIDH1 into hMSCs, 2-HG production was quantified with GC-MS, and both of osteogenic and chondrogenic induction were performed. Gene specific histone modification was investigated with ChIP assay. For the doxycycline inducible expression of mutIDH1 in osteosarcoma cell line-ANOS, PiggyBac transposon system was used.
Results: The induction of mutIDH1 promoted the chondrogenic differentiation of hMSCs by enhancing the expression of SOX9 and COL2A1 in association with an increase in the active mark (H3K4me3) in the promoters of these genes, but disrupted cartilage matrix formation. When the expression of SOX9 was downregulated by siRNA in mutIDH1 expressing cells, the expression of COL2A1 was not affected, suggesting the enhanced expression of COL2A1 was due to direct histone modification of promoter. However, the expression of ALPL the key enzyme initiating ECM mineralization was suppressed in association with an increase in the repressive mark (H3K9me3) in the promoter, and subsequently the osteogenic differentiation of hMSCs was inhibited by mutIDH1. The inhibition of mineralization by mutIDH1 was recaptured in the osteocarcoma cell line-ANOS.

Conclusion: Since osteogenic properties are an indispensable feature for the diagnosis of osteosarcoma, the inhibitory effects of mutIDH1 on osteogenic properties may contribute to the lack of osteosarcomas with mutIDH1. These results suggested that mutIDH1 contributed to the formation of cartilaginous tumors by dysregulating the differentiation properties of hMSCs via gene-specific histone modulation.

P1 - Poster 138 2568392

A PHASE 1 STUDY OF AG-120, AN IDH1 MUTANT ENZYME INHIBITOR: RESULTS FROM THE CHONDROSARCOMA DOSE ESCALATION AND EXPANSION COHORTS

William Tap[2]; Victor M. Villalobos[3]; Gregory M. Cote[4]; Howard Burris[5]; Filip Janku[6]; Olivier Mir[7]; Murali Beeram[8]; Andrew Wagner[9]; Julia Auer[1]; Hua Liu[1]; Bin Wu[1]; Katharine Yen[1]; Sam Agresta[1]; Shuchi S. Pandya[1]; Jonathan Trent[10]
[1]Agios Pharmaceuticals, Cambridge, MA, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]University of Colorado, Denver, CO, USA; [4]Massachusetts General Hospital, Boston, MA, USA; [5]Sarah Cannon Research Institute, Nashville, TN, USA; [6]MD Anderson Cancer Center, Houston, TX, USA; [7]Gustave Roussy Cancer Institute, Paris, France; [8]The START Center for Cancer Care, San Antonio, TX, USA; [9]Dana-Farber Cancer Center, Boston, MA, USA; [10]University of Miami, Miami, FL, USA

Objective: Mutations in the metabolic enzyme, isocitrate dehydrogenase 1 (IDH1) occur in over 50% of chondrosarcomas. These mutations lead to an increase in the oncometabolite 2-hydroxyglutarate (2-HG) which results in epigenetic and genetic dysregulation leading to oncogenesis. AG-120 is a first in-class potent oral inhibitor of mutant IDH1 and has completed the dose escalation phase of an ongoing Phase 1 study in solid tumors. AG-120 was

escalated in a 3+3 design from 100mg twice daily up to 1200mg once daily for a 28 day cycle (N=62). Based on the safety, tolerability, pharmacokinetic and pharmacodynamic data from the dose escalation phase, the 500mg dose was selected for expansion in 4 solid tumor cohorts including patients with locally advanced or metastatic chondrosarcoma not amenable to surgical resection.

Methods: Key eligibility: IDH1 gene-mutated disease that has recurred or progressed following standard therapy, measurable disease by RECIST 1.1, and ECOG 0-1. Responses (RECIST 1.1) were assessed every 8 weeks. Plasma, archived tissue, and optional tumor biopsies were collected for exploratory analyses.

Results: As of 14April2016, 15 chondrosarcoma patients were enrolled in the dose escalation (n= 12) and expansion cohorts (n=3). Demographics: M/F=8/7, median prior therapy=1 (range 1-5), ECOG 0/1=6/9. Common treatment emergent adverse events (≥20% patients) regardless of causality were mostly grades 1/2: decreased appetite, QTc prolongation, nausea, anemia, diarrhea, and peripheral edema. In the dose escalation phase there were eleven efficacy evaluable chondrosarcoma patients with 64% (n=7) achieving stable disease and 36% (n=4) experiencing stable disease lasting ≥ 6 months. There were no partial responses.

Conclusion: Updated response, safety, and exploratory analyses will be presented.

P1 - Poster 139 2541711

IDENTIFICATION OF A POSSIBLE THERAPEUTIC CANDIDATE FOR ADVANCED CHONDROSARCOMA WITH AN IDH1 MUTANT INHIBITOR

Makoto Nakagawa[1]; Fumihiko Nakatani[2]; Makoto Endo[2]; Eisuke Kobayashi[2]; Yoshikazu Tanzawa[2]; Akira Kawai[2]; Hirokazu Chuman[2]; Akihiko Yoshida[3]; Takehiko Seki[4]; Kazushi Araki[4]; Yukihide Iwamoto[5]; Issay Kitabayashi[1]
[1]Hematological Malignancy, National Cancer Center Research Institute, Tokyo, Japan; [2]Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [3]Pathology and Clinical Laboratories, National Cancer Center Hospital, Tokyo, Japan; [4]R&D Division, Daiichi-Sankyo, Tokyo, Japan; [5]Orthopaedic Surgery, Kyushu University, Fukuoka, Japan

Objective: Mutations in isocitrate dehydrogenase (IDH) genes are observed in various malignant tumors including chondrosarcoma. IDH mutations have been reported to contribute to the malignant transformation of the tumors through the production of 2-hydroxyglutarate (2-HG) and the competitive inhibition of α-KG-dependent dioxygenases. Therefore, we have presumed that IDH mutant inhibitors can be novel anticancer drugs for IDH mutated tumors and proceed to develop specific IDH1 mutant inhibitors. In this study, we examined the potential anticancer effect of the specific IDH1 mutant inhibitor for chondrosarcoma cell lines with IDH1 mutations in vitro and in vivo.

Methods: Three IDH1 mutated cell lines, JJ012 (IDH1R132G), L835 (IDH1R132C) and HT1080 (IDH1R132C) were treated with different concentration of the IDH1 mutant inhibitor or DMSO (0 to 10μM) for 14 and 28 days, and effect on cell proliferation was assessed. In addition, intracellular 2-HG levels of these cell lines were measured using LC-MS with absence or presence of the IDH1 mutant inhibitor. We also established xenograft model of a chondrosarcoma cell lines (JJ012) and examined antitumor effect of the drug as well as the intra-tumoral and plasma 2-HG levels during the treatment.

Results: We have found that the developed specific IDH1 mutation inhibitor suppress the proliferation of all cell lines in accompany with decreasing 2-HG levels in a dose dependent-manner. Furthermore, the IDH1 mutant inhibitor significantly impaired the tumor growth in JJ012 xenograft model (109.44±120.33 mm^3 vs 481.42±198.21 mm^3, p = 0.002). The intra-tumoral and plasma 2-HG levels of treated mice were also decreased significantly compared to those of controls (intra-tumoral: 433.4±214.6 vs 2,467.7 ±1,193.4 pmol/mg/tissue; p=0.00008, plasma: 1.10±0.69 vs 2.02±0.35 μM; p=0.006).

Conclusion: These data support that IDH1 mutant inhibitor treatment can be a promising candidate for the therapy of unresectable chondrosarcoma. For the next step, we are planning to analyze IDH mutation status and 2-HG levels of the clinical samples from chondrosarcoma patients in our institute to search for the possible clinical trials of IDH mutated chondrosarcoma.

P1 - Poster 140 2570238

D-2HG LEVELS AND IDH MUTATION TYPE CORRELATE WITH DISEASE FREE SURVIVAL IN CHONDROSARCOMA

Makoto Hirata[1]; Nalan Gokgoz[2]; Qingxia Wei[1]; Shingo Sato[1]; Yuning J. Tang[1]; Irene L. Andrulis[2]; Benjamin Alman[3]; Jay Wunder[4]
[1]Developmental and Stem Cell Biology, Hospital for Sick Children, Toronto, ON, Canada; [2]Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, ON, Canada; [3]Department of Orthopaedic Surgery, Duke University, Durham, NC, USA; [4]University of Toronto Musculoskeletal Oncology Unit, Mount Sinai Hospital, Toronto, ON, Canada

Objective: Accumulated evidences have shown that a variety of tumors, including chondrosarcoma, are associated with isocitrate dehydrogenase 1 (*IDH1*) or *IDH*2 mutations. IDH-mutations in gliomas and AMLs have been reported to predict favorable clinical outcomes, while a

previous study on chondrosarcoma showed no significant difference in clinical measures between patients with and without IDH-mutations. Here we analyzed the prevalence of chondrosarcomas with IDH-mutations in our cohort, characterized IDH-mutant chondrosarcomas, and investigated association of *IDH1/2* status with survival.

Methods: The present study population consisted of 142 patients with chondrosarcoma. Median follow up was 3.4 years, ranging from 0 to 17 years. *IDH1* and *IDH2* genes were genotyped by capillary sequence. D-2HG level was quantified by liquid-chromatography-mass spectrometry analysis (LC/MS). Mann-Whitney and Fisher's exact tests were performed to compare continuous and dichotomous variables, respectively. Log-rank test and multivariate cox regression analysis were performed to compare disease-specific and disease-free survivals among subgroups by IDH mutation status. P<0.05 was defined as significant.

Results: 116 of 142 chondrosarcomas were central or periosteal chondrosarcomas (CCS), and the remaining 26 were peripheral chondrosarcomas (PCS). Of 116 CCS, 58 harbored IDH-mutations, while one of 26 PCS also had an IDH1 mutation. The most frequent mutation was IDH1-R132C, followed by IDH1-R132G and -R132L. LC/MS revealed a significant increase of D-2HG levels in tumor tissues with IDH mutations, though the increase level was comparable between IDH1 and IDH2 mutations. Characterization of the patients showed that IDH mutant CCS occurred at a significantly older age (median age of 56 years in IDH-mutant vs 40 years in IDH-wild type; P=0.0405) and were more likely in the extremities. Survival analysis revealed that IDH1-R132G was associated with a more favorable disease-specific and disease-free survival than IDH1-R132C mutation or other IDH1-R132 mutations. In addition, higher D-2HG levels were associated with significantly worse disease-free survival.

Conclusion: Specific IDH1 mutations and D-2HG levels are prognostic factors for survival in patients with chondrosarcoma. This raises the possibility that drugs that target D-2HG levels may be of clinical benefit for these patients, and requires further study.

P1 - Poster 141 2552801

FORTY-EIGHT CASES OF LEIOMYOSARCOMA OF BONE: A MULTICENTER STUDY IN JAPAN

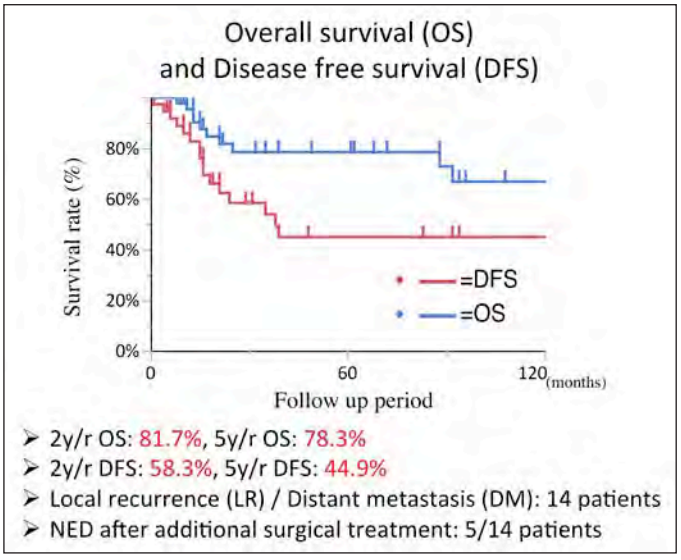
Tomoaki Mori[1]; Robert Nakayama[2]; Makoto Endo[1]; Eisuke Kobayashi[1]; Akira Kawai[1]; Takafumi Ueda[3]; Hideo Morioka[2]

[1]Division of Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [2]School of Medicine, Keio University, Tokyo, Japan; [3]National Hospital Organization Osaka National Hospital, Osaka, Japan

Objective: Leiomyosarcoma of bone (LMSoB) is a rare malignant bone tumor. This multicenter retrospective study was conducted to investigate the diagnosis and the clinical outcome of primary LMSoB in Japan.

Methods: Forty-eight patients (average age: 52 years [range 14-88 years]) with primary LMSoB who were treated at registered institutes in Japan between 1991 and 2014 were recruited. The median follow-up period was 44 months (range: 2-273).

Results: The 5-year overall survival rates and disease-free survival rates were 78.3% and 44.9% respectively. Surgical treatment was performed in 42 patients, and R0 resection was achieved in 31 patients. Neoadjuvant chemotherapy was administered in 18 patients. The most common regimen (cisplatin-based chemotherapy) was administered in 15 patients, however, no patient achieved a good response in both radiological and histological evaluations. The presence of metastasis at the first visit and a lack of definitive surgery were significantly correlated with poor overall survival, and the surgical margin was a significant prognostic factor for disease-free survival.



Conclusion: This study is the largest LMSoB case series ever reported. The 5-year overall survival and disease free survival of Leiomyosarcoma of bone in Japan was 78.3% and 44.9%, which was slightly better than the previous study. Surgical treatment with wide margins was the only

treatment that proved to be effective, whereas adjuvant chemotherapy in the present setting did not improve the overall survival.

P1 - Poster 142 2554149

DIFFERENTIAL MIRNA EXPRESSION PROFILING OF PDGFRA-MUTATED GASTROINTESTINAL STROMAL TUMORS (GIST)

Margherita Nannini, MD[1]; Gloria Ravegnini[2]; Milena Urbini[1]; Sabrina Angelini[2]; Annalisa Astolfi[3]; Valentina Indio[1]; Maristella Saponara[1]; Lidia Gatto[1]; Guido Biasco[3]; Maria A. Pantaleo[1]

[1]Department of Specialized, Experimental and Diagnostic Medicine, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; [2]Department of Pharmacy and Biotechnology, University of Bologna, Bologna, Italy; [3]"Giorgio Prodi" Cancer Research Center, University of Bologna, Bologna, Italy

Objective: PDGFRA mutations are by far the less common of the two known driving kinase gene mutations in gastrointestinal stromal tumors (GIST) and occur in about 5–7 % of cases. The major issue related with this tumor genotype is that D842V-mutant GIST patients, unlike the others, do not benefit from standard therapies and are still orphan from a codified medical treatment. Given these considerations, there is the urgent need to better understand the biological background of this rare subset of GIST in order to clarify what lies beyond their primary resistance to standard therapies and discover novel potential therapeutic targets. With the aim to deeper investigate the molecular biology of this rare subset of GIST and open novel potential therapeutic horizons, we evaluated miRNA expression profiles comparing PDGFRA D842V-mutated and imatinib-sensitive mutated GIST (PDGFRA non-D842V and KIT exon 11 mutated GIST).

Methods: We analyzed the miRNA profiles of 6 GIST samples, of which 2 harboring PDGFRA D842V mutation, 2 harboring an imatinib sensitive PDGFRA non-D842V mutation and 2 harboring a KIT exon 11 mutation (Table 1). Specifically, miRNA profiling was performed using TaqMan® Low Density Arrays (Applied Biosystems), pool A and B, which allow to analyze 754 miRNA. Data were analyzed with SDS Relative Quantification Software (Applied Biosystems); miRNA with Ct values ≥ 35 were considered as not expressed and were excluded from analysis. Normalization was carried out by subtracting the mean U6 Ct from individual Ct values.

Results: Unsupervised and supervised hierarchical clustering of the miRNA profiles showed that PDGFRA D842V mutant GIST clustered together in a distinctive pattern compared to PDGFRA non-D842V mutant GIST and to KIT exon 11 mutated GIST (Figure 1A , Figure 1B). A total of 12 significantly deregulated miRNA were found ($p<0.05$) (Table 2). In particular, the expression of 5 miRNA was up-regulated and 7 miRNA were down-regulated in PDGFRA D842V mutant GIST compared to PDGFRA not D842V mutant GIST and to KIT exon 11 mutated GIST respectively.

Conclusion: PDGFRA D842V mutant GIST display a distinctive miRNA expression profile, different from both PDGFRA not D842V and KIT exon 11 mutated GIST. Future developments plan the miRNA validation on a larger sample size and the correlation with gene expression profiles in order to understand the biological role of the epigenetic signature of this rare subset of GIST still orphan from effective medical treatment.

Table 1: Description of patients' mutational status and imatinib response

#Samples	Mutation	Imatinib response
GIST_1	PDGFRA D842V	Resistant
GIST_2	PDGFRA D842V	Resistant
GIST_3	PDGFRA del 842-5	Sensitive
GIST_4	PDGFRA V561D	Sensitive
GIST_5	KIT del 557-558	Sensitive
GIST_6	KIT del 557-558	Sensitive

Table 2: Significant deragulated miRNA

miRNA	pvalue
hsa-miR-373	0.021
hsa-miR-15a	0.00058
hsa-miR-486-3p	0.0358
hsa-miR-101	0.00239
hsa-miR-19a	0.0379
hsa-miR-17	0.0140
hsa-miR-1267	0.0148
hsa-miR-29b	0.0458
hsa-miR-149*	0.0468
hsa-miR-9	0.0493
hsa-miR-122	0.0492
hsa-miR-1267	0.0148
hsa-miR-17*	0.0140

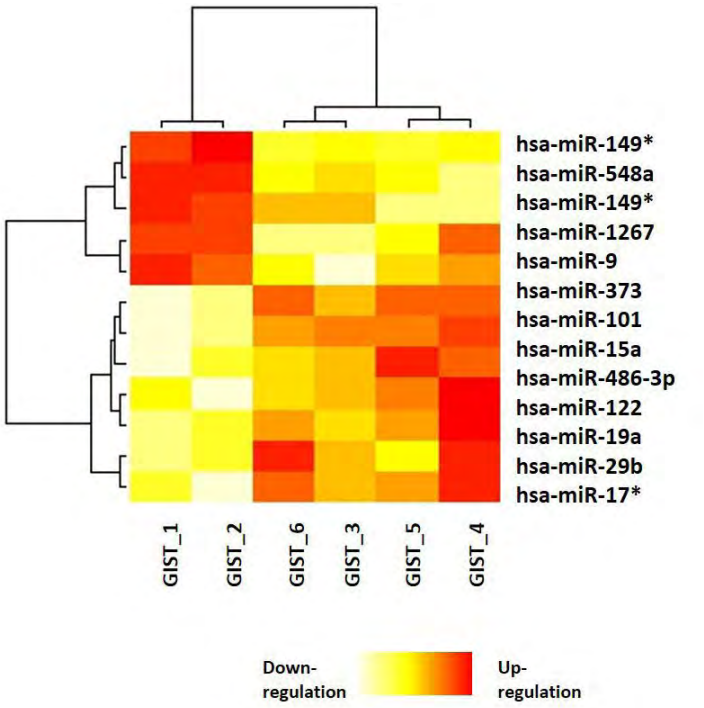


Fig. 1a: the heatmap reports the significant deregulated miRNA comparing imatinib resistant PDGFRA D842V-mutated GIST and imatinib sensitive KIT/PDGFRA mutated GIST (PDGFRA non-D842V and KIT exon 11 mutated GIST).

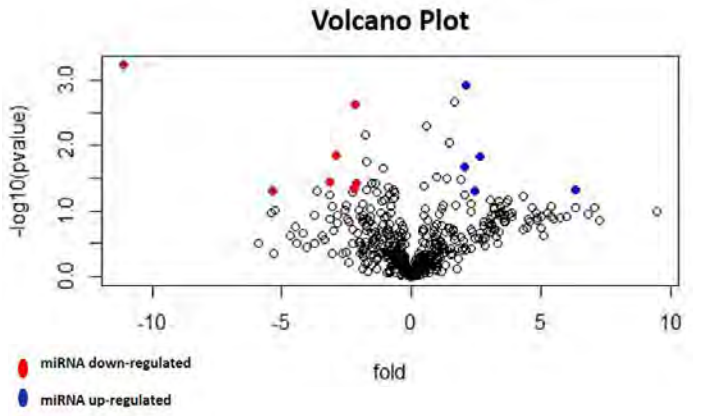


Fig.1b: Volcano plot. Red spots represent significant down-regulated miRNA whereas the blu spots indicate up-regulated miRNA.

P1 - Poster 143 2571368

EVALUATION OF DMD DELETIONS IN NON-METASTATIC GIST PATIENTS TREATED WITH ADJUVANT IMATINIB

Ana Sebio, MD, PhD[1]; Pia Gallano[2]; Maria Jose Rodriguez[2]; Silvia Bague[3]; Juliana Salazar[2]; Lidia Gonzalez[2]; Vicenç Artigas[4]; Ana Virgili[1]; Oscar Gallego[1]; Agusti Barnadas[1]; Antonio Lopez-Pousa[1]
[1]Medical Oncology, Santa Creu I Sant Pau Hospital, Barcelona, Spain; [2]Genetics, Santa Creu I Sant Pau Hospital, Barcelona, Spain; [3]Pathology, Santa Creu I Sant Pau Hospital, Barcelona, Spain; [4]Surgery, Santa Creu I Sant Pau Hospital, Barcelona, Spain

Objective: The dystrophin gene (DMD) has been recently described as a tumor suppressor in cancers with myogenic programs. In metastatic GIST, DMD deletions have been reported to be present in 65% of the cases. We evaluated the presence of DMD deletions in patients with non-metastatic GIST receiving adjuvant imatinib and its relationship with disease recurrence.

Methods: We studied 13 non-metastatic GIST patients (11 patients harboring Kit exon 11 mutations and 2 patients exon 9 mutations) treated with adjuvant imatinib with a follow up of at least 2 years after the end of treatment. Of those, 8 patients relapsed after or during adjuvant treatment and 5 patients were free of recurrence. DNA was extracted from formalin fixed paraffin embedded (FFPE) tissue samples and DMD deletion was evaluated by MLPA (Multiplex ligation-dependent probe amplification) technique.

Results: DMD deletions were found in 2 out of 8 (25%) non-metastatic GIST patients that developed recurrence despite of adjuvant imatinib. Both patients harboured tumors with Kit exon 11 mutation (Patient 1: p.E554_K558del and patient 2: p.V560D) and presented mosaic deletions in multiple exons in the DMD gene (Patient 1: exons 2,4,8 ,13>16,18,19,23>29,38>40,43,44,48,56,66,75 and patient 2: exons 1>17). No deletions were found in the group of patients free of recurrence.

Conclusion: DMD deletions can be evaluated in FFPE tissue samples. DMD deletions are present in non-metastatic GIST patients and, in this small cohort DMD deletions are restricted to patients developing recurrence. Larger studies are needed to evaluate the value as a prognostic biomarker of DMD deletions in non-metastatic GIST patients treated with adjuvant imatinib.

P1 - Poster 144 2559490

BUSULFAN-MELPHALAN WITH BLOOD STEM CELL RESCUE (BUMEL) FOR HIGH RISK LOCALISED EWING SARCOMA (ES): RESULTS OF R2LOC RANDOMISED STUDY

Jeremy Whelan, MD MBBS FRCP[1]; Marie-Cecile De Leley[2]; Uta T. Dirksen[3]; Nathalie Gaspar[2]; Ian Judson[4]; Bernadette Brennan[5]; Andreas Ranft[3]; Jendrik Hardes[3]; Perrine Marec-Bérard[6]; Michael Paulussen[7]; Gwenael Le Teuff[2]; Ian Lewis[8]; Alan Craft[9]; Heribert Juergens[3]; Odile Oberlin[2]
[1]Oncology, University College Hospital London, London, United Kingdom; [2]Gustave Roussy, Villejuif, France; [3]University Hospital Muenster, Muenster, Germany; [4]Royal Marsden Hospital, London, United Kingdom; [5]Royal Manchester Childrens Hospital, Manchester, United Kingdom; [6]Centre Léon Bérard, Lyon, France; [7]Witten/Herdecke University, Datteln, Germany; [8]University of Leeds, Leeds, United Kingdom; [9]Newcastle University, Newcastle, United Kingdom

Objective: EE99R2Loc (NCT00020566) evaluated the effect on event-free (EFS, main endpoint) and overall survival (OS) of BuMel compared to standard chemotherapy in ES presenting with localized disease and either a poor histologic response to induction chemotherapy or large tumor volume (>200ml) unresected or initially resected. It was conducted in 12 countries, by 4 cooperative groups: GPOH, SFCE/GSF, UK-CCLG, and EORTC.

Methods: Eligible pts were aged <50, received 6 VIDE courses (vincristine, ifosfamide, doxorubicin, etoposide) and 1 VAI (vincristine, actinomycin-D, ifosfamide) before randomization to BuMel or VAI x 7 courses. The estimate of hazard ratio, HR, and the p-value were corrected for the 4 previous interim analyses by the Inverse Normal Method.

Results: Between 2000 and 2013, from 477 pts classified as high-risk pts, 216 pts (median age, 17 yrs) were randomized to VAI (107) or BuMel (109). Some pts requiring radiation therapy to the primary site were excluded to avoid excess organ toxicity from interaction between RT and Busulfan. 80% entered the trial because of poor histologic response after chemotherapy alone. Median follow up is 8.0 yrs, with only 3 pts lost to follow up before 3 yrs. Overall, 3yr EFS is 60.0% and OS, 73.9%. In the intention to treat analysis, the risk of an event was significantly decreased by BuMel compared to VAI: HR =0.64 (95%CI, 0.43-0.94) p=.024; 3yr-EFS of 67% (57.6-75.0) vs. 53% (43.6-62.3). OS also favored BuMel, 78% vs. 70%, HR=0.60 (0.39-0.92) p=.019. Results were consistent across subgroups, and in the sensitivity analyses. Two pts died of BuMel-related toxicity and 1 after standard chemotherapy. Significantly more BuMel pts experienced severe acute toxicities, but these arose from a single high-dose course vs. multiple VAI courses.

Conclusion: In patients with poor histological response to VIDE and/or with tumour volume>200ml in whom prior resection or RT prevents histological response data being available, BuMel improves EFS and OS without unacceptable excess toxicity. For this selected group of patients BuMel is the new standard of care.

P1 - Poster 145 2550561

EFFICACY OF BUSULFAN-MELPHALAN HIGH DOSE CHEMOTHERAPY CONSOLIDATION (BUMEL) COMPARED TO CONVENTIONAL CHEMOTHERAPY COMBINED WITH LUNG IRRADIATION IN EWING SARCOMA (ES) WITH PRIMARY LUNG METASTASES: RESULTS OF EURO-EWING 99-R2PULM RANDOMIZED TRIAL (EE99R2PUL)

Douglas S. Hawkins, MD[1]; Marie-Cecile Le Deley[2]; Bernadette Brennan[3]; Ian Judson[4]; Richard Gorlick[5]; Richard B. Womer[6]; Nathalie Gaspar[2]; Gwenael Le Teuff[2]; Perrine Marec-Berard[7]; Andreas Faldum[8]; Michael Paulussen[9]; Heribert Juergens[8]; Keith Wheatley[10]; Mark Krailo[11]; Uta T. Dirksen[8]
[1]Pediatrics, Seattle Children's Hospital, Seattle, WA, USA; [2]Institute Gustave Roussy, Villejuif, France; [3]Royal Manchester Children's Hospital, Manchester, United Kingdom; [4]The Royal Marsden Hospital, Sutton, United Kingdom; [5]The Children's Hospital, Bronx, NY, USA; [6]Children's Hospital of Philadelphia, Philadelphia, PA, USA; [7]Institut d'Hématologie et d'Oncologie Pédiatrie, Lyon, France; [8]Westfälische Wilhelm's-Universität Münster, Muenster, Germany; [9]Witten-Herdecke University, Datteln, Germany; [10]University of Birmingham, Birmingham, United Kingdom; [11]Department of Preventive Medicine, University of Southern California, Los Angeles, CA, USA

Objective: EE99R2pul (ISRCTN61438620) was conducted in 16 countries, by 5 cooperative groups: COG, SFCE/GSF, GPOH, UK CCLG, EORTC. It evaluated the effect on event-free (EFS, main endpoint) and overall survival (OS) of BuMel without radiation to the lung, compared to standard chemotherapy with lung irradiation in ES presenting with metastases to the lung or pleura.

Methods: Eligible pts had histological confirmation of ES, lung or pleural metastases, no other metastatic site, were aged < 50, received chemotherapy with 6 VIDE (vincristine, ifosfamide, doxorubicin, etoposide) courses and 1 VAI (vincristine, actinomycin-D, ifosfamide) before randomization to BuMel with stem cell rescue or VAI x 7 courses and lung irradiation (VAI-RT). The analysis was conducted as intention-to-treat. The estimate of the hazard ratio, HR, and the p-value were corrected for the 3 previous interim analyses by the Inverse Normal Method. The presented data will represent the final analytic data cohort.

Results: Between 2000 and 2014, from 576 pts with lung or pleural metastases, 265 pts (median age, 14 yrs) were

randomized to VAI-RT (132) or BuMel (133). Some pts requiring radiation therapy to the primary site were excluded from randomization to avoid excess organ toxicity from interaction between RT and Busulfan. Median follow up is 7.8 yrs. We did not observe any significant difference in survival outcomes between treatment groups: For BuMel pts, 3yr-EFS was 55% vs. 51% for VAI-RT pts, hazard ratio (HR) of 0.82 (0.58-1.15), p = 0.24. OS was 68% for BuMel vs. 68% for VAI-RT, HR 0.96 (0.65-1.40), p = 0.82. Results were consistent across subgroups, and in the sensitivity analyses, with the exception of histologic response, in which BuMel was superior among pts with good pathologic response (< 10% viable cells) and VAI-RT was superior among pts with poor pathologic response (> 30% viable cells), p=0.0003. Three pts died of BuMel-related toxicity and none after standard chemotherapy. Significantly more pts in BuMel-arm experienced severe acute toxicities than in the VAI-RT arm.

Conclusion: In ES with lung metastases, there is no clear benefit associated with BuMel high-dose chemotherapy without lung irradiation compared to conventional chemotherapy combined with lung irradiation.

P1 - Poster 146 2566848

INSTITUTIONALLY-REPORTED HISTOLOGIC RESPONSE (HR) AND OUTCOME IN EWING SARCOMA: A REPORT FROM CHILDREN'S ONCOLOGY GROUP STUDY AEWS0031

Richard B. Womer, MD[1]; Mark Krailo[2]; Daniel C. West[9]; Bruce R. Pawel[3]; Paul Dickman[4]; John Healey[10]; John P. Dormans[11]; Karen Marcus[5]; Neyssa Marina[6]; Holcombe E. Grier[7]; Aaron Weiss[12]; Richard Gorlick[8]

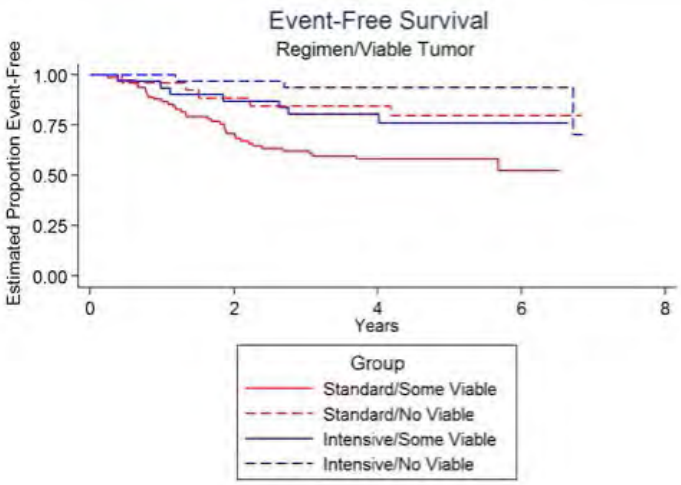
[1]Pediatrics / Oncology, Children's Hosp of Phila / Univ of Penn, Philadelphia, PA, USA; [2]Children's Oncology Group, Monrovia, CA, USA; [3]Pathology, Children's Hosp of Phila / Univ of Penn, Philadelphia, PA, USA; [4]Pathology, Phoenix Children's Hospital, Phoenix, AZ, USA; [5]Radiation Oncology, Dana-Farber Cancer Center, Boston, MA, USA; [6]Pediatrics, Lucille Packard Children's Hospital, Palo Alto, CA, USA; [7]Pediatrics, Dana-Farber Cancer Institute, Boston, MA, USA; [8]Pediatrics, Montefiore Medical Center, New York, NY, USA; [9]Pediatrics, University of California, San Francisco, San Francisco, CA, USA; [10]Orthopedics, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [11]Orthopedics, Texas Children's Hospital, Houston, TX, USA; [12]Pediatrics, Maine Medical Center, Portland, ME, USA

Objective: Several previous studies have associated histologic response at primary tumor surgery with outcome in Ewing sarcoma. AEWS0031 (accrual 2001-2005) compared standard timing (ST) 3-weekly chemotherapy with interval compressed (IC) 2-weekly treatment. We assessed the association between HR, treatment assignment, and outcome in that study, and assessed the impact of IC.

Methods: AEWS0031 did not require submission of HR data on excised specimens, nor did the protocol provide instructions for such assessment; however many investigators reported it. To be considered a valid necrosis assessment (VNA), patients had to have surgery as their first local control method, and it had to occur between 56 and 120 days after enrollment. The endpoint was 5 year event-free survival (EFS) from the time of local control.

Results: Of 568 eligible patients, 230 had surgery as their first method of local control, and 171 had VNAs (86 ST and 85 IC). Analyzing all surgical patients, EFS was the same for the groups with and without VNA. Patients with 90% or more necrosis (65% of the total) had better 5y EFS than those with less than 90% (77% v. 61%, p=0.038). Further analysis revealed that the patients with no viable tumor (NVT) (41% of the total) underlay this advantage: 5 year EFS for patients with NVT v 90-99% necrosis v less than 90% necrosis was 87%, 65%, and 61% respectively (p=0.003). IC provided slightly more NVT than ST (38% v 30%, p=0.34), but it produced much superior 5y EFS regardless of HR (82% v 61%, p=0.002). Combining HR and regimen, IC and NVT provided the best 5y EFS (94%), ST and viable tumor the worst (58%), and the other combinations were in between (p=0.0005) (Figure).

Conclusion: Every-2-week IC chemotherapy provides a slightly higher proportion of good histologic responses, and much better EFS regardless of histologic response, than ST every-3-week chemotherapy in localized Ewing sarcoma. Necrosis (NVT v some viable tumor) and regimen are significantly independently prognostic. We plan to repeat these analyses with centrally reviewed pathology.



P1 - Poster 147 2559012

GEIS-21: A MULTICENTRIC PHASE II STUDY OF INTENSIVE CHEMOTHERAPY INCLUDING GEMCITABINE/DOCETAXEL FOR THE TREATMENT OF EWING SARCOMA OF CHILDREN AND ADULTS: A REPORT FROM THE SPANISH GROUP OF SARCOMA INVESTIGATION (GEIS)

Jaume Mora, MD, PhD[1]; Alicia Castañeda[1]; Antonio Lopez-Pousa[4]; Claudia Valverde[3]; Javier Martin-Broto[2]; Xavier Garcia del Muro[5]; Enrique de Alava[2]; Carmen de Torres[1]
[1]Pediatric Oncology, Hospital Sant Joan de Déu, Barcelona, Spain; [2]Hopsital Virgen del Rocio, Sevilla, Spain; [3]Hospital Vall de Hebron, Barcelona, Spain; [4]Hospital de Sant Pau, Barcelona, Spain; [5]Institut Català d'Oncologia, Barcelona, Spain

Objective: first Spanish trial of Ewing sarcoma (ES) with the aim to reproduce the mP6 results and test the efficacy of the Gemcitabine/Docetaxel (G/D) regimen.

Methods: prospective, multicentric, non-randomized study of ES pts ≤40 years with tumor rearrangements of EWSR1. Centralized bone marrow screening for micrometastatic spread and radiological review was performed. All pts received 5 mP6 courses of chemotherapy; surgical resection after course 3; and radiotherapy after course 5. High-risk (HR) pts received 2 window cycles of G/D, Gemcitabine 1000 mg/m2 IV on days 1 and 8, and Docetaxel 100 mg/m2 on day 8 of a 21-day cycle. HR pts with an objective response (OR) to G/D received 12 monthly cycles of G/D after mP6.

Results: 43 (22 SR, 21 HR) pts were enrolled, median age 17y (range, 3 - 40). 10/21 HR pts evaluable for G/D window therapy response showed 1 complete (CR) and 3 partial (PR) responses, 3 stable disease (SD). 30/43 pts were evaluable at the end of mP6. 24 (80%) CR; 3 (10%) PR; 1 SD (3%); and 2 (7%) progressed. 11 HR entered maintenance and 1 year later 5 remain CR. Grade 4 adverse events during mP6 occurred in 28/39 (72%) and did not correlate with age. Statistically significant differences were detected for risk groups: SR 4-y OS 74% (CI=51,100) and 4-y EFS 67% (CI=47,95); HR 4-y OS 42% (CI=25,73) p=0.011 and EFS 27% (CI=13,56) p=0.0028; and age: <18y 4-y OS 78% (CI= 58,100) and 32% for >18y (CI= 15,69) p<0.001; 4y-EFS 62% (CI= 43,89) <18y and 28% (CI= 13,61) >18y, p=0.0087. Multivariate analysis for OS showed HR and < 18y vs HR >18y, p= 0.0070; HR and >18y vs SR and < 18y, p <0.001. Cox model for HR and >18y vs SR and <18y, p<0.001; 18y vs same risk group, p= 0.0021, superior to same age vs risk group, p=0.014.

Conclusion: The G/D regimen resulted in objective responses to 70% HR-ES. Age is stronger predictive marker than risk group. Monthly G/D benefited 50% of HR-ES providing a backbone regimen for managing minimal residual disease.

P1 - Poster 148 2571077

PEDIATRIC PATIENT WITH SIADH RELATED TO HIGH DOSE METHOTREXATE REGIMEN

Jennifer A. Misasi, Masters[1]; Anil P. George[2]; Paul Kent[1]
[1]Pediatrics-Oncology, Rush University Medical Center, Chicago, IL, USA; [2]Pediatrics-Oncology, University of Illinois, Chicago, IL, USA

Objective: The case we are presenting is one of pediatric oncology and osteosarcoma. In our practice we see many sarcomas and have administered quite a bit of high dose methotrexate and have not seen SIADH occur. The objective is to understand the importance of recognizing this severe side effect in order to treat immediately and assertively for the best patient outcome.

Methods: A 14 year old female with localized right tibia osteosarcoma was treated following the COG protocol AOST0331 "MAP," during her fourth dose of HDMTX experienced acute fluid retention with a weight gain of of 2.5kg, edema of face, hands and feet, diminished urine output (from 5 to 1.2 cc/kg/hr), increasing urine specific gravity (1.005 to 1.017), free water retention (hemoglobin dropped from 8.7 to 7.8/dl, Na+ dropped from 138 to 133mmol/L), BUN/Cr 12/0.64 mg/dl to 9/0.66 mg/dl simultaneous urine/serum osmolality of 725 and 292 mos/kg, with delayed clearance of methotrexate and on no renal toxic medications. After diagnosis of SIADH the patient was successfully treated with intravenous furosemide without further complication or delay in treatment.

Results: The standard chemotherapeutic agents used in osteosarcoma, "MAP" (cis-platinuum, high dose methotrexate (HDMTX), and doxorubicin) have been associated with hyponatremia and renal salt wasting (Turner, N. et al, Asia-Pacific Journal of Clinical Oncology,2012, 8: 9-11). And although the syndrome of inappropriate antidiuretic hormone (SIADH) has been associated with several cancers and several chemotherapy drugs (most commonly small-cell lung carcinoma and the drugs cyclophosphamide, vinblastine and vincristine), there have been no cases associated with osteosarcoma or high dose methotrexate (HDMTX). The proposed mechanisms for methotrexate-induced hyponatremia in the literature include toxic effects on the neurosecretory areas of the cerebrum, activation of natriuretic peptides, or changes in the distribution of body fluid volumes, but not excessive ADH secretion.

Conclusion: We wish to raise awareness of the rare complication of SIADH associated with HDMTX in the setting of osteosarcoma treatment in the hopes that if others experience the same scenario they can benefit from our report.

P1 - Poster 149 2570646

OUTCOMES IN PATIENTS WITH RECURRENT DESMOID TUMOR MANAGED WITH SURGERY ALONE, COMBINED SURGERY AND RADIATION THERAPY OR RADIATION THERAPY ALONE

Michelle S. Gentile, MD, PhD[1]; Alex Jacobson[1]; Haotong Wang[1]; Saveli Goldberg[1]; Edwin Choy[3]; John T. Mullen[2]; Kevin Raskin[4]; Nielsen Petur[5]; Francis Hornicek[4]; Thomas F. DeLaney[1]; Yen-Lin Chen[1]
[1]Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [2]General Surgery, Massachusetts General Hospital, Boston, MA, USA; [3]Medical Oncology, Massachusetts General Hospital, Boston, MA, USA; [4]Orthopedic Oncology, Massachusetts General Hospital, Boston, MA, USA; [5]Pathology, Massachusetts General Hospital, Boston, MA, USA

Objective: Desmoid tumor is a benign tumor that can be locally aggressive and is managed with a variety of treatments including surgery, radiation therapy (RT) and systemic agents in the recurrent setting. The purpose of this study was to determine the disease free survival (DFS) in patients with recurrent desmoid tumor treated with one of the above named modalities.

Methods: The medical records of 90 patients with recurrent desmoid tumor treated at our institution from 1970 through 2015 were reviewed to collect patient, tumor and treatment related characteristics. Kaplan Meier method was used to analyze survival outcomes.

Results: Median age at first recurrence was 33.1 years old (range,9.5-78.4). There were 34 (37.8%) male patients. Breakdown of tumor locations were 54 (60.0%) in the extremity, 17 (18.9%) in the spine/sacrum/bony pelvis, 9 (10.0%) in the trunk, 4 (4.4%) in the head and neck with 4 (4.4%) in the thorax and 1 (1.1%) in the retroperitoneum. Median size of tumor at intial surgery was 7 cm (range,1.5–32) and 32 (35.6%) of patients had close/positive margins. Margin status was not available for 28 (31.1%) patients. Median time to recurrence was 15.4 months (range, 1.9–107.6). Median follow-up was 7.4 years (range, 0.1–41.6). At first recurrence, 23 (25.6%) patients were treated with surgery alone, 48 (53.3%) patients were treated with surgery and RT, and 9 (10.0%) patients were treated with RT alone. Other patients were treated with observation, systemic therapy alone or a combination of modality and systemic therapy. Two patients in the RT alone group were treated with systemic therapy. Of patients treated with RT, the median dose was 54.0 Gy (range,45.0–64.6). 26 (28.9%) were treated with conventional RT, 6 (6.7%) patients were treated with protons, 3 (3.3%) were treated with IMRT, and 1 (1.1%) was treated with IORT. RT modality was not specified for 22 (24.4%) patients. 5 year DFS was 33.1% (95% CI:14.3–53.4), 64.2% (95% CI:47.7–76.8), 88.9% (95% CI:43.3–98.3) for patients treated with surgery alone, combination of RT and surgery and RT alone respectively (p-value=0.002). For patients with subsequent recurrence, 5 years DFS was 44.3% (95% CI:24-62.9) and 67.8% (95% CI:52.7-79.0) for treatment without and with RT, respectively (p-value=0.01).

Conclusion: DFS is best in patients treated with RT alone or a combination of surgery and RT at recurrence. Inclusion of RT may be considered for patients with recurrent desmoid tumor when technically feasible and the risk of morbidity is small.

P1 - Poster 150 2565620

THE SAFETY AND RESULTS OF INTRATUMORAL STERIOD INJECTION FOR PROGRESSIVE FIBROMATOSIS: PHASE-I CLINICAL TRIAL STUDY

Dumnoensun Pruksakorn, MD, PhD[1]; Areerak Phanphaisarn[1]; Saratwadee Lorsomradee[2]; Natthapong Kosachumhanun[3]; Pimpis Piyakasem[1]; Jongkolnee Settakorn[4]
[1]Department of Orthopedics, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [2]Department of Anesthesiology, Chiang Mai University, Chiang Mai, Thailand; [3]Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; [4]Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Objective:
1. Short and intermediate term complications monitoring from procedures and local steroid used
2. Outcome of treatment monitoring including pain, functional score, and tumor size

Methods: This is Phase I clinical trial study of intratumoral steroid injection in fibromatosis. The protocol approved by ethical committee of Faculty of Medicine, Chiang Mai University ORT-12-1184-FB(ID:1184). Ten patients with recurrent, and progressive fibromatosis were enrolled. Particulated steroid (10 mg/mL Kenacort-A suspension of total dose 3 mg/kg) was injected in tumor under ultrasound guidance. The injection was operated monthly for 3 consecutive months. Patients were followed up until 3 months after last injection (totally 6-month period of study). Short and long term complications from procedures and from locally steroid use, as well as pain, functional score, and tumor size were monitored.

Results: Eight patients were able to comply the full evaluation process. No minor and major procedure-related complications were reported. Two cases presented the significant high blood pressure during injection protocol and returning to normal level within the study period. The serum triamcinolone level was increased after 24 hours of injection. There was no interruption of hypothalamus-pituitary-adrenal (HPA) axis in one month after finishing procedure (the fourth month of study). The significant improvement ($p<0.05$) of pain from 6.75±3.24 of before injection and 3.38(±1.60),

3.13(±1.64), 2.50(±1.41), 2.63(±1.92), 2.63(±1.60), and 2.50(±1.60), after the 1st, 2nd, 3rd, 4th, 5th and 6th month, respectively. The significant improvement of functional score from 2.38(±0.74) of before injection and 1.50 (±1.07) and 1.63(±1.06), at the 4st and 6st month, respectively. Tumor size were stabilized from progression in 6 of 8 cases (75%). No regression of tumor was observed, and two cases continually progressed despite receiving steroid.

Conclusion: High dose intra-tumoral steroid injection is an alternative procedure for controlling recurrent and progressive fibromatosis with good safety margin. Locally steroid application also has the systematic distribution and presented some steroid effects, but without HPA-axis suppression. Phase II clinical trial would be further study with a larger group and longer term of follow up to identify the optimum frequency of injection with minimal complications from steroid used.

P1 - Poster 151 2555901

CLINICAL FEATURES AND TREATMENT OUTCOME OF DESMOID-TYPE FIBROMATOSIS BASED ON DATA OF THE BONE AND SOFT TISSUE TUMOR REGISTRY IN JAPAN

Yoshihiro Nishida, MD, PhD[1]; Akira Kawai[2]; Junya Toguchida[3]; Akira Ogose[4]; Keisuke Ae[5]; Toshiyuki Kunisada[6]; Tomoya Matsunobu[7]; Shunsuke Hamada[1]; Tomohisa Sakai[1]
[1]Orthopaedic Surgery, Nagoya University Graduate School and School of Medicine, Nagoya, Aichi, Japan; [2]National Cancer Center, Tokyo, Japan; [3]Kyoto University, Kyoto, Japan; [4]Uonuka Kikan Hospital, Niigata University, MInami Uonuma, Japan; [5]Cancer Institute Hospital, Tokyo, Japan; [6]Okayama University, Okayama, Japan; [7]Kyusyu Rosai Hospital, Kitakyusyu, Japan

Objective: Treatment modality for patients with desmoid-type fibromatosis (desmoid) has been changed from surgery with negative operative margin to conservative therapy including watchful waiting. To establish appropriate practice guideline for patients with desmoid in our country, Japan, we should know the ongoing treatment modality and clinical outcome of recent years. The aims of this study were to clarify the registration status, transition of treatment modality, and treatment outcome of patients with desmoid in Japan.

Methods: Registration and follow-up data of primary soft tissue tumors has been collected to National Cancer Center, from most of the specialized hospitals for bone and soft tissue tumors in Japan. This registration has been directed by Musculoskeletal Tumor Committee (MSTC) of Japanese Orthopaedic Association (JOA). Registration data regarding desmoid from 2006 to 2012, and follow-up data of registered cases from 2006 to 2010 were also retrieved. This retrospective study was approved by Ethical Review Board of JOA. Demographics were investigated, and clinical outcome and prognostic factors of patients with surgical treatment was analyzed with Kaplan-Meier method and logrank test.

Results: The number of registered desmoid has been increasing yearly (Fig. 1). In total, 530 cases, female 323 cases (61%) and male 207 were registered. Mean age was 44. Site of predilection was lower extremity, trunk, and abdominal wall. The number of case with surgical treatment was similar to that with conservative treatment. Whereas, from 2011 to 2012, 65 cases (33%) received surgical treatment among registered 196 cases (Fig. 2). Among 103 cases, which were registered from 2006-2010, with follow-up data, three-year recurrence-free survival with surgical treatment was 77.7% (Fig. 3). Extremity location (P=0.11) and tumor size (>8cm, P=0.091) tended to be poor prognostic factors. There was no significant difference in recurrence between wide and marginal margin (P=0.34).

Conclusion: We have collected and investigated the basic data for desmoid in Japan. Treatment modality for desmoid has been shifted to conservative treatment in Japan, which is similar to European countries. Cases with extremity location and/or large tumor size will not be suitable for surgical treatment. To establish adequate practice guideline for patients with desmoid, other factors including treatment outcome of conservative therapy and significance of CTNNB1 mutation status should be further clarified.

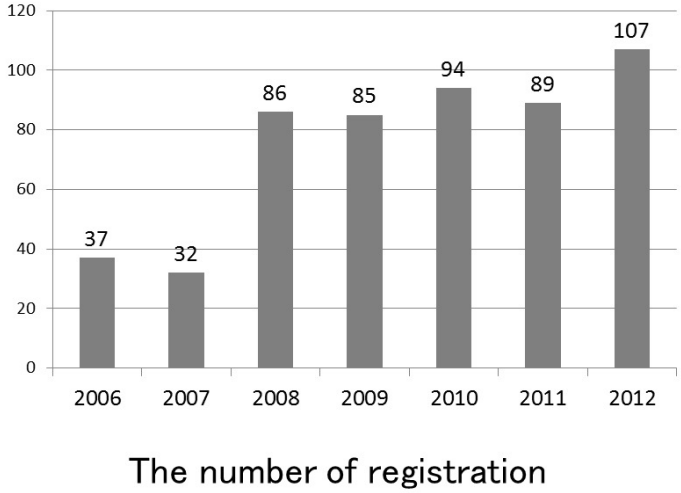


Fig. 1. The number of registration in desmoid.

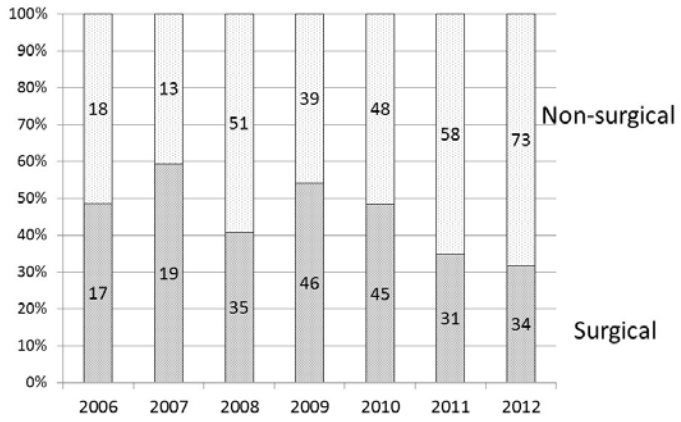


Fig.2 The ratio of operative and non-operative treatment for desmoid.

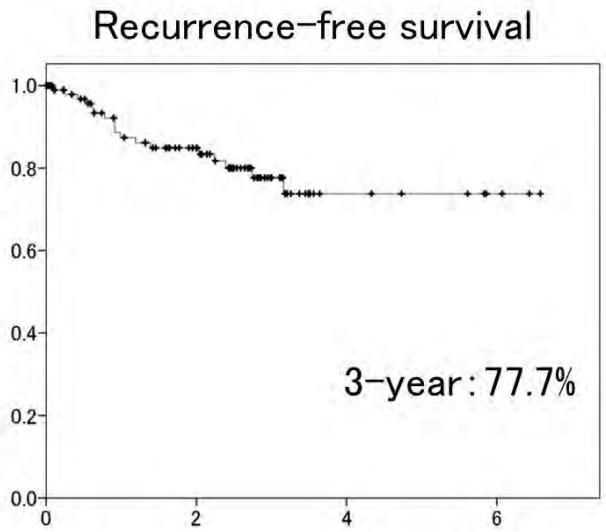


Fig. 3. Recurrence-free survival in all cases.

P1 - Poster 152 2531917

IS SYMPTOM WORSENING (SW) ASSOCIATED WITH RECIST RESPONSE IN DESMOID TUMORS (DT) PATIENTS (PTS)?

Nuria Kotecki[1]; Armelle Renaud[2]; Meriem Ben Haj Amor[2]; Desfachelles Anne-Sophie[3]; Thomas Ryckewaert[1]; Vincent Gamblin[4]; Yves-Marie Robin[5]; Sophie Taieb[2]; Nicolas Penel[1]

[1]Medical Oncology, Centre Oscar Lambret, Lille, France; [2]Imaging Department, Centre Oscar Lambret, Lille, France; [3]Pediatric Oncology Unit, Centre Oscar Lambret, Lille, France; [4]Palliative Care Unit, Centre Oscar Lambret, Lille, France; [5]Pathology Unit, Centre Oscar Lambret, Lille, France

Objective: DT is a rare, locally infiltrative tumor. Front-line 'watch-and-wait' policy with monitoring by MRI is recommended.

Methods: We retrospectively reviewed data from 27 consecutive pts with histologically-proven DT from 01/2007 to 12/2015. The study aims to investigate if WS is correlated with disease progression according to RECIST 1.1, volumetric changes or contrast enhancement (CE) over time. Clinical and MRI characteristics were measured at diagnosis and at last follow up.

Results: The cohort consisted in 6 men (22%) and 21 women (77%) with a median age of 33 (10-77). The most common location was the abdominal wall (11, 40%). Median follow-up was 40 months (5-98). 15/27 (55%) pts received at least 1 systemic treatment including NSAID, tamoxifen, imatinib or methotrexate based chemotherapy**.** Increasing in pain, retraction, functional impairment were seen respectively in 11 (40%), 10 (37%) and 10 (37%) patients. Objective response, stable disease and disease progression according to RECIST 1.1 was found respectively in 7 (26%), 13 (48%) and 7 (26%) pts, respectively. Objective response, stable disease and progressive disease according to volumetric changes was found in 8 (30%), 10 (37%), 9 (33%) pts, respectively. Size and volume changes were highly correlated (p<.00001.). We have described 2 "false" progressions characterized by increased of only 1 axis and decrease of other axis; this could be related tumor retraction along the muscle fibers. We found that response assessment according RECIST was not associated with WS.. CE was assessable in 26 pts, with decrease CE in 10 pts (38%) and stable CE in 16 pts (62%). CE change and RECIST response were not correlated (p=0.697). CE changes were not associated with worsening of pain (p=0.676), retraction (p=0.126) and functional impairment (p=0.126)

Conclusion: SW was not associated with the response according to RECIST or CE change. Innovative methods for monitoring pts are needed.

P1 - Poster 153 2558252

A REFRACTORY DESMOID-TYPE FIBROMATOSIS WITH A REMARKABLE RESPONSE TO PAZOPANIB TREATMENT

Eisuke Kobayashi, MD, PhD; Makoto Endo; Yoshikazu Tanzawa; Fumihiko Nakatani; Hirokazu Chuman; Akira Kawai

Orthopaedic, National Cancer Research Center Hospital, Tokyo, Japan

Objective: Desmoid-type fibromatosis (DTF) usually behaves as an indolent disease. A wait-and-see policy at the initial presentation is the current standard treatment. Although some cases of DTF have a very aggressive course with a high tendency toward local recurrence, the significance of surgery is still controversial, and systemic treatment options are limited.

Methods: A 19-year-old male Japanese patient with unresectable recurrent DTF in his thigh was admitted to our institution 6 months after initial surgical resection by a referring surgeon. He did not have a history of Gardner's syndrome or colonic polyps. Magnetic resonance imaging (MRI) confirmed a huge recurrent tumor involving his sciatic nerve. As the tumor was considered to be unresectable, he had started systemic treatment with NSAIDS or tamoxifen or methotrexate two years previously. However, there was a gradual increase in the size of the mass and worsening of pain. Eventually he started treatment with the multi-targeted tyrosine kinase inhibitor pazopanib (800 mg daily orally) due to the progressive increase in size.

Results: Pazopanib treatment brought about a significant improvement in clinical symptoms after three months of treatment. MRI demonstrated a remarkable radiological response with significantly decreased gadolinium enhancement and persistent regression. The dose was reduced to 600 mg due to mild diarrhea and palmer erythema three months after starting pazopanib. Second-look biopsy confirmed the histological degeneration of this tumor. Pazopanib was subsequently reduced to 200 mg after the confirmation of a radiological response every four months. He remains on a 200 mg dose of pazopanib without significant adverse events, and his tumor has remained stable in size one year after starting pazopanib treatment.

Conclusion: The patient achieved a dramatic improvement in his symptoms and radiological response after starting pazopanib treatment. Pazopanib may therefore be an effective and promising treatment option for progressive and refractory DTF.

P1 - Poster 154 2570475

THERAPY AND PROGNOSIS IN DESMOID TUMOR

Laura Wirth[1]; Falk Roeder[2]; Andrea Baur-Melnyk[3]; Thomas Knösel[4]; Lars Lindner[5]; Alexander Klein[1]; Volkmar Jansson[1]; Hans R. Dürr[1]
[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany;
[2]Institute of Radiotherapy, LMU Munich, Munich, Germany;
[3]Institute of Radiology, LMU Munich, Munich, Germany;
[4]Institute of Pathology, LMU Munich, Munich, Germany;
[5]Medical Clinic III, LMU Munich, Munich, Germany

Objective: Desmoid tumors are totally unpredictable in their behavior. Established are the surgical treatment, as well as radiation therapy and various systemic therapies. The aim of this study was to clarify the impact of margins in surgery.

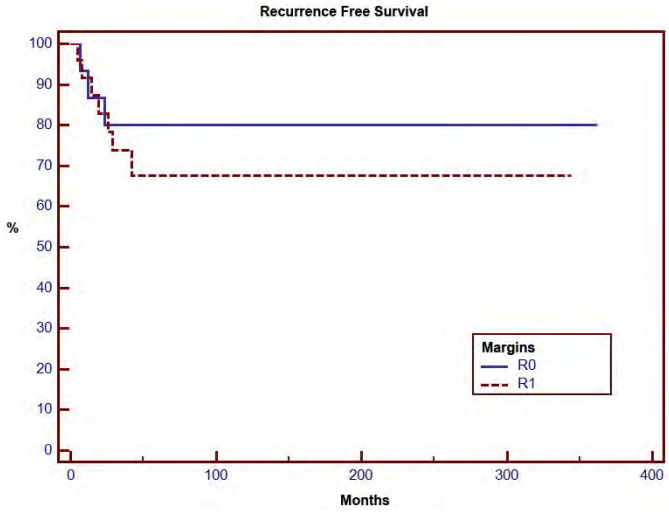
Methods: From 1981 to July 2014. 53 treatments were performed in 44 patients. At the time of diagnosis the average age of the 19 mals was 40.9 years, of the 25 females 39.9 years. In total 53 treatments in 37 primary patients and 16 recurrent cases had been done. Performed had been in 16 cases a R0-resection in 28 cases, a resection with positive margins (R1) and in 6 cases a R2-resection. 5 patients received therapy with NSAIDs, 20 patients were irradiated, one patient received tamoxifen, 3 patients received Imatinib and one patient did undergo chemotherapy. In 53 treated cases follow-up was possible in 47 cases.

Results: 2 patients died independently to the desmoid tumour. In case of a R0-resection we saw local recurrence in 20%. In case of a R1-resection in 29% (Figure 1, p=0.54). Considering radiation, neither in the R0-resected patients (in 4 cases, radiotherapy) nor in R1-resected patients (12 radiotherapy), a significant difference was seen.

In 6 R2-resections in 2 cases, additonal radiotherapy was done. One patient remained without progression, one patient could not be reached for follow-up. In 4 cases, there was no further therapy. 2 patients showed no progression, one patient was progressive, another patient could not be tracked.

In 3 cases (each recurrence) there was no further surgical treatment. One patient received NSAIDs and remained without progression. One patient is progressive after radiation and one patient showed a response with Imatinib. From 47 trackable cases 36 (77%) were free of tumour. 2 out of 16 relapsed cases are not trackable and 10 are free of tumour (71%). In 37 primary cases 4 are not trackable and 26 free of tumour (79%).

Conclusion: In all but one case (end of a toe) amputation could be avoided. The course of the disease was found completely unpredictable, both in watchfull waiting, as well as under systemic therapy, stable or regressive follow-ups had been seen. Regarding surgery, no benefit of a R0-resection was seen, as also no positive effect of radiation could be shown neither in the R0 as also the R1-resected patients. Whether it was a primary or recurrent tumor remained without significance to local recurrence. In total free of tumour was achieved in more than ¾ of the cases.



P1 - Poster 155 2553792

USE OF HYDROXYUREA IN CHILDREN, ADOLESCENTS AND ADULTS WITH RECURRENT AND/OR REFRACTORY AGGRESSIVE FIBROMATOSES

Caroline J. Gross, BS[1]; Arun S. Singh[2]; Bartosz Chmielowski[2]; Frederick C. Eilber[3]; Nicholas Bernthal[4]; Susan Bukata[4]; Leanne Seeger[5]; Scott Nelson[6]; Mitchell Kamrava[7]; Noah Federman[8]
[1]UCLA David Geffen School of Medicine, Los Angeles, CA, USA; [2]Medicine, Hematology & Oncology, UCLA, Los Angeles, CA, USA;
[3]Surgical Oncology, UCLA, Los Angeles, CA, USA;
[4]Orthopaedic Surgery, UCLA, Los Angeles, CA, USA;
[5]Radiological Sciences, UCLA, Los Angeles, CA, USA;
[6]Pathology, UCLA, Los Angeles, CA, USA;
[7]Radiation Oncology, UCLA, Los Angeles, CA, USA;
[8]Pediatrics, Hematology & Oncology, UCLA, Los Angeles, CA, USA

Objective: Aggressive fibromatosis or desmoid tumor (DT) is a rare neoplastic proliferation characterized by the presence of locally aggressive, fibroblastic disease. Surgical resection has been considered the mainstay of treatment, though commonly associated with adverse functional sequelae and high rates of tumor recurrence. Systemic pharmacotherapy is generally reserved for unresectable tumors and/or recurrent/refractory disease. Limited data exists on the use of hydroxyurea (HU) in DTs.

Methods: We performed an IRB approved retrospective chart review for treatment and outcomes for 10 patients with recurrent and/or refractory aggressive extra-abdominal DTs who were treated with HU at UCLA medical center. Patients were treated with 20mg/kg of HU rounded to nearest 500mg tablet with dose escalation secondary to signs of pain or tumor growth. Tumor burden was monitored by serial MRIs every 3 to 12 months. Response to treatment was evaluated by Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 through comparison of pre- and post-treatment imaging. Toxicities were graded with standard Common Terminology Criteria for Adverse Events (CTCAE) v4.0.

Results: Since initiation of HU, 1 patient has had partial response (30% tumor reduction) and 9 patients have had stable disease, with an average progression free survival of 36.7 months [range 10.5-58.7mo]. Zero patients have had disease progression since the initiation of HU treatment. No grade 3-4 toxicities were observed. Toxicities included grade 1 neutropenia (n=1), which resolved after holding the medication for 1 week; Grade 1 thrombocytopenia (n=2), which resolved after holding the medication for 2 months; 4 patients discontinued the medication due to complaints of fatigue (n=1), questionable tumor progression (n=1) and non-specific complaints with taking a daily medication in the context of stable disease (n=2). Prior to initiating HU, patients had received an average of 1.3 lines of therapy [range 0-3], including Tamoxifen/Indomethacin, Naproxen, Methotrexate/Vinblastine and Doxorubicin/Dacarbazine, and patients had undergone an average of 1.9 surgical resections [range 0-3]. 4 patients had received prior adjuvant radiation therapy.

Conclusion: HU is a non-toxic, safe and potentially effective treatment modality for long term control of DT. Initial evaluation has shown the potential for this treatment to be an important addition to the armamentarium of aggressive fibromatosis therapy supporting the initiation of a prospective clinical trial.

P1 - Poster 156 2561516

DESMOID PATIENTS AND THE RISK OF FAMILIAL ADENOMATOUS POLYPOSIS: WHO SHOULD HAVE A COLONOSCOPY?

Winan van Houdt, MD, PhD[1]; Deborah Kuk[3]; Li-Xuan Qin[3]; Anthony Villano[2]; Meera Hameed[4]; Frits van Coevorden[5]; Samuel Singer[2]; Aimee M. Crago[2]
[1]Department of Surgery, Royal Marsden Hospital, London, United Kingdom; [2]Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Department of Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA;
[4]Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, USA;
[5]Surgery, Netherlands Cancer Institute, Amsterdam, Netherlands

Objective: A fraction of patients with desmoid-type fibromatosis have undiagnosed familial adenomatous polyposis (FAP). We sought to define subsets of desmoid patients who require colonoscopy to rule out underlying FAP.

Methods: Patients (n=652) presenting with desmoids during 1982-2015 were identified by query of a single-institution pathology database and prospectively maintained database of surgical outcomes. Retrospective review identified those who underwent colonoscopy. *CTNNB1* mutations were identified by Sanger sequencing. Fisher's tests were used to compare patient subsets.

Results: 26 patients (4.0%) with desmoids had FAP. In 20, diagnosis of FAP predated desmoid diagnosis, and in 6, desmoid was the initial manifestation of FAP. Compared with those with sporadic desmoids (n=626), patients with FAP were younger (median 26 vs 38 years, $p<0.001$) and more likely to have intraabdominal tumors (53% vs 21%, $p<0.001$), multiple primary tumors (62% vs 3%, $p<0.001$), and first-degree relatives with colonic neoplasms (46% vs. 5%; $p<0.001$). Colonoscopy results were reported for 161 (25%) of the 632 patients without FAP diagnosis at presentation. The test identified the 6 patients in whom desmoid was the initial sign of FAP (6/161 patients undergoing colonoscopy; 3.7%). Probability of finding FAP on

colonoscopy tended to be higher in patients with clinicopathologic features characteristic of FAP (Table 1), such as intraabdominal disease (4/74 patients; OR=2.4) or positive family history (3/36 patients with 1st-degree relative having colon neoplasm or unknown family history; OR=3.3) and was statistically higher in those with multifocal desmoids (4/14 patients; OR=29, p<0.001) and age <40 years (6/55; OR=2.8 x 10^8, p=0.0013). All patients diagnosed with FAP following presentation with a de novo desmoid had at least 2 of these 4 risk factors, and all were younger than age 40 (Table 2). *CTNNB1* mutation status was known in tumors of 50 patients who underwent colonoscopy. No cases of FAP was identified in the 34 patients with *CTNNB1* mutation; 4 were identified in 16 patients with 'wild-type' *CTNNB1* (25%, p <0.001).

Conclusion: Desmoid-type fibromatosis is rarely the initial presentation of FAP; in these instances, patients have multiple risk factors associated with the genetic condition. Therefore, colonoscopic screening can be recommended selectively in patients with new diagnosis of desmoid. *CTNNB1* sequencing and identification of gene mutation may provide an alternative means of FAP screening.

Table 2: Characteristics of patients presenting with desmoid before diagnosis of FAP

GENDER	AGE	FAMILY HISTORY	MULTIPLE PRIMARIES	LOCATION
male	29	mother, colon cancer (42 y.o.)	yes	intra-abdominal
female	18	no	yes	intra-abdominal
male	13	no	yes	mandibula
female	28	unknown on father's side	yes	abdominal wall
female	35	no	no	intra-abdominal
female	36	mother, colon cancer (28 y.o.)	no	intra-abdominal

Table 1: Colonoscopies positive for FAP, by risk factor

	Total	No FAP (n = 155)	FAP (n=6)	p-value
AGE:				
< 40	55	49 (89)	6 (11)	0.0013
>= 40	106	106 (100)	0 (0)	
LOCATION:				
Intra-abdominal	74	70 (55)	4 (5)	0.4148
Other	87	85 (98)	2 (2)	
MULTIPLE PRIMARIES:				
No	147	145 (99)	2 (1)	< 0.001
Yes	14	10 (71)	4 (29)	
POSITIVE FAMILY HISTORY:				
1st degree	25	23 (92)	2 (8)	0.3078
2nd degree	8	8 (100)	0 (0)	
None	114	111 (97)	3 (3)	
Unknown	14	13 (93)	1 (7)	
NUMBER OF RISK FACTORS:				
0	40	40 (100)	0 (0)	<0.001
1	69	69 (100)	0 (0)	
2	44	42 (95)	2 (5)	
3	7	4 (57)	3 (43)	
4	1	0 (0)	1 (100)	

Risk factors were age <40 years, 1st degree relative or unknown family history, multiple primaries, and intra-abdominal tumor

P1 - Poster 157 2570645

CONSERVATIVE MANAGEMENT OF DESMOID TUMORS IS SAFE AND EFFECTIVE

Jiwon S. Park[1]; Robert D. Boutin[2]; Arta M. Monjazeb[3]; Robert J. Canter[1]
[1]Surgery, UC Davis, Sacramento, CA, USA;
[2]Radiology, UC Davis, Sacramento, CA, USA;
[3]Radiation Oncology, UC Davis, Sacramento, CA, USA

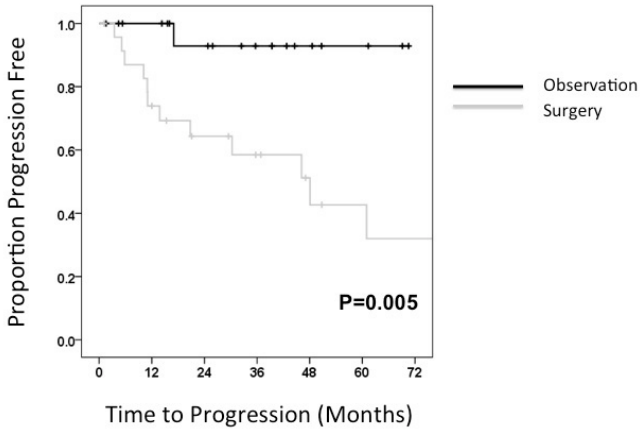
Objective: Surgical resection of desmoid tumors has traditionally been the mainstay of therapy, but this is a potentially morbid approach with high rates of recurrence. Given increasing reports of active surveillance in this disease, we sought to evaluate our experience with conservative management, hypothesizing this would be an effective strategy.

Methods: Using a prospectively maintained database of sarcoma patients from 2008 to 2015, we identified 47 patients with a diagnosis of desmoid tumor from all anatomic sites. Data points were abstracted on clinical and pathologic factors, disease stability or progression, and follow-up time. Main outcome measurements were tumor recurrence following surgical resection versus tumor progression with conservative management.

Results: In our cohort, 20 patients were managed with surveillance, 24 patients with surgery, and 3 patients with other approaches. Clinical and tumor characteristics between treatment groups were not significantly different. With a median follow-up of 35.7 months, there was 1 complete regression, 5 partial regressions, and 13 stable diseases among the surveillance group. Only one patient under observation progressed, crossing over to surgical resection. Among 24 patients managed with surgery, 13 patients developed local recurrence. Kaplan-Meier analysis revealed a statistically superior progression-free survival in the surveillance group (P=0.001).

Conclusion: This retrospective analysis adds to the growing body of evidence that observation of desmoid tumors is safe and effective with high rates of stable disease. These data further support an initial conservative approach to desmoid tumors that may spare patients the morbidity and risk of recurrence that accompanies potentially extensive operations.

Figure 2



Kaplan-Meier curve depicting progression-free survival/ local recurrence free survival comparing the observation and surgical treatment groups.

Clinicopathologic Characteristics among Treatment Cohorts

Characteristic	Observation (N=20)	Surgical Resection (N=24)	P value
Female Gender	14 (70%)	14 (58%)	0.53
Median Age (range)	40.2 (24.9 - 76.3)	36.7 (18.7 - 86.0)	0.54
Site Extremity Trunk Retroperitoneal/ Intra-abdominal Head and Neck	 9 (45%) 9 (45%) 1 (5%) 1 (5%)	 12 (50%) 6 (25%) 6 (25%) 0 (0%)	0.15
Median Tumor Size (range)	8.0 (2.6 - 24.0)	10.0 (1.6 - 22.6)	0.23
Deep Superficial	18 (90%) 2 (10%)	22 (92%) 2 (8%)	1.0
Presentation Status Referral before Surgery Referral after Surgery	 20 (100%) 0 (0%)	 16 (67%) 8 (33%)	0.005
Recurrence/Progression after Treatment	1 (5%)	13 (54%)	0.001

P1 - Poster 158 2543288

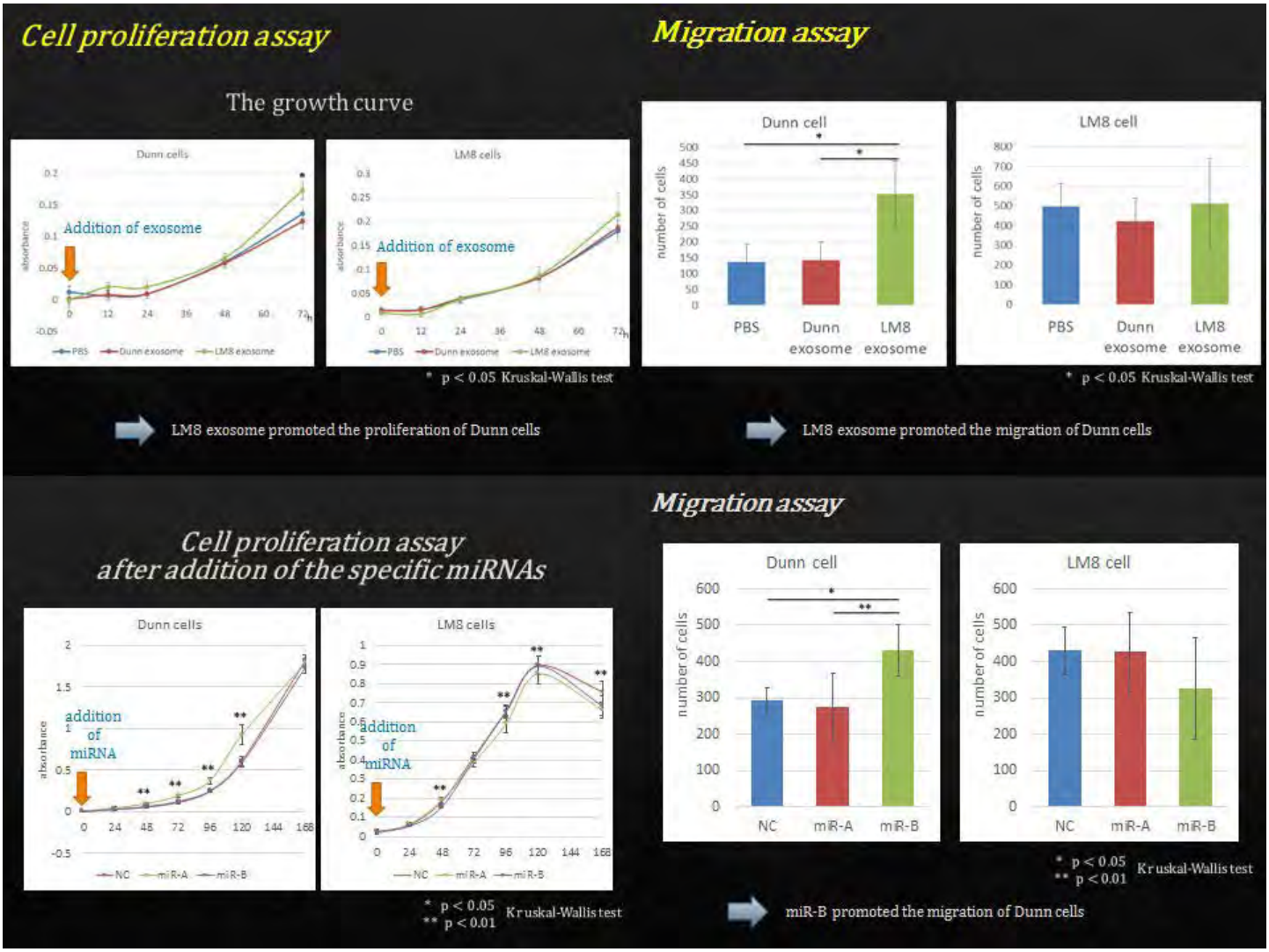
EXOSOME DERIVED FROM OSTEOSARCOMA CELL LINE WITH HIGHLY PULMONARY METASTATIC POTENTIAL PROMOTE CELL PROLIFERATION AND MOVEMENT OF OSTEOSARCOMA CELLS

Takuya Kakimoto[2]*; Akihiko Matsumine*[1]*; Kunihiro Asanuma*[1]*; Takao Matsubara*[1]*; Tomoki Nakamura*[1]*; Yuki Yada*[1]*; Tomohito Hagi*[1]*; Takahiro Iino*[1]*; Atsushi Kitao*[2]*; Akihiro Sudo*[1]

Objective: Pulmonary metastasis is the major risk factor of poor prognosis for osteosarcoma (OS) patients. Because the molecular mechanism regulating the processes of the pulmonary metastases remain unclear, to identify the novel factors which regulate the pulmonary metastases is crucial in order to find new therapeutic targets. Recently, exosomes have emerged as an important mediator of cell-to-cell signaling through the transfer of molecules such as mRNAs, miRNAs, and proteins between cells. Here, we investigated the effect of exosomes on cell proliferation and migration, both of which may be an important step to form pulmonary metastases of OS.

Methods: Two types of mouse OS cell line (Dunn and LM8) were used in this study. Exosomes were purified from conditioned medium by differential ultracentrifugation. To investigate the effect of exosomes on cell proliferation, MTS assay was used. To investigate the effect of exosomes on cell migration, transwell migration assays was employed. To measure Rho family activation after exosome treatment, pull-down assay was performed. To identify the differentially expressed exosomal miRNAs between Dunn and LM8, screening of miRNA with miRNA array was done, validated the candidates of miRNA by qRT-PCR. Finally, the function of the candidates' exosomal miRNAs were examined.

Results: LM8 exosomes significantly promoted cell proliferation and migration of Dunn cells. The protein expression and autophosphorylation of cdc42 were elevated in Dunn cell after LM8 exosome treatment. The miRNA array showed the different expression pattern of exosomal miRNA between LM8 and Dunn. miR-A and miR-B were more included in exosome from LM8 than Dunn. miR-A promoted the proliferation of Dunn. miR-B promoted the migration of Dunn cells.



Conclusion: Exosome from LM8 with highly pulmonary metastatic potential significantly promoted cell proliferation and migration of Dunn with low metastatic potential. Two candidates of differentially expressed exosomal miRNA were identified by the screening with miRNA array. miR-A promoted the proliferation of Dunn, and miR-B promoted the migration of Dunn cells. These results suggest that exosomes released from OS cells with highly metastatic potential may play an important role in the formation of pulmonary metastases.

– SOFT TISSUE SARCOMAS –

P2–Poster 001 2557776

ACTIVATION OF THE PI3K/MTOR PATHWAY PROVIDES A THERAPEUTIC TARGET FOR FGFR4-DRIVEN RHABDOMYOSARCOMAS

Timothy McKinnon[1]; Rosemarie E. Venier[1]; Marielle Yohe[2]; Berkley Gryder[2]; Brendan C. Dickson[4]; Krista Schleicher[1]; Abha Gupta[3]; Javed Khan[2]; Rebecca Gladdy[1]
[1]Lunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada; [2]Oncogenomics, National Cancer Institute, Gaithersburg, MD, USA; [3]Hematology/Oncology, The Hospital for Sick Children, Toronto, ON, Canada; [4]Pathology, Mount Sinai Hospital, Toronto, ON, Canada

Objective: Rhabdomyosarcoma (RMS) is the most common pediatric soft tissue sarcoma and, while survival rates have increased over the past few decades, intermediate and high risk patients still have dismal outcomes. Comprehensive genomic analyses have revealed that 93% of RMS have RTK/RAS/PI3K alterations and that fibroblast growth factor receptor 4 (FGFR4) is frequently mutated or overexpressed. The point mutation V550E constitutively activates FGFR4, stimulating downstream signaling pathways.

Methods: We have demonstrated that $FGFR4^{V550E}$ is a potent oncogene in mouse models of RMS and that secondary tumor models can be generated following transplantation of $FGFR4^{V550E}$ overexpressing tumor cells into immunocompetent host mice. These models have been employed in a translational study to uncover the mechanism of transformation in $FGFR4^{V550E}$ driven RMS and to uncover experimental compounds that inhibit RMS growth.

Results: Immunoblot analysis on myoblasts overexpressing $FGFR4^{V550E}$ demonstrated activation of AKT and mTOR signalling pathways. Likewise, $FGFR4^{V550E}$ overexpressing tumors and tumor-derived cells also showed AKT and mTOR phosphorylation. Mass cytometry at single cell resolution validated phosphoprotein abundance using these cell populations. Additionally, murine tumor cells overexpressing $FGFR4^{V550E}$ were subjected to a single agent, in vitro dose-response drug screen. Compounds were grouped by target class, and potency was determined using average percent area under the dose response curve (AUC). Using this technique, $FGFR4^{V550E}$ over-expressing tumor cells were highly sensitive to PI3K/mTOR inhibitors. In particular, GSK2126458 (omipalisib) was a potent inhibitor of $FGFR4^{V550E}$ tumor-derived cell and human RMS cell viability. $FGFR4^{V550E}$ overexpressing myoblasts and tumor cells had low nanomolar GSK2126458 EC_{50} values. In a preclinical study, GSK2126458 inhibited tumor growth in vivo. A statistically significant increase in disease specific survival (DSS) was observed in mice treated with GSK2126458 compared to mice treated with vehicle alone ($p<0.001$) or standard of care, vincristine ($p<0.05$).

Conclusion: In summary, this functional genomics platform is amenable to study RMS driver mutations and as a preclinical tumor model to test therapeutic agents. Importantly, these results suggest a role for PI3K/mTOR inhibition in precision therapy regimens for RMS with FGFR4 mutations. This study provides further evidence for clinical studies involving mTOR inhibitors (e.g. temsirolimus).

P2–Poster 002 2556403

OPPORTUNITIES FOR NOVEL MOLECULAR THERAPEUTIC INTERVENTION TARGETING THE EPIGENETIC/MIRNA SIGNATURE OF CLEAR CELL SARCOMA OF THE SOFT TISSUES (CCSST)

Peter W. Halcrow, PhD Candidate[1]; Christopher D. Walden[1]; Joyce E. Ohm[2]
[1]Biomedical Sciences, University of North Dakota, Grand Forks, ND, USA; [2]Cancer Genetics, Roswell Park Cancer Institute, Buffalo, NY, USA

Objective: The prognosis for individuals diagnosed with Clear Cell Sarcoma of Soft Tissue (CCSST) is poor; the five-year survival rate is ~50%, the recurrence rate is as high as 84%, and the morbidity and mortality in children and young adults is higher than in adults. The best treatment for CCSST is wide-excision surgery and localized radiation; <10% of tumors are responsive to cytotoxic chemotherapy. As such, there is a significant need for novel molecular therapies for CCSST. Mature microRNAs (miR) are aberrantly expressed in tumors and some miRNAs have established roles in tumor proliferation or suppression. They may be targeted *in vivo* via the use of miR antagonists (used to inhibit endogenous miRNAs showing a gain-of-function) and miR mimics (used to restore a loss-of-function).

Methods: We have utilized multiple –omics platforms to help determine the epigenetic and transcriptomic landscape of CCSST cell lines. RNA-sequencing was used to measure gene expression in CCSST cell lines and non-cancerous controls. RT-qPCR was used to determine the expression of specific mature miRNAs and their precursors. This study also utilized the Illumina Infinium 450K DNA methylation array to identify genomic loci with abnormal patterns of DNA methylation in CCSST, normal human mesenchymal stem cells (MSCs), primary human melanocytes, and other sarcoma cell lines.

Results: We have identified a unique global DNA methylation signature for CCSST based on whole genome DNA methylation analysis of CCSST cell lines; this pattern is

distinct from non-cancerous primary cells (MSCs and melanocytes) as well as other sarcoma cell lines (osteosarcoma, fibrosarcoma, and leiomyosarcoma). Further, we have shown that 204 of 612 (33%) annotated miRNA promoter regions on the 450K array are differentially methylated between CCSST and non-cancerous cells ($P = 3.39e^{-36}$); and that expression of the vast majority of corresponding mature miRNAs is significantly altered in CCSST.

Conclusion: These data suggest a wide-spread disruption of miRNA regulation and expression in CCSST. We hypothesize that the EWSR1-ATF1 translocation drives a global epigenomic reprogramming event and disrupts endogenous EWSR1 RNA binding and chaperone activity, and specifically altering miRNA processing. As key regulators of both oncogenic proteins and tumor suppressors, manipulation of these microRNAs may offer a unique potential therapeutic opportunity for CCSST patients.

P2–Poster 003 2565140

CIRCSARC - DISEASE MONITORING BY LIQUID BIOPSIES IN SARCOMAS

Heidi M. Namløs, PhD[1]; Olga Zaikova[1]; Bodil Bjerkehagen[1]; Anders Ståhlberg[2]; Synnøve Granlien[1]; Stefan Filges[2]; Daniel Vodák[1]; Lars B. Aasheim[1]; Stine Næss[1]; Eivind Hovig[1]; Ola Myklebost[1]; Kjetil Boye[1]; Kirsten S. Hall[1]; Leonardo A. Meza-Zepeda[1]

[1]Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway; [2]Sahlgrenska Cancer Center, University of Gothenburg, Gothenburg, Sweden

Objective: At present, mutational profiles of solid tumours are obtained from tissue biopsies or surgical specimens. Recent advances in technology now allows to use blood plasma as a "liquid biopsy", examining circulating tumour DNA (ctDNA) shed by the tumour cells into peripheral blood. ctDNA in plasma carries tumour-specific alterations that can be used to monitor minimal residual disease, tumour burden and evolution throughout the course of the disease. The CircSarc study aims to provide new insights into the clinical utility of liquid biopsies in soft tissue sarcomas.

Methods: We have enrolled 30 high-grade soft tissue sarcoma patients, with localised disease, that are beeing followed throughout the course of their disease. The patient's tumour and germline DNA is sequenced after surgery to identify tumour-specific mutations. Plasma from each patient is collected before and after surgery, and we are currently monitoring the patients over time, collecting plasma at routine controls and before and after each treatment cycle. We are using targeted resequencing to compare the mutation patterns observed in plasma and the primary tumour. The level of ctDNA in plasma, represented by the tumour-specific biomarkers, are monitored throughout the course of the treatment, and acts as an indicator of tumour burden. We are also collecting a cohort of GIST samples, where *KIT* and *PDGFRA* mutations in ctDNA and levels of ctDNA will be correlated with clinical and pathological features.

Results: We have established targeted resequencing protocols for ctDNA based on amplicons, multiplex-PCR and capturing, giving a balance between complexity and sensitivity. In the first screening, we have successfully detected somatic mutations in ctDNA,collected at time of surgery, for 70% of the patients. In addition, mutations only present in cfDNA and not in DNA from the primary tumour were detected, possibly reflecting intra-tumour heterogeneity. In a proof-of-concept study, we have shown that that levels of tumour-specific mutations in liquid biopsies can be correlated to clinical manifestation of metastatic disease in aggressive sarcoma, and have the potential to detect disease progression at an early stage.

Conclusion: Our study will provide new insights into the clinical significance of ctDNA in sarcomas. By repeated sampling of liquid biopsies, somatic mutations identified in ctDNA can be used as unique non-invasive tumour-specific biomarkers for monitoring tumour burden throughout the disease course.

P2–Poster 004 2555233

TERTIARY LYMPHOID STRUCTURES IN WELL DIFFERENTIATED / DEDIFFERENTIATED LIPOSARCOMA: POTENTIAL IMPLICATIONS IN DISEASE BIOLOGY?

William W. Tseng, MD[1]; Shefali Chopra[2]; Susan Groshen[3]; Sophia Hernandez[1]; Eric E. Jung[1]

[1]Surgery, Section of Surgical Oncology, University of Southern California, Keck School of Medicine, Los Angeles, CA, USA; [2]Pathology, University of Southern California, Keck School of Medicine, Los Angeles, CA, USA; [3]Biostatistics, University of Southern California, Keck School of Medicine, Los Angeles, CA, USA

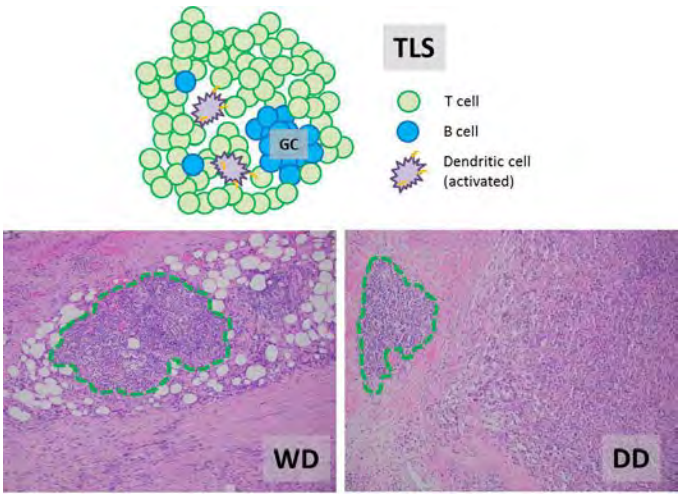
Objective: The immune response plays a critical role in shaping the tumor microenvironment in many cancers. Tertiary lymphoid structures (TLS) are organized aggregates of immune cells that may be sites of antigen presentation within tumors. TLS have been described in several solid tumor types and we have previously reported their intratumoral presence in well differentiated / dedifferentiated (WD / DD) liposarcoma (Tseng et al., Am J Surg Path 2012; Tseng et al., Sarcoma 2015). We sought to further characterize TLS in this disease.

Methods: Clinically-available H&E slides were retrieved for consecutive cases of WD / DD liposarcoma resected at our institution between 2011-2016. Each case was scored for overall TLS density (none, rare, few, some, many, inflam-

matory) and immunologic maturity (none, aggregate, follicle, germinal center). Demographic, clinicopathologic and outcome data were also collected. Associations between the data were analyzed for statistical significance using a two sided Cochran-Mantel-Haenszel test (for ordered categorical variables) and Spearman correlation coefficients (for continuous variables). Clinical outcome data were represented with Kaplan-Meier plots and analyzed using the logrank test.

Results: In total, 43 cases were studied, 51% of which had evidence of DD. The presence of TLS was noted in 72% of all cases, more commonly in DD than WD tumors (82% vs. 62%, p = 0.19). There was no significant association with TLS density scores and histology (WD versus DD); however higher TLS maturity scores were seen in DD tumors compared to WD tumors (p = 0.012). Tumors found in deep body locations (retroperitoneum, mediastinum) had both higher TLS density (p = 0.032) and maturity (p = 0.027) scores compared to tumors in superficial locations (extremity, trunk). After stratifying by histology and then presence of TLS, tumors with TLS were more likely to recur, but this pattern was not statistically significant (p > 0.25); however in a post hoc analysis comparing DD tumors with TLS to all others, this subset was particularly likely to recur (p = 0.002).

Conclusion: TLS are commonly found in WD / DD liposarcoma and may play a role in the disease biology. TLS appear to be specifically associated with DD and seem to confer a greater likelihood of recurrence. These unique aggregates of immune cells may have potential utility as a clinical biomarker. Further investigation of the intratumoral immune response in WD / DD liposarcoma is warranted.



Tertiary Lymphoid Structures (TLS) are organized intratumoral aggregates of immune cells that may also contain germinal centers (GC). TLS, shown in green outlines, are found in both well differentiated (WD) and dedifferentiated (DD) liposarcoma.

P2–Poster 005 2535507

THE EFFECT OF SS18-SSX ON TUMOR-GROWTH AND INITIATION OF SYNOVIAL SARCOMA

Hidetatsu Otani[2]; Takaaki Tanaka[2]; Yoshinori Imura[2]; Kazuya Oshima[2]; Nobuhito Araki[2]; Takaaki Nakai[1]; Kenichiro Hamada[1]; Takafumi Ueda[3]; Hideki Yoshikawa[1]; Norifumi Naka[1]

[1]Orthopaedic Surgery, Osaka University Graduate School of Medicine, Osaka, Osaka, Japan; [2]Musculoskeletal Oncology Service, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Osaka, Japan; [3]Orthopaedic Surgery, Osaka National Hospital, Osaka, Japan

Objective: Synovial sarcoma is an aggressive soft tissue malignancy that predominantly affects young adults and can arise in almost all parts of the body. This sarcoma is defined by t(18;X) (p11;q11) translocation that leads to fusion of the SSX gene to the SS18 gene, producing a chimeric SS18-SSX fusion gene. Previous studies reported that SS18-SSX is involved in chromatin remodeling and alters gene expression by epigenetic mechanisms. However, these studies were based on murine (mouse) models, where epigenetic status is different from that of humans. In addition, the detailed role of SS18-SSX also remains unclear. The aim of this study is to examine the role of SS18-SSX on tumorigenesis and tumor-growth using the human synovial sarcoma cell line.

Methods: We generated the synovial sarcoma cell line 'YSSi' from human synovial sarcoma cell line Yamato-SS. We induced Yamato-SS cells with shSS18-SSX1 using doxycycline-regulated silencing system. We examined the effects of SS18-SSX on tumor growth and tumor initiation using YSSi cells *in vitro* and *in vivo*.

Results: Doxycycline-induced shSS18-SSX1 down-regulated the expression of the SS18-SSX1 fusion protein in YSSi cells both *in vitro* and *in vivo*. Doxycycline suppressed cell growth in vitro. Cell cycle analysis revealed that doxycycline enhanced G0/G1 population of YSSi cells. In YSSi xenografts, administration of doxycycline significantly delayed tumor growth. In addition, doxycycline treatment significantly reduced the tumor formation ability of YSSi cells. These results suggest that SS18-SSX1 is essential for tumor growth and tumorigenesis in the human synovial sarcoma cell line YSSi cells.

Conclusion: We established the human synovial sarcoma cell line YSSi, and could silence the expression of SS18-SSX1 by doxycycline treatment. Then, we demonstrated that silencing of SS18-SSX1 could suppress the growth and tumorigenesis of YSSi cells. Given that, the fusion gene could be a potential target of this difficult disease. This cell line and xenograft model may be a useful tool for further in-depth investigation of the role of SS18-SSX in human synovial sarcoma.

P2–Poster 006 2570166

MESENCHYMAL TUMORS CAN DERIVE FROM NG2-EXPRESSING PERICYTES WITH β-CATENIN MODULATING THE NEOPLASTIC PHENOTYPE

Shingo Sato, MD, PhD[1]; Yuning J. Tang[2]; Qingxia Wei[3]; Makoto Hirata[4]; Ilkyu Han[5]; Shu Takeda[1]; David Kirsch[6]; Jay Wunder[7]; Benjamin Alman[2]

[1]Department of Physiology and Cell Biology, Tokyo Medical and Dental University Graduate School and Faculty of Medicine, Tokyo, Japan; [2]Department of Orthopaedic Surgery, Duke University, Durham, NC, USA; [3]Developmental and Stem Cell Biology, The Hospital for Sick Children, Toronto, ON, Canada; [4]The Institute of Medical Science, The University of Tokyo, Tokyo, Japan; [5]Department of Orthopaedic Surgery, Seoul National University Hospital, Seoul, Korea (the Republic of); [6]Department of Pharmacology & Cancer Biology, Duke University, Durham, NC, USA; [7]Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, ON, Canada

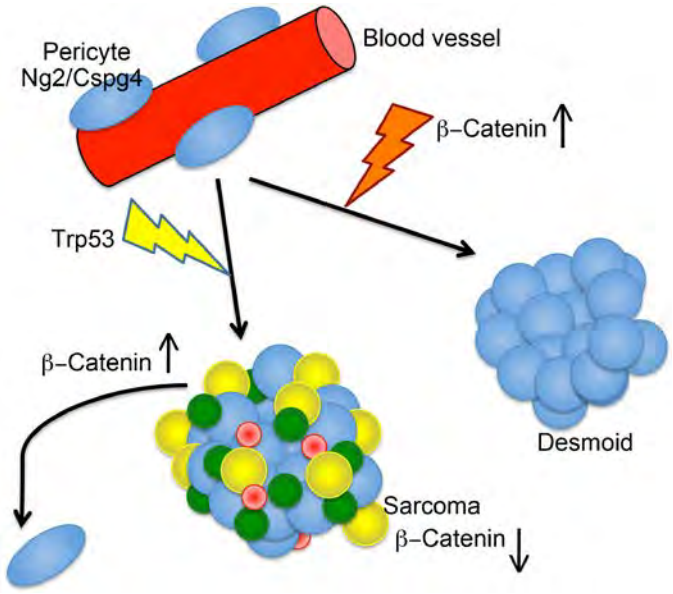
Objective: Pericytes are mesenchymal cells which surround endothelial cells in small vessels, and are implicated as mesenchymal progenitor cells. Since human sarcomas express markers for pericytes and are thought to be initiated from mesenchymal progenitor cells, sarcomas could be derived from pericytes with genetic mutations. In this study, we addressed the role of *Ng2*-expressing pericytes and β-catenin in the origin of mesenchymal tumors.

Methods: NG2 is a cell surface protein expressed by pericytes. To label pericyte-derived cells, we crossed *Ng2-Cre* mice or *Ng2-CreER* mice with *Rosa26R^{lacZ}* mice. We then crossed these mice with *p53* deficient mice or *APC1638N* mutant mice. Lineage tracing studies in sarcomas driven by the deletion of *p53* or desmoid tumors driven by a mutation in *Apc* were performed to show the presence of percicyte-derived tumor cells in the mesenchymal tumors. Next, to determine if mutations in *Ng2*-expressing pericytes could induce sarcomas, we generated *Ng2-Cre;p53$^{flox/flox}$* mice in which *p53* gene was deleted in pericytes, or *Ng2-CreER;Ctnnb1^{ex3}* mice in which Wnt/β-catenin signaling was upregulated in pericytes.

Furthermore, to determine gene expression differences between *Ng2*-expressing pericytes and sarcomas that arose from deletion of *p53* in pericytes, RNA sequencing analysis was performed, identifying decreased β-catenin signaling in sarcomas.

Finally, to determine if β-catenin activation might alter the growth of sarcomas, human sarcoma cells were implanted into immune-deficient mice, and these mice were treated with lithium to activate β-catenin signaling.

Results: Using lineage tracing, we demonstrated that murine sarcomas driven by the deletion of the *p53* or desmoid tumors driven by a mutation in *Apc* can derive from pericytes expressing *Ng2*. Deletion of the *p53* in these cells resulted in osteosarcomas or soft tissue sarcomas that closely resemble human sarcomas, while stabilizing β-catenin in the same cell type caused desmoid tumors. Comparing expression profile between pericytes and percicyte-derived sarcomas showed inhibition of β-catenin signaling in the sarcomas. Furthermore, activation of β-catenin inhibited the growth of sarcomas.



Conclusion: Our data showed that pericytes can be a cell of origin for mesenchymal tumors. Malignant sarcomas exhibited a lower level of β-catenin activity, while β-catenin stabilization suppressed the malignant phenotype (Figure). Modulating the level of β-catenin could be developed into therapeutic approach for these mesenchymal tumors.

P2–Poster 007 2565770

SS18-SSX, THE ONCOGENIC FUSION PROTEIN IN SYNOVIAL SARCOMA, IS A CELLULAR CONTEXT-DEPENDENT EPIGENETIC MODIFIER

Sakura Tamaki[1]; Makoto Fukuta[2]; Kazuya Sekiguchi[3]; Kazuo Hayakawa[2]; Yonghui Jin[1]; Takeshi Okamoto[4]; Knut Woltjen[5]; Hiroyuki Yoshitomi[1]; Junya Toguchida[1]
[1]Department of Tissue Regeneration, Institute for Frontier Medical Sciences, Kyoto University, Kyoto, Japan; [2]Department of Orthopaedic Surgery, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan; [3]Department of Cell Growth and Differentiation, Center for iPS Cell Research and Application, Kyoto University, Kyoto, Japan; [4]Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan; [5]Department of Life Science Frontiers, Department of Reprogramming Sciences, Kyoto University, Kyoto, Japan

Objective: The prevalence and specificity of unique fusion oncogenes are high in a number of soft tissue sarcomas (STSs). The close relationship between fusion genes and clinicopathological features suggests that a correlation may exist between the function of fusion proteins and cellular context of the cell-of-origin of each tumor. However, most STSs are origin-unknown tumors and this issue has not yet been investigated in detail. In the present study, we examined the effects of the cellular context on the function of the synovial sarcoma (SS)-specific fusion protein, SS18-SSX.

Methods: Using human pluripotent stem cells (hPSCs) containing the drug-inducible *SS18-SSX* gene, we induced SS18-SSX at various differentiation stages from PSCs to neural crest cell (NCC)-derived mesenchymal stromal cells (MSCs), and compared its biological effects on each type of cell.

Results: We found that the expression of *FZD10*, identified as a SS-specific gene, was induced by SS18-SSX at the PSC and NCC stages, but not at the MSC stage. This stage-specific induction of *FZD10* correlated with stage-specific changes in histone marks (H3K4me3 and H3K27me3) associated with its locus and also with the loss of the BAF47 protein, a member of the SWI/SNF chromatin-remodeling complex. Furthermore, the global gene expression profiles in hPSCs, hPSC-derived NCCs (hPSC-NCCs), and hPSC-NCC-derived MSCs (hPSC-MSCs) with or without the induction of SS18-SSX identified a large number of one-stage-specific genes, suggesting that SS18-SSX regulated different downstream genes depending on the cell type. Intriguingly, the profile of hPSC-NCCs after the induction of SS18-SSX was the closest to that of SS cell lines.

Conclusion: Our results clearly demonstrated that the cellular context is an important factor in the function of SS18-SSX as an epigenetic modifier. Although we employed the neural crest lineage in this study, our inducible system is applicable to other lineages in order to identify the cells-of-origin of SS. In addition, the cellular context-specific function of fusion proteins represents an important issue in the search for target molecules for the treatment of SS, and our inducible system will be a powerful tool for investigating this issue.

P2–Poster 008 2557497

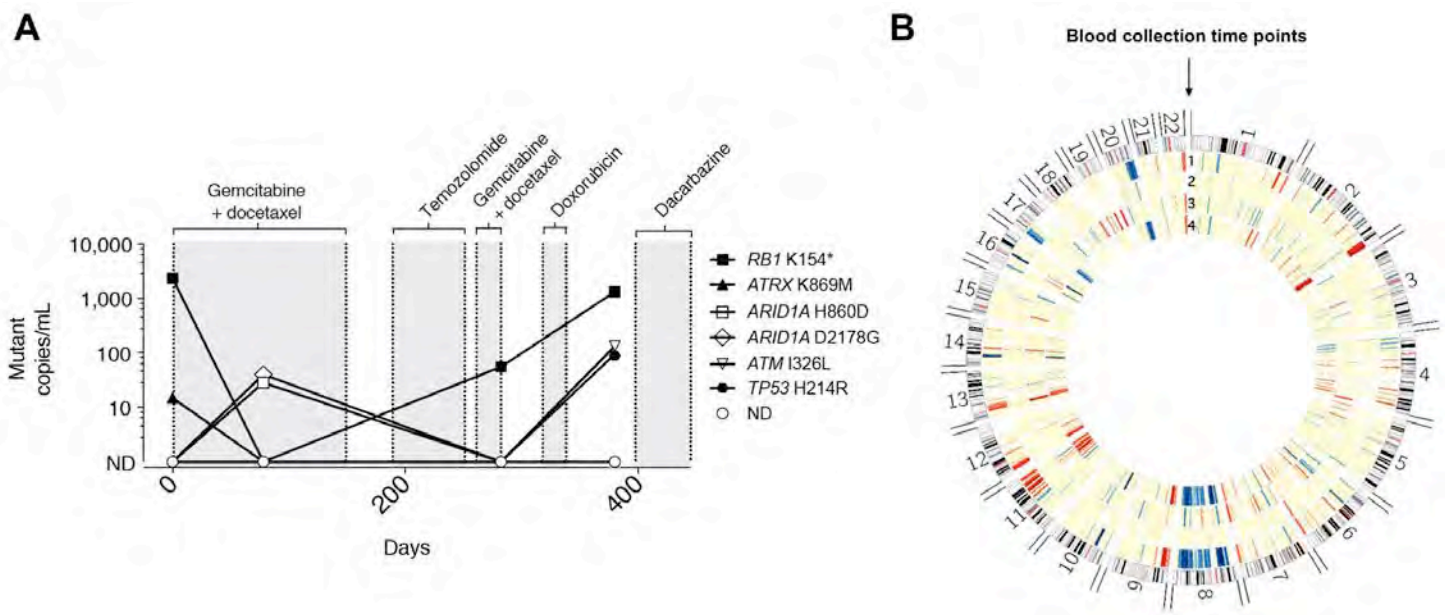
MONITORING RESPONSE TO TREATMENT IN LEIOMYOSARCOMA PATIENTS USING CIRCULATING TUMOR DNA

Joanna Przybyl, PhD[1]; Jacob J. Chabon[2]; Lien Spans[3]; Kristen Ganjoo[4]; Sujay Vennam[1]; Aaron M. Newman[2]; Erna Forgó[1]; Agnieszka Wozniak[5]; Raf Sciot[6]; Patrick Schöffski[5]; Maria Debiec-Rychter[3]; Ash Alizadeh[2]; Maximilian Diehn[2]; Matt van de Rijn[1]
[1]Department of Pathology, Stanford University, Stanford, CA, USA; [2]Institute for Stem Cell Biology and Regenerative Medicine, Stanford University, Stanford, CA, USA; [3]Department of Human Genetics, KU Leuven and University Hospitals Leuven, Leuven, Belgium; [4]Medical Oncology, Stanford Medical Institute, Stanford, CA, USA; [5]Department of Oncology, KU Leuven and Department of General Medical Oncology, University Hospitals Leuven, Leuven Cancer Institute, Leuven, Belgium; [6]Department of Pathology, KU Leuven and University Hospital Leuven, Leuven, Belgium

Objective: Circulating tumor DNA (ctDNA) has significant potential for diverse clinical applications, including assessment of treatment response, monitoring of recurrent/residual disease, and characterization of tumor heterogeneity. However, few studies have evaluated ctDNA profiling in sarcomas.

Methods: To assess the utility of ctDNA analysis in leiomyosarcoma (LMS), we profiled single nucleotide variants (SNVs) and copy number changes in 11 tumor specimens and an initial set of 24 serial plasma samples from 9 LMS patients. SNVs were detected using Cancer Personalized Profiling by deep Sequencing, a highly sensitive capture-based sequencing approach (CAPP-Seq; PMIDs: 24705333, 27018799). Copy number changes in ctDNA were analyzed by genome representation profiling (PMIDs: 25585704, 26687610) and in tumors by SNP arrays.

Results: We designed a 184kb CAPP-Seq panel targeting 306 exons from 89 genes recurrently mutated in LMS based on the analysis of whole exome sequencing data for 77 LMS patients from TCGA. Our panel identified a median of four SNVs per tumor specimen and five SNVs per ctDNA sample. The most frequently mutated genes in ctDNA were enriched for those previously implicated in LMS tumorigenesis (e.g. *TP53, RB1, ATM, ATR* and *ATRX*). While genetic aberrations identified in paired ctDNA and tumor DNA samples were largely concordant,



some mutations were detected only in ctDNA. Since ctDNA profiling integrates contributions from multiple tumor deposits, we hypothesize that the latter may reflect geographic tumor heterogeneity or clonal evolution. Our results also indicate that ctDNA monitoring may allow for early prediction of disease progression in LMS patients. Figure 1 shows CAPP-Seq (A) and genome representation profiling (B) results from serial plasma specimens in a patient with a lower leg LMS who continued to progress on multiple therapies and developed metastases to lung, bone and liver. Loss of the most abundant *RB1* stop-gain mutation (A) and decreased copy number changes (B) in the second plasma sample suggest an initial response to gemcitabine/docetaxel treatment while emergent mutations during therapy suggest clonal evolution. Profiles of subsequent plasma samples indicate a gradual return of aberrations detected at the first time point, in parallel with the occurrence of new somatic mutations.

Conclusion: Our results suggest that serial analysis of ctDNA is a promising approach for the evaluation of treatment response in LMS patients.

P2–Poster 009 2568664

COMPREHENSIVE GENOMIC SEQUENCING OF LIPOSARCOMA PATIENTS IDENTIFIES A NOVEL NTRK2 SUBGROUP

Sherri Z. Millis, PhD[1]; Sujana Movva[2]; James Chen[3]; Gregory M. Cote[4]; Edwin Choy[5]; Julia Elvin[1]; Alexa Schrock[1]; Jeffrey Ross[1]; Philip Stephens[1]; Vincent Miller[1]; Arun S. Singh[6]; Siraj Ali[1]
[1]Medical Affairs, Foundation Medicine, Phoenix, AZ, USA; [2]Fox Chase Cancer Center, Philadelphia, PA, USA; [3]Ohio State University Medical Center, Columbus, OH, USA; [4]Massachusetts General Hospital, Boston, MA, USA; [5]Harvard University, Cambridge, MA, USA; [6]UCLA, Los Angeles, CA, USA

Objective: Liposarcomas (LPS) account for ~20% of soft tissue sarcomas; common disease sites include retroperitoneal, trunk, and lower extremities. A subset of liposarcoma patients recur after an initial surgical resection and have a clinically aggressive course. These patients may benefit from systemic therapy. Identification of genomic alterations in those LPS may inform therapeutic opportunities.

Methods: Tissue from 407 liposarcoma patients (dedifferentiated [DDLPS], well differentiated [WDLPS], pleomorphic, myxoid) were assayed by comprehensive genomic profiling (CGP) to identify possible targets for therapy. All samples were assayed by DNA sequencing of 315 genes for genomic alterations (GA), including base substitutions, indels, amplifications, copy number alterations and fusions/rearrangements; 347 cases were assayed for 405 genes with additional RNA sequencing of 265 genes frequently altered in cancer, to evaluate targeted therapy opportunities in this disease.

Results: Review of genomic profiles was consistent with previously published data (median age, 56; 60% male;

SELECT GA	NTRK2 Subgroup n = 10 (%)	Non-NTRK2 Subgroup n = 397 (%)	P value
GNAQ	3 (30%)	2 (1%)	0.0005
CDKN2A	5 (50%)	22 (7%)	0.0004
CDKN2B	6 (60%)	16 (5%)	0.0001
CD274, PDCD1LG2	2 (20%)	6 (2%)	0.0211

variety of disease sites; *MDM2, CDK4* GAs ~60%, *FRS2* GA's ~40%). Additional RNA analysis of 347 cases identified 10 (2.9%) that harbored an *NTRK2* alteration (one with 2 *NTRK2* GA). These 10 cases were further evaluated. The *NTRK2*-altered subset included 5 DDLPS/WDLPS, 2 pleomorphic LPS, and 3 myxoid LPS and was 60% female, with a median age of 50. Half of the *NTRK2*-altered cases had abdominal or omental tumors, which differed significantly from the overall site incidence in the liposarcoma cohort we analyzed (p=0.03 and 0.01, respectively). *NTRK2* alterations included 4 amplifications, 3 fusions: *NTRK2-CTDSP2, NTRK2-STRN, NTRK2-PRRX1,* and 3 missense point mutations (G401E, I71V, S257F). The *NTRK2* subgroup also had an apparent enrichment of *CDKN2A/B*, *CD274, PDCD1LG2,* and *GNAQ* amplifications (table below).

Conclusion: Chromosome 9 GA's are involved in a subpopulation of liposarcomas. This region includes *NTRK2, GNAQ, CDKN2A/B, CD274,* and *PDCD1LG2*. These GA's were found more commonly in females and in the abdomen, when compared to the entire liposarcoma cohort evaluated. These alterations may inform the use of targeted therapies such as *NTRK2* inhibitors, currently in clinical trials, and *CD274/PDCD1LG2* targeted immunotherapies. Based on their genomic profiles, 2 patients in this cohort were identified for *NTRK2* inhibitor or immunotherapy and were entered into trials.

P2–Poster 010 2568085

ESTABLISHMENT OF JAPANESE SARCOMA GENOME CONSORTIUM (JSGC) FOR GENOMIC ANALYSIS

Makoto Hirata[1]; Koichi Matsuda[2]
[1]Institute of Medical Science, University of Tokyo, Tokyo, Japan; [2]Graduate School of Frontier Sciences, University of Tokyo, Tokyo, Japan

Objective: Previous analysis of musculoskeletal tumors identified various structural abnormalities such as chromosomal translocations and amplification. However, these alterations cannot fully explain the initiation and progression of malignancies. Recent cancer genome analysis revealed a number of genes frequently mutated in various cancer tissues. To comprehensively understand the genomic abnormalities of musculoskeletal tumors, genomic and transcriptome analysis using next generation sequencer is essential. However, it is difficult to identify low-frequency mutations when the number of samples are limited. To overcome rarity of musculoskeletal tumors, nation-wide collaborating network is required.

Methods: In 2014, we launched Japanese Sarcoma Genome Consortium. For now, a total of 20 hospitals and 8 research institutes throughout Japan participate this consortium. Under the standard operation procedure, we collected frozen tumor tissue as well as normal tissue, including skin, blood or adipose tissue. Clinical information; basic and tumor-specific information and outcomes, was also collected. Cryosections were obtained from the frozen tumor tissue to extract DNA and RNA and to perform pathological evaluation. To enhance the validity of the tumor samples, pathological diagnosis was confirmed by two expert pathologists. For sample preparation, qualities and tumor contents of frozen tumor samples were histologically evaluated by referring to pathological information of original tumors. Purified DNA and RNA were subjected with whole exome and RNA sequence, respectively to identify novel mutations or structural alterations.

Results: Currently several bone and soft tissue tumors including both benign and malignant diseases were under investigation. In a certain histological type of malignant soft tissue tumors, whole exome and RNA sequence analysis was completed and identified some recurrent genetic alterations. Further association studies between such genetic alterations with clinical variables including mortality were conducted.

Conclusion: We hope that our research activities would contribute to the understanding of disease pathogenesis as well as the development of novel therapeutics for musculoskeletal tumor.

P2–Poster 011 2569560

PATIENT-DERIVED XENOGRAFTS (PDX) AS RELIABLE PRECLINICAL MODELS TO COMPARATIVELY ASSESS THE ACTIVITY OF NOVEL DRUGS IN SOLITARY FIBROUS TUMOR (SFT)

Denis Cominetti[1]; Silvia Stacchiotti[2]; Roberta Frapolli[5]; Monica Tortoreto[1]; Tiziana Negri[4]; Gian Paolo Dagrada[4]; Ezia Bello[5]; Maristella Saponara[2]; Alessandro Gronchi[3]; Chiara Colombo[3]; Paolo Casali[2]; Silvana Pilotti[4]; Maurizio D'Incalci[5]; Nadia Zaffaroni[1]

[1]Experimental Oncology and Molecular Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milan, Milan, Italy; [2]Cancer Medicine Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Italy; [3]Department of Surgery, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Italy; [4]Department of Diagnostic Pathology and Laboratory, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy, Milan, Italy; [5]Department of Oncology, IRCCS, Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy

Objective: Since PDXs mostly retain the main molecular, genetic and histological features of their donor tumors, closely recapitulating the original heterogeneity, they represent excellent preclinical models to predict therapeutic response to anticancer agents and inform drug treatment scheduling. Here, we take advantage of the availability of SFT PDX to comparatively assess the activity of a novel cytotoxic drugs and targeted agents with the aim of generating new hypotheses to be confirmed in prospective clinical studies.

Methods: The antitumor activity of novel cytotoxic drugs and targeted agents of interest for the management of soft tissue sarcoma patients was comparatively assessed in a pleomorphic osteochondro-like NAB2-STAT6-positive high-grade dedifferentiated-SFT PDX (SFT-1). The tested compound included the novel microtubule inhibitor eribulin, the CRM1/XPO1 inhibitor selinexor and the EZH2 inhibitor DZNeP. For comparative purposes, the antitumor activity of regorafenib, that we previously identified as the most potent anti-angiogenic compound against SFT-1 tumors, was also tested.

Results: Preliminary results obtained in the SFT-1 PDX model showed an excellent antitumor activity of eribulin (max tumor volume inhibition (TVI) >90%), which was superimposable to that induced by regorafenib (TVI=88%). As single agents, selinexor and DZNeP induced a disease stabilization also in a late-stage tumor setting (max TVI=63 and 53%, respectively). Experiments are ongoing to dissect the determinants of response to the different agents.

Conclusion: Our PDX-derived preclinical data suggest a possible relevance of the novel microtubule inhibitor eribulin for the management of SFT patients. In addition, both CRM1/XPO1 and EZH2 inhibitors seems to be promising as single agents and, based on their action mechanisms, may have the potential to enhance the effect of other anticancer agents, which make them suitable for combination regimens.

P2–Poster 012 2560400

H3K27ME3 IMMUNOHISTOCHEMISTRY IN THE DIAGNOSIS OF MALIGNANT PERIPHERAL NERVE SHEATH TUMORS: INSIGHTS FROM A VALIDATION STUDY

Naofumi Asano[1]; Hitoshi Ichikawa[2]; Taisuke Mori[3]; Masaya Nakamura[4]; Nobuyoshi Hiraoka[3]; Akira Kawai[5]; Akihiko Yoshida[3]

[1]Rare Cancer Research, National Cancer Center, Tokyo, Japan, Tokyo, Japan; [2]Clinical Genomics, National Cancer Center, Tokyo, Japan, Tokyo, Japan; [3]Pathology and Clinical Laboratories, National Cancer Center, Tokyo, Japan, Tokyo, Japan; [4]Orthopaedic Surgery, Keio University School of Medicine, Tokyo, Japan; [5]Musculoskeletal Oncology, National Cancer Center, Tokyo, Japan, Tokyo, Japan

Objective: The diagnosis of malignant peripheral nerve sheath tumor (MPNST) can be challenging. The discovery of frequent inactivation of polyclomb repressive complex 2 in MPNSTs suggests that immunohistochemical detection of trimethylated lysine 27 of histone 3 (H3K27me3) could be of diagnostic aid. Several recent studies have indeed shown the usefulness of this marker, but close scrutiny of the actual data reveals some unresolved issues. We performed a detailed validation study to better understand the utility of H3K27me3 immunohistochemistry for the diagnosis of MPNSTs.

Methods: We performed parallel immunohistochemical assays, using monoclonal and polyclonal antibodies, which were applied to whole sections of 57 MPNSTs (54 conventional and 3 epithelioid) and a 232 non-MPNST tumors representing 16 tumor types. The percentage of cells that lacked staining was assessed semiquantitatively. Cases were categorized as "complete loss" when ≥95% of the tumor cells lost staining, "intact" when <5% of the tumor cells lost staining, or "mosaic loss" when the percentages of loss were ≥5% and <95%.

Results: By monoclonal antibody, 56% of 54 conventional MPNSTs showed complete loss of staining, whereas 17% displayed mosaic loss and 28% showed intact staining. Three MPNSTs demonstrated a novel geographic pattern of complete loss. All 3 epithelioid MPNSTs retained intact staining. Among 232 non-MPNST tumors successfully evaluated, only 2 (0.9%) showed complete loss of staining. Mosaic loss of staining was observed in 39% of non-MPNSTs, whereas remaining 60% retained intact staining. For conventional MPNSTs, a complete loss of H3K27me3 was significantly associated with a higher TNM stage (*P*

= 0.013), deeper location (P = 0.004), and the presence of heterologous differentiation (P = 0.003), with a trend towards decreased disease-free survival (P = 0.068). Polyclonal antibodies did not recognize 34% of cases that showed complete loss with the use of monoclonal antibodies.

Conclusion: We demonstrated that a complete loss of H3K27me3 labeling by immunohistochemistry is a moderately sensitive and highly specific phenomenon for MPNSTs, and therefore could be diagnostically useful. We also revealed a novel geographic pattern of complete loss in rare cases. A mosaic loss of H3K27me3 staining may occur in a subset of non-MPNSTs, and therefore should not be considered diagnostic. The use of a monoclonal antibody over a polyclonal reagent resulted in enhanced performance and easier interpretation.

P2–Poster 013 2570712

ACTIVATION OF INHIBITED GSK3 MALIGNANT PERIPHERAL NERVE SHEATH TUMORS (MPNST) WITH AUL12 LEADS TO RAPID CELL DEATH

Bethany Prudner; Davinelle Daniels; Jeff Kremer; Richa Rathore; Brian Van Tine
Washington University in Saint Louis, St. Louis, MO, USA

Objective: Malignant peripheral nerve sheath tumors (MPNSTs) are Ras pathway driven nerve-associated tumors that occur either in association with mutated neurofibromin in the neurofibromatosis type 1 (NF1; ~50%) or sporadically (~50%). Several signaling pathways have been tested over the past decade, but there have not been any therapeutic advances specifically targeting MPNSTs. We have demonstrated that in cellular environments with high glucose levels, glycogen synthase kinase 3 (GSK) is inhibited. This inhibition protects MPNSTs from cell death by preventing the mitochondrial permeability transition pore (PTP) from opening. We hypothesized that activation of GSK by a complex I inhibitor, AUL12, would relieve this inhibition and induce apoptosis in a caspase-independent process.

Methods: AUL12 was applied to MPNSTs cell lines and immortalized human Schwann cells (iHSC). Cell death was measured using propridium iodide (PI) Fluorescence-Activated Cell Sorting (FACS). Additionally, a peptide specific to the inhibited phosphorylated site of GSK3 was utilized to demonstrate the specificity of GSK3 inhibition. Knockdown of GSK3 with shRNA was performed and a peptide mimetic of GSK was used.

Results: We demonstrated that inhibiting OXPHOS, the preferred source of energy production in MPNSTs, by AUL12 induced cell death. These results were recapitulated by a peptide specific to the phosphorylated inhibition site on GSK3.

Conclusion: Our results show that MPNSTs depend on a carbon source utilizing OXPHOS for the energy production needed for survival. Disrupting this by shutting down the metabolic processes OXPHOS, greatly reduced MPNST survival, thus leading to a potential new strategy for the development of MPNST therapeutics.

P2–Poster 014 2570248

MALIC ENZYME 1 (ME1) EXPRESSION CORRELATES WITH ROS-MEDIATED CELL DEATH IN SYNOVIAL SARCOMA

Sara Lange; Jeff Kremer; Bethany Prudner; Richa Rathore; Brian Van Tine
Washington University in Saint Louis, St. Louis, MO, USA

Objective: Synovial sarcoma (SS) is a lethal form of soft-tissue sarcoma with high metastatic potential that occurs in young adults. We have demonstrated that SS displays both a unique glucose addiction and a deficiency in malic enzyme 1 (ME1). ME1 deficiency in SS results in insufficient NADPH production to sufficiently defend the cell against ROS damage, and results in the rapid cell death noted in glucose deprivation. As no targeted chemotherapeutic strategy has been developed for SS, we have built a therapeutic approach to treating SS based upon this unique glucose metabolism of ME1-negative SS.

Methods: Overexpression of malic enzyme 1 was achieved in SYO-1 and FUJI SS cell lines using a retroviral system. Knockdown of ME1 in MG63 cells was achieved through short hairpin RNA. Cell death was analyzed by trypan blue exclusion assay and fluorescence-assisted flow cytometry (FACS). Sensitivity assays were performed using DHEA, DHEA analogs, and sigma-erastin. Protein expression was analyzed by western blotting.

Results: SS cell lines are acutely sensitive to glucose withdrawal, as they die within two hours of glucose deprivation. ME1 was not expressed in SS cell lines, patient sample microarrays, spontaneous SS transgenic mice, monophasic SS patient samples, or the sarcomatoid morphology of biphasic SS patient samples. Knockdown of ME1 in MG63 cells conferred acute sensitivity to glucose withdrawal. Suppression of ME1 makes SS dependent on the PPP for NADPH production. Treatment with DHEA (G6PD inhibitor) and sigma-erastin in SS lines resulted in significant cell death. Overexpression of ME1 in SS cell lines resulted in decreased susceptibility to glucose deprivation, G6PD inhibition, and sigma-erastin treatment. Taken together, these findings suggest that ME1 expression correlates directly with ROS-mediated cell death, recognizing that in

SS, decreased NADPH leads to an increased oxidative stress and cell death in SS that lack ME1 expression.

Conclusion: These findings suggest that decreased NADPH leads to an increased oxidative stress and cell death in SS where ME1 is not expressed. Overexpression of ME1 in SS decreases the susceptibility of SS to ROS-mediated cell death. This is the first report of a metabolic deficiency unique to SS that can be exploited therapeutically and may allow for targeted therapy of ME1 in other cancers.

P2–Poster 015 2543698

ATRX-ASSOCIATED ALTERNATIVE LENGTHENING OF TELOMERE (ALT) MAY BE CORRELATED WITH CHEMOTHERAPY RESPONSE IN LEIOMYOSARCOMA (LMS)

Brett Po-Hsiang Huang[1]; Jau-Yu Liau[2]; Yung-Ming Jeng[2]; Tom W. Chen[1]
[1]Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan; [2]Department of Pathology, National Taiwan University Hospital, Taipei, Taiwan

Objective: Response to systemic chemotherapy in LMS varies and no predictive biomarker exists. ALT, a common mechanism to maintain telomere in sarcoma, is associated with altered DNA repair mechanism. Loss of a chromatin modifierα-thalassemia/mental retardation syndrome X-linked (ATRX) has been implicated as one of the factors leading to ALT. We aimed to determine the relationship between ALT, ATRX and chemotherapy response in patients with advanced LMS.

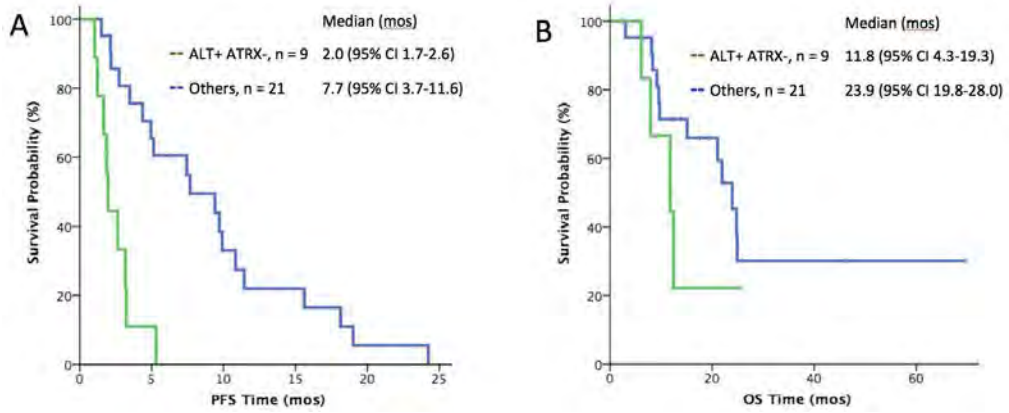
Methods: Histology-proven advanced LMS patients (pts) treated with systemic chemotherapy in National Taiwan University Hospital from January 2001 to December 2015 were selected. Patient demographic data and clinical outcomes including tumor response, progression-free survival (PFS) and overall survival (OS) were recorded. We used formalin-fixed paraffin-embed tumor samples for ALT and ATRX status assessment by telomere-specific fluorescence in situ hybridization and immunohistochemistry, respectively.

Results: 30 pts with advanced LMS treated with systemic chemotherapy were identified. Table 1 summarizes the clinicopathological information. 21 pts received anthracycline-based first line chemotherapy. 20 pts (67%) were ALT-positive (ALT+). 10 pts (33%) were ATRX-negative (ATRX-), among which all but 1 were also ALT+. ALT positivity was not correlated with chemotherapy response (odds ratio (OR) 1.25, p = 0.78). Comparing the 9 ALT+/ATRX- pts to others (n = 21, including 11 ALT+/ATRX+ pts , 9 ALT-/ATRX+ pts and 1 ALT-/ATRX- pt), a trend for much lower odds of response to chemotherapy was noted (11.3% vs 42.9%, OR 0.17, 95% CI = 0.01-1.58, p = 0.11). PFS was significantly shorter in ALT+/ATRX- pts vs others (median 2.0 mos vs 7.7 mos, hazard ratio (HR) 6.5, 95% CI = 2.4-17.7, p < 0.001). No significant difference in OS was noted (median 11.7 mos vs 23.9 mos, HR 1.84, 95% = CI 0.58-5.78, p = 0.314) between ALT+/ATRX- pts and others.

Conclusion: ALT+/ATRX- phenotype may be correlated with poorer response to chemotherapy in advanced LMS.

Patient Demographics and Clinicopathologic Features

	n = 30 (%)
Age, median (range)	51 (28-67)
Sex	
Male	2 (7)
Female	28 (93)
Tumor origin	
Uterus	22 (73)
Retroperitoneum/intra-abdomen	3 (10)
Others	5 (17)
Metastatic site	
Lung	25 (83)
Liver	14 (47)
Bone	7 (23)
Intra-abdomen (excluding liver)	7 (23)
Cell morphology	
Spindle	19 (63)
Epithelioid/pleomorphic	11 (37)
FNCLCC Grade	
Grade 1/2	12 (40)
Grade 3	18 (60)
ALT FISH	
Positive	20 (67)
Negative	10 (33)
ATRX expression	
Loss	10 (33)
Present	20 (67)
1st-line chemotherapy	
Anthracycline-based	21 (70)
Nonanthracycline-based	9 (30)



sion of ASS1 was suppressed, the expression of P-gp was upregulated in comparison to negative controls.

Conclusion: These results indicate that the reduced expression of ASS1 expression in Dox-resistant sarcomas may contribute to drug resistance. ASS1 deficiency is a potential target for novel drug therapies. The combination of arginine deprivation therapy and an autophagy inhibitor may have anti-tumor effects in drug-resistant sarcomas.

P2–Poster 016 2558429

REDUCED ARGINOSUCCINATE SYNTHETASE EXPRESSION IN REFRACTORY SARCOMAS: THE IMPACT ON THERAPEUTIC POTENTIAL AND DRUG RESISTANCE

Youngi Kim[1]; Eisuke Kobayashi[1]; Daisuke Kubota[2]; Yoshiyuki Suehara[2]; Kenta Mukaihara[2]; Keisuke Akaike[2]; Ayumu Ito[3]; Kazuo Kaneko[2]; Hirokazu Chuman[1]; Akira Kawai[1]; Shigehisa Kitano[4]
[1]Division of Musculoskeletal Oncology, National Cancer Center Hospital (Tokyo, Japan), Tokyo, Japan; [2]Department of Orthopaedic Surgery, Juntendo University School of Medicine, Tokyo, Japan; [3]Department of Hematopoietic Stem Cell Transplantation, National Cancer Center Hospital (Tokyo, Japan), Tokyo, Japan; [4]Department of Experimental Therapeutics, National Cancer Center Hospital (Tokyo, Japan), Tokyo, Japan

Objective: Treating drug-resistant sarcomas remain a major challenge. The present study aimed to identify a novel therapy for drug-resistant sarcomas based on a metabolic errors involving argininosuccinate synthetase1 (ASS1).

Methods: We assessed the expression of ASS1 and P-glycoprotein (P-gp) in epithelioid sarcomas (ES-X and VAESBJ), alveolar soft part sarcoma (ASPS-KY) and doxorubicin (Dox)-resistant osteosarcoma ($KHOS_{R2}$). Each cell was cultured in arginine-containing and arginine-free media. Cell growth was assessed using an XTT assay and flow cytometry. We analyzed autophagy and also added chloroquine to the arginine-free medium. In addition, we assessed the expression of P-gp in after suppressing the expression of ASS1.

Results: The expression of ASS1 was reduced in Dox-resistant sarcoma cells. Interestingly, there was an inverse relationship between the expression of ASS1 and the expression of P-gp. Furthermore, the inhibition of cellular proliferation, with G1-arrest, was shown to lead to autophagy with arginine deprivation. In addition, the combination of chloroquine plus arginine deprivation was more effective than arginine deprivation alone. In cells in which the expres-

P2–Poster 017 2570609

MATRIGEL SUPPORTS FORMATION OF SARCOSPHEROIDS AND UPREGULATION OF CANCER STEM CELL MARKERS

Jonathan Mandell; Shibing Yu; Jessica Tebbets; Adel Mahjoub; Mitchell S. Fourman; David Hirsch; Kurt Weiss
University of Pittsburgh, Gibsonia, PA, USA

Objective: Sarcoma is cancer of the connective tissue, and is comprised of many diverse subtypes. Although sarcoma only makes up 1% of new cancer diagnoses in the United States each year, it accounts for nearly 15% of pediatric diagnoses. Evidence of metastatic disease at the time of sarcoma diagnosis continues to remain the primary predictor of mortality. Culturing primary patient-derived sarcoma samples on Matrigel better represents the in vivo characteristics of the tumor and metastatic microenvironments, and will lead to improved translational studies as well as novel treatments.

Methods: Matrigel (Corning) was diluted with un-supplemented DMEM to obtain 50%, 25%, and 5% Matrigel concentrations. Primary samples of three different histologic subtypes (LM10-leiomyosarcoma, RM2- rhabdomyosarcoma, DS5-desmoid) which were previously cultured, were added to both Matrigel containing wells and control wells with no Matrigel. Cells were incubated for five days, and wells were photographed with a Leica DM IRB Microscope using QCapture software. cDNA was probed using Applied Biosystems Power SYBR Green PCR Mix (ThermoFisher Scientific).

Results: On 50% Matrigel LM10 formed large, dense spheroids with protrusions; RM2 formed slightly smaller, dense spheroids; and DS5 did not display any spheroid structures. LM10 and RM2 only formed spheres on 50% Matrigel. DS5 formed no obvious spheroid structures at

any Matrigel concentration. Cells grown on plastic alone showed lower transcriptional expression of CXCR4, which increased significantly when cells were grown on 50% Matrigel. Nanog expression was increased significantly in RM2 and decreased significantly in DS5 on 50% Matrigel. Oct 3/4 increased significantly in LM10 and RM2 when grown on 50% Matrigel.

Conclusion: Growth of primary sarcoma cells on Matrigel causes upregulation of known metastatic markers as well as cancer stem markers. RM2 is a known metastatic cell population, LM10 has no history of metastasis, while DS5 is a benign but aggressive fibromatosis. All three cell populations upregulated CXCR4, a known metastatic marker, when grown on Matrigel. Oct 3/4 and Nanog, both known cancer stem cell markers, were significantly elevated in the known metastatic cell population RM2 when grown on 50% Matrigel. Culturing tumor samples on Matrigel or other extracellular matrix concentrates in order to best match the natural rigidity of the tissue of origin will more accurately replicate in vivo the tumor microenvironment and improve research methodologies.

P2–Poster 018 2561311

CIRCULATING TUMOR CELLS USING TELOMERASE-SPECIFIC REPLICATION-SELECTIVE ADENOVIRUS AS A PROGNOSTIC FACTOR IN SOFT TISSUE SARCOMA

Toshihiro Matsuo, MD, PhD[1]; Masataka Deie[1]; Shoji Shimose[2]; Yasuo Urata[3]; Katsuhisa Kawanami[1]; Keiji Sato[1]

[1]Orthopaedic Surgery, Aichi Medical University, Nagakute, Japan; [2]Kure Medical Center, Kure, Japan; [3]Oncolys BioPharma, Tokyo, Japan

Objective: Sarcomas have specific molecular characteristics and poor prognosis due to the tendency to spread to distant organs, especially the lungs, via the vascular system. Therefore, circulating tumor cells (CTCs) in the peripheral blood may be very important for analysis of the metastatic biology of sarcomas. We attempted to detect viable CTCs in the peripheral blood of sarcoma patients using a telomerase-specific viral agent. We looked for a correlation between the numbers of CTCs and other clinical features of sarcomas.

Methods: For CTC analysis, 20 blood samples were obtained from 10 patients with soft tissue sarcoma of the trunk or extremities before and after surgery. Five patients were diagnosed with grade 2 and five with grade 3 sarcoma. The average duration of postoperative observation was 36.6 months. The oncological prognosis was as follows: 6 patients were continuously disease-free, 2 patients were no evidence of disease, and 2 patient were dead on disease. Three patients developed lung metastases after surgery. All clinical data are shown in Table. We incubated 7.5-ml blood samples with a telomerase-specific, replication-selective, oncolytic adenoviral agent carrying the green fluorescent protein (GFP) gene and were then able to detect viable CTCs. GFP-positive cells were counted under a fluorescence microscope.

Results: The average number of CTCs was 1.9 in preoperative and 2.6 in postoperative patients. There was no significant difference in numbers of CTCs between pre-operation and post-operation ($p = 0.704$). All patients with an increased number of postoperative CTCs compared to the number of preoperative CTCs had lung metastases. The number of postoperative CTCs was significantly related to metastasis ($p = 0.022$) and life prognosis ($p = 0.014$). With regard to the number of postoperative CTCs, patients with metastasis had a significantly higher than those without metastasis. With regard to the number of postoperative CTCs, dead patients had a significantly higher than alive patients.

Clinical Data and CTCs

age	gender	site	pathology	grade	preoperative CTC	postoperative CTC	metastasis	prognosis	period (month)	size (cm)
86	female	thigh	myxofibrosarcoma	G2	1	1	none	CDF	26	6
84	male	chest	undifferentiated pleomorphic sarcoma	G3	3	0	none	CDF	45	10
82	male	chest	myxofibrosarcoma	G2	0	0	none	NED	48	12
71	male	lower leg	myxofibrosarcoma	G3	0	0	none	CDF	48	6
77	female	thigh	pleomorphic liposarcoma	G3	0	3	lung	DOD	12	15
64	female	lower leg	myxofibrosarcoma	G3	4	18	lung	DOD	28	8
82	male	chest	pleomorphic liosarcoma	G3	0	4	lung	NED	25	5
67	female	lower leg	myxofibrosarcoma	G2	0	0	none	CDF	49	4
44	male	chest	fibrosarcoma	G2	5	0	none	CDF	45	5
70	female	iliopsoas	leiomyosarcoma	G2	6	0	none	CDF	40	7

Conclusion: We demonstrated that an increase in the number of postoperative CTCs compared to the number of preoperative CTCs was related to lung metastasis. The number of postoperative CTCs was significantly related to metastasis and prognosis. This assay is remarkably simple method that was able to detect viable human CTCs in the peripheral blood of sarcoma patients. Detection of CTCs using this method may be useful for prognostic evaluation of sarcoma patients.

P2–Poster 019 2570249

ARGININE DEPRIVATION INDUCED AUTOPHAGY RENDERS ASS1 DEFICIENT SARCOMAS DEPENDENT ON SERINE METABOLISM AND SENSITIVE TO 3-PHOSPHOGLYCERATE DEHYDROGENASE (PHGDH) INHIBITION

Jeff Kremer[1]; Bethany Prudner[1]; Assama Ketegou[2]; Brian Van Tine[1]
[1]Oncology, Washington University In St. Louis, University City, MO, USA; [2]New York University, New York City, NY, USA

Objective: Argininosuccinate Synthetase 1 (ASS1) is silenced in ~90% of sarcomas. Loss of this enzyme causes cells to become dependent upon extracellular arginine for continued cell growth and proliferation. Upon arginine starvation, ASS1(-) sarcoma cells undergo autophagy and growth arrest. In order to identify potentially exploitable targets arising from the induction of autophagy, we investigated the metabolic alterations caused by pegylated arginine deiminase (ADI-PEG20) mediated arginine deprivation. Mass spectroscopy revealed a significant increase in serine biosynthesis concomitant with an upregulation of PHGDH. When paired with ADI-PEG20 treatment, inhibition of serine metabolism results in significant cell death. With new studies showing the importance of serine biology in cancer, as well as recent generation of a small molecule inhibitor to PHGDH, this newly identified synthetic lethality proves to be an exploitable therapeutic option for ASS1 deficient sarcomas.

Methods: The cell lines were with ADI-PEG20 for three days and subjected to metabolite extraction and capillary electrophoresis mass spectrometry (CE-MS). Similarly, additional samples were cultured for 2 days, with or without ADI-PEG20, and subsequently treated with U-C^{13} labeled glucose for an additional 24 hours before being subjected to metabolite extraction. Cell death was measured by propidium iodide fluorescent activated cell sorting after inhibition of serine metabolism by the small molecule inhibitor of PHGDH (CBR-5884) or genetic knockdown of key enzymes, with and without ADI-PEG20.

Results: Upon treatment with ADI-PEG20 and subsequent autophagy induction, the radiolabeled glucose derived component of a vast majority of metabolites decreased significantly. The pathway with the largest increase in metabolic flux was serine biosynthesis, including subsequent conversion into glycine. Significant changes in the enzyme responsible for the rate limiting step of serine biosynthesis, PHGDH, as well as serine catabolism, serine hydroxymethyltransferase (SHMT1/2) were induced upon arginine deprivation. Cell death levels were significantly higher in samples when inhibition of PHGDH or SHMT1/2 was paired with ADI-PEG20 treatment.

Conclusion: Arginine deprivation causes global changes in cellular metabolism. By determining the alterations in the fate of glucose upon treatment with ADI-PEG20, we were able to illustrate a significant increase in the level of serine biosynthesis. Inhibition of this escape pathway resulted in cell death.

P2–Poster 020 2570660

COMPREHENSIVE GENOMIC SEQUENCING OF TUMORS OF PEDIATRIC PATIENTS WITH HEMANGIOMAS

Sherri Z. Millis, PhD[1]; Julie Blatt[2]; Alexa Schrock[1]; Julia Elvin[1]; Laurie Gay[1]; Jeffrey Ross[1]; Philip Stephens[1]; Vincent Miller[1]; Siraj Ali[1]
[1]Medical Affairs, Foundation Medicine, Phoenix, AZ, USA; [2]University of North Carolina, Research Triangle Park, NC, USA

Objective: Cutaneous and soft tissue hemangiomas are the most common childhood neoplasms, occurring in ~10% of Caucasians. Although the vast majority of hemangiomas spontaneously regress or can be managed with local treatments such as corticosteroids or propranolol, a small subset of cases either persist or progress, causing both cosmetic and structural challenges for the treating physicians. Some also present a diagnostic challenge. These issues have prompted a new interest in uncovering the genomic nature of these histologically benign, but clinically aggressive lesions to learn whether targeted therapies could be of potential benefit.

Methods: Ten cases of clinically advanced, therapy resistant histologically benign hemangiomas were assayed by comprehensive genomic profiling (CGP) of up to 405 genes and selected introns (frequently involved in fusion), to evaluate genomic alterations (GA) and opportunities for targeted therapy approaches in this disease. GA included base substitutions, indels, amplifications, copy number alterations and fusions/rearrangements. Seven of the ten specimens had an additional 265 genes analyzed by targeted RNA-seq for rearrangements.

Results: Ten (100%) of cases featured at least 1 GA. Three of 10 (30%) hemangiomas harbored a *KRAS* GA (all male), and a 4th (female) harbored an *NRAS* alteration. Of 7 patients who had sequencing of the larger gene set, 3

(43%) harbored a PCLO missense point mutation (Q1292L, E1576Q, A2123V). *PIK3CA* or *PIK3R2* alterations were identified in 3 cases and 2 of the 10 cases had an AR alteration (1 male/1 female). Hemangioma incidence was 60% male/40%female. The median patient age was 10 years, with a range of 0-20 years. Overall 7/10 cases had either a RAS pathway lesion, an AR alteration, or a mutation in the PI3K pathway, as shown in the table.

Conclusion: 40% of hemangiomas have activating lesions of the RAS pathway, with KRAS alterations exclusively found in male. KRAS driven hemangiomas could potentially respond to MEK inhibitors, both approved and in clinical trials. The 43% of hemangiomas which harbored *PCLO* alterations were mutually exclusive of the 30% patients whose tissue harbored KRAS alterations. These results indicate a potential for targeted therapies for aggressive childhood hemangiomas and further study of the genomic alterations in these tumors appears warranted.

Gene/Case	1	2	3	4	5	6	7	8	9$	10$
KRAS	*	*	*							
NRAS				*						
PCLO				*	*	*				
AR	*				*					
PIK3CA						*	*			
NOTCH1							*	*		
PIK3R2		*					*			

$GA's were identified but not included in this list.
All other genes were seen in only 1 case.

P2–Poster 021 2570405

TRANSCRIPTOME ANALYSIS OF METASTATIC AND NON-METASTATIC PATIENT SARCOMA REVEALS DIFFERENCES IN ALDH ACTIVITY AND NOTCH SIGNALLING

Jonathan Mandell; Stuti Patel; Mitchell S. Fourman; David Hirsch; Adel Mahjoub; Jessica Tebbets; Shibing Yu; Kurt Weiss
University of Pittsburgh, Gibsonia, PA, USA

Objective: ALDH is a known cancer stem cell (CSC) marker and has been shown to correlate with a more metastatic phenotype. ALDH activity is regulated at least in part by Notch signaling pathway, which controls stemness and proliferative capabilities of normal stem cell populations. Sarcoma is a cancer that originates from vastly different tissue, and we should suspect primary formation and metastatic ability would be operating using different aberrant signaling mechanisms. We examined transcriptome of 12 primary patient sarcoma cell lines as a first step in examining differences in sarcoma signaling mechanisms, and finding novel targets for personalized for each patient post-surgery.

Methods: Samples obtained from patients with metastatic as well as non-metastatic medical histories. Samples used; chondrosarcoma (CS9, CS10, CS8, MC1) osteosarcoma (OS8, OS10) leiomyosarcoma (LM1, LM7, LM10) high grade sarcoma (SC9, SC10a), and a rhabdomyosarcoma (RM2). Metastatic cell lines (CS9, LM1, LM7, RM2, OS10, SC10a) non- metastatic cell lines (MC1, CS10, CS8, SC9, OS8). RNA was extracted using Dneasy Kit (Qiagen). cDNA was probed using (Invitrogen) Custom Primers and Power SYBR Green PCR Mix (Applied Biosystems).

Results: Differences in ALDH, Notch1, Notch3, Jag1, and Hes1 could be seen in metastatic vs. non metastatic lines within histologic subtypes. Metastatic leiomyosarcoma have increased ALDH expression over 50 fold compared to non-metastatic leiomyosarcoma. Metastatic leiomyosarcoma have decreased Notch3, Jag1, and Hes1 expression compared to increased expression in non-metastatic leiomyosarcoma. Osteosarcoma showed the opposite trend, having decreased ALDH expression and increased Notch3, Jag1, and Hes1 in metastatic lines compared to non-metastatic. Chondrosarcomas show metastatic lines show increased ALDH expression and decreased Notch1, Jag1, and Hes1, compared to non-metastatic.

Conclusion: Analysis of primary human tumor cell isolates has shown complexities to sarcoma signaling biology and metastatic phenotypes. A mechanism can be shown in which a minor subset of high ALDH expressing cancer stem cells within a tumor is driving tumorigenesis and metastasis. This constitutive ALDH expression produced by the cells is a result of many possible permutations of aberrant Notch signaling. Targeting both ALDH enzyme activity and blocking Notch pathway crosstalk, may yield higher tumoricidal effects and improve patient outcomes.

P2–Poster 022 2569798

FACTORS IMPACTING THE ESTABLISHMENT OF INDIVIDUAL SOFT TISSUE SARCOMA PATIENT-DERIVED ORTHOTOPIC XENOGRAFT (PDOX) MOUSE MODELS: A UCLA SARCOMA PROGRAM PROSPECTIVE CLINICAL TRIAL

Mark A. Eckardt[1]; Tara A. Russell, MD, MPH[2]; Takashi Murakami[3]; Arun S. Singh[4]; Tasuku Kiyuna[3]; Kentaro Igarashi[3]; Kei Kawaguchi[3]; Yunfeng Li[5]; Joseph G. Crompton[2]; Sarah M. Dry[5]; Noah Federman[6]; Bartosz Chmielowski[4]; Elizabeth Shurell[2]; Robert M. Hoffman[7]; Frederick C. Eilber[1]

[1]Department of Surgery, Yale University School of Medicine, New Haven, CT, USA; [2]Division of Surgical Oncology, Jonsson Comprehensive Cancer Center Sarcoma Program, University of California Los Angeles, Los Angeles, CA, USA; [3]Department of Surgery, University of California San Diego, San Diego, CA, USA; [4]Division of Hematology-Oncology, Jonsson Comprehensive Cancer Center Sarcoma Program, University of California Los Angeles, Los Angeles, CA, USA; [5]Department of Pathology, Jonsson Comprehensive Cancer Center Sarcoma Program, University of California Los Angeles, Los Angeles, CA, USA; [6]Department of Pediatrics, Jonsson Comprehensive Cancer Center Sarcoma Program, University of California Los Angeles, Los Angeles, CA, USA; [7]AntiCancer Inc., San Diego, CA, USA

Objective: Soft tissue sarcomas(STS) are among the most aggressive chemotherapy(CT) resistant neoplasms. Understandably there is great interest in personalizing STS therapy and avoiding trial & error toxic CT. The surgical specimen offers a unique opportunity to obtain information to individualize therapy, particularly if immortalized in a murine model. Prior attempts to develop clinically relevant STS xenograft models were limited by small numbers, pre-clinical/lab settings & subcutaneous tumor implantation. The aims of this prospective clinical trial were to: 1) determine if we could develop STS patient-derived orthotopic xenografts(PDOX) models in the clinical setting & 2) identify the clinical-pathologic factors associated with successful PDOX establishment.

Methods: 5/2015-5/2016 all 107 patients with biopsy-proven or potential STS offered enrollment signed pre-operative consent. Sarcoma surgeon (FCE) obtained a portion of the tumor in OR, which was transported fresh for surgical orthotopic implantation(SOI) in nude mice. Once a PDOX reached 500 mm^3 & was passaged it was considered established. Mice without tumor growth by ≥6 months were classified as a failure. To date no low grade(LG) STS established. 44 high grade(HG) STS PDOX attempts either established or failed (completed surveillance ≥6mo). This cohort was analyzed for factors associated with PDOX establishment. All 71 HG-STS PDOX attempts (27 additional) will be able to be analyzed by meeting date.

Results: 107 STS underwent SOI; 71 HG, 36 LG. 28/44(64%) of the HG-STS that completed surveillance(≥-6mo) successfully established a PDOX(Table 1). Median interval for establishment was 46.5 days. Take-rates varied only by preoperative therapy(Pre-Tx). Untreated patients (No Pre-Tx) were 10.1 times more likely to successfully establish a PDOX compared to Pre-Tx patients(p=0.002). Univariate & multivariate analysis demonstrated only pre-operative radiation(XRT) significantly impacted likelihood of PDOX establishment (97% less likely w/ Pre-XRT,p=0.002). Preoperative CT did not significantly diminish successful establishment(p=0.552). Figure 1 Pre-Tx impact on PDOX establishment.

Conclusion: This study demonstrates a very high (82%) establishment rate for PDOX in HG STS patients without pre-tx, which was not significantly impacted by preoperative CT, but was impacted by preoperative XRT. In the largest PDOX study to date, we demonstrate that this is a feasible model for immortalizing individual patient HG-STS & potentially personalizing therapy.

Figure 1

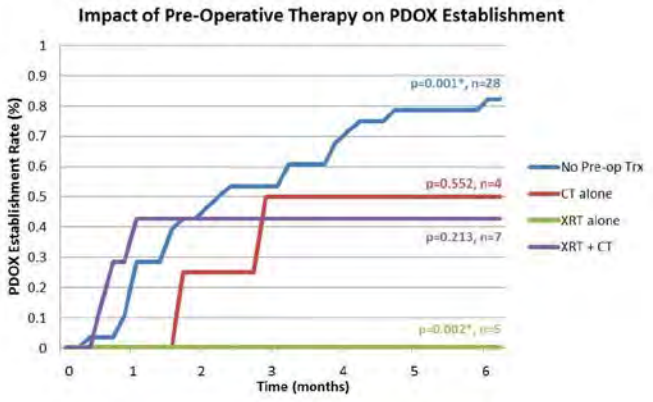


Table 1

		Sample n = 44		Take-Rate by Individual Factors		Univariate Logistic Regression		Multivariate Logistic Regression^	
		n	%	% (n)	p-value	OR (SE)	p-value	OR (SE)	p-value
Gender	Female	23	52.27%	60.87% (14)	0.690	0.778 (0.490)	0.690		
	Male	21	47.70%	66.67% (14)		Ref			
Grade	Low grade	0	0.00%	0.00% (0)					
	High grade	44	100.00%	63.64% (28)					
Presentation	Primary	27	61.36%	62.69% (17)	0.907	0.927 (0.598)	0.907		
	Recurrent or Metastatic	17	38.64%	64.71% (11)		Ref			
Location	Trunk	22	50.00%	59.09% (13)	0.531	Ref			
	Extremity	22	50.00%	68.18% (15)		1.484 (0.935)	0.532		
Subtype	Leiomyosarcoma	9	20.45%	66.67% (6)	0.832	1.333 (1.176)	0.744		
	Liposarcoma	9	20.45%	66.67% (6)	0.832	1.333 (1.176)	0.744		
	NOS/Spindle Cell/UPS	11	25.00%	63.64% (7)	1.000	1.167 (0.955)	0.851		
	Other	15	34.09%	60.00% (9)	0.718	Ref			
Pre-operative CT	Yes	11	25.00%	41.67% (5)	0.830	0.362 (0.259)	0.155	2.682 (2.797)	0.344
	No	33	75.00%	45.10% (23)		Ref			
Pre-operative XRT	Yes	12	27.27%	25.00% (3)	0.001*	0.093 (0.074)	0.003*	0.033 (0.038)	0.002
	No	32	73.73%	78.13% (25)		Ref			
Pre-operative Therapy	None	28	63.64%	82.14% (23)	0.001*	10.120 (7.398)	0.002*		
	CT alone	4	9.09%	50.00% (2)	0.552	0.538 (0.567)	0.557		
	XRT alone	5	11.36%	0.00% (0)	0.002*	--	--		
	CT + XRT	7	15.91%	42.86% (3)	0.213	0.360 (0.303)	0.224		
Xenograftability	Success	28	63.64%						
	Failure	16	36.36%						
		Median	**Range**						
Age		61	16 - 91			1.037 (0.022)	0.086	1.067 (0.030)	0.024
Size (cm)		7.15	0.9 - 35.5			0.971 (0.046)	0.536	1.007 (0.070)	0.925
Time to Establish (days)		46.5	9 - 184						

* significant at p<0.05, CT: chemotherapy, XRT: radiation therapy, NOS: not otherwise specified

^ Multivariate logistic regression model included the following factors: age, size, neoadjuvant chemotherapy, neoadjuvant radiation. Pseduo R-squared 0.2971, likehood ratio chi squared 17.14 (p=0.0018)

P2–Poster 023 2566129

SIRT1 AND SIRT2 INHIBITION IMPAIRS PEDIATRIC SOFT TISSUE SARCOMA GROWTH

limin Ma; Bertha A. Brodin
Oncology & Pathology, Karolinska institutet, SOLNA, Stockholm, Sweden

Objective: Sirtuins are NAD+ dependent deacetylases and/or ADP-ribosyl transferases active on histone and non-histone substrates. The first sirtuin was discovered as a transcriptional repressor of the mating-type-loci (Silent Information Regulator sir2) in the budding yeast, where it was shown to extend yeast lifespan. Seven mammalian sirtuins (SIRT1-7) have been now identified with distinct subcellular localization, enzymatic activities and substrates. These enzymes regulate cellular processes such as metabolism, cell survival, differentiation, DNA repair and they are implicated in the pathogenesis of solid tumors and leukemias.

Methods: The purpose of the present study was to investigate the role of sirtuin expression, activity and inhibition in the survival of pediatric sarcoma cell lines. We have analyzed the expression of SIRT1 and SIRT2 in a series of pediatric sarcoma tumor cell lines and normal cells, and we have evaluated the activity of the sirtuin inhibitor and p53 activator tenovin-6 (Tv6) in synovial sarcoma and rhabdomyosarcoma cell lines.

Results: We show that SIRT1 is overexpressed in synovial sarcoma biopsies and cell lines in comparison with normal mesenchymal cells. Tv6 induced apoptosis as well as impaired autophagy flux. Using siRNA to knock down SIRT1 and SIRT2, we show that the expression of both proteins is crucial for the survival of rhabdomyosarcoma cells and that the loss of SIRT1 expression results in a decreased LC3II expression.

Conclusion: Our results show that SIRT1 and SIRT2 expressions are crucial for the survival of synovial sarcomas and rhabdomyosarcomas, and demonstrate that the pharmacological inhibition of sirtuins impairs the autophagy process and induces tumor cell death.

P2–Poster 024 2563283

DECIPHERING THE GENE REGULATORY NETWORKS OF MESENCHYMAL-EPITHELIAL TRANSITIONS IN SARCOMAS

Jason Somarelli, PhD[1]; Samantha Shetler[1]; Mohit Jolly[2]; Sarah Wang[3]; Suzanne Bartholf DeWitt[4]; Alexander Hish[1]; Shivee Gilja[1]; William Eward[4]; Kathryn Ware[1]; Herbert Levine[2]; Andrew Armstrong[1]; Mariano Garcia-Blanco[5]
[1]Medicine, Duke University, Durham, NC, USA; [2]Rice University, Houston, NC, USA; [3]Johns Hopkins University, Baltimore, MD, USA; [4]Orthopaedics, Duke University, Durham, NC, USA; [5]Biochemistry, University of Texas Medical Branch, Galveston, TX, USA

Objective: Phenotypic plasticity involves a series of events through which cells transiently acquire phenotypic traits of another lineage. Sarcomas appear to exhibit phenotypic plasticity, with a subset of sarcomas undergoing a transition to a more epithelial-like state. Interestingly, the transition to a more epithelial-like phenotype appears to have prognostic benefit in sarcomas. Our research objective was to understand the gene regulatory networks responsible for phenotypic plasticity in sarcomas.

Methods: Using mathematical models, we developed a predictive framework to identify a core regulatory circuit that controls mesenchymal-epithelial transitions in sarcomas. We tested this predictive framework using wet bench experiments. We also analyzed the prognostic relevance of these transitions in sarcoma samples from the The Cancer Genome Atlas.

Results: We found that combined expression of miR-200s and GRHL2 further upregulates epithelial genes to induce a mesenchymal-epithelial transition-like state in sarcomas. This effect is phenocopied by downregulation of either ZEB1 or the ZEB1 co-factor, BRG1. In addition, a mesenchymal-epithelial transition gene expression signature is prognostic for improved overall survival in sarcoma patients.

Conclusion: Together, our results suggest that a miR-200, ZEB1, GRHL2 gene regulatory network may drive sarcoma cells to a more epithelial-like state with prognostic relevance.

P2–Poster 025 2562298

MIR-X AND MIR-Y ARE POTENTIAL BIOMARKERS IN LIPOSARCOMA AND AFFECT THE TUMOR MICROENVIRONMENT INDUCING INFLAMMATORY RESPONSE

Lucia Casadei, PhD; Federica Calore; Kara Batte; Abeba Zewdu; Danielle Braggio; Carlo Maria Croce; Raphael Pollock
CCC, Ohio State University, Columbus, OH, USA

Objective: Liposarcoma (LPS) is the most common soft tissue sarcoma histological subtype. Despite the development of combined modality treatments in recent years, a significant proportion of patients respond poorly to chemotherapy. Thus, early detection of recurrent or metastatic disease could improve patient prognosis; however, there are no useful biomarkers for these purposes.
MicroRNAs (miRNAs) are short non-coding RNAs (ncRNAs) that regulate gene expression by binding to specific mRNA targets and promoting their degradation and/or translational inhibition. Circulating blood-borne miRNAs are being investigated for their potential as minimally invasive biomarkers of several diseases, including tumors.
The goal of this study is to identify potential biomarkers in the peripheral blood of LPS patients that could be useful for LPS diagnostic, prognostic, and therapeutic purposes.

Methods: A series of 16 human LPS patient specimens and 8 healthy controls was analyzed on a miRNA high throughput platform. Validation of the array was performed by qRT-PCR on an independent set of samples. Moreover LPS tissues and microvesicles (MVs) from different cells lines were analyzed. Murine peritoneal macrophages were stimulated with synthetic miRNAs and MVs respectively for 48 h; then ELISAs for IL-6 were performed following the manufacturer's instructions.

Results: A total of 26 miRNAs were significantly upregulated and 3 miRNAs were significantly down regulated ($p<0.004$) in the peripheral blood exosomes of LPS samples. Validation of the miRNA panel in an independent cohort of LPS patients confirmed this signature. Receiver-operating characteristic (ROC) curve analysis indicated that miR-X and miR-Y may be used as diagnostic biomarkers with the ability to discriminate between the healthy cohort and patients with LPS. Furthermore, in the *in vitro* study phase, these miRNAs were found to be secreted from LPS cell lines in MVs, suggesting their tumor origin. Importantly, these miRNAs extracted from tumor cell MVs were shown to be able to bind the toll-like receptors (TLRs) and induce inflammatory response in the tumor microenvironment.

Conclusion: This study has identified a specific miRNA signature in circulating exosomes that may lead to improvements in the diagnosis, prognosis, and/or treatment of LPS patients in a clinical setting. Moreover, we showed that miR-X and miR-Y also participate in the protumoral inflammatory process by activating the TLRs response in immune cells.

P2–Poster 026 2558863

TARGETING FGFR1 FOR TREATMENT OF SOFT-TISSUE SARCOMA

Priya Chudasama, PhD[1]; Marcus Renner[2]; Melanie Straub[3]; Barbara Hutter[6]; Matthias Scheffler [4]; Simon Schimmack[5]; Christof von Kalle[1]; Jürgen Wolf[4]; Benedikt Brors[6]; Wilko Weichert[3]; Hanno Glimm[1]; Claudia Scholl[1]; Gunhild Mechtersheimer[2]; Katja Specht[3]; Stefan Fröhling[1]

[1]Translational Oncology, German Cancer Research Center and National Center for Tumor Diseases, Heideleberg, BW, BW, Germany; [2]Institute of Pathology, Heidelberg University Hospital, Heidelberg, Germany; [3]Institute of Pathology, Technische Universität München, Munich, Germany; [4]Department of Internal Medicine I, Center for Integrated Oncology, Cologne University Hospital, Cologne, Germany; [5]Heidelberg University Hospital, Heidelberg, Germany; [6]Division Applied Bioinformatics, German Cancer Research Center and National Center for Tumor Diseases, Heidelberg, Heidelberg, Germany

Objective: Soft-tissue sarcomas (STS) are highly diverse and clinically challenging malignancies. In the setting of metastatic STS, systemic therapy using a limited spectrum of conventional cytotoxic drugs may provide symptom palliation and prevent rapid disease progression, but does not prolong survival in the majority of cases. Hence, there is an unmet need for novel, molecularly targeted STS therapies. Alterations of the FGFR1 receptor tyrosine kinase have been identified as oncogenic drivers in various cancers, and small-molecule FGFR inhibitors are being evaluated as anticancer drugs; however, the role of FGFR1 in STS has not been established. Prompted by the detection and subsequent therapeutic inhibition of amplified FGFR1 in a patient with metastatic leiomyosarcoma, we investigated the oncogenic properties and potential as drug target of FGFR1 in STS.

Methods: The frequency of FGFR1 amplification and overexpression, as assessed by fluorescence in situ hybridization, microarray-based comparative genomic hybridization and mRNA expression profiling, SNP array profiling, and RNA sequencing, was determined in three independent patient cohorts. The sensitivity of STS cell lines with or without FGFR1 alterations to genetic and pharmacologic FGFR1 inhibition and the signaling pathways engaged by FGFR1 were investigated using viability assays, colony formation assays, and biochemical analysis.

Results: Increased FGFR1 copy number was detected in 74 of 190 (38.9%; Cohort 1), 13 of 79 (16.5%; Cohort 2), and 80 of 254 (31.5%; Cohort 3) patients. FGFR1 overexpression occurred in 16 of 79 (20.2%, Cohort 2) and 39 of 254 (15.4%; Cohort 3) patients. FGFR1 alterations were detected in nine different categories of STS, including subtypes with specific genetic alterations as well as subtypes characterized by complex karyotypes. Targeting of FGFR1 by RNA interference and small-molecule inhibitors (PD173074, AZD4547, BGJ398) revealed that the requirement for FGFR1 signaling in STS cells is primarily dictated by FGFR1 expression levels, and identified the MAPK-ERK1/2 axis as critical FGFR1 effector pathway.

Conclusion: These data identify FGFR1 as oncogenic driver in multiple STS subtypes and suggest that FGFR1 inhibition, guided by patient selection according to FGFR1 expression and monitoring of MAPK-ERK1/2 signaling, may broaden the therapeutic armamentarium against STS, a hypothesis that can readily be tested in molecularly stratified clinical trials.

P2–Poster 027 2556643

ANTI-PHAGOCYTIC MARKER CD47 EXPRESSION IN SARCOMAS

Amanda R. Dancsok, MD, PhD Student[1]; David Thomas[3]; Jean Yves Blay[4]; Robert G. Maki[2]; Torsten Nielsen[1]; Elizabeth G. Demicco[2]

[1]University of British Columbia, Vancouver, BC, Canada; [2]Mount Sinai Hospital, New York, NY, USA; [3]Garvan Institute of Medical Research, Sydney, New South Wales, Australia; [4]Centre Léon Bérard, Lyon, France

Objective: CD47 is an immune checkpoint molecule, expressed in most normal cells and overexpressed in some cancer cells, that prevents ingestion by macrophages and other phagocytic immune effector cells. The interaction between CD47 and its receptor SIRPα is targeted by novel immunotherapy agents currently accruing for phase I trials. The objective of this study was to characterize expression of CD47 in sarcomas, which has not previously been reported.

Methods: Immunohistochemistry was performed on tissue microarrays containing duplicate cores representing 1896 sarcomas spanning 23 sarcoma subtypes, using CD47 mouse monoclonal antibody B6H12. Tissues were scored by the percentage of tumor cells exhibiting positive cytoplasmic and/or membranous staining.

Results: The distribution of CD47 scores was distinctly bimodal across the sample set, with most cores staining at either 0% or 100% positive tumor cells. This bimodality persisted in some subtypes (osteosarcoma, chondrosarcoma, gastrointestinal stromal tumors), while in other subtypes, samples skewed in one direction. Translocation-associated sarcomas were notably and consistently low-expressors of CD47, particularly dermatofibrosarcoma protuberans, low-grade fibromyxoid sarcoma, and Ewing sarcoma. Notable high expressors of CD47 included dedifferentiated liposarcoma and chordoma, which demonstrated 100% tumor cell staining in 36/77 (47%) and 23/28 (82%) samples, respectively. Angiosarcoma and epithelioid sarcoma

also had consistently high expression of CD47, though this was based on smaller numbers of samples (Table 1).

Conclusion: CD47 demonstrated all-or-nothing expression in our sample set, suggesting that CD47-SIRPα signaling is present and active in some sarcomas. CD47 staining may prove useful the selection of patients appropriate for anti-CD47 based therapies now in development.

CD47 immunohistochemistry scores in sarcoma tissue microarrays

number of cases% positive tumor cells	n	0%CD47	100%CD47	median	Q1-Q3
TRANSLOCATION-ASSOCIATED SARCOMAS					
Synovial sarcoma	137	67	12	0.5	0-45
Solitary fibrous tumor	118	73	16	0.5	0-65
Myxoid liposarcoma	41	14	5	25	0-78
Dermatofibrosarcoma protuberans	23	17	2	0	0-15
Low-grade fibromyxoid sarcoma	16	12	1	0	0-11
Ewing sarcoma	13	11	1	0	0-0
Alveolar rhabdomyosarcoma	10	5	2	2.5	0-95
Alveolar soft part sarcoma	8	5	1	0	0-67
Clear cell sarcoma	7	4	1	0	0-90
SARCOMAS WITH RECURRENT GENETIC ALTERATIONS					
Gastrointestinal stromal tumor	636	264	286	85	0-100
Dedifferentiated liposarcoma	77	15	36	95	38-100
Well-differentiated liposarcoma	62	22	8	50	0-84
Chondrosarcoma	46	26	12	0	0-33
Chordoma	28	0	23	100	100-100
Epithelioid sarcoma	8	2	5	100	14-100
SARCOMAS WITH COMPLEX KARYOTYPES					
Osteosarcoma	260	143	59	0	0-85
Undifferentiated pleomorphic sarcoma	86	66	9	0	0-0
Malignant peripheral nerve sheath tumor	77	51	9	0	0-16
Myxofibrosarcoma	59	50	1	0	0-0
Leiomyosarcoma	23	12	3	0	0-50
Embryonal rhabdomyosarcoma	10	6	0	0	0-90
Fibrosarcoma	9	7	2	0	0-50
Angiosarcoma	5	0	4	100	75-100
OVERALL	1896	872	498	2.5	1-100

P2–Poster 028 2556570

THE REGULATION OF MALIGNANT TRANSFORMATION BY PPP2R1A IN ALVEOLAR RHABDOMYOSARCOMA BASED ON A PROTEOMIC APPROACH CORRESPONDING TO THE PAX3-FOXO1 FUSION GENE

Keisuke Akaike[1]; Yoshiyuki Suehara[1]; Shinji Kohsaka[2]; Kenta Mukaihara[1]; Midori Ishii[1]; Daisuke Kubota[1]; Yu Tanabe[1]; Saiko Kazuno[3]; Reiko Mineki[3]; Tsutomu Fujimura[3]; Kazuo Kaneko[1]; Marc Ladanyi[2]; Tsuyoshi Saito[4]

[1]Orthopaedic Surgery, Juntendo University School of Medicine, Bunkyo-ku, Tokyo, Japan; [2]Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [3]Laboratory of Biochemical Analysis, Central Laboratory of Medical Sciences, Juntendo University School of Medicine, Tokyo, Japan; [4]Human Pathology, Juntendo University School of Medicine, Tokyo, Japan

Objective: Two fusion gene, PAX3-FOXO1 and PAX7-FOXO1, have been detected in approximately 70% of Alveolar rhabdomyosarcoma (ARMS). ARMSs with the PAX3-FOXO1 variant have a poorer outcome than those with PAX7–FOXO1, therefore it has been suggested that the PAX3-FOXO1 fusion protein is associated with the pathogenesis or malignant transformation of ARMS. In this study, in order to identify the relationship between the PAX3-FOXO1 fusion gene and oncogenic or malignant transforming factors of ARMS, we conducted proteomic studies using PAX3-FOXO1 knockdown in ARMS cell lines.

Methods: We performed proteomic analyses using isobaric tags for relative and absolute quantitation (iTRAQ) to determine proteins profiles regulated by PAX3-FOXO1. We utilized 4 ARMS cell lines with PAX3-FOXO1 gene fusion and gene knockdown by 2 siRNA transfections of PAX3-FOXO1 followed by i-TRAQ methods. In order to further understand these biological processes and networks, we applied the protein profiles to the Oncomine databases and Ingenuity Pathways Analysis (IPA) system. We also performed functional assays using the ARMS cell lines to elucidate malignant potentials regarding the proteins which were identified by iTRAQ profiling.

Results: Eight distinct protein silenced profiles from each transfected ARMS cell lines were observed, in which approximately 1,300-2,400 altering protein expressions were identified. In order to narrow down the protein profiles, we selected significantly altered proteins that were observed in two or more of the 8 protein profiles and found 74 consistently upregulated and 92 consistently downregulated proteins. These up- or downregulated protein profiles were further analyzed using the Oncomine or IPA databases and PPP2R1A was determined to play a critical functional role in the setting of ARMS. To further characterize the role of PPP2R1A, we subsequently performed cell proliferation assays in ARMS cell lines using PPP2R1A siRNA and silencing of PPP2R1A significantly increased the cell growth of all ARMS cells. Furthermore, a cytotoxicity assay with FTY720, a PP2A-activating drug, was performed and the cell growth of all ARMS cell lines was suppressed.

Conclusion: Our data suggest that the identified proteins associated with PAX3-FOXO1 may play an important role in the acquisition of malignant potential of ARMS cells. We believe that these findings will help to elucidate the malignant progression of ARMS achieved by PAX3-FOXO1 and may lead to the development of novel therapeutic strategies.

P2–Poster 029 2553539

MUTATIONAL SPECTRUM OF UNDIFFERENTIATED PLEOMORPHIC SARCOMAS

Andrew Seto[1]; Nalan Gokgoz[1]; Yael Babichev[1]; Qingxia Wei[2]; Richard de Borja[3]; Brendan C. Dickson[4]; Adam Shlien[3]; Benjamin Alman[2]; Rebecca Gladdy[1]; Jay Wunder[1]; Irene L. Andrulis[1]

[1]Lunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada; [2]Developmental and Stem Cell Biology, Hospital for Sick Children, Toronto, ON, Canada; [3]Genetics & Genome Biology, Hospital for Sick Children, Toronto, ON, Canada; [4]Department of Laboratory Medicine and Pathobiology, Mount Sinai Hospital, Toronto, ON, Canada

Objective: Undifferentiated pleomorphic sarcomas (UPS) are high grade soft tissue sarcomas (STS) with no apparent line of differentiation. Despite overall gains in the management of STS, progress in therapies based on molecular targets and understanding the unknown genetic diversity is needed, especially in UPS where response to therapy is limited. Using integrated multi-omic analysis, we aim to characterize UPS for recurrent genetic mutations, altered pathways and mutational spectrum. These insights into UPS may enable robust classification, identify prognostic markers and lead to novel treatment approaches.

Methods: Well clinically annotated cases of UPS with matched blood specimens were retrieved from the Sarcoma Tumor Bank at Mount Sinai Hospital, Toronto. Using current WHO histopathological classification, re-evaluated cases were subjected to exome and RNA sequencing. Cell lines and in one case, a xenograft model, have been generated from 4 primary tumors. We are integrating the annotated somatic mutations, expressed transcripts, mRNA fusions and copy number aberrations to detect recurrent molecular features.

Results: At present, 14 UPS tumor, 4 cell lines and 1 xenograft have been analyzed. TP53, ATRX and RB1 were recurrently mutated and one case had a RB1 and ATXN10 fusion transcript that lacked RB1 tumor suppressing domains. The matched cell line also expressed the RB1-ATXN10 fusion. Somatic point mutations among the tumors occurred at ~5 muts/Mb with a single hypermutated case (>10 muts/Mb). In examining the base changes, the

hypermutated case displayed a C>A bias and 3 other cases displayed a C>A bias, but were not hypermutated. The 5' and 3' bases flanking the C>A alterations in the hypermutated case had a distinct pattern (TpCpN, CpCpA) from the 3 other C>A biased cases (CpCpN). These C>A biases are not detected in >10K cases across 33 cancer types sequenced by TCGA. The cell line and xenograft models retained 8-71% of their matched tumors' point mutations. Changes in the variant allele frequency between the tumors and cell lines showed neutral dynamics, a diagonal pattern, (UPS1, UPS3 and UPS4) and possible clonal selection (UPS2) (Figure 1).

Conclusion: Initial integrated analysis of UPS tumors identified recurrently mutated genes and unique patterns of C>A biases in 4/14 cases not previously seen. Ongoing multi-omic analysis of 20 additional UPS tumors may reveal further genomic events that may aid in stratification of UPS, identify actionable targets and realize novel therapeutics.

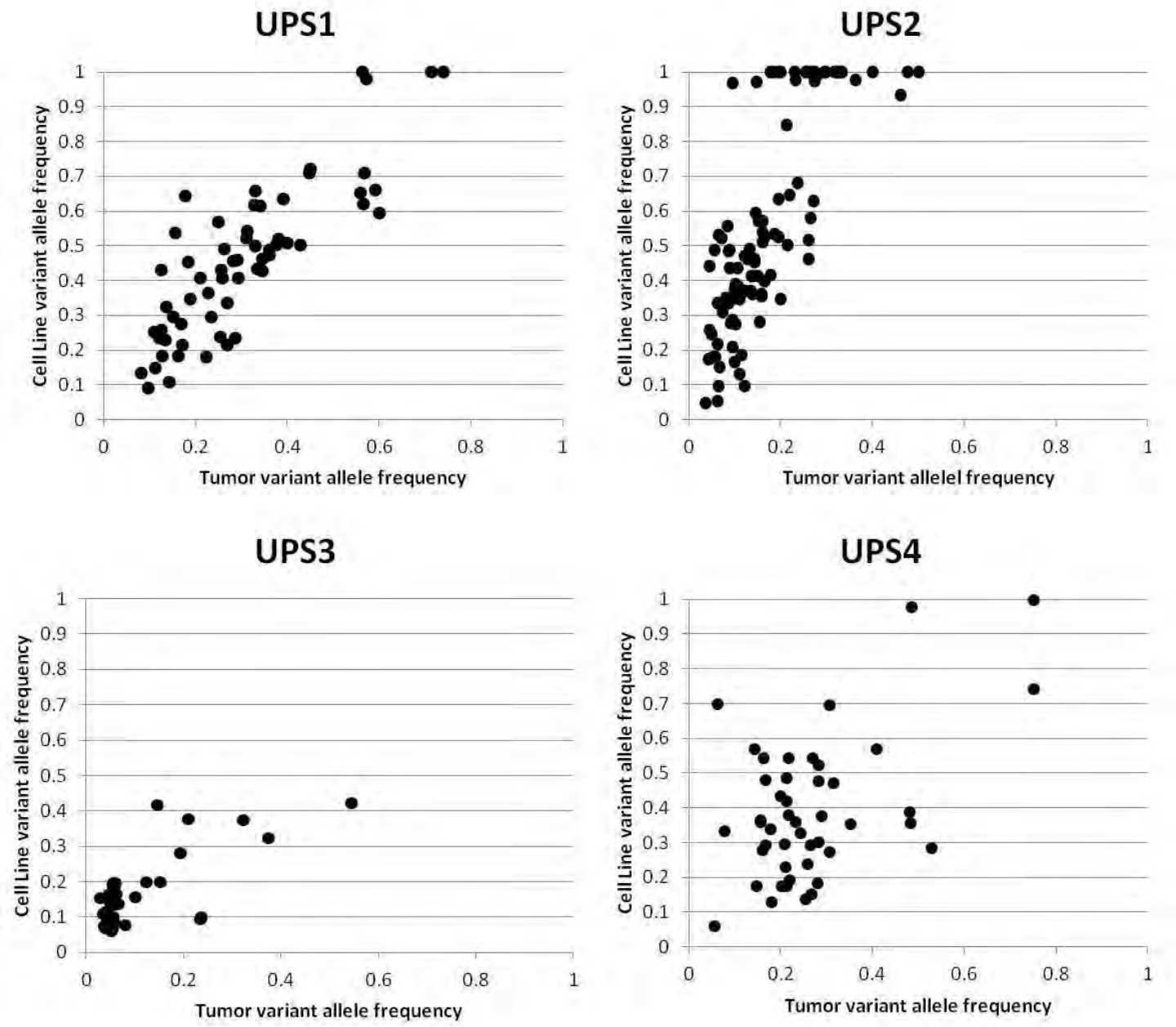


Figure 1. Comparison of the variant allele frequency of the shared variants between the UPS tumors and matched cell lines.

P2–Poster 030 2551164

HDAC AND PROTEASOME INHIBITORS SYNERGIZE AGAINST SYNOVIAL SARCOMA

Aimee N. Laporte[1]; Robert Ren Jie Yao[1]; Jared J. Barrott[2]; Neal Poulin[1]; Kevin B. Jones[2]; T. Michael Underhill[1]; Torsten Nielsen[1]
[1]University of British Columbia, Vancouver, BC, Canada; [2]University of Utah, Salt Lake City, UT, USA

Objective: Conventional therapies do not target the synovial sarcoma oncoprotein and patients remain at high risk for recurrence and death. HDAC inhibitors disassociate the driving SS18-SSX oncoprotein complex, but monotherapy trials in patients have only produced stable disease as best response. A high-throughput drug screen was undertaken in a panel of synovial sarcoma cell lines to uncover novel sensitizing agents and targetable pathways.

Methods: A 900 compound library comprised of known and experimental anticancer drugs, tyrosine kinase inhibitors and epigenetic modulators was screened on panel of fusion oncogene-confirmed synovial sarcoma cell line models. Compound efficacy was evaluated based on potency and specificity in all synovial sarcoma cell lines. Combinational studies were utilized to measure potential compound synergy. Effective compounds were validated in specific assays of drug activity, including the proximity ligation assay, apoptotic induction assays, mechanism of synergy studies, and *in vivo* drug treatment studies. HDAC inhibition in this model was further assessed by transcriptome analysis and supporting functional studies.

Results: Top hits in the unbiased screen were HDAC (including quisinostat) and proteasome (bortezomib, carfilzomib) inhibitors. In combination, these agents induce cytosolic stress, increase reactive oxygen species and activate pro-apoptotic factors. The combination of the HDAC inhibitor quisinostat and the proteasome inhibitor bortezomib significantly inhibits tumour growth in a murine model of synovial sarcoma. HDAC inhibition prevents aggresome formation, reactivates expression of tumor suppressors including EGR1 and CDKN2A, downregulates the mitotic cell cycle phenotype and initiates apoptotic marker expression.

Conclusion: HDAC inhibition has significant effects in activating a tumor suppressive phenotype in synovial sarcoma, and synergizes with proteasome inhibition to elicit apoptosis and inhibit tumor growth. This study identifies and provides mechanistic support for the combination of quisinostat with proteasome inhibitors against synovial sarcoma, a combination known to have limited toxicity in phase I myeloma studies, and therefore amenable to evaluation in human sarcoma clinical trials.

P2–Poster 031 2550053

IN VITRO SCREEN IDENTIFIES NOVEL DRUG TARGETS IN PRIMARY UNDIFFERENTIATED PLEOMORPHIC SARCOMA CELL LINES

Rosemarie E. Venier[1]; Yael Babichev[1]; Winan van Houdt[2]; Leah Kabaroff[1]; Alessandro Datti[1]; Adrian Pasculescu[1]; Richard Marcellus[3]; David Uehling[3]; Brendan C. Dickson[4]; Rima Al-awar[3]; Albiruni A. Razak[5]; Jay Wunder[1]; Irene L. Andrulis[1]; Rebecca Gladdy[1]
[1]Lunenfeld Tanenbaum Research Institute, Toronto, ON, Canada; [2]Department of Surgery, University of Toronto, Toronto, ON, Canada; [3]Drug Discovery Group, Ontario Institute for Cancer Research, Toronto, ON, Canada; [4]Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada; [5]Medical Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada

Objective: Undifferentiated pleomorphic sarcoma (UPS) is a heterogeneous group of tumors with no identifiable line of differentiation. Tumors are characterized genetically by complex and unstable karyotypes, with limited knowledge of their molecular pathobiology. As part of a UPS translational research pipeline at our institution, we aimed to detect recurrent molecular pathway alterations, with the intention of drug repurposing and functionally identifying novel drug targets for this disease.

Methods: Primary UPS cell lines were established from confirmed cases of UPS surgical specimens in accordance with institutional research ethics. Short tandem repeat (STR) analysis confirmed genetic identity with the original tumor. Four UPS and 1 control fibroblast cell line were initially screened with 3,346 compounds at two concentrations (0.4 and 2 μM). Incubation times were dependent on cell cycle duration. Response was measured by cell viability (B-score >3 StDev). Top hits were validated with EC_{50} assays.

Results: Four UPS cell lines were analyzed by STR and found to be >80% concordant with banked tumor sample, indicating a match. We confirmed that the cell lines were immunohistologically (IHC) similar to original tumors by examining IHC markers, as well as morphological similarities. Four cell lines were screened using 3,346 compounds and top hits included: cytotoxics, and inhibitors of receptor tyrosine kinases, protein synthesis, PI3K/mTOR/IRE-1 pathways and cyclin-dependent kinases. Twenty-five compounds were prioritized based on FDA-approval status, known oncologic activity, minimal human toxicity, and mechanism of action. The majority of these (23/25), were subsequently validated with a 12-point EC_{50} assay. A validated hit was generally defined as a compound that elicited a response from at least 3/4 UPS cell lines (EC_{50} < 1 μM), but was not toxic to the normal control. Dose response curves indicated 6 selective hits, 7 non-selective hits, 3 mixed response and 7 inactive compounds. Selective hits included novel sarcoma therapeutics.

Conclusion: In this study, 4 primary UPS cell lines were analyzed to determine sensitivity to 3,346 compounds. Following triage, 6 compounds were highly selective for UPS cell lines (3/4 cell lines responded, excluding the control) and had an EC_{50} of < 1 μM. Ongoing validation consists of confirming on-target effects in vitro and determining in vivo efficacy using pre-clinical UPS xenograft models to vet which compounds are valuable for further clinical development.

P2–Poster 032 2544296

MYXOID LIPOSARCOMA FUSION PROTEIN FUS-DDIT3 ASSOCIATES WITH PARP1, RNA PROCESSING AND DBHS FAMILY PROTEINS (SFPQ, NONO, PSPC1)

Jamie S. Yu[1]; Chia-Chin Wu[2]; Hannah C. Beird[2]; Judith V. Bovée[3]; Alexander Lazar[2]; Neeta Somaiah[2]; Torsten Nielsen[1]

[1]University of British Columbia, Vancouver, BC, Canada; [2]MD Anderson Cancer Center, Houston, TX, USA; [3]Leiden University Medical Center, Leiden, Netherlands

Objective: Myxoid liposarcoma (MLS) is characterized by a balanced translocation involving *FUS* (12q13) and *DDIT3* (16p11). While the resultant FUS-DDIT3 oncoprotein has been hypothesized to form an aberrant transcriptional complex, its exact mechanism of action has remained unclear, rendering it difficult to formulate rational strategies for targeted therapy. We used mass spectrometry to interrogate the FUS-DDIT3 interactome, and integrated this proteomic data with RNA-seq gene expression profiles. We sought to validate top FUS-DDIT3 interacting proteins, and use bioinformatics to identify the key pathways represented in the FUS-DDIT3 interactome to elucidate its major functions.

Methods: Anti-DDIT3 immunoprecipitation-mass spectrometry experiments in 3 MLS cell lines identified 73 potential proteins in the FUS-DDIT3 interactome. RNA-seq was performed on 9 untreated frozen MLS primary tumors and 1 normal adipose tissue sample. Top candidate proteins were validated by co-immunoprecipitation and proximity ligation assays in 3 MLS cell lines.

Results: Four of the top 5 enriched GO biological processes for the FUS-DDIT3 protein interactome were related to RNA processing and splicing, while the top GO molecular functions were poly(A) RNA binding and RNA binding. The mRNA surveillance pathway was the only enriched KEGG pathway in the protein interactome. Several FUS-DDIT3 protein interactors were also upregulated in MLS vs adipose tissues on the transcript level, including *PARP1*, *NONO* and *SFPQ*. The protein products of the latter two belong to the drosophila behavior/human splicing (DBHS) family of proteins, while the last DBHS protein, PSPC1, is also present in the putative interactome. We validated the association of NONO, SFPQ and PSPC1 with FUS-DDIT3 by reciprocal co-immunoprecipitation and proximity ligation assay.

Conclusion: The FUS-DDIT3 interactome is enriched in RNA processing proteins, which mirrors the recently published protein interactome of EWSR1-FLI1, in which the 5' half of the fusion protein, EWSR1, is a close homologue of FUS. This suggests a potential common function between fusion proteins harboring FUS or EWSR1 partners that could be applicable in additional mesenchymal tumors. We also observed a novel association of FUS-DDIT3 with PARP1, and the DBHS family of proteins (SFPQ, NONO PSPC1), that have been implicated in several other cancer types, and have critical roles in gene regulation (including transcription and RNA processing).

P2–Poster 033 2564681

IMMUNOHISTOCHEMISTRY SCREENING TO INCREASE THE EFFICIENCY OF NEXT GENERATION SEQUENCING FOR DETECTION OF RARE NTRK, ROS1, AND ALK GENE FUSIONS IN SARCOMA PATIENTS

K. Kumar Sankhala[2]; Steven J. Potts, PhD[1]; Jason Christiansen[1]; Patrick Foley[1]; Katherine Kim[2]; Suzan Arasheben[2]; Bryan Leong[2]; Shayan Senaati[2]; Pratik Multani[1]; Zach Hornby[1]; Danielle Murphy[1]; Jennifer Lamoureux[1]; Sant P. Chawla[2]

[1]Ignyta Pharmaceuticals, San Diego, CA, USA; [2]Sarcoma Oncology Center, Santa Monica, CA, USA

Objective: The STARTRK-2 trial is a potentially registration-enabling Phase 2 global basket trial of the tyrosine kinase inhibitor entrectinib in patients with solid tumors harboring *NTRK1, NTRK2, NTRK3*, *ROS1*, or *ALK* gene fusions. Phase 1 studies of entrectinib reported a 79% ORR across multiple histology types in patients with gene fusions who were naïve to inhibitors of these targets, received an efficacious dose, and had extracranial disease. Patients harboring these gene fusions are rare (<3%); however, sarcoma patients may have a relatively higher prevalence, particularly in the *NTRK* genes (that encode the Trk proteins), where preliminary clinical evidence of benefit has been demonstrated with Trk inhibitors. Unfortunately, diagnostic testing to identify sarcoma patient populations with such low molecular prevalence poses efficiency and cost challenges, as molecular testing for these gene fusions is not yet part of standard clinical practice. We report on the prevalence of NTRK, ROS1, and ALK fusions in sarcoma based on Ignyta's internal and 3rd party testing. We also discuss the development of an assay for sarcoma samples and report on immunohistochemistry (IHC) screening rates in a clinical sarcoma cohort.

Methods: The prevalence of NTRK, ROS1, and ALK gene fusions were reviewed for sarcoma from Ignyta's aggregate diagnostic experience to date (internal testing in Ignyta's

CLIA/CAP lab and testing by third parties). In order to effectively identify sarcoma patients eligible for STARTRK-2, we developed a 2-step diagnostic test to identify *NTRK1, NTRK2*, *NTRK3*, *ROS1*, and *ALK* gene fusions in FFPE clinical specimens. This test is comprised of IHC screening using an antibody cocktail followed by an RNA-based anchored multiplex PCR next generation sequencing (NGS) assay.

Results: Table 1 shows the prevalence of the five gene fusions in sarcoma, ranging from 0 percent to 11 percent. Out of 86 samples, no instances were detected where the IHC was screened negative and gene fusions were observed by NGS. An IHC assay enriches detection of the patient population for gene fusions from 2- to 4-fold (Table 2), depending on the sarcoma subtype or tumor location, and has a 100% negative predictive value.

Conclusion: NTRK, ROS1, and ALK fusions have 3 to 11% prevalence in soft tissue sarcoma in important histological subtypes. This 2-step assay is an efficient method for detection of gene rearrangements in both high-volume clinical testing and studies of archival formalin-fixed paraffin-embedded specimens.

Table 2. Representative IHC positive screening rate by sarcoma location and histology

Sarcoma Location	Number of Samples	Number of IHC Positives	Percent Positive By IHC
Abdomen	9	4	44%
Arm/shoulder	4	2	50%
Bone	3	2	67%
Chest wall	2	0	0%
Leg	12	5	42%
Liver	4	1	25%
Lung	16	5	31%
Retroperitoneum	8	5	63%
Uterus	6	3	50%
Results by Histology			
Sarcoma Histology	Number of Samples	Number of IHC Positives	Percent Positive By IHC
Chondrosarcoma	7	5	71%
Fibrosarcoma	3	1	33%
Leiomyosarcoma	19	8	42%
Liposarcoma	15	6	43%
Osteosarcoma	2	1	50%
PEComa	1	0	0%
Sarcoma - NOS	12	7	58%

Table 1. Prevalence of NTRK, ROS1, and ALK gene rearrangements from internal testing and partner collaborations

Sarcoma Type	NTRK1, 2, and 3 (%)	ROS1 (%)	ALK (%)
Fibrosarcoma	5	0	2
Neurosarcoma	2	0	2
Uterine and ovarian sarcomas	1	4	2
Stomach and small intestine sarcomas	11	3	3
Breast sarcomas	9	*	*
Liposarcoma	*	2	*
Leiomyosarcoma	*	*	5

Data from Ignyta's aggregate diagnostic experience to date in a larger volume data set (includes internal testing in Ignyta's CLIA/CAP diagnostic lab and testing by third parties) *no available data

P2–Poster 034 2569357

VERSICAN AS A KEY DETERMINANT OF TUMOR GRADE IN SOFT TISSUE SARCOMAS

Paul Keire[2]; Prakash Vishnu[3]; Thomas Wight[2]; Kevin MacDonald[1]

[1]Department of Orthopedics, Virginia Mason Medical Center, Seattle, WA, USA; [2]Benaroya Research Institute, Virginia Mason Medical Center, Seattle, WA, USA; [3]Department of Medical Oncology, Virginia Mason Medical Center, Seattle, WA, USA

Objective: The need for effective systemic treatment options for soft tissue sarcomas is clear. While the pathogenesis of this heterogeneous group of tumors remains unknown, versican is one potential target that has shown promise in preliminary studies as both a marker of tumor grade and potential modulator of sarcoma activity. Versican, a proteoglycan, and its partner molecule hyaluronan, a high molecular weight polysaccharide are two major components of the extracellular matrix. In this study we sought to further explore the role of versican as a predictor of tumor behavior and potential treatment target by asking if versican and hyaluronan are highly expressed in various sarcoma subtypes and if the level of expression correlates to tumor grade.

Methods: From consenting patients, we collected a range of benign and malignant soft tissue tumors. We analyzed versican and hyaluronan expression via targeted histology stains of the tumor samples as well as cell lines derived from the tumor samples. Histological analysis of versican and hyaluronan was related to patient pathology reports and tumor characteristics including diagnosis, size, metastasic status, neo-adjuvant treatment, histologic grade and mitotic index. In addition, we identified the mutational state of molecules upstream of versican expression via exome and RNASeq analysis and correlated this to the relative benign or the metastatic state of the tumor.

Results: Samples identified as high grade, metastatic, pleomorphic sarcoma, and of high mitotic index, displayed high levels of both versican and hyaluronan expression. Lipoma, well differentiated liposarcoma, and gastrointestinal stromal tumors, and tumors of comparably low mitotic index displayed lower or only localized areas of versican accumulation. Preliminary data indicates that the versican expression pathway is mutated in those tumors deemed benign and was associated with lower levels of versican expression, while those highly metastatic and highly proliferative tumors with high versican and hyaluronan expression, the versican expression pathway remained without key mutational errors.

Conclusion: Versican and hyaluronan are highly expressed in high grade sarcomas. This correlation between degree of expression and tumor grade makes versican and hyaluronan potential markers of tumor behavior and potential treatment targets for novel systemic treatment options.

P2–Poster 035 2568571

A CRISPRI SCREEN REVEALS SYNTHETIC LETHALITY BETWEEN PAX3-FOXO1 AND GATOR2

Amit J. Sabnis, MD[1]; Jonathan Weissman[3]; Trever G. Bivona[2]

[1]Pediatric Hematology-Oncology, UCSF Benioff Children's Hospital, San Francisco, San Francisco, CA, USA; [2]Hematology-Oncology, University of California, San Francisco, San Francisco, CA, USA; [3]Howard Hughes Medical Institute/University of California, San Francisco, San Francisco, CA, USA

Objective: Rhabdomyosarcoma (RMS) is the most common pediatric soft tissue sarcoma. The *PAX3-FOXO1* translocation predicts poor RMS patient outcomes, but no oncogene-directed therapy exists for fusion-positive RMS. To address this, we employed a CRISPRi loss-of-function screen to find genes that, when lost, were specifically toxic to PAX3-FOXO1 expressing cells.

Methods: We created an isogenic system of PAX3-FOXO1 dosage by clonally selecting Rh30 cells transduced with an shRNA that tiled the fusion boundary. We then expressed a dCas9-KRAB chimera in both Rh30 cells transduced with a control vector ($P3F^{+}$) or the PAX3-FOXO1 shRNA ($P3F^{KD}$). Both groups of cells were infected with a lentiviral library consisting of 10 sgRNAs targeting each of 2000 genes involved in protein homeostasis and grown for 10 population doublings. The abundance of each sgRNA through the experiment was calculated by deep sequencing genomic DNA, and fold-change was tabulated for genes in aggregate.

Results: $P3F^{KD}$ cells exhibited 80% decreases in PAX3-FOXO1 levels and loss of anchorage independent colony formation, but preserved growth in 2D culture, allowing successful completion of our screen. Intriguingly, many genes were essential for $P3F^{+}$ cells although $P3F^{KD}$ cells tolerated their loss. We postulated that their loss created synthetic lethality in PAX3-FOXO1 positive cells. STRING analysis grouped screen hits by function and highlighted multiple members of the GATOR2 complex, a positive regulator of mTORC1. We validated that loss of GATOR2 suppressed the growth of $P3F^{+}$ but not $P3F^{KD}$ cells. Loss of GATOR2 attenuated mTORC1 activity after amino acid stimulation in $P3F^{+}$ cells, but to a lesser extent in $P3F^{KD}$ cells. As independent evidence of PAX3-FOXO1 dependence on mTORC1, we found that $P3F^{+}$ cells were much more sensitive to the mTOR kinase inhibitor MLN-0128 than $P3F^{KD}$ cells.

Conclusion: Our data highlight an unexpected synthetic lethality whereby cells with native, but not reduced levels of PAX3-FOXO1 require GATOR2 for growth. The essential role of GATOR2 appears to be to convey amino acid sufficiency to mTORC1, and inhibition of mTORC1 also has PAX3-FOXO1 dependent effects. Future work will establish the molecular connection between PAX3-FOXO1, GATOR2, and mTORC1 in RMS, and identify the specific outputs of mTORC1 that are required by PAX3-FOXO1 positive cells. These insights will inform current efforts to target mTOR in RMS and suggest novel biomarkers and alternative targets for even more precise PAX3-FOXO1 targeting.

P2–Poster 036 2556322

ACTIVATION OF THE CANONICAL WNT/β-CATENIN SIGNALING PATHWAY IN SOFT TISSUE SARCOMA TUMORIGENESIS: A COMPARATIVE STUDY OF SYNOVIAL SARCOMAS AND LEIOMYOSARCOMAS

Laurence M. Briski, MD[1]; Dafydd G. Thomas[1]; Rajiv M. Patel[1]; Elizabeth R. Lawlor[2]; Rashmi Chugh[3]; Jonathan B. McHugh[1]; David R. Lucas[1]

[1]Department of Pathology, University of Michigan, Ann Arbor, MI, USA; [2]Department of Pediatrics, University of Michigan, Ann Arbor, MI, USA; [3]Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA

Objective: Soft tissue sarcomas encompass a diverse array of malignant entities with different origins and histologic features. Despite this diversity, surgery remains the mainstay of treatment for a vast majority of these malignancies. Although adjuvant therapies may be indicated depending on factors such as site, size, grade, and stage, therapeutic options remain rather limited. Several previous expression-profiling studies have demonstrated a consistent role of the canonical Wnt/β-catenin signaling pathway in the tumorigenesis of synovial sarcoma (SS), implicating potential molecular targets for this particular translocation-associated sarcoma phenotype. In the current study, we investigate whether the Wnt/β-catenin pathway is activated in leiomyosarcoma (LMS), a soft tissue sarcoma phenotype with a complex karyotype.

Methods: Cancer Outlier Profile Analysis (COPA) was performed on sarcoma expression datasets (n=11) in Oncomine using LMS (7 datasets), SS (4 datasets), affymetrix platform, and either LEF1 or β-catenin as filters. These datasets represent 178 LMS and 70 SS. The results were expressed in median-centered intensity. To confirm these results, we created tissue microarray slides for immunohistochemical (IHC) analysis. Seventy-eight LMS and 57 SS were analyzed for LEF1 nuclear expression; 77 LMS and 56 SS were analyzed for β-catenin nuclear expression. IHC staining intensity was scored as 0, 1+, or 2+. Tumors with unequivocal 2+ nuclear staining involving ≥5% of cells were interpreted as positive.

Results: Although COPA of β-catenin mRNA expression did not detect a significant difference between SS and LMS (p = 0.868), there was a higher level of LEF1 expression in SS than in LMS (p = <0.0001). This was supplemented by our IHC data in which the majority of SS showed strong nuclear positivity for LEF1 (79%) and β-catenin (84%), while only a minority of LMS showed strong nuclear positivity for LEF1 (5%) and β-catenin (6%).

Conclusion: While the canonical Wnt/β-catenin pathway is consistently activated in SS, our data show that it is not universally activated in LMS. These results suggest that disrupting the interactions between various constituents of this pathway might represent a novel therapeutic approach in the treatment of SS but not in the treatment of LMS. Further investigation on a wider variety of mesenchymal tumors will be required to ascertain whether LEF1 and/or β-catenin expression may have diagnostic, prognostic, or therapeutic implications in other sarcoma phenotypes.

P2–Poster 037 2543033

GENERATING PRIMARY SOFT TISSUE SARCOMAS IN MICE BY CRISPR/CAS9 TECHNOLOGY

Jianguo Huang, PhD[1]; Melodi J. Whitley[1]; Mark Chen[1]; Hsuan-Cheng Kuo[1]; Yvonne Mowery[1]; David V. Mater[1]; Lixia Luo[1]; Yan Ma[1]; Jacqueline Robinson-Hamm[2]; Christopher Nelson[2]; Anupama Reddy[3]; Charles Gersbach[2]; Sandeep Dave[3]; Rebecca D. Dodd[1]; David Kirsch[1]

[1]Radiation Oncology, Duke University Medical Center, Durham, NC, USA; [2]Department of Biomedical Engineering, Duke University Medical Center, Durham, NC, USA; [3]Center for Genomic and Computational Biology, Duke University Medical Center, Durham, NC, USA

Objective: Soft tissue sarcomas are rare connective tissue tumors that are often fatal. Genetically engineered mouse models (GEMMs) are important platforms for pre-clinical studies and for investigating sarcoma biology. Using Cre-loxP technology, we have generated autochthonous high-grade soft tissue sarcomas by intramuscular delivery of an adenovirus expressing Cre recombinase to mice with conditional mutations in *Kras* and *Trp53*. However, this approach is costly and time-consuming. Here, we generate a mouse model of soft tissue sarcoma with CRISPR/Cas9 technology.

Methods: Mouse embryonic fibroblasts (MEFs) with genotypes of *LSL-Kras*^{G12D}, *LSL-Cas9-EGFP* or *LSL-Kras*^{G12D}; *LSL-Cas9-EGFP* were isolated from mouse embryos. The MEFs were transiently transfected with pX333-sgTrp53-Cre. We subsequently performed DNA analysis, soft agar assays, and an allograft study to test the system for cell transformation. Mice received intramuscular injections of either the naked pX333-sgTrp53-Cre plasmid or an adenovirus expressing Cre and sgTrp53. Immunohistochemical analysis of the tumors was performed with staining for MyoD and Myogenin. Sanger sequencing were to study the clonality of CRISPR/Cas9 induced primary sarcomas. We also examined off-target effects by deep sequencing and whole exome sequencing by comparing the mutational load and copy number variation between tumors generated via Cre-loxP and CRISPR/Cas9 technology.

Results: Transient transfection of px333-sgTrp53-Cre plasmid is sufficient to activate conditional mutant *Kras* and mutate *Trp53* in MEFs resulting in oncogenic transformation. Adenoviral delivery of Cre and sgTrp53 efficiently induced primary sarcomas by expressing mutant *Kras* with Cre and by inactivating *Trp53* via the CRISPR/Cas9

system. However, tumor induction by naked plasmid was inefficient and delayed. The majority of tumors resembled undifferentiated pleomorphic sarcoma (UPS), while a small number were rhabdomyosarcoma (RMS)-like. Clonality studies suggest that the CRISPR/Cas9 induced sarcomas are predominantly monoclonal. There was no significant difference in mutational load between the Cre-loxP and CRISPR/Cas9 tumor models.

Conclusion: CRISPR/Cas9 technology can be applied to generate a primary mouse model of soft tissue sarcoma with similar tumor kinetics and mutational load compared to Cre-initiated tumors. This approach can be employed to rapidly develop models to assess the roles of genes mutated in human soft tissue sarcomas.

P2–Poster 038 2566226

PDGFRA PROTEIN EXPRESSION IN RHABDOMYOSARCOMA PATIENT SAMPLES

Yvonne M. Versleijen-Jonkers, PhD[1]; Melissa H. Hillebrandt-Roeffen[1]; Uta E. Flucke[2]; Erik Wiemer[3]; Stefan Sleijfer[3]; Winette Van der Graaf[4]
[1]Medical Oncology, Radboud University Medical Center, Nijmegen, Netherlands; [2]Pathology, Radboud University Medical Center, Nijmegen, Netherlands; [3]Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; [4]The Institute of Cancer Research and the Royal Marsden NHS Foundation Trust, London, United Kingdom

Objective: The PAX3-FOXO1 fusion gene functions as an essential oncogenic driver in alveolar rhabdomyosarcoma (ARMS) pathogenesis and is described to activate PDGFRA expression. However, a genome-wide approach to identify PAX3-FOXO1 binding sites in RMS failed to detect PDGFRA. Nevertheless PDGFRA is frequently found overexpressed in ARMS and considered a valid therapeutic target. An interesting study using phosphoproteomics to identify driver tyrosine kinases demonstrated overexpression of PDGFRA in 13% of RMS cases. Others report a more general expression in ARMS and embryonal RMS (ERMS) by immunohistochemistry.

Since conflicting results are described in literature, PDGFRA could serve as druggable target, and only small series have been investigated so far, we aimed to determine PDGRA expression in a large number of RMS samples and to correlate it with available follow-up data.

Methods: Paraffin-embedded RMS tissue samples were collected on tissue microarrays. PDGFRA protein expression was evaluated by immunohistochemistry (D13C6, Cell Signaling Technology). A semiquantitative scoring system was used in which staining was scored negative"0", weak"1" or strong"2" when present in at least 10% of tumor cells.

Results: We analyzed PDGFRA protein expression in 118 primary RMS tumor samples (91 ERMS and 27 ARMS). Cytoplasmic expression was detected in only 1 of 27 primary ARMS samples (4%, weak expression) versus 21 of 91 ERMS samples (23%, 12 weak and 9 strong). Apparent membranous expression was observed in 8 ERMS samples (9%) with cytoplasmic expression. None of the ARMS samples showed apparent membranous expression. PDGFRA expression was occasionally detected in stromal cells.

PDGFRA expression was thus significantly more frequently expressed in ERMS versus ARMS (p=0.023). The tumors from patients that already experienced metastases at diagnosis (n=13) were all PDGFRA negative, whereas 25% of the patients without metastases at diagnosis had PDGFRA positive tumors (p=0.041).

No correlations were found between the expression of PDGFRA and survival.

Conclusion: Although further research is warranted we expect from these results that PDGFRA targeting on the tumor cells will only be useful in a small subset of ERMS. Since most positive tumors seem to only express cytoplasmic PDGFRA, a tyrosine kinase inhibitor seems more relevant than an antibody. However, since PDGFRA expression is also visible in the stromal microenvironment of a subset of the tumors, an interaction with stromal PDGFRA cannot be excluded.

P2–Poster 039 2565149

HDAC8 INHIBITION FOR THE TREATMENT OF LEIOMYOSARCOMA

Gonzalo Lopez, PhD[1]; Wei-Jan Huang[2]; Abeba Zewdu[1]; Danielle Braggio[1]; Anne M. Strohecker[1]; Dina Lev[3]; Raphael Pollock[1]
[1]Comprehensive Cancer Center, The Ohio State University, Grandview Heights, OH, USA; [2]Taipei Medical University, Taipei, Taiwan; [3]Sheba Medical Center, Tel Aviv, Israel

Objective: Leiomyosarcoma (LMS) is a malignant soft tissue sarcoma (STS) with a dismal prognosis following metastatic disease. Chemotherapeutic intervention has shown modest clinical efficacy with no curative potential in LMS patients. Previously, we demonstrated pan-HDAC inhibition to have superior anti-LMS effect alone and in combination with gemcitabine. Pan-HDAC inhibitors (pan-HDACis) have an affinity for class 1 HDAC isoforms (HDAC1, HDAC2, HDAC3, and HDAC8). Isoform-specific inhibitors may possibly improve the therapeutic window while limiting pan-HDACi toxicities. HDAC8 inhibitors (HDAC8i) are novel compounds and demonstrate potential as anti-cancer therapeutics; however, little is known about their activity in LMS. In this study, our goal is to evaluate

the therapeutic efficacy of HDAC8 inhibition alone and in combination with gemcitabine in LMS.

Methods: Human leiomyosarcoma (LMS) cell lines and cell strains were used for *in vitro* studies. HDAC8 inhibitor (11a) was created and provided by Dr. Ching-Shih Chen and Dr. Wei-Jan Huang. The nucleoside analog, gemcitabine (Gem) was purchased commercially. MTS and clonogenic assays were used to evaluate the effect of 11a on LMS cell growth. Annexin V PI/FACS analysis was used to determine the effects of 11a alone and in combination with Gem on apoptosis. Compusyn software was used to determine *in vitro* synergy studies for 11a combined with gemcitabine.

Results: 11a abrogated LMS cell growth and clonogenic potential. 11a enhanced apoptosis in LMS cell lines and strains. The combination of 11a + Gem exhibited a synergistic effect in LMS cells *in vitro*.

Conclusion: LMS are aggressive, metastatic tumors with poor prognosis where effective therapeutic interventions are lacking. We demonstrate the potential utility of HDAC8 inhibition combined with gemcitabine for the treatment of LMS. Future studies (already underway) include testing the efficacy of 11a alone and in combination in PDX LMS models and elucidating the molecular mechanisms underlying HDAC inhibition in LMS.

P2–Poster 040 2562822

TAMOXIFEN INDUCES APOPTOSIS IN RHABDOMYOSARCOAM VIA ESTROGEN-RECEPTOR ACTIVATION OF STRESS-ACTIVATED PROTEIN KINASES

Zainab A. Motala, PhD Candidate[1]; Kevin Chen[2]; Adam D. Durbin[3]; Gino R. Somers[4]; David Malkin[1]
[1]Department of Pediatrics, The Hospital for Sick Children, Toronto, ON, Canada; [2]MD Program, University of Toronto, Toronto, ON, Canada; [3]Department of Pediatric Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [4]Department of Pediatric Laboratory Medicine, The Hospital for Sick Children, Toronto, ON, Canada

Objective: The goals of this study were to identify and define key pathways involved in regulation of 4-hydroxy-tamoxifen (4OHT) and tamoxifen-induced apoptosis in rhabdomyosarcoma (RMS).

Methods: RMS cell cultures and xenograft models were established and exposed to a spectrum of doses and time course of treatment of 4OHT or tamoxifen alone, or in combination with vincristine and the mTOR inhibitor, temsirolimus.

Results: In RD, RH4 and RH30 cells, induction of apoptosis by 4OHT is accompanied by phosphorylation of JNK and p38, which is blocked by small molecule inhibition of either kinase. Inhibition of ER signaling results in suppression of JNK phosphorylation and rescue of 4OHT-driven apoptosis. 4OHT inhibits activation of cell survival protein AKT and mTORC1 activity in association with apoptosis. Further, 4OHT potentiates the anti-proliferative effects of vincristine and temsirolimus. In an mouse RMS xenograft model, tamoxifen (150 mg/kg given 5 days/week) inhibits tumour growth compared to vehicle-treated control group by 2 weeks.

Conclusion: This work suggests the molecular mechanism and provides a pre-clinical rational for use of tamoxifen and 4OHT alone, or in combination with vincristine and temsirolimus in the treatment of RMS.

P2–Poster 041 2562413

IDENTIFICATION OF ESSENTIAL SIGNALING PATHWAYS IN SYNOVIAL SARCOMA AND MYXOID LIPOSARCOMA USING FUNCTIONAL GENOMICS

Ya-Yun Cheng[1]; Patrizia Jensen[1]; Priya Chudasama[1]; Sophie Rabe[1]; Thomas Kindler[2]; Claudia Scholl[1]; Stefan Fröhling[1]
[1]Department of Translational Oncology, National Center for Tumor Diseases and German Cancer Research Center, Heidelberg, Germany; [2]Department of Medicine III, Johannes Gutenberg University Mainz, Mainz, Germany

Objective: Soft-tissue sarcomas (STS) are a heterogeneous group of difficult-to-treat mesenchymal malignancies that comprise more than 50 histologic subtypes. Many STS subtypes carry chromosomal translocations that serve as important diagnostic markers; however, direct targeting of these rearrangements for therapeutic benefit has been challenging. We focus on two common STS subtypes, synovial sarcoma (SS) and myxoid liposarcoma (MLS). SS accounts for 10% of all STS, and 50% of patients develop metastases. The most important diagnostic marker is the *SS18-SSX1/2* fusion gene, which is caused by the t(X;18) chromosomal translocation that occurs in approximately 90% of SS patients. MLS accounts for 10% of STS cases. More than 90% of MLS cases harbor a t(12;16), which results in expression of the *FUS-DDIT3* fusion gene. *SS18-SSX1/2* and *FUS-DDIT3* are known to be important for sarcomagenesis. However, the underlying molecular mechanisms are incompletely understood. Therefore, our aim is to identify signaling pathways that become essential specifically in the context of *SS18-SSX1/2* and *FUS-DDIT3*.

Methods: To investigate whether *SS18-SSX1/2* and *FUS-DDIT3* lead to "rewiring" of signaling pathways, thereby creating context-specific functional dependencies, we generated isogenic cell line pairs expressing *SS18-SSX1/2* or *FUS-DDIT3* and an empty control vector, respectively, as *in vitro* models. These cells were subjected to genome-wide, "drop-out" RNA interference (RNAi) screens using a pooled, lentivirally delivered short hairpin RNA library, followed by

validation and mechanistic study of screening potential hits.

Results: The screening results showed good representation of the library and high correlation between biological replicates. Two different algorithms (cut-off method and RNAi Gene Enrichment Ranking) were used for data analysis, and 65 candidate genes in the SS model and 21 candidate genes in the MLS model were selected for further study. These genes are currently being validated using panels of established human SS and MLS cell lines, providing the basis for further functional and mechanistic investigations.

Conclusion: Our data indicate that isogenic cell line pairs represent useful *in vitro* models for functional genomic analysis of the molecular regulatory networks associated with the *SS18-SSX1/2* and *FUS-DDIT3* fusion genes, which may provide new insights into sarcomagenesis and uncover potential targets for therapeutic intervention in patients with SS and MLS.

P2–Poster 042 2553268

A NOVEL SYNOVIAL SARCOMA MOUSE MODEL IDENTIFIES COOPERATIVE GENETIC PATHWAY WITH SS18-SSX1

Miwa Tanaka; Takuro Nakamura, MD, PhD
Division of Carcinogenesis, The Cancer Institute, Japanese Foundation for Cancer Research, Tokyo, Japan

Objective: SS18-SSX fusion proteins play a central role in synovial sarcoma development, disrupting SWI/SNF complex and modulates transcriptional programs involviong ATF2 and TLE1. However, genetic network and mechanisms of synovial sarcomagenesis remain largely unknown. To clarify such unknown mechanisms, we have established a new *ex vivo* mouse model for synovial sarcoma.

Methods: An *ex vivo* mouse model for synovial was generated according to the method described previously (Tanaka et al, J Clin Invest, 2014). Briefly, mouse embryonic mesenchymal cells were transduced with SS18-SSX1 retrovirus and the cells were transplanted subcutaneously to nude mice or syngeneic mice. The animals were observed daily for tumor development and pathological and genomic analyses of tumors were performed. Retroviral integration sites were identified by inverse-PCR.

Results: Subcutaneous tumors develop in 100% of recipients with an average latency of 25 weeks. Histological analysis has shown invasive proliferation of short spindle tumor cells with frequent biphasic appearance (Figure 1). Cytokeratin expression was observed in epithelial components in tumors (Figure 2). Frequent expression of TLE1 and BCL2 was also shown. Gene expression profiling indicates modulation of the SWI/SNF pathway by introduction of *SS18-SSX1* into mesenchymal cells, and upregulation of *Tle1* and *Atf2* in tumors. Collectively, these findings indicate the model exhibits typical phenotypes of human synovial sarcoma. Retroviral tagging of the tumor identified 15 common retroviral integration sites with *Dnm3* locus as the most frequent in 30 mouse synovial sarcomas. Up-regulation of micro RNAs *miR199a2* and *miR214* within Dnm3 locus was observed. Co-introduction of *SS18-SSX1* and *miR214* indeed accelerated sarcoma onset, indicating that *miR214* is a cooperative onco-miR in synovial sarcomagenesis.

Conclusion: We have succeeded to generate a novel mouse model for human synovial sarcoma. The model well recapitulated not only the phenotypes but also gene expression profiles of synovial sarcoma. As miR214 overexpression in human synovial sarcoma was reported, our results underscore the important role of miR214 in tumor development and disease progression.

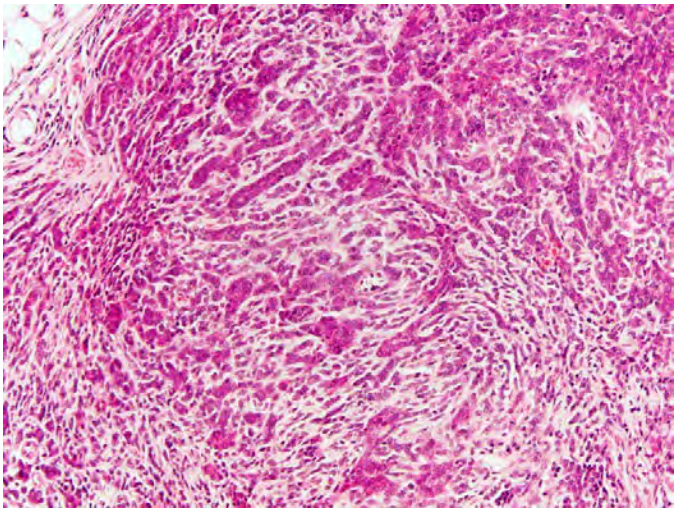


Figure 1. Biphasic morphology of murine synovial sarcoma expressing SS18-SSX1.

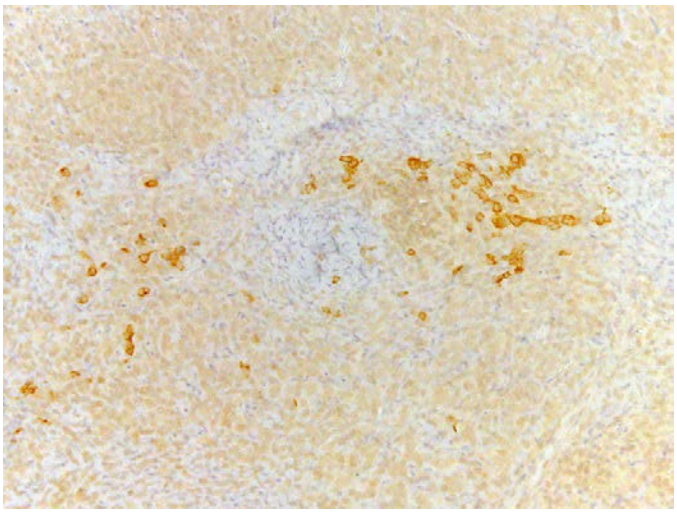


Figure 2. Expression of cytokeratin in murine synovial sarcoma.

P2–Poster 043 2570585

COMPARATIVE PROTEOMICS OF PRIMARY SARCOMA AND THEIR PAIRED METASTASES REVEALS HIGH EXPESSION OF PARP-1 IN SACROMA METASTASES

Winan van Houdt, MD, PhD[1]; Hester van Boven[3]; Tim Schelfhorst[2]; Linde Braaf[4]; Thang Pham[2]; Jaco Knol[2]; Sander Piersma[2]; Frits van Coevorden[1]; Connie Jimenez[2]

[1]Surgery, Netherlands Cancer Institute, Amsterdam, Netherlands; [2]OncoProteomics Laboratory, Department of Medical Oncology, VU University Medical Center, Amsterdam, Netherlands; [3]Pathology, Netherlands Cancer Institute, Amsterdam, Netherlands; [4]Division of Molecular Pathology, Netherlands Cancer Insitute, Amsterdam, Netherlands

Objective: Soft tissue sarcomas (STS) is a group of mesenchymal malignancies consisting of over 60 different subtypes. Each of these subtypes has distinct biological characteristics and behavior, resulting in a widely varying sensitivity to systemic therapy. Treatment of metastatic sarcoma is challenging, partly due to this high variety in subtypes. This study is designed to find common up regulated pathways in the metastases of different sarcoma subtypes, in order to unravel their biology and identify promising targets specifically for metastases, as they most often determine the prognosis of patients.

Methods: Fresh frozen tissue from untreated surgical specimens or biopsies of 7 primary sarcomas and 9 matching metastases was collected and protein was extracted. Proteomics based on one-dimensional gel electrophoresis coupled to nano liquid chromatography tandem mass spectrometry were used to identify proteome differences between the primary tumors and their metastases. A subsequent data and pathway analysis was performed with David bioinformatics resources and STRING.

Results: The histological diagnoses of the selected tumors were UPS (2x), Spindle cell sarcoma (2x), high grade SFT (1x), Synovial sarcoma (1x) and myxofibrosarcoma (1x). Out of a total data set of 7772 identified proteins, 309 proteins were at least 1,5 fold up-regulated in the metastatic tumors when compared with their primary tumors, with a p-value of <0.05. Analysis for activated cellular networks in metastatic tumors revealed a significantly higher expression of proteins involved in metabolism and cellular respiration, chromatin remodeling, chromosome organization and DNA repair. Interestingly, PARP1 (Poly (ADP-ribose) polymerase-1), an enzyme that plays a role in the detection of DNA damage and DNA repair, was highly up-regulated in all tumors except for synovial sarcoma. Also, proteins involved in PDGFB (platelet derived growth factor receptor beta) signaling in the metastases were up-regulated, including PDGFB itself.

Conclusion: Sarcoma metastases show higher expression of proteins involved in chromatin remodeling and DNA repair, including PARP-1. Therefore, treatment of different sarcoma subtypes with PARP-1 inhibitors might be more effective in sarcoma metastases than in primary sarcoma.

P2–Poster 044 2570584

VERTICILLIN A INHIBITS LEIOMYOSARCOMA AND MALIGNANT NERVE SHEATH TUMOR GROWTH VIA INDUCTION OF APOPTOSIS

Abeba Zewdu, PhD[1]; Gonzalo Lopez[1]; Danielle De Almeida Braggio[1]; Hemant Bid[2]; Connor Kenney[1]; Kara Batte[1]; Kate Lynn Bill[1]; O. Hans Iwenofu[1]; Nicholas Oberlies[3]; Cedric Pearce[5]; Anne M. Strohecker[1]; Dina Lev[4]; Raphael Pollock[1]

[1]Surgical Oncology, The Ohio State University, Columbus, OH, USA; [2]Resonant Therapeutics, Ann Arbor, MI, USA; [3]University of North Carolina, Greensboro, NC, USA; [4]Sheba Medical Center, Tel Aviv, Israel; [5]Mycosynthetix, Hillsborough, NC, USA

Objective: The heterogeneity of soft tissue sarcoma (STS) represents a major challenge for therapeutic development. Comprised of over 50 different histology subtypes of various etiologies, STS subsets are further characterized as either karyotypically simple or complex. The number of genetic anomalies associated with karyotypically complex STS renders the development of therapies especially difficult. Verticillin A is a small molecule drug with demonstrated anticancer activity; however, the efficacy of this agent has never been evaluated in STS. Therefore, the goal of this study was to explore verticillin A as a potential STS therapeutic.

Methods: Survival (MTS) and clonogenic analyses were performed to measure the impact of this agent on the viability and colony formation capability of two karyotypically complex cell lines, malignant peripheral nerve sheath tumor (MPNST) and leiomyosarcoma (LMS). Effects on apoptotic levels were assessed via annexin V/PI analysis and cleaved caspase 3 activity. Cell cycle progression was determined via PI inclusion. *In vivo* studies were performed using MPNST xenograft models. Tumors were processed and analyzed using immunohistochemistry (IHC).

Results: Treatment with verticillin A significantly inhibited cellular growth after 24 hours (96.7, 88.7, 72.7, 57, and 39.7% reduction in LMS1, S462, ST88, SKLMS1, and MPNST724, respectively). Furthermore, all STS cell lines displayed elevated annexin, no cell cycle arrest, and a nearly two fold increase in cleaved caspase 3/7 activity. Normal human Schwann (HSC) and aortic smooth muscle (HASMC) cells displayed higher tolerance to verticillin A treatment, though toxicity was seen in HSC at the 100nM dose. *In vivo* studies mirrored the *in vitro* results: tumor size was significantly reduced in MPNST724 xenograft models with treatment of 0.5 mg/kg verticillin A by day 11.

IHC assessment of tumors showned increased cleaved caspase 3 and decreased Ki67 expression following treatment with verticillin A.

Conclusion: The multiple chromosomal abnormalities associated with genetically complex STS complicate the treatment of these diseases. Consequently, the identification of novel therapies is imperative. Our data propose that verticillin A selectively inhibits MPNST and LMS growth via induction of apoptosis while exhibiting lesser effects on normal cells. These findings suggest verticillin A as a potential treatment for MPNST and LMS, justifying the further preclinical evaluation of this agent.

P2–Poster 045 2569570

IDENTIFICATION OF NOVEL GENETIC DEPENDENCIES IN SYNOVIAL SARCOMA MODELS

Samuel E. Jones, BSc (PhD submitted by meeting)[1]; Christopher Williamson[1]; Emmy Fleuren[1]; Helen Pemberton[1]; Dragomir Krastev[1]; Rachel Brough[1]; Alan Ashworth[2]; Winette Van der Graaf[1]; Janet Shipley[1]; Christopher Lord[1]

[1]Breakthrough Breast Cancer/Cancer Therapeutics, Institute of Cancer Research, London, United Kingdom; [2]University College San Francisco, San Francisco, CA, USA

Objective: Synovial sarcoma (SS) is a difficult to treat disease, with poor prognosis and no approved targeted therapies. Synovial sarcomas are defined by a chromosomal translocation that results in expression of SS18-SSX fusion proteins. SS18-SSX interacts with chromatin remodelling complexes including BAF and polycomb, and causes an aberrant transcriptional program proposed to drive tumour growth. However, the dependency of SS tumours on such transcriptional programs remains unclear, thus there is a requirement to further understand the genetic and epigenetic dependencies associated with these tumours.

Methods: We set out to identify novel therapeutic targets in SS using a series of high-throughput siRNA screens in a panel of SS cell lines. Five synovial sarcoma cell lines were transfected with a 384-well plate arrayed library of 1600 siRNAs and cell viability measured after 5 days.

Results: Using our siRNA libraries, we generated genetic dependency profiles for each SS cell line. Z-score analyses were used to idenfity genes required for SS cell line survival. By comparing these profiles with siRNA screen data generated for a wider panel of 117 tumour cell lines, we identified siRNAs that selectively inhibited SS cells, providing us with an initial map of the genetic dependencies in SS tumour cell lines.

Conclusion: Ongoing research is aiming to investigate the therapeutic potential of the genetic dependencies idenfitied using chemical inhibition of druggable targets, and to investigate the mechanistic connections between SS18-SSX expression and drug sensitivity.

P2–Poster 046 2567792

A WHOLE-BODY IMAGEABLE PATIENT-DERIVED ORTHOTOPIC XENOGRAFT (PDOX) MOUSE MODEL OF UNDIFFERENTIATED PLEOMORPHIC SOFT-TISSUE SARCOMA FOR RAPID DRUG SCREENING OF INDIVIDUAL PATIENT TUMORS

Tasuku Kiyuna[1]; Takashi Murakami[1]; Yasunori Tome[3]; Kentaro Igarashi[1]; Kei Kawaguchi[1]; Tara A. Russell[4]; Mark A. Eckardt[5]; Joseph G. Crompton[4]; Arun S. Singh[6]; Nicholas Bernthal[7]; Susan Bukata[7]; Noah Federman[8]; Fuminori Kanaya[3]; Frederick C. Eilber[4]; Robert M. Hoffman, PhD[2]

[1]AntiCancer Inc., San Diego, CA, USA; [2]Department of Surgery, University of California San Diego, San Diego, CA, USA; [3]Department of Orthopedic Surgery, University of the Ryukyus, Okinawa, Japan; [4]Department of Surgery, University of California Los Angeles, Los Angeles, CA, USA; [5]Department of Surgery, Yale School of Medicine, New Haven, CT, USA; [6]Division of Hematology-Oncology, University of California Los Angeles, Los Angeles, CA, USA; [7]Department of Orthopedic Surgery, University of California Los Angeles, Los Angeles, CA, USA; [8]Department of Pediatrics, University of California Los Angeles, Los Angeles, CA, USA

Objective: Our laboratory pioneered patient-derived orthotopic xenograft (PDOX) mouse models using surgical orthotopic implantation (SOI). PDOX models are patient-like, in contrast to the ectopic subcutaneous-transplant cancer models. In the present study, we demonstrate that an undifferentiated pleomorphic soft-tissue sarcoma (UPS-STS) PDOX model acquired bright RFP-expressing stroma through one passage in red fluorescent protein (RFP) transgenic mice, which upon passage to non-colored nude mice was non-invasively imageable.

Methods: A PDOX nude mouse model of UPS-STS was established in the biceps femoris of nude mice. After the tumors grew to a diameter of 10 mm, the tumors were subsequently-passaged to RFP transgenic mice, and after tumor growth were then passaged to non-transgenic nude mice. Tumors were divided into small fragments and transplanted in the biceps femoris at each passage. The OV100 Small Animal Fluorescence Imaging System and FV1000 laser scanning confocal microscope were used to image RFP fluorescence in the UPS-STS PDOX models.

Results: UPS-STS PDOX tumors, previously-grown in RFP transgenic nude mice for only one passage, had very bright fluorescence and after passage to non-transgenic nude mice were non-invasively imageable (Figure 1). FV1000 confocal imaging revealed diffusely-distributed bright RFP stromal cells in the PDOX tumor, both in RFP

transgenic mice and after passage to non-transgenic mice (Figure 2). These results demonstrate a powerful method to make the PDOX UPS-STS model brightly-fluorescent for non-invasive imaging, as well as for confocal microscopy of individual stromal cells associated with the tumor.

Conclusion: In the present study, we established an imageable PDOX model of UPS-STS brightly-labeled with RFP-expressing stroma in non-transgenic nude mice passaged from RFP transgenic nude mice. The RFP-labeled UPS PDOX has the potential to rapidly screen for novel effective agents for individual patients, including stroma-targeting drugs, whereby the stromal cells are a visual target.

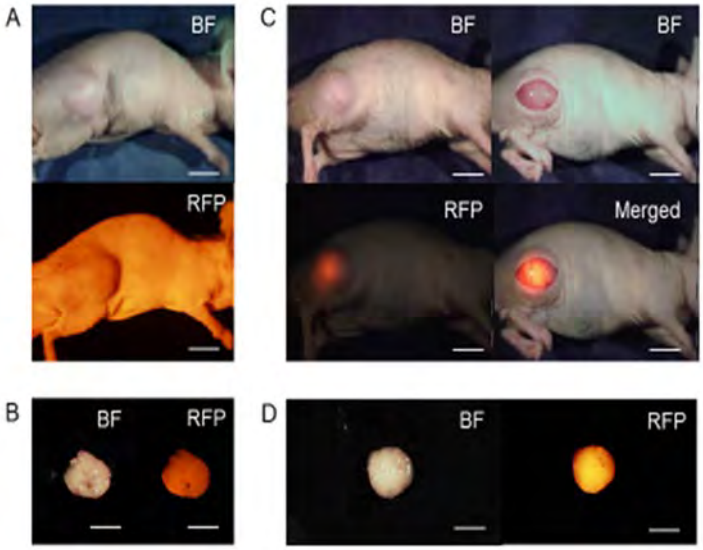


Figure 1. Establishment of a fluorescent undifferentiated pleomorphic soft-tissue sarcoma (UPS) PDOX model. A. A growing PDOX tumor in the right biceps femoris of an RFP-expressing nude mouse. **B.** Images of the resected tumor derived from the RFP-expressing nude mouse. The RFP-expressing PDOX tumor was passaged to the right biceps femoris of a non-transgenic non-colored nude mouse. **C.** Non-invasive imaging of RFP-expressing UPS PDOX tumor in the non-transgenic nude mouse (left). Imaging of the RFP-expressing UPS PDOX after a skin-flap was raised (right). **D.** Images of the resected tumor derived from a non-transgenic PDOX nude mouse model. Tumor RFP expression was still strongly detectable. Imaging with the OV100. UPS: undifferentiated pleomorphic sarcoma, PDOX; patient-derived orthotopic xenograft, RFP: red fluorescent protein, BF: bright field. Scale bars: 10 mm **(A-D)**.

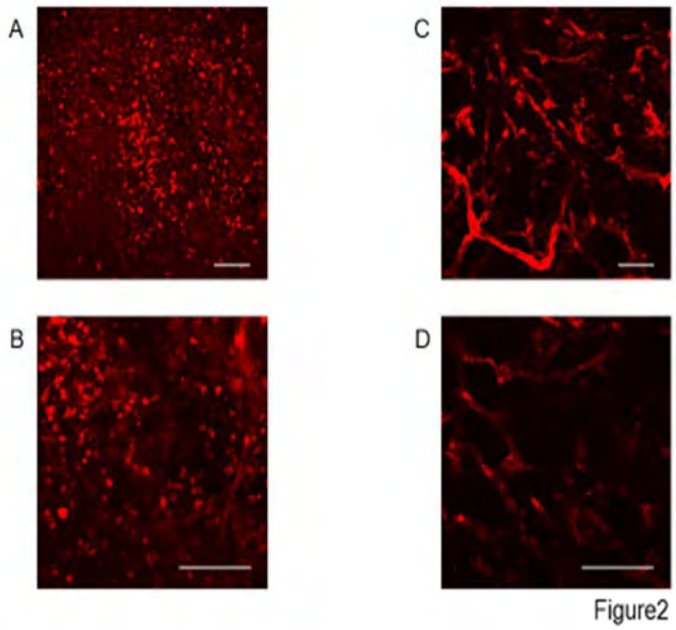


Figure 2. Confocal fluorescence microscopy of individual stromal cells of the UPS PDOX. FV1000 confocal laser microscopy imaged RFP-expressing stroma of PDOX tumors grown in the RFP-expressing nude mouse **(A, B)** and after passage and growth in non-transgenic nude mice **(C, D)**. Bright and diffusely-distributed RFP expressing stroma could be seen both in the UPS PDOX grown in the RFP transgenic nude mouse and after passage and growth in a non-transgenic nude mouse. Scale bars: 100 μm.

P2–Poster 047 2567790

EFFICACY OF NOVEL ANIONIC AND CATIONIC PLATINUM COMPLEXES AGAINST UNDIFFERENTIATED PLEOMORPHIC SARCOMA IN A PATIENT-DERIVED ORTHOTOPIC XENOGRAFT (PDOX) MODEL

Kentaro Igarashi[1]; Takashi Murakami[1]; Tasuku Kiyuna[1]; Kei Kawaguchi[1]; Akira Odani[3]; Arun S. Singh[4]; Noah Federman[5]; Hiroyuki Tsuchiya[6]; Frederick C. Eilber[7]; Robert M. Hoffman, PhD[2]

[1]AntiCancer Inc., San Diego, CA, USA; [2]Department of Surgery, University of California San Diego, San Diego, CA, USA; [3]Division of Pharmaceutical Sciences, Kanazawa University, Kanazawa, Japan; [4]Division of Hematology-Oncology, University of California Los Angeles, Los Angeles, CA, USA; [5]Department of Pediatrics, University of California Los Angeles, Los Angeles, CA, USA; [6]Department of Orthopaedic Surgery, Kanazawa University, Kanazawa, Japan; [7]Division of Surgical Oncology, University of California Los Angeles, Los Angeles, CA, USA

Objective: Soft tissue sarcomas are a rare and heterogenous group of malignancies for which new therapies are an unmet clinical need. Our group has recently developed novel platinum complexes for cancer treatment that may overcome some of the limitations of current platinum che-

motherapies. The novel platinum complexes were evaluated in a patient-derived (PDOX) model of undifferentiated pleomorphic soft-tissue sarcoma (UPS), also developed by our laboratory.

Methods: Freshly-harvested tumor from a patient with UPS of the thigh was grown orthotopically in the right biceps femoris muscle of nude mice to establish a PDOX model. After establishment, this tumor was serially transplanted into a second generation of nude mice. Two weeks after transplantation, when tumor sizes reached 50-100 mm^3, groups of mice were treated intraperitoneally once a week for three weeks with cisplatinum (CDDP) (6 mg/kg), doxorubicin (DOX) (3 mg/kg) and the novel platinum complexes, 1Pt (anionic) (42.7 mg/kg) and 3Pt (Cationic) (41.1 mg/kg). Tumor sizes were measured with calipers every week. A cell line was established from the PDOX model by passaging dissociated xenograft cells on tissue culture plates in RPMI-1640 medium. IC_{50} values were calculated for each compound using a 72hr WST-8 assay. Six weeks after transplantation, all mice were sacrificed and analyzed.

Results: 1Pt and 3Pt caused concentration-dependent cytocidal effects on the UPS cell line. The IC_{50} value of 1Pt was relatively high compared to CDDP, but 3Pt had a lower IC_{50}. Treatment of the UPS PDOX with 1Pt and 3Pt resulted in the largest decreases in tumor volume compared to other treatment groups: CDDP vs. control (P=0.0001); DOX vs control (P=6.56E-7); 1Pt vs control (P=4.8E-8); 3Pt vs. control (P=2.8E-9); CDDP vs. 1Pt (P=0.0005); CDDP vs. 3Pt (P=0.0002); DOX vs. 1Pt (P=0.01); DOX vs. 3Pt (P=0.001). There were no animal deaths in any of the four groups.

Conclusion: 3Pt and 1Pt were highly-effective against a UPS PDOX model and superior to CDDP and DOX.

P2–Poster 048 2562942

DISIALOGANGLIOSIDE GD2 EXPRESSION IN PEDIATRIC RHABDOMYOSARCOMA

Amanda Saraf[2]; Paul Dickman[1]; Pooja Hingorani[1]
[1]Center for Cancer and Blood Disorders, Phoenix Children's Hospital, Phoenix, AZ, USA;
[2]Nationwide Children's Hospital, Columbus, OH, USA

Objective: Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma in children. Outcome for patients with metastatic as well as recurrent RMS is poor and novel therapies are needed for this patient population. GD2 is a membranous protein that is expressed in a variety of malignancies and has been targeted successfully in neuroblastoma with several clinical trials showing improvement in survival with anti-GD2 therapy. Anti-GD2 therapy is also being studied in osteosarcoma due to a high percentage of patient samples expressing GD2 antigen. Limited data exist about GD2 expression in RMS, with one study showing expression in 3/5 embryonal RMS samples and a more recent study evaluating GD2 expression in pediatric cancers, both using the 3F8 antibody. In this study, we evaluated the expression of GD2 in both alveolar and embryonal RMS (ARMS and ERMS respectively) patient samples to identify if GD2 may be a rational therapeutic target.

Methods: Fresh-frozen archived RMS samples were analyzed using anti-GD2 antibody (Ganglioside GD2 Antibody (14G2a): sc-53831; Santa Cruz Bio) via immunohistochemistry. Neuroblastoma samples were used as a positive control. Membranous staining was graded as 0 (<10% positive tumor cells), 1+ (10-50% positive tumor cells) and 2+ (>50% positive tumor cells).

Results: A total of 16 RMS and one undifferentiated pleomorphic sarcoma samples were available for analysis with seven ERMS and nine ARMS. Four of the 16 RMS specimens were positive for GD2 expression (2 ERMS and 2 ARMS) and one pleomorphic sarcoma specimen was positive for GD2 expression. Out of the 4 positive RMS specimens, 2 were 1+ and 2 were 2+ in staining intensity.

Conclusion: Our results suggest that a small subset (approx. 25%) of RMS express GD2 antigen and this data is consistent with other small published series using the 3F8 antibody. A universal well-validated test for GD2 staining in paraffin-embedded tissues would help in evaluating GD2 expression in a larger cohort of RMS patients and confirming the results of these smaller studies. Anti-GD2 therapy may be a rational therapeutic strategy for the GD2 positive subset of RMS patients especially in the setting of recurrent or metastatic disease. Further evaluation of GD2 expression in undifferentiated pleomorphic sarcomas is warranted.

P2–Poster 049 2562145

EFFICACY OF BORTEZOMIB IN SARCOMAS WITH HIGH LEVELS OF MAP17 (PDZK1IP1)

Amancio Carnero, PhD; Marco Perez;
Javier Peinado-Serrano; Jose Manuel Garcia-Heredia;
Irene Felipe-Abrio; Cristina Tous; Irene Ferrer;
Javier Martin-Broto; Carmen Saez
Oncohematology and Genetics, IBIS/CSIC/HUVR, Sevilla, Spain

Objective: Sarcomas are malignant tumors accounting for a high percentage of cancer morbidity and mortality in children and young adults. Surgery and radiation therapy are the accepted treatments for most sarcomas; however, patients with metastatic disease are treated with systemic chemotherapy. Many tumors display marginal levels of chemoresponsiveness and new treatment approaches are needed.

Methods: MAP17 is a small non-glycosylated membrane

protein overexpressed in carcinomas. The levels of MAP17 could be used as a prognostic marker to predict the response to bortezomib in hematological malignancies and in breast tumors. Therefore we have analyzed the levels of expression of this oncogene in sarcomas, it relationship with clinico-pathological features and tested whether it can be used as new biomarker to predict the therapeutic response to bortezomib and new therapy for sarcomas. We have explored this using Immunohistochemistry, cell culture and animal experiments in PDX models.

Results: We have found that the levels of MAP17 were related to clinical features and poor survival in a cohort of 69 patients with different sarcoma types, not being restricted to any special subtype of tumor. MAP17 expression is associated with poor overall survival ($p<0.001$) and worse disease-free survival ($p=0.002$). Cell lines with high levels of MAP17 show a better response to bortezomib *in vitro*. Furthermore, patient derived xenografts (PDX) with high levels of MAP17 respond to bortezomib *in vivo*. Our results showed that this response is due to lower levels of NFkB and autophagy activation.

Conclusion: MAP17 is a new biomarker to predict the efficacy of bortezomib as new therapy for sarcomas.

P2–Poster 050 2559109

INSERTIONAL MUTAGENESIS SCREEN FOR IDENTIFICATION OF DRUG RESISTANCE MECHANISMS IN SOFT-TISSUE SARCOMA

Tim Rath; Priya Chudasama; Martina Tedesco; Claudia Scholl; Manfred Schmidt; Stefan Fröhling
Translational Oncology, German Cancer Research Center and National Center for Tumor Diseases, Heidelberg, Germany

Objective: Emergence of drug resistant clones leading to relapse of tumors is a major challenge pertaining to both cytotoxic chemotherapy as well as targeted drugs for majority of tumor entities, including soft-tissue sarcoma (STS). Insight into mechanisms leading to drug resistance in STS is required to improve therapeutic outcome. We employed a forward genetic approach utilizing lentiviral vectors for insertional mutagenesis to identify genes involved in drug resistance. Lentiviral integration induces genetic aberrations, e.g. activation of genes and generation of chimeric virus-host fusion transcripts or truncated transcripts, which enable inquiry of genetic lesions affecting selected phenotypes. In the present study, we utilized this tool combined with drugs currently employed for treatment of STS to identify genes involved in drug resistance.

Methods: A panel of STS cell lines was tested for sensitivity towards chosen drugs. Responsive cell lines were treated with full LTR-driven 'toxic' lentiviral vectors at different doses. Subsequently, the cells were exposed to treatment with drug doses lethal for the respective cell lines and kept in an adherent monolayer or anchorage-independent setting. Potentially resistant bulk cells or colonies were isolated, expanded and analyzed using linear amplification-mediated PCR and high-throughput sequencing to detect clustered viral integration loci and nearby genes.

Results: Leiomyosarcoma and synovial sarcoma cell lines showed sensitivity towards doxorubicin and pazopanib. Cell lines highly sensitive to the drugs were transduced with lentiviral vectors. Transduction led to a higher amount of surviving bulk cells or colonies in comparison to treatment-matched untransduced cells. Subsequent bioinformatical analysis for identification of integration sites and hotspots of clustered integrations is ongoing. Subtraction of genomic loci identified in controls (pre-drug and DMSO treatment) will reveal genes potentially involved in resistance mechanisms to respective drugs. Selected genes will be functionally investigated using suitable model systems.

Conclusion: Our approach allows detection of clustered viral integration sites potentially generating genomic alterations that may drive drug resistance in STS. Functional characterization of the resistance genes will enable to nominate novel drug targets and combinations to achieve sustained responses to treatment.

P2–Poster 051 2548496

NEXT GENERATION SEQUENCING WITH LINKED CASE REPORTS FOR GRANULAR CELL SARCOMAS

Elizabeth T. Loggers, MD, PhD[1]; Bradley J. Petek[2]; Julia Elvin[3]; Seth M. Pollack[1]; Edward Y. Kim[2]; Gabrielle M. Kane[2]; Darin Davidson[2]; Ernest U. Conrad[2]; Lee D. Cranmer[2]
[1]Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [2]University of Washington, Seattle, WA, USA; [3]Foundation Medicine, Boston, MA, USA

Objective: Granular cell tumors are rare soft tissue neoplasms believed to arise from Schwann cells that arise most commonly in the head and neck of females, ages 30-50 years. Malignant cases are rare but frequently fatal and little is known about genomic drivers of these tumors. This study presents next generation sequencing (NGS) results for 19 granular cell sarcoma (GCS), including clinical correlation for 2 GCS cases.

Methods: Comprehensive genomic profiling of 14 granular cell sarcomas, including 2 known institutional cases (indicated with *) was performed on formalin fixed paraffin embedded archival clinical specimens by hybridization-capture for up to 405 cancer-related genes (FoundationOneHeme®). All classes of genomic alterations (GA; SV, indels, CNA, rearrangements) and tumor mutational

burden (TMB) calculated by counting mutations across a 1.25Mb region encompassing these genes, was assessed. A COSMIC database search identified 5 more cases yielding a total of 19 cases for this analysis.

Results: 7 of the 19 cases harbored known somatic variants, including alterations in *MYST3, CDKN2A, PDCD11*, MLL2, GNAS, EWSR1,* as well as amplification in *HRAS**. 2 cases demonstrated amplification of *SDHA* in conjunction with *PDCD11 and HRAS*; 1 demonstrated amplification of both *ARFRP1* and *GNAS.* Multiple variants of unknown significance (VUS) were found. Of note, in 6 of 19 (32%) cases somatic or VUS of *MLL2, MLL3, MLL4 or TLL2* genes were identified. These genes are associated with the *KMT2* gene (encoding myeloid/lymphoid or mixed-lineage leukemia (MLL) protein 1), which plays an essential role in early development and hematopoiesis. The MLL1/MLL complex mediates epigenetic transcriptional activation and acts as a coactivator for estrogen receptor(ER), which is also related to beta catenin-TCF complex assembly. ER may interact with the ERK pathway (as does constitutive activation of HRAS). 2 known malignant cases occurred in white females aged 46 and 39 with tumor originating in left buttock and right arm, respectively.

Conclusion: The role of MLL1/MLL signaling in the etiology of granular cell sarcoma, and whether KMT2 and MEK inhibition may offer additional therapeutic approaches, should be explored further. Updated results will be presented.

P2–Poster 052 2563399

ACIDIC MICROENVIRONMENTS CREATED BY VACUOLAR-ATPASE PROMOTES SARCOMA PROGRESSION

Toshihiko Nishisho; Ryo Miyagi; Shunichi Toki; Koichi Sairyo

Orthopedics, The University of Tokushima Graduate School, Tokushima, Japan

Objective: Acidic microenvironment is one of the characteristic features of malignant tumors. Accumulating evidence indicates that the acidic microenvironments critically influence malignant behaviors of cancer including invasiveness, metastasis and chemoresistance. For sarcoma, it was reported that sarcomas were significantly more acidic than benign soft tissue tumors. However, the precise role of acidic microenvironment in sarcoma is still unclear. Vacuolar proton-ATPase (V-ATPase) is a multi-subunit enzyme that regulates proton transport and presents in the membranes of many organelles, where its proton-pumping action creates the low pH. In the present study, we examined whether the V-ATPase expressed in sarcoma cells took a part in the sarcoma activity by producing acidic microenvironments as well.

Methods: The human dedifferentiated liposarcoma (DDLS) cell line SW872 were cultured in pH 6.4 and 7.4 DMEM for 24 hours. Cell invasion assay and cell proliferation assay were performed. We extracted total RNA from the fresh frozen sample that obtained by open biopsy or wide resection. All experiments were conducted according to the ethical guidelines of the Institutional Review Boards and approved by the Ethics Committee of the Tokushima University.

Results: SW872 liposarcoma cells treated with acidic medium (pH6.4) showed increased cell proliferation and invasion at 24 hours compared with cells with normal pH medium (Fig.1, Fig.2). Next, we investigated all V-ATPase subunit in lipoma and DDLS. RT-PCR revealed that high-expression of the a1, a3, A, E2, F, G1, G2, H subunit in DDLS compared with lipoma (Fig. 3). Real-time PCR showed high-expression of a3, A, E2, F, G2, H in DDLS (Fig 4).

Conclusion: These data suggest that acidic microenvironment promotes sarcoma aggressiveness. Furthermore, the V-ATPase may be responsible for the creation of sarcoma-associated acidic microenvironment.

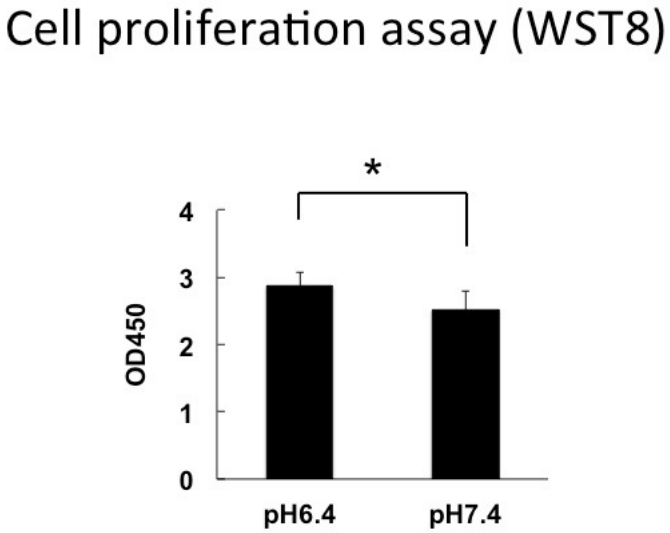


Fig.1 Acidic pH (6.4) promotse invation of SW872 liposarcoma cell line.

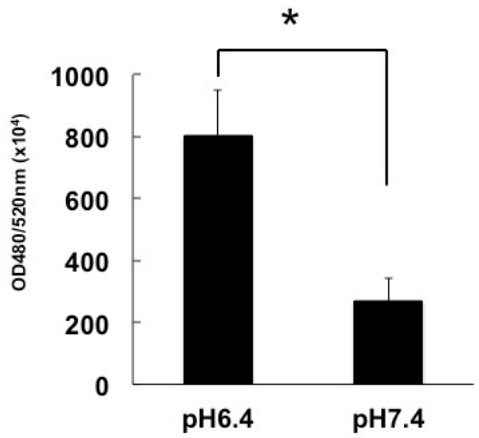


Fig.2 Acidic pH (6.4) promotes cell invasion in SW872 liposarcoma cell.

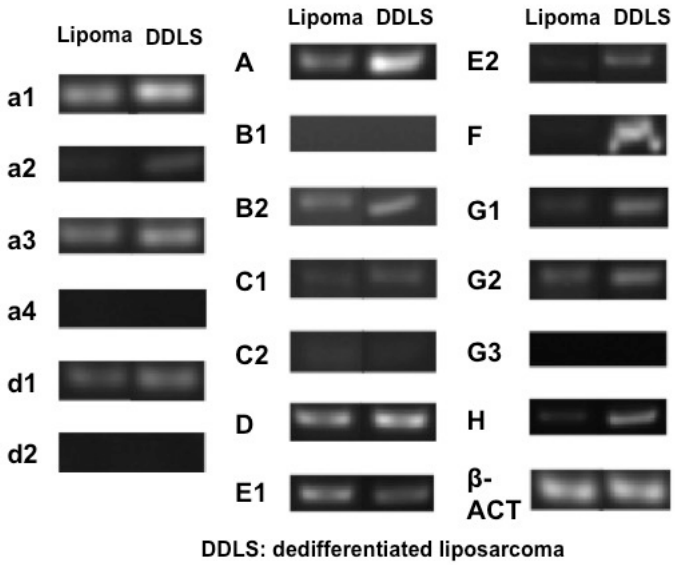


Fig.3 RT-PCR revealed that high-expression of the a1, a3, A, E2, F, G1, G2, H subunit in DDLS compared with lipoma.

P2–Poster 053 2571158

DRUG SENSITIVITY TESTING ON PATIENT DERIVED SARCOMA CELLS: NEW POSSIBILITIES FOR PATIENT-TAILORED TREATMENT

Christina Linder Stragliotto[2]; Elisabet Lidbrink[2]; Swapnil Potdar[6]; Otte Brosjö[3]; Henrik Bauer[3]; Asle Hesla[3]; limin Ma[1]; Tani Edneia[4]; Johan Wejde[4]; Olli Kallioniemi[5]; Krister Wennerberg[6]; Bertha A. Brodin[1]
[1]Oncology and Pathology, Karolinska Institutet, Stockholm, Sweden; [2]Breast and Sarcoma, Oncology Clinic, Karolinska University Hospital, Stockholm, Sweden; [3]Tumor Orthopedic Surgery, Karolinska University Hospital, Stockholm, Sweden; [4]Pathology, Karolinska University Hospital, Stockholm, Sweden; [5]Karolinska Institutet, ScienceLifeLaboratory, Stockholm, Sweden; [6]FIMM, Institute for Molecular Medicine Finland, Helsinki, Finland

Objective: To identify new treatment possibilities for individual sarcoma patients by implementing a systems medicine approach that combines drug sensitivity testing of patient's sarcoma cells to a library of oncology drugs and whole transcriptome profile.

Methods: A drug sensitivity and resistance test (DSRT): Patient-derived sarcoma cells and normal tissue are isolated from surgical specimens or by fine needle aspiration, expanded, characterized and exposed to 528 oncology drugs with known targets. The sensitivity of the patient tumor cells to the drugs (drug sensitivity score, DSS) is calculated in relation to normal bone marrow cells and to normal mesenchymal cells. The most active drugs and selective hits are selected and the results are discused by the sarcoma team as a guide for treatment decisions.

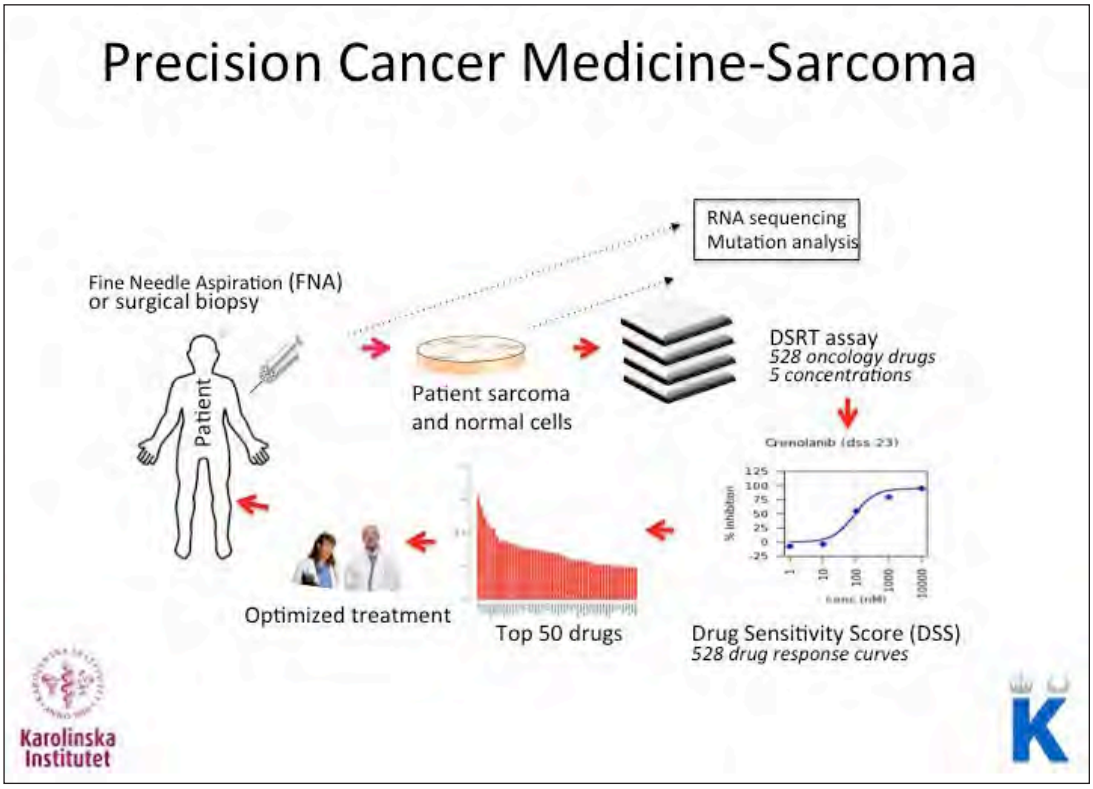
In parallel we are profiling the transcriptome in the a) sarcoma biopsies, b) matched normal tissue, and in c) the derived primary cultures using RNAseq.

We have also developed methods for the in situ detection of fusion oncoproteins using proximity ligation assay to characterize primary sarcoma cultures with chromosomal translocations prior to drug screening.

Results: Application of DSRT on 15 patient sarcomas and matched normal mesenchymal cells uncovered taxonomic drug-response subtypes and identified target inhibitors indicative of cancer pathways active on specific sarcoma subtypes.

DSRT could identify cytostatic drugs used in treatment protocols for a Ewing sarcoma patient with clinical response indicating this approach has potential to predict patient response to treatment.

Conclusion: Our preliminar results indicate that DSRT is a feasible and faster approach to identify therapeutic



possibilities for sarcoma patients. It has a potential to be a predictor of treatment response.

The combination of drug library screening and transcriptome profile on sarcoma biopsies, normal tissue and derived cultures will give information of the phenotypic differences that may be generated by culturing primary cells in vitro and shed information on cancer pathways active on rare sarcoma subtypes

P2–Poster 054 2557744

DCE-MRI IN PATIENTS WITH EXTREMITY SOFT TISSUE SARCOMA TREATED WITH PRE-OP RADIOTHERAPY

Ying Hitchcock, MD[1]; Matthias Schabel[2]; Michael Mclaughlin[2]; Matthew Poppe[1]; Lor Randall[3]; Kevin B. Jones[3]; Dennis C. Shrieve[1]; Christopher Hanrahan[2]

[1]Radiation Oncology, Huntsman Cancer Hospital, University of Utah, Salt Lake City, UT, USA; [2]Radiology, University of Utah, Salt Lake City, UT, USA; [3]Huntsman Cancer Hospital, University of Utah, Salt Lake City, UT, USA

Objective: To assess the potential for DCE-MRI to identify intrinsic characteristics of STS for use in diagnosis, prognosis, and response to preop RT.

Methods: 20 patients with STS of the extremities were recruited 8/2008-11/2014 to undergo high-temporal resolution DCE-MRI prior to and 2-4 weeks after preop-RT. DCE-MRI data of adequate quality for analysis were acquired in 19 of the 20 pre-RT and 17 of the 20 post-RT scans. All, except 1 patient, received 50 Gy in 25 fractions. DCE-MR were analyzed by voxelwise nonlinear regression using a novel quantitative pharmacokinetic model providing estimates of interstitial volume, blood volume, interstitial fraction, first pass extraction fraction, vascular transit time, vascular heterogeneity index, delay time for bolus arrival, blood flow, transfer constant, permeability-surface area product, and washout rate, as well as the tumor volume fraction with significant blood volume at the 1-sigma level. Tumor regions of interest (ROIs) for each imaging study were drawn by a radiologist blinded to DCE-MRI results and tumor diagnosis. Median model parameter values for pre-RT, post-RT, and change from pre- to post-RT were computed over all voxels with significant blood volume. Correlation between these model statistics were computed using the two-sided Kolmogorov-Smirnov test for four separate groups: (1) myxoid liposarcoma vs. other STS, (2) with local recurrence and/or metastasis vs. no recurrence, (3) tumor histological grade 1/2 vs. grade 3, and (4) alive vs. dead at last follow-up time.

Results: With mean follow-up 36.3 months (range, 2-87), 6 had LR and/or distant disease, 12 ANED at last follow-up. Significant differences between myxoid liposarcoma and other STS were found in multiple pre-RT parameters: including lower (p=0.045), (p=0.045), F (p=0.001), (p=0.018), and (p=0.006), and longer (p=0.018), along with decrease in post-RT (p=0.031). The only significant predictor for recurrence or metastasis was a decrease in with RT (p=0.025). Higher pre-RT E was predictive of lower tumor grade (1/2) (p=0.027). Pre-RT E was also significantly (p=0.025) higher in patients who were alive at last follow-up. Increase in with RT was also observed in patients who were alive (p=0.032). , PS, , and were not found to be significant in any measurement.

Conclusion: There are a number of DCE-MRI parameters that may help differentiate myxoid liposarcomas from other STS, while other parameters may be of use in determining prognosis and risk of recurrence or metastasis.

P2–Poster 055 2565637

NOVEL MR IMAGING METHOD -MAVRIC- FOR METAL ARTIFACT SUPPRESSION AFTER MUSCULOSKELETAL TUMOR SURGERY

Michiro Susa[1]; Sota Oguro[2]; Kazutaka Kikuta[2]; Kazumasa Nishimoto[2]; Keisuke Horiuchi[2]; Masahiro Jinzaki[2]; Kazuhiro Chiba[1]; Hideo Morioka[2]
[1]National Defense Medical College, Tokorozawa, Saitama, Japan; [2]Keio University, Tokyo, Japan

Objective: Standard imaging modality for the follow-up after musculoskeletal tumor surgery using metal implants has been conventional radiography. This technique is effective in detecting local recurrence in the bone adjacent to implants, but in many cases, radiographs do not lead to definitive diagnosis, especially after soft tissue tumor resection. Conventional MRI sequences have not been effective due to metal artifacts. In this study, we tried to elucidate the effectiveness of metal artifact suppression using novel sequence, multiacquisition variable-resonance image combination (MAVRIC), after musculoskeletal tumor surgeries.

Methods: We analyzed 7 cases of bone and soft tissue malignant tumor patients who were reconstructed with metal implants. Images obtained using MAVRIC and short tau inversion recovery (STIR) were compared side by side. The paired images were qualitatively compared independently by two specialists for 4 parameters: visualization of bone - implant interface, visualization of surrounding soft tissues, image blurring, and overall image quality. Quantitatively, paired images were reviewed to identify the slice where the metal artifact was maximal, and region of interest encompassing the implant and surrounding artifact was analyzed.

Results: By utilizing MAVRIC, visualization of the bone - implant interface and visualization of the surrounding soft tissue were significantly improved. Although blurring was worse on the MAVRIC acquisitions, the overall image quality was still better on MAVRIC. Quantitatively, the area of metal artifact measured using MAVRIC was less compared to STIR (79.5 cm^2 vs 154.6 cm^2).

Conclusion: Several variations of metal artifact suppression techniques have been reported, but there is still significant challenges in detecting small lesions near metal implants. MAVRIC was able to improve the quality of images by decreasing the artifact caused by metal implants and has the potential to improve patient managements. However, further prospective studies are needed to establish the optimum use of MAVRIC for early diagnosis of local recurrences after sarcoma surgeries.

P2–Poster 056 2570172

FEASIBILITY OF VOLUMETRIC ADC MAPPING TO TUMOR HABITATS DERIVED FROM DYNAMIC CONTRAST ENHANCED MRI IN SOFT TISSUE SARCOMAS

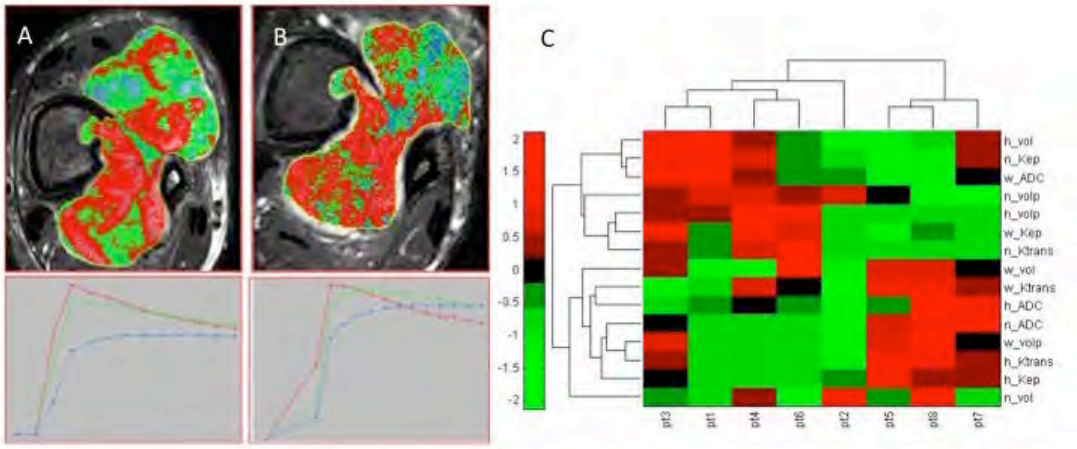
Jared Mahan[1]; Ty K. Subhawong[1]; Breelyn A. Wilky, MD[3]; Yu-Cherng C. Chang[2]; Raphael Yechieli[2]; Radka Stoyanova[2]
[1]Radiology, University of Miami, Miami, FL, USA; [2]Radiation Oncology, University of Miami, Miami, FL, USA; [3]Department of Medicine, Division of Hematology/ Oncology, University of Miami, Miami, FL, USA

Objective: To determine feasibility of semi-automated volumetric delineation of soft tissue sarcoma habitats from Dynamic Contrast Enhanced (DCE) MRI data, and compare volumetric Apparent Diffusion Coefficient (ADC) measurements among those habitats.

Methods: Eight patients with soft tissue sarcomas underwent MRI with DWI (b-values 50 and 600 s/mm2) and DCE with 10 sec temporal resolution. Tumors were manually segmented in 3D using T1 post-contrast. Tumor habitats were delineated using a previously developed technique that automatically identifies three unique temporal patterns from DCE-MRI datasets corresponding to well-perfused, hypoxic, and necrotic tumor environments. ADC maps were co-registered with T1 MRI and ADC mean values were derived for each habitat. ADC were compared across tumor environments.

Results: The DCE-MRI dataset allowed identification of three habitats in 7 patients, and 2 habitats in one patient with a small residual subcutaneous tumor. Mean tumor volume was 151 cc. Mean ADC of hypoxic, well-perfused, and necrotic tumor compartments were 1.25, 1.33, and 1.33 x 10^{-3} mm^2/sec, respectively; although there was a slight increase in ADC values in the necrotic habitat, this small 0.08 x 10^{-3} mm^2/sec within-subject difference between well-perfused and necrotic compartments was not statistically significant ($p = 0.27$, paired t-test). The volumetric % necrosis correlated with % histologic necrosis in 5 patients where available ($r = 0.91$). K^{trans} values in hypoxic, well-perfused, and necrotic tumor compartments were 0.16, 0.097, and 0.049 min^{-1}, respectively; there was little correlation with tumor habitat mean ADC (Pearson r range -0.0.19 to 0.047).

Conclusion: Volumetric mean ADC values showed little correlation with automatically delineated tumor habitats in soft tissue sarcoma regardless of treatment response; the non-overlapping nature of these results suggests they may serve complementary roles in assessing tumor viability in different sarcoma microenvironments.



Mapping of tumor habitats in soft tissue sarcoma. Axial DCE in the lower leg of patient with adult fibrosarcoma A) pre-treatment and B) after treatment. Tumor habitats are presented as follows: well-perfused – red; hypoxic – green; and necrotic – blue. (below) Corresponding average signal-versus-time curve from each habitat. The two imaging exams were 5 months apart; post-treatment exam is one month after completion of neoadjuvant chemotherapy. Subsequent amputation revealed only 10% histologic necrosis. Note that the fraction of the hypoxic/necrotic habitats is higher in the anterior portion of the tumor while the posterior compartment is better perfused and harbors viable, infiltrating tumor. C) Heatmap shows clustering of the eight patients based on quantitative imaging features: volumes, ADC and DCE parameters, associated with each habitat (n=necrotic; h=hypoxic; w = well-perfused).

P2–Poster 057 2543067

CONTRAST-ENHANCED ULTRASOUND (CEUS) IN DIAGNOSIS, EVALUATION, AND MANAGEMENT OF SOFT TISSUE SARCOMA (STS)

Mittul Gulati, MD[1]; William W. Tseng[2]; James Hu[3]; Sant P. Chawla[3]; Darryl Hwang[1]; Bhushan Desai[1]; Vinay Duddalwar[1]

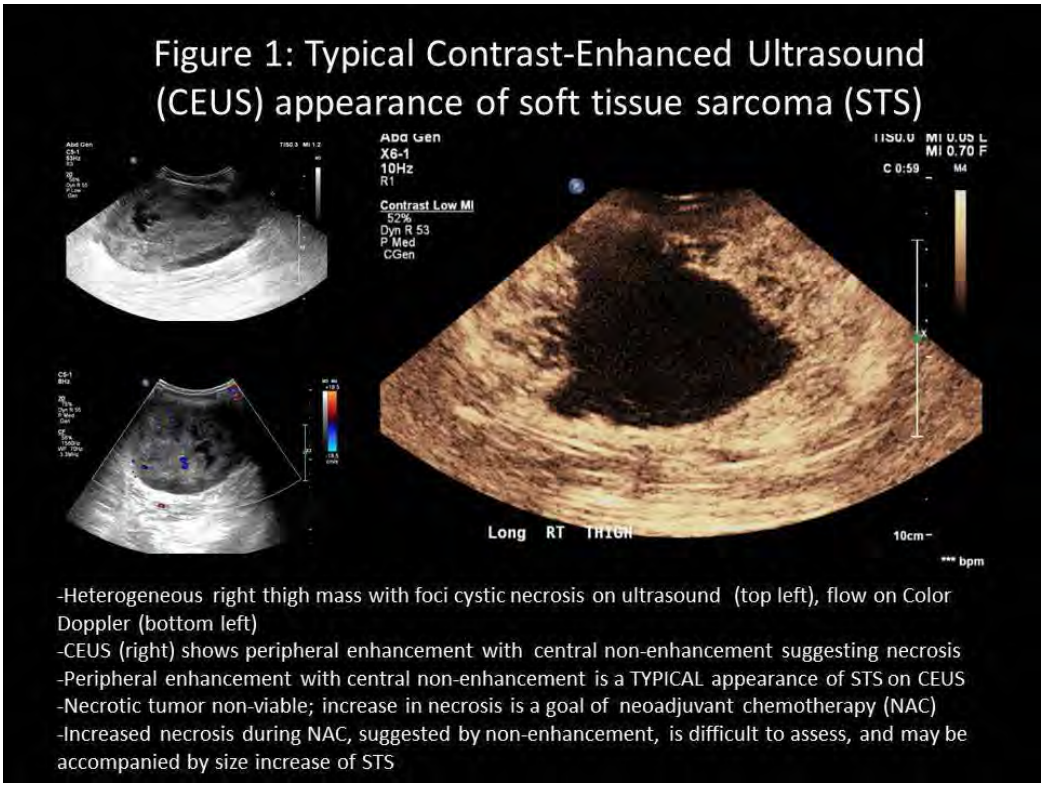
[1]Radiology, Keck USC School of Medicine, La Canada Flintridge, CA, USA; [2]Surgery, Keck USC School of Medicine, Los Angeles, CA, USA; [3]Medicine, Keck School of Medicine of USC, Los Angeles, CA, USA

Objective: Contrast-enhanced ultrasound (CEUS) is a novel imaging modality with advantages over CT/MRI, including lack of nephrotoxicity and unmatched temporal resolution due to continuous imaging. Contrast enhanced ultrasound (CEUS) was used to assess clinically suspected soft tissue sarcomas (STS). Evaluation included enhancement pattern and quantitative analysis (QA) of enhancement kinetics, as well as comparison to CT/MRI.

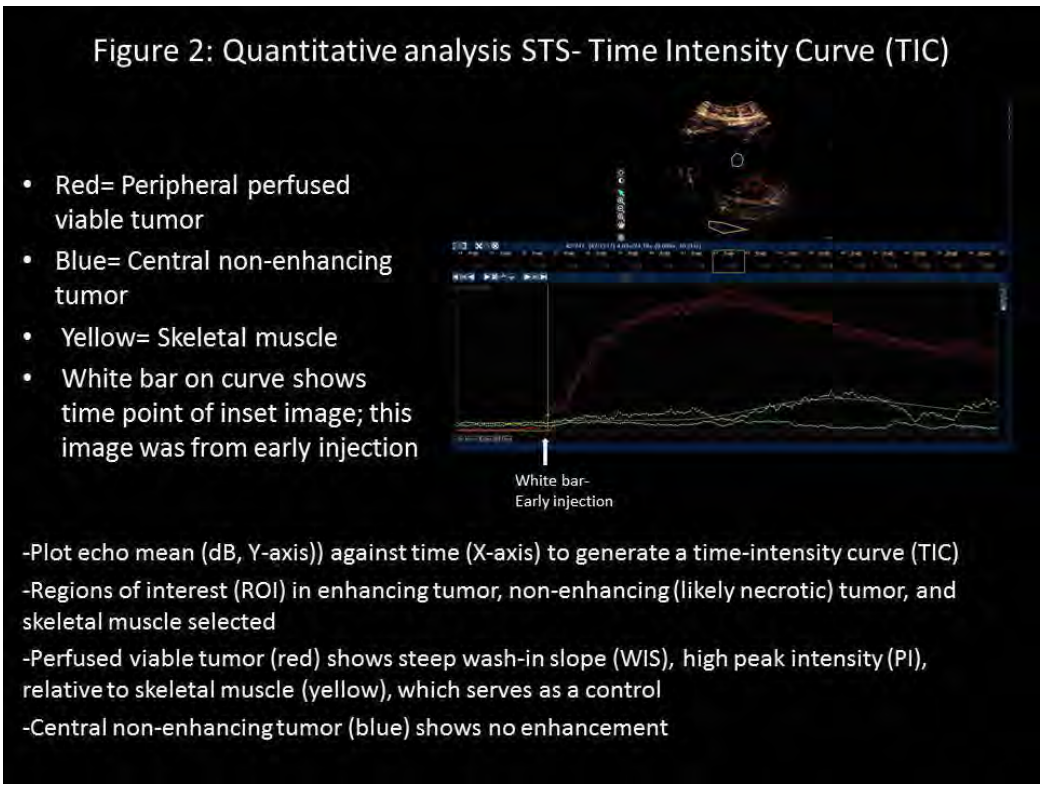
Methods: 20 patients with clinically suspected STS underwent CEUS. All underwent subsequent image-guided biopsy. Enhancement pattern: masses were categorized as P1 (non-enhancing), P2 (peripherally enhancing with central non-enhancement), P3 (heterogeneously enhancing with non-enhancing foci), or P4 (homogeneously enhancing). QA included evaluation of enhancing tumor, non-enhancing tumor, and adjacent skeletal muscle (control) parameters including time to peak (TTP) and wash in slope (WIS), with generation of time-intensity curves (TIC). Comparison was made to contrast-enhanced CT/MRI as available. Follow-up CEUS exams were also performed on 3 patients after neoadjuvant chemotherapy (NAC).

Results: Enhancement pattern: Of the 20 masses, none were non-enhancing (P1) on initial CEUS. 7 (35%) were peripherally enhancing with central non-enhancement (P2), and 11 (55%) were heterogeneously enhancing with internal non-enhancing foci (P3). All 18 masses with either P2 or P3 enhancement patterns were biopsy proven STS (100%). 2 masses demonstrated homogenous enhancement (P4); both were biopsy-proven lymphoma. Interestingly, both masses with P4 pattern were clinically suspected to be STS until CEUS and biopsy. QA: All 18 biopsy-proven STS demonstrated a typical enhancement pattern on TIC, with higher PI and steeper WIS of tumor relative to control (skeletal muscle). 3 patients demonstrated a quantifiable increase in non-enhancing tumor following NAC, from a mean of 21% non-enhancement on pre-therapy CEUS to 54% non-enhancement following NAC. CEUS exam results correlated closely with contemporaneous CT/MRI (available in 18 of 20 patients, or 90%).

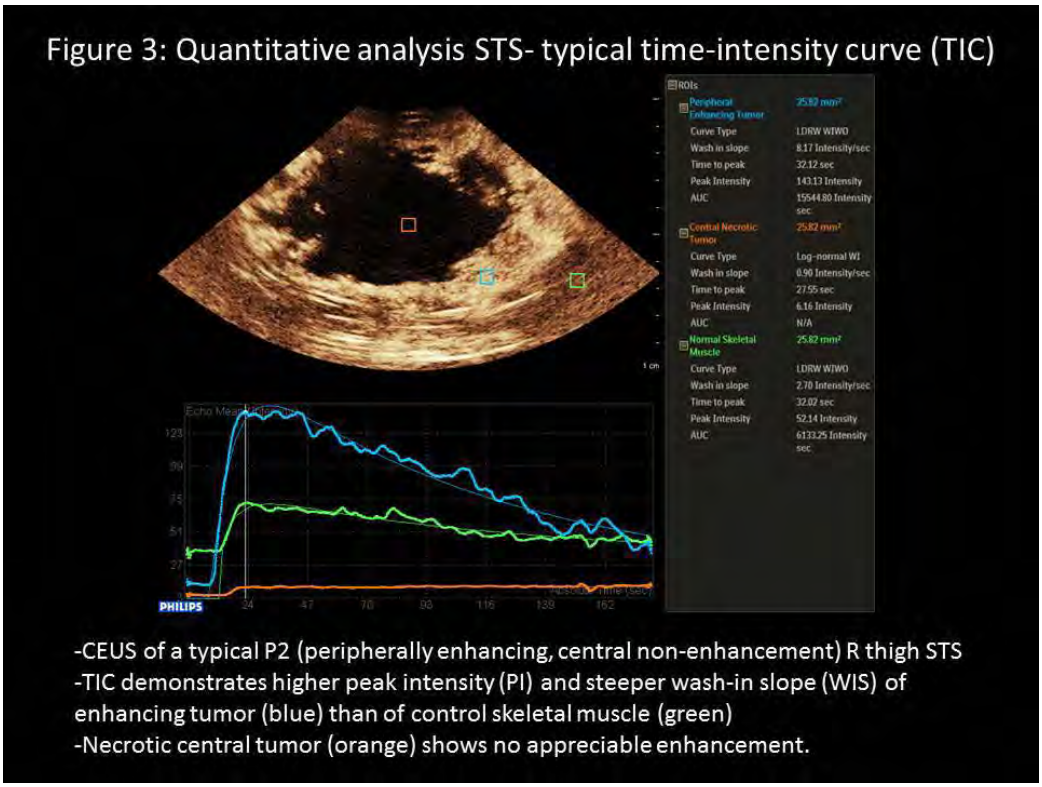
Conclusion: CEUS enhancement pattern may differentiate STS from lymphoma, as the latter typically shows homogeneous enhancement; STS demonstrate a typical TIC, with higher PI and steeper WIS than adjacent muscle. Finally, a subgroup of patients undergoing NAC demonstrated a quantifiable increase in non-enhancing tumor during STS treatment, correlating closely with CT/MRI. CEUS may aid in diagnosis, evaluation, and treatment monitoring of STS.



Typical Contrast-Enhanced Ultrasound (CEUS) appearance of Soft Tissue Sarcoma (STS)



Quantitative Analysis STS- Time-Intensity Curve (TIC)



P2–Poster 058 2544489

EFFECTIVENESS OF CONTRAST COLOR DOPPLER ULTRASONOGRAPHY IN PREOPERATIVE DIAGNOSIS BETWEEN MALIGNANT AND BENIGN OF SOFT TISSUE TUMORS

Naoto Oebisu; Manabu Hoshi; Yoshitaka Ban; Hiroaki Nakamura
Osaka City University, Osaka, Japan

Objective: The aim of the present study was to elucidate the usefulness of contrast enhanced color Doppler (CD) ultrasonography for preoperative differential diagnosis between benign and malignant soft tissue tumors.

Methods: Between January 2010 and December 2013, a total of 180 patients (87 male, 93 female) were enrolled in the present study. The patient ages ranged from 1 to 91 years (mean 58.1±20.0 years). The patients were treated at Osaka City University Hospital in Osaka, Japan. The institutional Ethics Review Board of Osaka City University Graduate School of Medicine approved the protocol of the present study.

The maximum size, depth, tumor margins, shape, echogenicity and textural pattern were measured on gray-scale images. CDUS was used to evaluate the intratumoral blood flow, using conventional criterion according to classical Giovagnolio classification with and without contrast medium, Sonazoid. Peak systolic flow velocity (Vp), mean flow velocity (Vm), resistivity index (RI) and pulsatility index (PI) of each detected intratumoral artery were automatically calculated with power Doppler US (PDUS). The elasticity of tumor was also measured, compared to a normal fat tissue using the elastgraphy.

Results: A total of 118 benign and 62 malignant tumors were included in the present study.

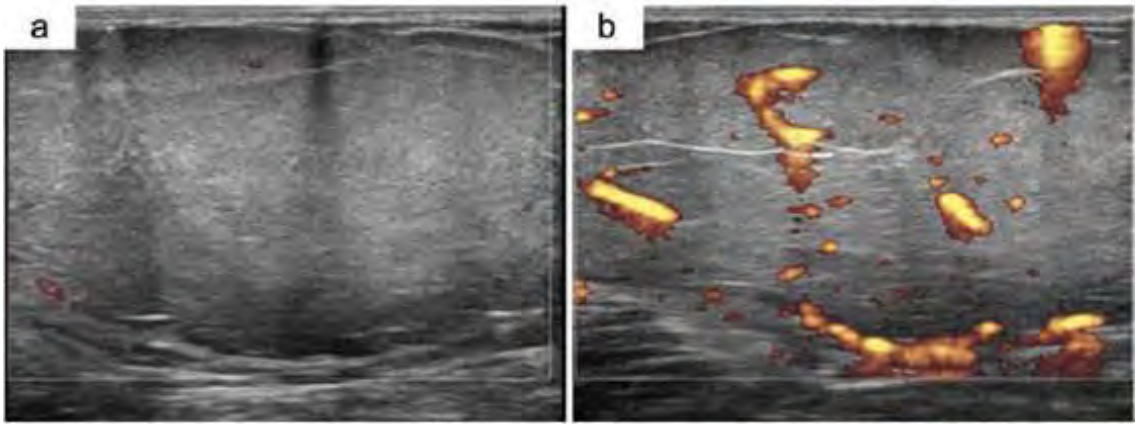
Statistical significances were found in size, depth, tumor margin and textural pattern but not in shape or echogenicity on gray-scale images. Before Sonazoid injection, CDUS findings showed 55% sensitivity, 77% specificity and 69% accuracy, whereas contrast-enhanced CDUS showed 87% sensitivity, 68% specificity and 74% accuracy. There were no statistically significant differences between malignant and benign tumors regarding the mean Vp, Vm, RI and PI values determined on PDUS. Elastgraphy was performed 124 masses (87 benign and 37 malignant). Elastic ratio average was 0.58 in benign and 0.25 in malignant tumor (P=0.004).

Conclusion: The tumor size, depth, textural pattern and tumor margin proved to be positive parameters on gray-scale US images for differentiating benign from malignant tumors. From the standpoint of vascularity within the tumor, CDUS showed lower sensitivity (54.8%) and lower accuracy (69.4%). Contrast medium administration enhanced sensitivity and accuracy up to 86.8 and 74.4%, respectively. PDUS provided no useful information. Contrast-enhanced CDUS proved to be a reliable diagnostic tool with which to screen for malignant potential in soft tissue tumors.

Comparison with CDUS findings of benign and malignant tumors

Variable	Beign (No.)	Malignant (No.)	Sensitivity (%)	Specificity (%)	Accuracy (%)
CDUS grade without CM			54.8	77.1	69.4
Grade I, II	91	28			
Grade III, IV	27	34			
CDUS grade with CM			86.8	67.6	74.3
Grade I, II	48	5			
Grade III, IV	23	33			

CDS, color Doppler ultrasonography; CM, contrast medium



Well-differentiated liposarcomas from the right thigh of a 36-year old woman.
(a)CDUS image (grade II) before injection with Sonazoid.
(b)CDUS image (grade IV) after administration of Sonazoid. CDUS, color Doppler ultrasonography.

P2–Poster 059 2566632

APPARENT DIFFUSION COEFFICIENT: A POTENTIAL IMAGING BIOMARKER FOR PREDICTION OF METASTATIC DEVELOPMENT IN SOFT TISSUE SARCOMAS?

Manpreet Bedi, MD[1]; David M. King[2]; Eric Paulson[1]; John Charlson[3]; Donald Hackbarth[2]; John Neilson[2]
[1]Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI, USA; [2]Orthopaedic Surgery, Medical College of Wisconsin, Milwaukee, WI, USA; [3]Medical Oncology, Medical College of Wisconsin, Milwaukee, WI, USA

Objective: The goal of this study was to assess if there is a change between pre- and post-therapy apparent diffusion coefficient (ADC) values & to evaluate the predictive value of ADC for the development of metastasis (DM) in pts with soft tissue sarcomas (STS).

Methods: From 2011-2016, 22 pts with stage I-III STS underwent preoperative RT +/- chemotherapy. 44 MRIs, one prior & one after neodjuvant therapy, were prospectively evaluated. Imaging at 3.0 T included conventional (T1-weighted & contrast enhanced) & functional (diffusion-weighted imaging (DWI) & ADC mapping) sequences. Tumors on T1-post contrast imaging were fused with their respective DWI scans & contoured using MIM (version 6.5.4, MIM Software, Cleveland, OH). A ROI representing the tumor was measured & between pre- and post-therapy MRIs on T1 and DWI scans (Figure 1). Pre- and post-therapy median ADC values were calculated using ADC maps derived from DWI-MRI. DMFS & OS were evaluated using the Kaplan-Meier estimate of survival.

Pre- and post-therapy ADC values between pts who had localized & developed DM were analyzed by the Mann-Whitney test. The cut-off ADC value of the receiver operating characteristic (ROC) curve with DM was established.
Results: Median follow-up was 2.7 yrs. 41% received neoadjuvant chemotherapy. 32% of pts developed DM.

Median pre- & post-therapy ADC value was 1666.24 & 1718.79 mm^2/s, respectively. Median post-/pre-therapy ratio ADC value was 1.02. 2-yr DMFS and OS was 77% & 95%, respectively.

Median pre-therapy ADC value in pts who developed DM was 1744.89 & 1368.84 mm^2/s in non-DM pts (p=0.14). Median post-therapy ADC value in pts who developed DM was 1700 & 1737.57 mm^2/s in non-DM pts (p=0.83). Median

post-/pre-therapy ratio ADC values was lower in pts who developed DM vs non-DM pts (0.98 vs 1.16, p=0.003). All pts who developed DM had a decrease in post-therapy ADC value.

Pts with DM had larger tumors (18.3 cm vs 7.8 cm, p<0.0001) & undifferentiated histologies (43% vs 27%, P=0.02, Table 1).

The ROC curve for the cut-off value of the ADC ratio between post- and pre-therapy ADCs was 0.98 mm^2/s (AUC 0.895, p<0.0001, 95% CI 0.690 to 0.984) with a sensitivity, and specificity of 100% & 86.7%, respectively.

Conclusion: In general, ADC values increased after neoadjuvant therapy. All pts who developed DM had a decrease in post-therapy ADC values. An ADC ratio (post-/pre-therapy) of ≤0.98 mm^2/s correlated with a higher risk of developing DM. DWI-MRI technology may predict the development of DM in pts with localized STS.

Table 1: Patient, Tumor and Treatment Characteristics in Localized and Metastatic Patients

Variable	Non-Metastatic Patients	Metastatic Patients	P-value
Age	59	55	NS
Karnofsky Performance Status ≥80	100%	100%	NS
Diabetes	14%	0%	NS
Cardiovascular Disease	14%	0%	NS
Median Tumor Size	18.3 cm	7.8 cm	<0.0001
Tumor Location	Upper Extremity: 29% Lower Extremity: 71%	Upper Extremity: 27% Lower Extremity:73%	NS
Histology	Undifferentiated: 43% Leiomyosarcoma/Liposarcoma: 57% Spindle Cell Sarcoma: 0% Other: 0%	Undifferentiated: 27% Leiomyosarcoma/Liposarcoma: 13% Spindle Cell Sarcoma: 27% Other: 33%	0.02
High Grade	100%	80%	NS
Neoadjuvant Chemotherapy	29%	47%	NS

NS=non-significant

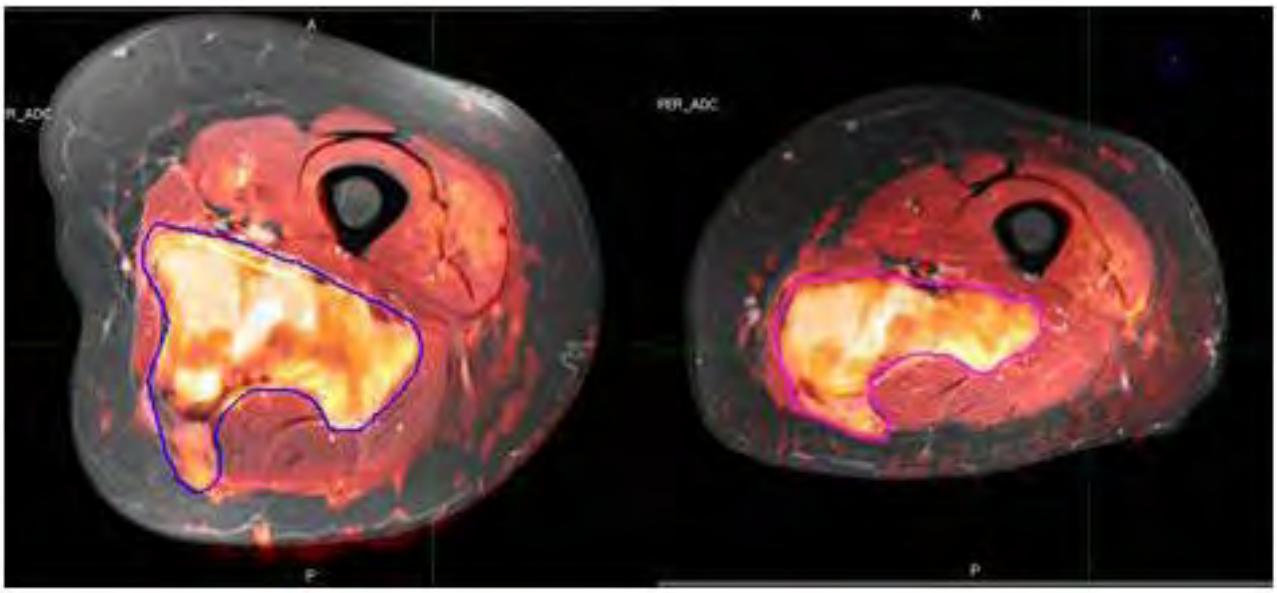


Figure 1: Fusion of DWI and T1 post-contrast MRIs A) Pre-Therapy B) Post-Therapy

P2–Poster 060 2566214

CLINICOPATHOLOGICAL INVESTIGATION OF LOW-GRADE FIBROMYXOID SARCOMA (EVANS TUMOR)

Naomasa Fukase, MD, PhD[3]; Ikuo Fujita[1]; Teruya Kawamoto[3]; Toshiko Sakuma[2]; Takanori Hirose[2]; Naoe Jimbo[4]; Tomoo Itoe[4]; Hitomi Hara[3]; Takuya Fujimoto[1]; Masayuki Morishita[3]; Etsuko Kamata[3]; Toshiyuki Takemori[3]; Ryosuke Kuroda[3]; Toshihiro Akisue[3]

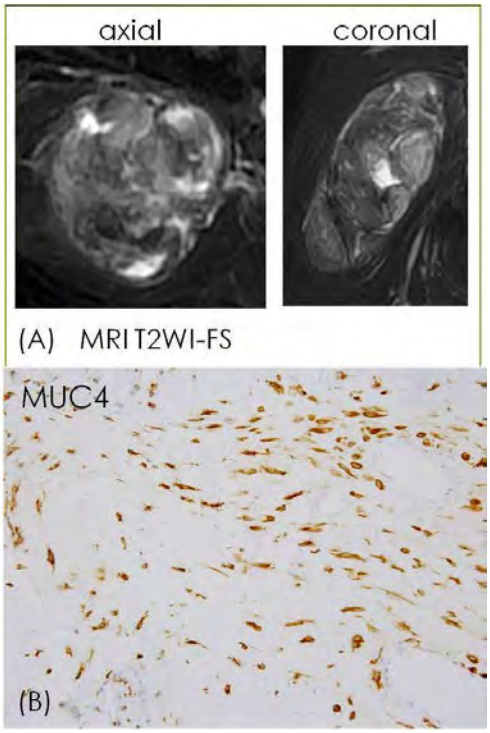
[1]Orthopaedic Surgery, Hyogo Cancer Center, Akashi, Japan; [2]Diagnostic Pathology, Hyogo Cancer Center, Akashi, Japan; [3]Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan; [4]Diagnostic Pathology, Kobe University Graduate School of Medicine, Kobe, Japan

Objective: Low-grade fibromyxoid sarcoma (LGFMS), proposed by Evans in 1987, is a rare soft tissue sarcoma. It may be treated as a benign disease because of its slow progression, hence the local recurrence, distant metastasis, and tumor death rates after excision were reported to be 64, 45, and 42%, respectively. In this study, we clinicopathologically investigated LGFMS.

Methods: The subjects were 6 LGFMS patients surgically treated at our hospital or an affiliated hospital between 2012 and 2014. There were 2 male and 4 female patients, aged 22-80 years old (mean: 49 years old). The time taken to visit a hospital after becoming aware of the tumor was one month to 20 years, and the duration of postoperative follow-up was 20-44 months (mean: 34 months). The imaging, pathological and genetic diagnosis were investigated. In addition, we investigated surgical procedure and outcome.

Results: The tumor arose from a deep region in 5 and subcutis in one. On MRI, 'low-isointensity on T1WI' and 'low-high-intensity on T2WI' were observed in all cases, and a gyrus-like morphology due to a mixture of fibrous and myxoma-like regions, termed the gyriform pattern characteristic to LGFMS, was noted in 5. On pathological examination, fibrous and myxoma-like regions were mixed in all cases and spindle-shaped tumor cells were arranged in a tortuous spiral pattern in it, but the cell density was low and nuclear division and atypia were noted in only a few cells, showing a benign fibroma-like lesion. Immunostaining of MUC4 was positive in all cases. The LGFMS-specific fusion gene, FUS-CREB3L2, was confirmed by RT-PCR and fluorescence in situ hybridization (FISH) in 3 and 3, respectively. On macroscopic evaluation of the resected margin, marginal resection was performed in one and wide resection was performed in 5. The resected stump was negative in all cases. Postoperative radiotherapy was performed in the patient treated with marginal resection. The outcome on the final follow-up was CDF in all patients.

Conclusion: The gyriform pattern on MRI was characteristic, and the diagnostic value of MUC4 positivity on immunostaining was very high. No local recurrence or distant metastasis occurred after wide resection, although these were short-term outcomes, suggesting the importance of accurate preoperative diagnosis made by combining imaging, histopathological, and genetic diagnoses.



MRI of the LGFMS in the buttock showed the gyriform pattern mimicking brain gyri. (A) .Tumor cells showed strong, diffuse immunoreactivity for MUC4 (B) .

Clinicopathologic features of patients with LGFMS

Case	Age/Sex	Site	AJCC Stage	Gyriform pattern on MRI	MUC 4 expression on immunostaining	Genetic abnormality	Surgical procedure	Outcome
1	56/M	hand	IB	(+)	(+)	(+)	wide	CDF
2	43/F	forearm	IA	(+)	(+)	(+)	marginal	CDF
3	22/F	thigh	IB	(+)	(+)	(+)	wide	CDF
4	80/M	buttock	IB	(+)	(+)	(+)	wide	CDF
5	52/F	pelvic region	IB	(+)	(+)	(+)	wide	CDF
6	39/F	chest wall	IA	(-)	(+)	(+)	wide	CDF

P2–Poster 061 2565681

ACCURACY OF IMAGE-GUIDED PERCUTANEOUS CORE NEEDLE BIOPSY OF PERIPHERAL NERVE SHEATH TUMORS

Tara A. Russell, MD, MPH[2]; Kambiz Motamedi[1]; Leanne Seeger[1]; Arun S. Singh[3]; Chmielowski Bartosz[3]; Nicholas Bernthal[4]; Susan Bukata[4]; Joseph G. Crompton[2]; Scott Nelson[5]; Sarah M. Dry[5]; Frederick R. Eilber[2]; Frederick C. Eilber[2]; Benjamin D. Levine[1]
[1]Department of Radiology, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [2]Division of Surgical Oncology, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [3]Department of Medicine, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [4]Department of Orthopedic Surgery, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [5]Department of Pathology and Laboratory Medicine, Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA

Objective: Accurate preoperative tissue diagnosis is critical in guiding appropriate surgical and oncologic management for patients with soft tissue tumors. Although image-guided core needle biopsy (IGCNBx) is the standard of care, there is often resistance to performing IGCNBx of peripheral nerve sheath tumors (PNST) due to potential discordant pathology and theoretic risk of nerve damage. The aim of this study was to 1) evaluate the accuracy of IGCNBx of PNSTs by comparing IGCNBx histology with tissue from surgical tumor resection & 2) determine prevelance of biopsy-related complications.

Methods: All cases of pathologically-proven PNST diagnosed at UCLA from 1/2002-5/2016 were reviewed. IGCNBx was done by an experienced musculoskeletal radiologist with CT or US guidance. Co-axial technique was employed for each biopsy using Cook® Quick-Core Biopsy needle set, which includes an 11gauge introducer and 14gauge biopsy needle. Moderate sedation was used in addition to local anesthesia at the radiologist's discretion.

Results: 207 PNSTs were diagnosed during the study period. Among these, 86(41.5%) had both IGCNBx & surgical resection performed at UCLA, 20(9.7%) had an outside hospital biopsy, 80(38.6%) had no pre-operative biopsy & 21(10.1%) had no surgical excision due to benign pathology. Among cases with both IGCNBx & surgical pathology, lesions occurred in the trunk(n=32, 37.2%), upper extremity(n=13,15.1%),& lower extremity(n=41, 47.7%). Median tumor diameter was 4.8cm(range 1.4-20cm). Final pathologic diagnoses included neurofibroma(n=9), Schwannoma(n=55), malignant PNST (MPSNT)(n=21), & PNST hybrid(n=1). Overall concordance between IGCNBx & surgical pathology was 88.4%(76/86). Among discordant cases, all 10 (11.6%) were due to upgrading pathology to MPNST. Of these, IGCNBx pathology was neurofibroma(n=4), spindle neoplasm(n=2), PNST NOS, myxoid sarcoma, Schwannoma, & low grade sarcoma. Concordance rates based on IGCNBx pathology were 100%(9/9) for MPNST, 58.3%(7/12) for neurofibroma, & 95.9%(47/49) for Schwannoma. Other than pain or soreness at the biopsy site following the procedure, there were no instances of long-standing nerve damage or other major complication reported in any of the IGCNBx cases.

Conclusion: Percutaneous IGCNBx is safe & accurate for the diagnosis of PNSTs, with 88% concordance between IGCNBx & surgical pathology. Neurofibromas diagnosed with IGCNBx should be interpreted with some caution due to potential risk of upgrade to MPNST on pathology after surgical resection.

P2–Poster 062 2565891

WHICH PERCUTANEOUS BIOPSY IN THE DIAGNOSIS OF BONE TUMOURS?

Pedro F. Cardoso[1]; João Esteves[1]; Vânia Oliveira[1]; André Coelho[2]; Tiago Couto[3]
[1]Orthopaedics, Centro Hospitalar do Porto, Porto, Portugal; [2]Pathology, Centro Hospitalar do Porto, Porto, Portugal; [3]Radiology, Centro Hospitalar do Porto, Porto, Portugal

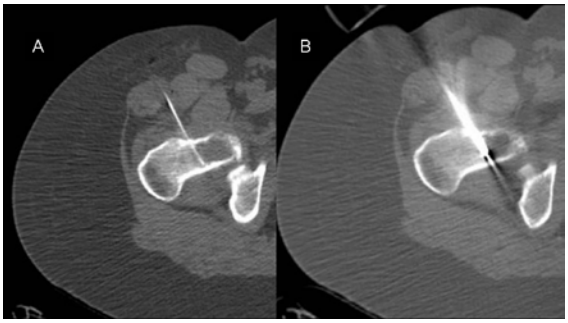
Objective: This study is a prospective evaluation of bone lesions in which fine needle aspiration (FNA) was performed followed by core needle biopsy (CNB) in order to compare the accuracy, the scarcity of samples and the possibility to initiate the treatment with each method.

Methods: 94 patients underwent this study being submitted to image-guided FNA. Immediately after the aspiration, an 8-gauge needle biopsy was introduced. Results of both techniques were compared with final diagnoses established by surgical specimen (41 patients) or ulterior clinical and imaging evaluation (53 patients) since in metastases, some benign and haematopoietic lesions no surgery is needed.

Results: Final diagnoses: 29 metastases, 28 malignant tumours, 13 benign tumours, 12 haematological diseases and 5 infections. In 7 cases pathology could be excluded. FNA diagnostic yield was 74,5% (n = 70) and accuracy 97,1% (n = 68). With this technique, 15 results (16%) were completely inconclusive but in 9 cases the pathologist could differentiate correctly a benign lesion (n = 5) from a malignant one (n = 4). Regarding determining malignancy, FNA had 98,3% sensibility, 100% specificity, 100% positive predictive value and 95,2% negative predictive value. CNB diagnostic yield was 97,9% (n = 92) and accuracy 98,9% (n = 91). Regarding determining malignancy CNB had 98,5% sensibility, 100% specificity, 100% positive predictive value and 96,2% negative predictive value. Diagnostic yield was

significantly lower (p<0.0001) with FNA than with CNB. There was no statistical difference (p=0.4046) between the diagnostic accuracy when using both techniques nor there were differences in the sensitivity, sensibility, PPV and NPV. Comparing the possibility of exclude malignancy FNA and CNB were statistically similar. However, FNA was inferior to CNB establishing an accurate diagnosis and initiating a treatment.

Conclusion: FNA is reliable and emables the initiation of treatment everytime it establishes a diagnostic or excludes malignancy. The number of onconclusive cases, the real problem with this technique can be decreased by a better selection of the lesionand a preliminary evaluation by the pathologist during the procedure. Until then, CNB remains the preferable method for bone tumours diagnosis.



Accuracy of Fine Needle Aspiration (FNA) and Core Needle Biopsy (CNB) regarding determining malignancy in comparison to the final diagnosis. P values indicate de differences of both biopsy techniques.

	Fine Needle Aspiration	Core Needle Biopsy	p value
Diagnostic yield #	70/94 (74.5%)	92/94 (97.9%)	<0.0001
Diagnostic accuracy #	68/70 (97.1%)	91/92 (98.9%)	0.4046
Specificity ##	100.0%	100.0%	1.0
Sensibility ##	98.31%	98.51%	0.9288
Positive predictive value ##	100.0%	100.0%	1.0
Negative predictive value ##	95.24%	96.15%	0.8792

Compared using the t test for proportion, set to a 95% confidence interval ## Analysed using MedCalc version® 15.11.4

Comparison of FNA and CNB excluding malignancy, establishing diagnosis and initiating treatment

	Fine Needle Aspiration	Core Needle Biopsy	p value
Excluding malignancy #	78/79 (98.7%)	91/92 (98.9%)	0.9047
Establishing diagnosis #	68/79 (86.1%)	91/92 (98.9%)	0.0011
Initiating treatment #	73/94 (77.7%)	91/94 (96.8%)	0.0001

Compared using the Chi-Square test

P2–Poster 063 2570472

EXPRESSION OF PAX7 DISTINGUISHES RHABDOMYOSARCOMA FROM HISTOLOGIC MIMICS

Gregory Charville, MD, PhD[1]; Sushama Varma[1]; Erna Forgó[1]; Sarah Dumont[2]; Eduardo Zambrano[1]; Jonathan Trent II[3]; Alexander Lazar[4]; Matt van de Rijn[1]
[1]Department of Pathology, Stanford University School of Medicine, Stanford, CA, USA; [2]Department of Medical Oncology, Institut Gustave-Roussy, Villejuif, France; [3]Division of Hematology/Oncology, Department of Internal Medicine, University of Miami Miller School of Medicine, Miami, FL, USA; [4]Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: Rhabdomyosarcoma (RMS) is a soft-tissue sarcoma defined by features of sketal muscle differentiation. Although there are specific morphologic characteristics of skeletal muscle differentiation (e.g., rhabdomyoblasts), these pathognomonic morphologic characteristics are often not present and therefore represent an insensitive diagnostic tool. Consequently, diagnosis of RMS often requires proving skeletal muscle differentiation by identifying expression of genes, namely myogenin (MYOG) or MYOD1, unique to this tissue. Previous studies have shown, however, that expression of MYOG or MYOD1 can be absent or focal in cases of RMS, especially those of the embryonal variant. We sought to expand the diagnostic sensitivity of immunohistochemical studies of skeletal muscle differentiation by analyzing expression of PAX7, a lineage-specifying transcription factor expressed early in the development and maintenance of myogenic progenitor cells.

Methods: We used a monoclonal anti-PAX7 antibody to analyze expression in over one-hundred RMS cases and over three-hundred other soft-tissue tumors or small round blue-cell neoplasms. The majority of cases were analyzed as cores on tissue microarrays. In a subset of alveolar RMS cases, the underlying genetic translocation was defined using fluorescence in situ hybridization analysis for PAX3/7-FOXO1 gene rearrangement.

Results: -- In non-neoplastic tissue, PAX7 is specifically expressed in adult skeletal muscle progenitors
-- PAX7 is expressed in a majority of embryonal RMS cases, including a subset with negative or focal MYOG expression
-- PAX7 is expressed in over half of alveolar RMS cases
-- PAX7 expression in alveolar RMS correlates with the underlying genetic translocation
-- Among other soft-tissue tumors and small

round blue-cell neoplasms, only Ewing sarcoma shows significant expression of PAX7.

Conclusion: Analysis of PAX7 is a useful adjunct in the diagnosis of soft-tissue neoplasms in which RMS is under consideration. Compared to currently used markers, such as MYOD1 and MYOG, PAX7 has greater sensitivity among the embryonal RMS cases analyzed in this study. Of note, PAX7 expression is also robust in Ewing sarcoma and therefore additional immunohistochemical or molecular tests are required if Ewing sarcoma is also in the differential diagnosis. Additional studies will help to define patterns of PAX7 expression in additional tumor sub-types and what, if any, prognostic significance can be assigned to PAX7 expression in RMS.

P2–Poster 064 2560449

TARGETED RNA-BASED NEXT-GENERATION SEQUENCING PANEL IN THE DIAGNOSIS OF SOFT TISSUE AND BONE TUMOURS

David Swanson; George S. Charames; Andrew Wong; Rita Kandel; Brendan C. Dickson, MD, MSc
Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada

Objective: The accurate diagnosis of soft tissue and bone tumours (STBT) is imperative to ensure appropriate patient treatment, in addition to creating a foundation on which future basic science and clinical studies can be predicated. Many STBT are characterized by disease-defining chromosomal translocations that can be exploited diagnostically using fluorescence *in situ* hybridization and/or reverse transcriptase-PCR (RT-PCR). These assays are expensive and time-consuming, particularly when multiple serial tests are required to achieve a definitive diagnosis. The purpose of this study was to assess whether these issues may be overcome with the simultaneous testing of multiple fusion transcripts in parallel, using a targeted RNA-based next-generation sequencing panel.

Methods: Using a 507 gene RNA-seq targeted fusion panel from Illumina, 18 cases of STBT containing RT-PCR-verified translocations were tested. RNA was extracted using Amsbio's ExpressArt FFPE Clear RNA Ready kit from formalin-fixed paraffin-embedded (FFPE) tissue. RNA-seq libraries were prepared using 20-100 ng total RNA and subsequently enriched by hybridization to the targeted fusion panel. Each sample was sequenced with 76 base-pair paired-end reads on an Illumina MiniSeq at 8 samples per flow cell (~3 million reads per sample). The results were analyzed using STAR aligner and Manta fusion caller.

Results: All 18 cases (100%) were correctly classified by the MiniSeq on-instrument analysis software. The results included the following translocations: *EWSR1-FLI1*; *EWSR1-ERG* [N=4]; *EWSR1-ATF1*; *EWSR1-WT1*; *EWSR1-CREB1* [N=2]; *WWTR1-CAMTA1* [N=2]; *SS18-SSX1*; *TLS-DDIT3*; *YWHAE-NUTM2B*; *JAZF1-SUZ12*; *MYH9-USP6* [N=2]; and *PAX3-FOXO1*.

Conclusion: This preliminary study illustrates the diagnostic utility of RNA-seq libraries using targeted fusion panels, in this case an Illumina-developed assay. A streamlined 8-sample run workflow can be performed manually, from paraffin block to final result, in 5-6 days, with automated library preparation promising even shorter turnarounds. These results suggest this technique may be of value in the routine analysis of STBT harboring known and potentially unique fusion products. While further testing is required, this targeted fusion panel appears to offer an efficient and accurate means of detecting gene fusions using conventional FFPE tissue.

P2–Poster 065 2570716

MAGEA3 EXPRESSION AND CLINICAL CORRELATION IN SARCOMA SUBTYPES

Anthony P. Conley, MD; Wei-Lien Wang; Vinod Ravi; Christina Roland; Neeta Somaiah; Patrick Hwu; Cassian Yee; Andrew Futreal; Alexander Lazar; Jason Roszik
Sarcoma Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA

Objective: MAGEA3 (Melanoma-associated antigen family A3), a member of the cancer-testis antigen family, has been shown to have increased expression in solid tumors, including sarcoma. MAGEA3-specific immunotherapies are currently in development for other cancers.

Methods: Publicly available data from the Cancer Genome Atlas (TCGA) and Cancer Cell Line Encyclopedia (CCLE) was analyzed for MAGEA3 expression in sarcoma subtypes and correlated with survival and other clinical variables. In addition, tumor and normal tissue expression comparisons were performed using data from the Genotype-Tissue Expression (GTEx) project (n = 8,555).

Results: MAGEA3 mRNA expression was available in the TCGA/CCLE for 104 leiomyosarcoma (LMS), 75 undifferentiated pleomorphic sarcoma / myxofibrosarcoma (UPS/MFS), 58 dedifferentiated liposarcoma (DDLPS), 10 synovial sarcoma, 9 malignant peripheral nerve sheath tumor (MPNST), and 46 various sarcoma cell lines. We found that MAGEA3 was highly expressed in UPS/MFS; the expression in these samples was significantly higher than in LMS ($p < 0.05$), DDLPS ($p < 0.001$), and synovial sarcoma ($p < 0.001$). Only UPS/MFS was associated with a survival difference in samples with undetectable MAGEA3 (median survival not reached) compared with detectable MAGEA3 (47.5 months; $p < 0.05$). In the CCLE cell line data variable MAGEA3 expression was noted, however, no

significant associations were observed. Of note, synovial sarcoma contained very low expression of MAGEA3 in TCGA and CCLE datasets.

Conclusion: To our knowledge, this is the first comprehensive analysis of MAGEA3 in multiple sarcoma subtypes. We report a statistically significant association in UPS/MFS and may be amendable to MAGEA3 specific immunotherapies.

P2–Poster 066 2570324

UNDIFFERENTIATED SARCOMA ACCOMPANIED BY INFLAMMATION: A CASE SERIES AND A COMPARISON WITH CONVENTIONAL UNDIFFERENTIATED SARCOMAS

Jun Sugaya[1]; Shintaro Iwata[2]; Yoko Hagiwara[1]; Tsukasa Yonemoto[2]; Hiroto Kamoda[2]; Yasuaki Murata[1]; Takeshi Ish[2]

[1]Orthopedics, Tokyo Women's Medical University, Tokyo, Japan; [2]Chiba Cancer Center, Chiba, Japan

Objective: Patients diagnosed with undifferentiated sarcoma (US) occasionally manifest symptoms of systemic inflammation, such as prolonged spiking fever, weight loss, or a leukaemoid reaction. This tumour type was formerly known as 'Inflammatory malignant fibrous histiocytoma', which is histologically characterized by numerous benign xanthomatous cells admixed with inflammatory cells. Most cases are retroperitoneal, and the prognosis is considered poor. On the other hand, this tumour rarely occurs in the extremities, and its clinical course is incompletely understood. The objective of this study is to identify clinical characteristics of US with inflammation (USI) occurring in the extremities, and to compare it with the conventional US presentation.

Methods: In this study, we defined USI as a tumour histologically diagnosed as US accompanied by an extreme inflammatory infiltrate composed of neutrophils, eosinophils and/or lymphocytes. Clinicopathological information of 9 USI patients and 62 US patients were obtained from 2 tertiary musculoskeletal oncology units. Overall survival (OAS) and event-free survival (EFS) were evaluated using the Kaplan–Meier method. Differences between the 2 groups were statistically analysed using the log-rank test and the Cox proportional hazards regression model.

Results: The median age at diagnosis of USI was 58 years (range, 29–81 years), and 6 patients were female. Continuous fever and elevation of white blood cell (WBC) counts, aspartate/alanine transaminase (AST/ALT), or c-reacting protein (CRP) level at presentation were observed in 8, 6, 4 and 8 patients, respectively. All patients underwent definitive surgery, including 3 amputations; sufficient surgical margins were achieved in all patients except 1. The median time for improvement of fever and WBC count, AST/ALT or CRP level normalisation were within 3, 6, 13 and 16.5 days after surgery, respectively. Five patients relapsed and 2 died of disease. Compared with conventional US cases, USI cases were significantly associated with larger tumours (median 13 cm vs. 8 cm, p = 0.026) and younger patients (median 58 years old vs. 70 years old, p = 0.029). The 5-year OAS of USI and US cases were 67% and 82% (p = 0.38) and that of EFS were 42% and 56% (p = 0.30), respectively.

Conclusion: USI occurring in the extremities have characteristics distinct from conventional US cases. USI had a tendency to show poorer survival comparing with conventional US.

P2–Poster 067 2566054

RETROSPECTIVE STUDY BETWEEN FNCLCC GRADE 2 AND GRADE 3 CASES IN RESECTABLE SYNOVIAL SARCOMAS

Yusuke Minami, Dr., PhD[2]; Seiichi Matsumoto[2]; Keisuke Ae[2]; Taisuke Tanizawa[2]; Tabu Gokita[2]; Keiko Hayakawa[2]; Yuki Funauchi[2]; Munehisa Kito[2]; Atsushi Okawa[1]

[1]Orthopedic Surgery, Tokyo Medical and Dental University, TOKYO, Japan; [2]Department of Orthopedic Surgery, The Cancer Institute Hospital of The Japanese Foundation for Cancer Research, Tokyo, Japan

Objective: Although FNCLCC grading system is broadly used as histopathological evaluation of soft tissue sarcomas, there are few previous reports about details. In case of synovial sarcomas, FNCLCC grade is at least more than grade 2 due to tumor differentiation. In this study, we compared FNCLCC grade 2 with grade 3 cases at the point of prognosis in synovial sarcomas.

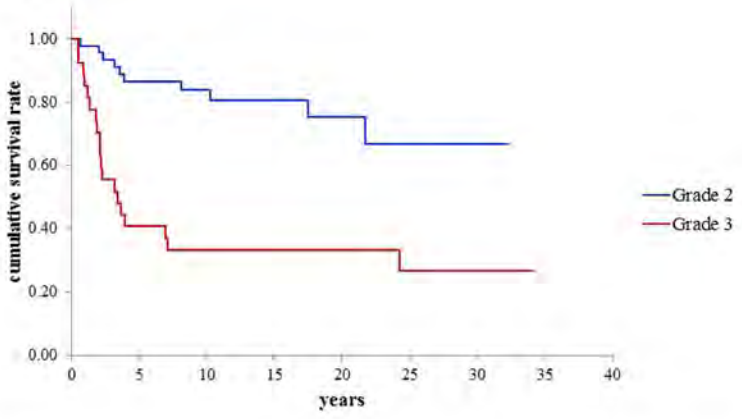
Methods: We investigated seventy-two resectable synovial sarcoma cases without metastasis from 1980 to 2011 in our institution. Moreover, between FNCLCC grade 2 and grade 3 cases, we examined how the presence of adjuvant chemotherapy improves their prognosis.

Results: The study population included forty-five FNCLCC Grade 2 and twenty-seven grade 3 cases. Five-cumulative survival rate and ten-cumulative survival rate were 86.6% and 83.8% in FNCLCC grade 2 cases, 40.7% and 33.3% in FNCLCC grade 3 cases respectively. FNCLCC Grade 3 cases resulted in poor prognosis than FNCLCC grade 2 cases (Figure1) ($p<0.05$). The presence of adjuvant chemotherapy couldn't improve five-cumulative survival rate and ten-cumulative survival rate in both FNCLCC grade 2 and grade 3 cases (Figure2, Figure3) (FNCLCC grade 2 cases; 87.1% and 68.2%, 92.3% and 68.3%, FNCLCC grade 3 cases; 50% and 50%, 27.2% and 18.1% respectively) (Grade2;p=0.85, Grade3;p=0.11).

Conclusion: FNCLCC grading system could be helpful

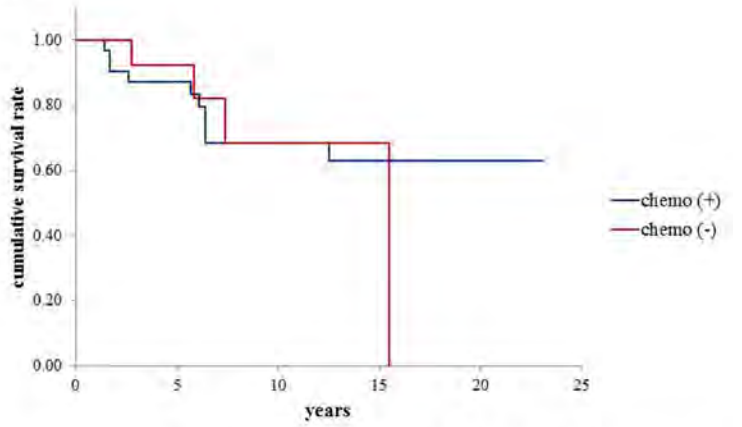
for the prediction of prognosis in resectable synovial sarcomas without metastasis. The presence of adjuvant chemotherapy couldn't improve their prognosis. It would be necessary that new drugs should be developed for synovial sarcomas, especially FNCLCC grade 3 cases, which resulted in poor prognosis.

Figure1



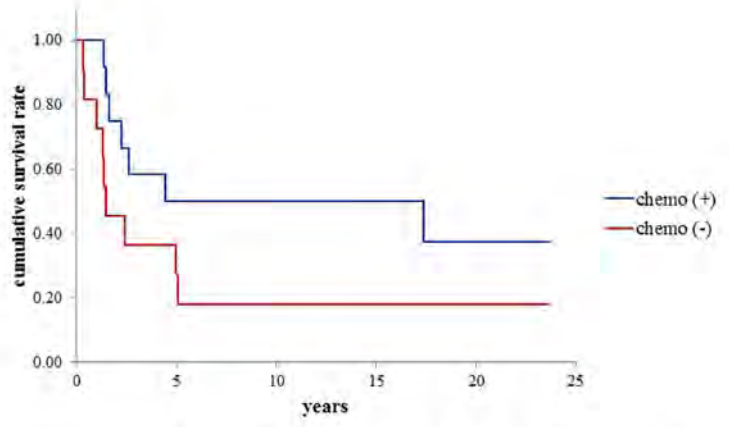
FNCLCC Grade 3 cases resulted in poor prognosis than FNCLCC grade 2 cases.

Figure2



The presence of adjuvant chemotherapy couldn't improve five-cumulative survival rate and ten-cumulative survival rate in FNCLCC grade 2.

Figure3



The presence of adjuvant chemotherapy couldn't improve five-cumulative survival rate and ten-cumulative survival rate in FNCLCC grade 3.

P2–Poster 068 2570484

GRM1 EXPRESSION IN CHONDROMYXOID FIBROMAS AND OTHER BONE AND SOFT TISSUE TUMORS

Arjen H. Cleven, MD, PhD[1]; Olaejirinde Olaofe[2]; Georgios Agrogiannis[3]; Inge Briaire-de Bruijn[1]; Karolin Nord[4]; Pancras Hogendoorn[1]; Karoly Szuhai[1]; Judith V. Bovée[1]

[1]Pathology, Leiden University Medical Center, Leiden, Netherlands; [2]Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University, Ile-Ife, Nigeria; [3]Pathology, School of Medicine National and Kapodistrian University of Athens, Athens, Greece; [4]Department of Clinical Genetics, University and Regional Laboratories, Skåne University Hospital, Lund, Sweden

Objective: Recently it was reported that glutamate receptor gene GRM1 is upregulated via gene fusion and promoter swapping in 90% of chondromyxoid fibromas (CMFs). Therefore we evaluated the usefulness of GRM1 immunohistochemistry as an easy applicable diagnostic marker for CMF.

Methods: Immunohistochemistry was performed for GRM1 (clone D5H10) on tissue microarrays constructed from decalcified formalin-fixed paraffin-embedded tissue of 19 CMFs, 16 chondroblastomas, 66 giant cell tumors of bone, 6 aneurysmal bone cysts, 158 osteosarcomas, 35 conventional chondrosarcomas, 20 clear cell chondrosarcomas, 8 mesenchymal chondrosarcomas, 32 dedifferentiated chondrosarcomas and many soft tissue sarcomas (n=75), including leiomyosarcomas, liposarcomas, rhabdomyosarcomas, solitary fibrous tumors, synovial sarcomas, desmoid-type fibromatosis, angiosarcoma, gastrointestinal stromal cell tumors, malignant peripheral nerve sheath tumors, sarcomas nos, dermatofibrosarcoma protuberans, myxofibrosarcoma, lipomas, diffuse type tenosynovial giant cell tumor and myxomas.

Results: We observed moderate/strong intensity staining of GRM1 in more than 80% of CMFs as well as in more than 80% of chondroblastomas, giant cell tumors of bone and aneurysmal bone cysts. In malignant bone tumors, GRM1 was also frequently expressed; in 40% of clear cell chondrosarcomas, 43% of conventional chondrosarcomas, 44% of dedifferentiated chondrosarcomas, 25% of mesenchymal chondrosarcomas and 61% of osteosarcomas. Strikingly, also more than 98% of all soft tissue sarcomas were positive for GRM1.

Conclusion: GRM1(clone D5H10) positive staining is a frequent finding in benign and malignant bone and soft tissue tumors other than CMF, implicating

that GRM1 (clone D5H10) immunohistochemistry has a low specificity and therefore cannot be used as a diagnostic marker for CMF. Since previous data showed that GRM1 expression at RNA levels was remarkably high in CMF compared to no or low expression in other tested tumors, detection of GRM1 RNA expression could be of additional value, although no reliable antibody is identified for this purpose yet.

P2–Poster 069 2554214

INSTRUMENTS AND GLOVES AS A SOURCE OF WOUND SEEDING IN SOFT TISSUE SARCOMA SURGERY

David Berger-Richardson, MD; Aaron Pollett; Peter Ferguson; Jay Wunder; Anthony Griffin; Roland Xu; Carol Swallow Mount Sinai Hospital, Toronto, ON, Canada

Objective: It has been hypothesized that following the extirpative phase of a sarcoma resection, malignant cells harboured on instruments and gloves can be exfoliated into the tumour bed and surgical wound, leading to recurrence. No evidence exists to support or refute this hypothesis. The purpose of this study was to determine whether sarcoma cells are present on surgical instruments and gloves, and whether such cancer cells retain viability and proliferative potential.

Methods: In a prospective clinical trial, we enrolled consecutive patients undergoing wide local excision (WLE) of extremity sarcoma. At a stipulated time point during surgery, surgeons' instruments and gloves were irrigated separately with normal saline, and the effluent collected, centrifuged and examined by microscopy. To ensure that microscopic detection of STS cells would be possible, the same protocol was followed for incisional biopsies performed for soft tissue masses of the extremity.

To examine the potential of harboured cells to survive and subsequently grow, cell lines (U2OS, STS 109, HEK293, DLD-1, HeLa, MDA MB-231) were seeded onto a stainless steel surface or a latex glove, left to air dry at room temperature, and washed off at serial time points. Effluent was collected, stained with propidium iodide to determine viability, and cultured by limiting dilution.

Results: In the cohort of patients undergoing incisional biopsy, washings obtained intra-operatively were positive for malignant cells on instruments and gloves in 73% and 36% of cases, respectively, validating the technique (n=11). In cases of WLE of extremity STS, there were no malignant or suspicious cells detected on either instruments or gloves (n=44).

For all cell lines investigated, >80% of cells seeded onto surgical steel were viable for a minimum of 10 mins, and on latex gloves for a minimum of 20 mins, and were capable of proliferation.

Conclusion: For procedures during which there is a high likelihood of direct contact with malignant tissue, such as incisional biopsy or marginal excision, sarcoma cells are retained on surgical instruments and gloves; such cells are viable for at least 10-20 minutes in room air. By contrast, there were no cases of detectable contamination of instruments or gloves during WLE of STS of the extremity. Routine changing of instrument trays and drapes have important financial and environmental consequences. Routine implementation of these practices may not be justified.

P2–Poster 070 2557681

ONCOLOGICAL OUTCOME AND QUALITY OF LIFE AFTER HINDQUARTER AMPUATION FOR SARCOMA: IS IT WORTH IT?

Winan van Houdt, MD, PhD[1]; Anthony Griffin[2]; Jay Wunder[2]; Peter Ferguson[2]
[1]Surgical Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; [2]Musculoskeletal Oncology Unit, Mount Sinai Hospital, Toronto, ON, Canada

Objective: Hindquarter amputations for sarcoma are associated with high complication rates, long rehabilitation times and drastically impaired mobility and can severely impact a patient's functional and social outcome. The goal of this study was to determine prognostic factors for oncologic outcome and evaluate quality of life after resection, in order to better select patients who are more likely to benefit from this operation.

Methods: Our prospectively collected sarcoma database was searched for patients treated with a hindquarter amputation for bone or soft tissue sarcoma between 1989 and 2015. Clinical and histopathological features were analyzed for their prognostic value using Kaplan-Meier and Cox proportional hazard analysis. Performance status, ambulatory status and pain were assessed from the hospital charts and clinical records in patients who were alive 1 year following surgery.

Results: The study included 78 patients of whom 62 presented with localized disease and were treated with curative intent, while 16 presented with metastatic disease. Median hospital stay was 25 days (6-217 days) and 55 patients (70%) had at least 1 complication. In-hospital mortality was 6% (5 patients) due to peri-operative complications. Patients with metastases at presentation had a significantly worse outcome, with a median survival of 5 months (0-38 months). Patients treated with curative intent had a 5 year overall survival of 39.8% (95% CI ±12.7%). 47 patients survived more than 1 year after surgery. Estimated 5-year local recurrence-free survival was 85.5% (95% CI±10.6%) while estimated 5-year metastasis-free survival was 41.4% (95% CI±13.5%). Age >65 years and tumor size >=15

cm was correlated with worse survival. Patients treated for recurrent sarcoma had the same outcome as patients with primary sarcoma. The long term performance status, ambulatory status and severity of pain varied widely, with approximately half of the patients having an acceptable performance status with reasonable pain levels and mobility. Younger patients had better ambulatory and performance status, but experienced more pain than the older patients.

Conclusion: Hindquarter amputations for sarcoma are still indicated for a select group of patients. Younger patients are more likely to benefit from this surgery in terms of survival and long term function. However, for older patients with large tumors and significant comorbidity, a hindquarter amputation might be an unreasonable treatment option.

P2–Poster 071 2525270

ASSOCIATION OF CORE NEEDLE BIOPSY TRACT RESECTION WITH LOCAL RECURRENCE IN EXTREMITY SOFT TISSUE SARCOMA

M. Ather Siddiqi[2]; Han-Soo Kim[1]; Jong Woong Park[1]; Ilkyu Han, MD, PhD[1]

[1]Orthopedic Surgery, Seoul National University Hospital, Seoul, Korea (the Republic of); [2]Department of Orthopaedic Surgery, Liaquat National Hospital and Medical College, Karachi, Pakistan

Objective: Percutaneous core needle biopsy (CNB) is being used increasingly as an alternative to open biopsy for diagnosis of extremity soft tissue sarcoma (STS). In open biopsy, resection of the biopsy tract is recommended because of the risk of tumor seeding along the biopsy tract. In CNB for extremity STS, however, due to the minimal tissue violation of the CNB, the risk of tumor seeding and subsequent local recurrence (LR) along the biopsy tract remains unclear. Thus, whether or not the biopsy tract needs to be resected remains controversial and little literature exist to address this issue. We sought to address this question by comparing the LR rates between the patients with their CNB tracts resected at the time of surgery and those without. We hypothesized that patients without their CNB tracts resected would have a higher risk of local recurrence as a result of CNB tract seeding.

Methods: 116 patients who underwent CNB prior to surgery for previously untreated non-metastatic extremity STS were reviewed. Among the patients who underwent CNB prior to surgery for previously untreated non-metastatic extremity STS, 36 patients who did not have CNB tracts resected (CNB-NR) were matched with 36 who had CNB tracts resected (CNB-R), for the tumor and treatment characteristics that are known to affect LR. Minimum follow-up was 1.0 years (mean, 4.5 years).

Results: Two patients (6%) developed LR in 5 and 13 months in the CNB-R group, whereas 3 patients (8%) developed LR in 13, 19 and 120 months in the CNB-NR group (P = 0.643). On Kaplan−Meier analysis, there was no significant difference between the two groups in metastasis–free survival (73.9%±7.5 for CNB-R group vs. 74.0%±7.5 for CNB-NR group, p = 0.786) and LR-free survival (94.3%±3.9 for CNB-R group vs. 93.8%±4.3 for CNB-NR group, P = 0.747).

Conclusion: Our data suggest any influence of a CNB tract resection on LR, within the limitations of this study, is likely to be of minor clinical importance in extremity STS. Although it would be prudent to resect CNB tract in most cases, not resecting the CNB tract is a feasible option if identification or removal of the CNB tract proves difficult.

P2–Poster 072 2570188

BIOPSY TRACT SEEDING: HISTOPATHOLOGICAL CONFIRMATION AND RELEVANCE IN CLINICAL PRACTICE

Irene Barrientos-Ruiz, MD[1]; Eduardo J. Ortiz Cruz[1]; Jose Serrano-Montilla[2]; Daniel Bernabeu-Taboada[1]; Juan Jose Pozo- Kreilinger[1]

[1]Pathology Department, Musculoskeletal Oncology Unit, University Hospital La Paz, Madrid, Madrid, Spain; [2]Traumatology and Orthopedics Department, Musculoskeletal Oncology Unit, University Hospital Rey Juan Carlos, Mostoles, Madrid, Spain

Objective: The complete resection of the biopsy tract is commonly recommended in musculoskeletal oncology guidelines since it is contaminated tissue that should be resected together with the tumor at the time of the oncologic surgery. We consider the contamination of the biopsy tract as the pathologically detected cell nest in the tissue resected together with the main tumor in the oncologic resection surgery. The aim of the study is to describe the incidence of contamination of the biopsy tract, the factors that can affect it and the relation woth the local prognosis.

Methods: This is a retrospective study with prospectively collected data from 221 sarcoma cases treated in a single center since 2000 until March 2013. 43 of the 221 patients were excluded due to lost of follow up or the biopsy samples resected with the main tumor were not eligible for the pathological analysis.The statistical analysis was performed by using SPSS software version 16.0 (SPSS, Chicago, Illinois). Minimum follow up was 24 months (24-150).

Results: 21 out of 180 biopsy tracts were contaminated (11%). 32% of the open biopsies and 0.8% of the percutaneous core needle biopsies had cell seeding (p<0.001). The contamination of the biopsy tract in soft tissue sarcomas (16%) was higher than bone sarcomas (5,4%) p=0.023. The local recurrence free survival (LRFS) was longer in patients without contaminated tracts (p<0.001).

	Contaminated Biopsy track	NOT Contaminated Biopsy track	Statistical significance (p) RR for 95% confidence interval
Bone sarcoma Soft tissue sarcoma	4 (5.4%) 17 (16%)	70 (94.6%) 89 (84%)	p=0.023 RR (CI 95%)=3,343 (1,076-10,382)
Neoadjuvant therapies • Chemotherapy • No adjuvant • Radiotherapy • Both	 3 (6.1%) 18 (16.1%) 0 0	 46 (93.9%) 94 (83.9%) 11 8	p=0.1
Biopsy • Open • Percutaneous	20 (32.3%) 1 (0.8%)	42 (68.7%) 117 (99.2%)	P<0.001 RR (CI 95%)=55,714 (7,251-428,081)
Grade 1 2 3 4	 2 (11.8%) 4 (10.5%) 15 (12.6%) 0	 15 (88.2%) 34 (89.5%) 104 (87.4%) 6 (100%)	p=0.815
Number of percutaneous procedures 1 >1	 18 (12.5%) 3 (8.3%)	 126 (87.5%) 33 (91.7%)	p=0.358
Tumor margins WR MR	 17/125 (13,6%) 3/35 (8.6%)	 8/125 (86,4%) 32/35 (91,4%)	P=0.411
Location Upper limbs Lower limbs Extra compartmental Axial skeleton	 5 (13.9%) 16 (12.6%) 0 0	 31 (86,1%) 111(87.4%) 14 3	p=0.47
Biopsy performed.... Our center Other hospitals	 3 (2.7%) 18 (26.5%)	 109 (97.3%) 50 (73.5%)	p< 0.001 RR (CI 95%)=13,080 (3,683-46,449)
Stage IA IB IIA IIB III +IV	 1 (8.3%) 1(3.8%) 5 (25%) 4 (7.1%) 10 (15.4%)	 11 (91,7%) 25 (96.2%) 15 (75%) 52 (92.9%) 55 (84.6%)	p=0.215

Univariate chi square analysis of the risk of contamination of the tract according to different variables.

Conclusion: The sarcoma cells can affect both, percutaneous and open biopsies, but in our series the contamination was increased in open biopsy and soft tissue sarcomas. In our hands no-contaminated biopsy tracts had a higher survival without local recurrence. Further studies with more homogeneous population are necessary to confirm these results.

P2–Poster 073 2541530

SURGICAL AND TUMOR-RELATED CONTRIBUTIONS TO INADVERTENT POSITIVE MARGINS AFTER SOFT TISSUE SARCOMA RESECTION

Kenneth R. Gundle, MD[1]; Sanjay Gupta[2]; Lisa Kafchinski[2]; Anthony Griffin[2]; Rita Kandel[3]; Brendan C. Dickson[3]; Peter Chung[4]; Charles Catton[4]; Brian O'Sullivan[4]; Peter Ferguson[2]; Jay Wunder[2]
[1]Orthopaedics & Rehabilitation, Oregon Health & Science University, Portland, OR, USA; [2]University of Toronto Dept of Surgery, Mount Sinai Hospital, Toronto, ON, Canada; [3]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada; [4]Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada

Objective: The context of a positive surgical margin after soft tissue sarcoma(STS) resection affects local recurrence(LR) risk, with the highest LR rates seen after inadvertent positive margins(IPM). This study aimed to elucidate tumor and surgeon-related contributions to IPM. Cumulative probability of LR with death as a competing risk was the primary outcome.

Methods: Retrospective review of a tertiary center database identified STS patients between 1989 and 2014. Tumors of the retroperitoneum, DFSP or well-differentiated liposarcoma, and metastatses at presentation were excluded. Patients with IPM were classified into two groups, by the context of their positive margin: tumor or surgery related.

Results: Of 2,234 resected STS, 309 had positive margins and 103(4.6%) met IPM criteria. The 103 cases were categorized as surgery(73%) or tumor-related(22%), or indeterminate(5%). Their mean follow-up was 52 months, with a median age of 66(range 21-97). There were differences in positive margin location between groups, with the deep margin often affected in surgery related IPM(65% vs 9%, p<0.001). The groups differed in tissue type in which IPM occurred(p=0.01), with surgery related IPM occurring frequently in muscle(36%) and tumor related IPM occurring often in subcutaneous tissues(39%). Surgery related IPM had larger tumor diameters(11 vs 7.5cm, p=0.002). The subtype distribution differed(p=0.036), with tumor related IPMs consisting predominantly of myxofibrosarcoma(30%, 7/23) and undifferentiated pleomorphic sarcoma(UPS, 52%, 12/23). There was no difference in age(p=0.52), follow-up(p=0.33), grade(p=0.88), and use of adjuvants(p=0.17).

The cumulative probability of LR in patients with IPM, with death as a competing event, was 27%(95%CI 18-35) at 5 years and 34%(95%CI 24-45) at 10 years. The risk of all-cause mortality in the study was 37%(95%CI 25-44) at 5 years and 45%(95%CI 32-54) at 10 years. There was no difference in the cumulative probability of LR(p=0.98) or OS(p=0.71) between the two groups.

Conclusion: Patients with IPM after STS resection have substantial risk for LR. Although this study identified distinct surgical and tumor-related contributions to IPM, no differences were seen in LR or OS rates between the two groups. These results corroborate with imaging studies showing a proportion of UPS and myxofibrosarcoma with infiltrative behavior and elevated risk of IPM and thereby LR. These cases provide insights that may aid surgeons in avoiding IPM and their poor clinical outcomes.

P2–Poster 074 2543689

FEASABILITY AND RESULTS OF SURGERY WITH FREE FLAP COVERAGE AFTER ISOLATED LIMB PERFUSION FOR SOFT TISSUE SARCOMA

Olivier Camuzart[1]; Andrea Cavalcanti[1]; Françoise Rimareix[1]; Olivier Mir[2]; Philippe Terrier[3]; Cecile Le Péchoux[4]; Axel Le Cesne[2]; Charles Honoré, MD, PhD[1]
[1]Surgical Oncology, Gustave Roussy Cancer Campus, Villejuif, France; [2]Medical Oncology, Gustave Roussy Cancer Campus, Villejuif, France; [3]Pathology, Gustave Roussy Cancer Campus, Villejuif, France; [4]Radiotherapy, Gustave Roussy Cancer Campus, Villejuif, France

Objective: To evaluate short and long term results after of surgery with free flap coverage after isolated limb perfusion (ILP) for soft tissue sarcoma (STS).

Methods: We retrospectively analyzed the files of all patients treated in our single tertiary care center with an ILP for a STS between 2000 and 2016 to select patients who had surgery with free flap coverage. Preoperative, operative, postoperative data and the long-term characteristics were analyzed.

Results: Among 177 patients, who had an ILP, 145 were subsequently operated and 24 had wound coverage with a free flap (17%). The median tumor size was at ILP 5 cm [range: 2-30]. Before ILP, 15 patients had already been operated at least once before (63%), 14 had previous chemotherapy (58%), 4 had previous radiotherapy (17%). Most tumors types (54%) were of uncertain differentiation or undifferentiated sarcoma, all of them were grade 2 or higher. Surgery was performed after a median time of 77 days after ILP [range: 51-114]. After surgery, 5 patients (21%) experience specific complication related to the flap: one deep hematoma, two flap venous thrombosis, one arterial thrombosis and one superficial flap necrosis. Three patients (12.5%) required reoperation with a flap salvage in one and subsequent early amputation in two patients (8%). R0 resection was achieved in 23 patients (96%). A complete pathological response was seen in 13 patients (54%). After a median follow-up of 41 months, 4 patients had a local relapse (8%).

Conclusion: Using free flap coverage in soft tissue sarcoma surgery after isolated limb perfusion is safe and feasi-

ble. It enables limb salvage in 92% of heavily pretreated patients. Nevertheless, the consequences of a flap failure are severe, with a loss of the limb in 2 thirds of the cases.

P2–Poster 075 2570195

SURGICAL MANAGEMENT OF LOCALLY RECURRENT SOFT TISSUE SARCOMA: PREVIOUS SURGICAL SCAR RESECTIONS REDUCE THE RISK OF SUBSEQUENT LOCAL RECURRENCE

Tabu Gokita, MD; Seiichi Matsumoto; Keisuke Ae; Taisuke Tanizawa; Keiko Hayakawa; Yuki Funauchi; Munehisa Kito
Orthopedic Oncology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Objective: Local control for recurrent soft tissue sarcoma (STS) is challenging. Optimal surgical margin for recurrent tumors is still controversial. This is because there is no sufficient analysis about how to deal with the previous surgical scars. The purpose of this study was to examine the impact of surgical scar resection on local control in recurrent STS.

Methods: A total of 137 patients with recurrent extremity/trunk sarcomas were enrolled in this retrospective study. All patients underwent wide resection for recurrent tumor in our institute between 1978 and 2010. In principle, recurrent tumor was resected with complete resection of previous surgical scar. However, if previous scar was widespread and huge functional impairment was anticipated, wide resection against only recurrent tumor was administered. The prognostic influence of previous surgical scar resection and other clinic-pathological characteristics were examined by the Kaplan–Meier survival analysis with log-rank tests.

Results: Median follow-up period was 73 months. The 5-year OS was 73.7%. The local recurrence free survival and recurrence free survival at 5-years was 66.7% and 48.4%, respectively. Only 27% (31 out of 137 patients) received radiation therapy pre or post-surgery for recurrent tumor. Previous surgical scar was completely resected in 84 patients (61.3%). A previous scar resection ($p=0.02$) and histologically low grade tumor ($p<0.001$) was associated with a lower rate of subsequent local recurrence. As a time from previous surgery to recurrent surgery became longer, subsequent local recurrence rate in patients without scar resection gradually decreased (3 years 47.1%, 4 years 35.7%, 5 years 30%, respectively), and there was no recurrence more than 6 years regardless of scar resection.

Conclusion: Previous surgical scar resection reduced the risk of subsequent local recurrence.

Histological grading is also important factor in the local control of recurrent tumor.

P2–Poster 076 2563279

INTRAOPERATIVE OPTICAL COHERENCE TOMOGRAPHY FOR SOFT TISSUE SARCOMA SURGICAL MARGIN ASSESSMENT

Laura E. Selmic, BVetMed (Hons), MPH[1]; Kelly J. Mesa[3]; Elizabeth A. Driskell[2]; Jonathan Samuelson[2]; Jennifer Reagan[1]; Marina Marjanovic[3]; Stephen A. Boppart[3]
[1]Department of Veterinary Clinical Medicine, University of Illinois at Urbana-Champaign, Urbana, IL, USA; [2]Department of Pathobiology, University of Illinois at Urbana-Champaign Urbana-Champaign, Urbana, IL, USA; [3]Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign, Urbana-Champaign, IL, USA

Objective: Surgical margin assessment is important for identification of residual local disease. The “gold standard” for assessment of surgical margins is post-operative histopathology and intra-operative frozen sections. Often intra-operative assessment is limited to only 1-2 small areas due to time constraints. Optical coherence tomography (OCT) is an alternative solution for intraoperative assessment of surgical margins allowing visualization of the microstructure of the surgical margins over a larger surface area within seconds. Prior to evaluation in humans, we conducted a study of intraoperative OCT imaging in pet companion animals with soft tissue sarcomas to assess the optical tissue properties of soft tissue sarcomas and their delineation from normal soft tissues. The primary aim was to create a training data set of the first 20 sarcomas to allow correlation of normal and abnormal features of surgical margins between OCT and histology. The secondary aim was to determine the diagnostic accuracy, sensitivity-specificity, and intra-inter-observer variability of OCT for detection of incomplete margins after surgical excision of sarcomas.

Methods: Pet companion animals with spontaneous soft tissue sarcomas underwent excision of their tumors and 4 areas of interest were imaged with a commercial OCT imaging system (Envisu C2300, Bioptigen) under IACUC approved protocols. Histology sections from these areas were taken for correlation with OCT images.

Results: Multiple types of normal tissue and delineation between these tissues and tumor were seen in imaged specimens. A representative OCT cross-sectional image of an excised feline sarcoma showing adipose, muscle, and tumor tissue, and with adipose-muscle and muscle-tumor tissue boundaries is shown in Fig. 1. Differences in scattering intensity in Fig. 1A helps to identify a tumor area (as shown encircled in the orange dashed line), while muscle tissue in the remaining areas of the image appears more homogenously lower scattering at these resolutions. The structural dissimilarity between adipose tissue and muscle tissue is clearly seen in Fig. 1B, with the boundary between these tissue types being identified by the blue arrow. The

images shown in Figs. 1A and 1B demonstrate the potential for OCT to differentiate among tissue types associated with soft tissue sarcomas.

Conclusion: Intraoperative imaging results show that OCT has potential for identification of soft tissue sarcoma from surrounding normal tissues at surgical margins.

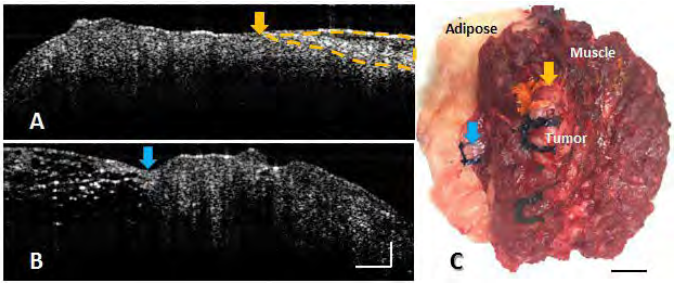


Fig. 1. (A) OCT intensity image of a muscle-tumor boundary (orange arrow). The orange dashed line encircles a region of tumor, with the remaining area composed of muscle. (B) OCT intensity image of a fat-muscle boundary (blue arrow). (C) Excised feline sarcoma specimen with 4 inked areas identifying selected regions submitted for histopathology sectioning and analysis. Adipose, muscle, and tumor tissue regions are identified, along with orange and blue arrows corresponding to the boundaries noted in (A) and (B). Scale bars are 500 μm for (A), (B), and 3 cm for (C).

P2–Poster 077 2553058

TARGET REGISTRATION ERROR COLORMAPS: GOING BEYOND THE SINGLE METRIC FOR SURGICAL NAVIGATION ACCURACY

Prakash R. Nayak, MD[1]; Michelle Arkhangorodsky[2]; Michael Daly[2]; Jimmy Qiu[2]; Harley Chan[2]; Robert Weersink[2]; David Jaffray[2]; Jonathan Irish[2]; Peter Ferguson[1]; Jay Wunder[1]

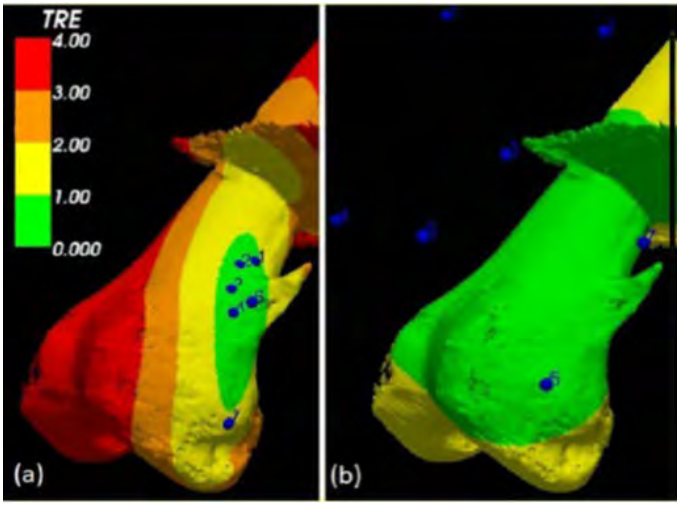
[1]Musculoskeletal Oncology, Mount Sinai Hospital and Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Guided Therapeutics (GTx) Program, Princess Margaret Cancer Centre, Toronto, ON, Canada

Objective: Real-time surgical navigation requires the registration of the image and tracking coordinate systems. Fiducial registration error(FRE) and fiducial configuration significantly impact target registration error(TRE) distribution. TRE has a direct impact on navigation accuracy during tumor surgery where close margins are expected. Purpose:To provide a dynamic,real time volumetric and surface rendering of TRE distribution using a color map of the surgical region of interest.

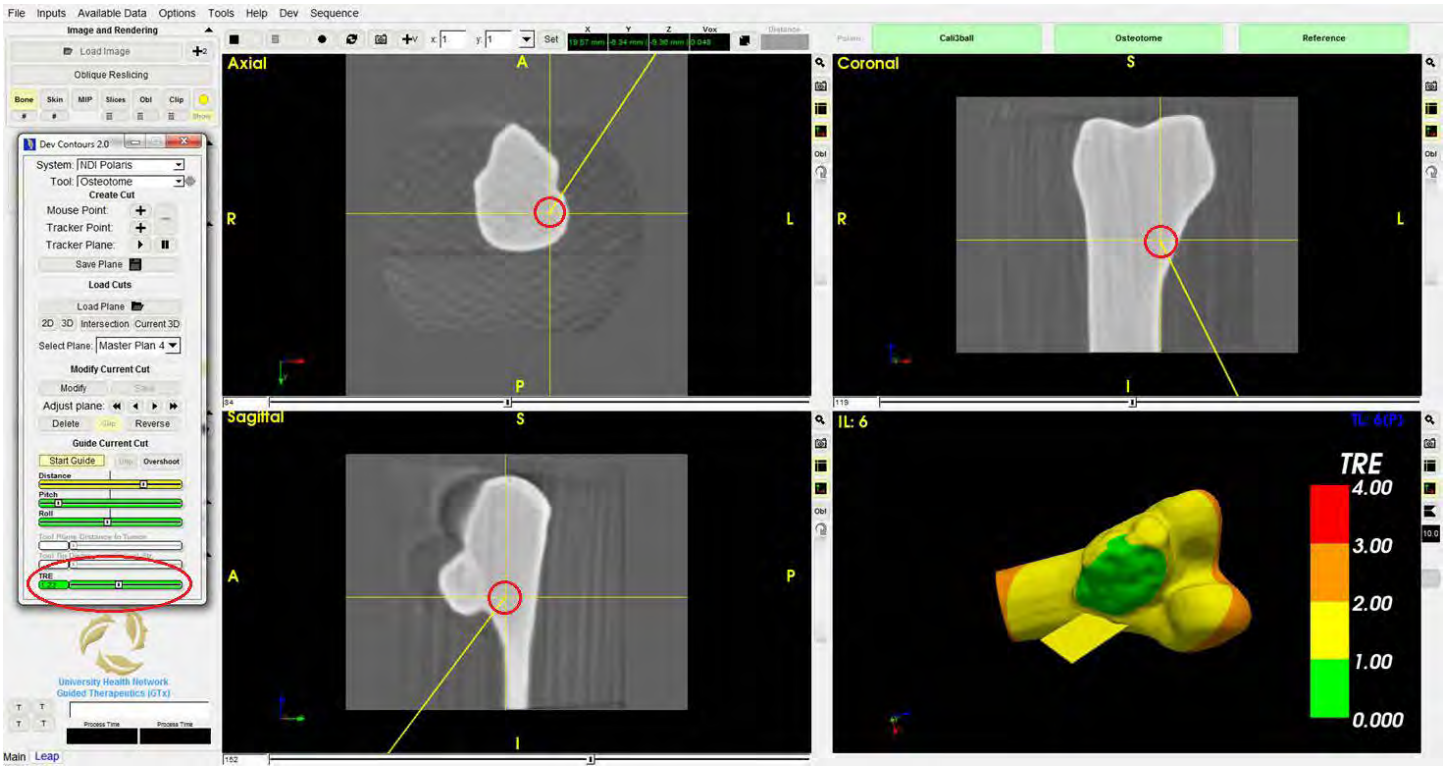
Methods: Once conventional registration is performed using image and tracking coordinates of a defined region of interest,a custom built tumor navigation software iterates over all points of the 3D CT image, storing values of TRE for each point(as calculated from the FRE value and the fiducial configuration).To render an intuitive map each point is assigned a discrete color based on its TRE value in millimeters :0-1 is green,1-2 is yellow,2-3 is orange, 3 and higher is red. (Fig1)

Results: The TRE color maps provide instant,dynamic,real-time,intuitive and accurate surgeon feedback.It has been successfully used as a tool to validate a novel registration method as a part of a larger clinical trial using a custom surgical navigation platform for navigation guided extremity bone tumor surgery.(Fig2) It provides real time target error value at the tool tip at the time of performing osteotomies using pointed(burr) or planar(osteotome,saw) cutting tools. (Fig 3)It has shown utility in a test bed for pre-operative optimization of fiducial configurations for challenging pelvi-sacral tumor resections. (Fig4)

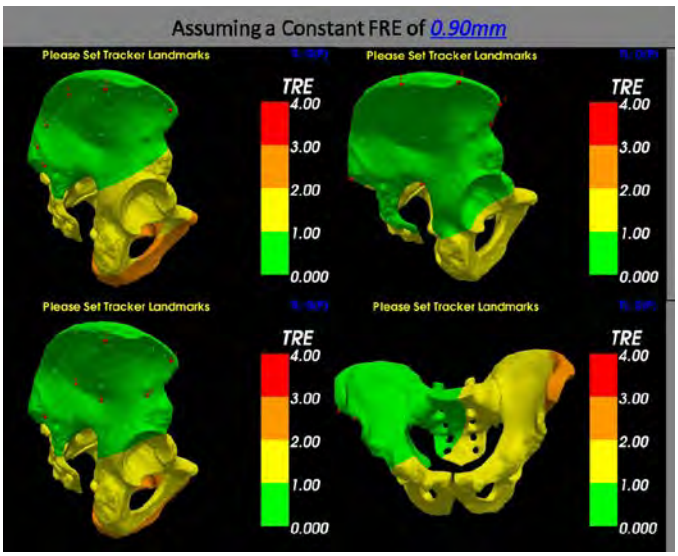
Conclusion: TRE color map is a simple yet powerful visualization tool that provides meaning and simplifies understanding of the impact of fiducial configuration on target error distribution.It is an effective tool for surgeons who use K wires or screws as fiducial surrogates to optimize their placement for an adequate target error distribution. Surgeons performing complex tumor surgery involving close margins may benefit from an intuitive 3D visualization tool for planning and evaluating navigation registrations.



Target registration error (TRE) maps with the legend (values in mm), showing the impact of different fiducial configurations



Live TRE map while navigating an osteotome through a saw bone model of a parosteal osteosarcoma. The TRE value of 1.23mm at the cutting tool tip is shown in the circled sliding bar on the bottom left of the image



Using TRE color map as a tool to test impact of fiducial configurations and optimize them in anatomically challenging pelvi-sacral surgeries.
(legend has values in mm)

P2–Poster 078 2538198

SYMPTOMATIC SMALL SCHWANNOMA IS A RISK FACTOR FOR POSTOPERATIVE NEUROLOGICAL DEFICITS AND CORRELATES WITH DIFFICULTY OF ENUCLEATION

Kensaku Abe; Norio Yamamoto; Katsuhiro Hayashi; Akihiko Takeuchi; Takashi Higuchi; Yuta Taniguchi; Hisaki Aiba; Hiroyuki Tsuchiya
Orthopaedic Surgery, Kanazawa University, Kanazawa, Ishikawa, Japan

Objective: Postoperative neurological deficits of schwannomas are the complications that we want to avoid most. Predicting postoperative neurological deficits is crucial; however, the correlation between preoperative symptoms and neurological findings with postoperative neurological complications has not yet been completely clarified. Here we analyzed the risk factors for postoperative neurological complications.

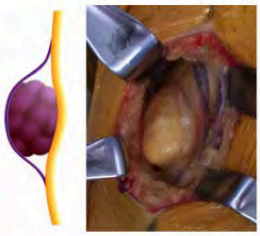
Methods: The study included 131 tumors from 107 patients histologically confirmed as schwannomas, which developed in the extremities and trunk without spinal cord involvement. The correlation between clinical findings and postoperative complications were statistically analyzed.

Results: One-hundred three tumors (78.6 %) had the preoperative neurological symptoms; these symptoms were detected in 93.3% of small tumors (<4 cm^3). We newly de-

fined it as follows about the anatomical location of schwannomas. One is “central type” that normal nerve bundles widely splayed over the tumor’s capsule (tumor located in the central region of the nerve) (Figure 1A). Another is “peripheral type” that easy to enucleate without neurolysis (tumor located in the peripheral region of the nerve) (Figure 1B). Then, static analysis showed a significant difference in the Tinel sign, numbness, and postoperative neurological deficits (p=0.04, 0.006, p<0.001, respectively) (Table 1). Twenty-one cases (16.0 %) showed new postoperative neurological symptoms, including numbness in 12 cases, dysesthesia in 3 cases, pain in 3 cases, and slight motor palsy in 2 cases. In statistical analysis, small tumors (<4 cm^3) significantly correlated with Tinel sign (p<0.001), and was marginally significant with postoperative neurological deficits (p=0.05) (Table 1). Moreover, small tumors (<4 cm^3) accompanying numbness preoperatively significantly correlated with postoperative neurological deficits (p=0.04) (Table 2).

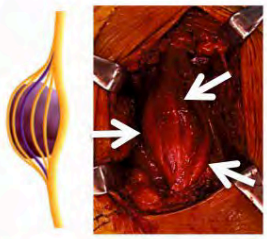
Conclusion: Small (<4cm^3) tumors significantly correlated with the preoperative neurological symptoms. Those tumors accompanying numbness also significantly correlated with the difficulty of the enucleation and postoperative neurological deficits. These findings will help to predict the neurological complication.

Figure 1A



Peripheral type

Figure 1B



Central type

P2–Poster 079 2561413

NEW VESSEL SEALING SYSTEM CAN REDUCE POST-OPERATIVE COMPLICATION ON SURGERY FOR MALIGNANT SOFT TISSUE TUMORS IN THE THIGH

Yoshitaka Ban; Manabu Hoshi; Naoto Oebisu; Hiroaki Nakamura
Osaka City University, Osaka, Osaka, Japan

Objective: New vessel sealing system, Ligasure® , has been used in several fields of abdominal, urological and gynecological surgeries, and many clinical studies have confirmed its efficiency and safety. However, little information is available concerning the clinical applications of this technology for bone and soft tissue tumors of the extremities. We applied this new vessel sealing system and investigated its utility.

Methods: Sixty two patients (36 males and 26 females, mean age: 61 years), who received surgery for malignant soft tissue tumor in the thigh, treated at our hospital between 2002 and 2014, were included in this study. During surgery, Ligasure® was applied to 33 patients (LS group), whereas, 29 patients received tumor surgery without Ligasure®(Control group). The common pathologies were 34 liposarcomas, 5 malignant peripheral nerve sheath tumor, and 4 leiomyosarcoma. Clinical information concerning operation time, blood loss, post-operative amount of drainage, recurrence rate, drainage interval and post-operative complications was retrospectively investigated. Statistical correlation was analyzed with Mann–Whitney U test and p<0.05 was deemed a statistically significant level.

Results: The operation time, blood loss, amount of drainage, recurrence rate, and drainage interval in LS group were 172 minutes, 90ml, 310ml, 15%,and 3 days, whereas those in control group were 195minutes, 90ml,

Table 1: Correlation of neurological symptoms with each factor

		Spontaneous pain		X^2 test	Logistic analysis			Tenderness		X^2 test	Logistic analysis			Tinel sign		X^2 test	Logistic analysis			numbness		X^2 test	Logistic analysis			Postoperative deficits		X^2 test	Logistic analysis		
		Y	N	P-value	OR	95% CI	P-value	Y	N	P-value	OR	95% CI	P-value	Y	N	P-value	OR	95% CI	P-value	Y	N	P-value	OR	95% CI	P-value	Y	N	P-value	OR	95% CI	P-value
Gender	Male	16	58	0.394	0.725	0.307-1.713	0.463	30	44	0.327	0.693	0.332-1.447	0.329	42	32	0.592	0.674	0.264-1.721	0.409	19	55	0.338	0.601	0.244-1.479	0.268	13	61	0.585	0.824	0.226-3.001	0.769
	Female	16	41		1			28	29		1			35	22		1			19	38		1			8	49		1		
Age	>50 years	15	52	0.578	0.706	0.297-1.678	0.431	26	41	0.197	0.536	0.255-1.126	0.1	42	25	0.353	1.424	0.574-3.534	0.446	21	46	0.547	1.072	0.442-2.600	0.878	9	58	0.407	0.479	0.137-1.670	0.248
	<50 years	17	47		1			32	32		1			35	29		1			17	47		1			12	52		1		
Region	Extremity	31	82	0.045	4.388	0.530-36.331	0.17	53	60	0.129	2.221	0.692-7.134	0.18	73	40	0.001	3.683	0.933-14.538	0.063	35	78	0.214	1.52	0.344-6.720	0.581	17	96	0.441	0.171	0.026-1.132	0.067
	Trunk	1	17		1			5	13		1			4	14		1			3	15		1			4	14		1		
Nerve origin	major	20	52	0.324	1.548	0.624-3.840	0.346	34	38	0.453	1.288	0.596-2.782	0.519	55	17	<0.001	4.67	1.846-11.816	0.001	30	42	<0.001	3.04	1.157-7.989	0.024	16	56	0.033	3.92	0.860-17.861	0.078
	minor	12	47		1			24	35		1			22	37		1			8	51		1			5	54		1		
Muscular location	Intermuscle	23	81	0.227	0.47	0.170-1.296	0.144	46	58	0.984	0.835	0.335-2.082	0.698	66	38	0.033	1.914	0.647-5.663	0.241	36	68	0.006	4.581	0.954-21.996	0.057	17	87	0.847	0.228	0.046-1.138	0.071
	Intramuscle	9	18		1			12	15		1			11	16		1			2	25		1			4	23		1		
Neuro-location	peripheral	27	79	0.567	1			46	60	0.677	1			56	50	0.004	1			23	83	<0.001	1			7	99	<0.001	1		
	central	5	20		0.794	0.251-2.509	0.694	12	13		1.216	0.472-3.131	0.686	21	4		3.772	1.018-13.984	0.047	15	10		4.209	1.517-11.681	0.006	14	11		32.04	7.566-135.704	<0.001
Volume	<4 cm^3	22	45	0.029	2.141	0.893-5.131	0.088	29	38	0.612	1.023	0.487-2.152	0.951	50	17	<0.001	6.594	2.487-17.480	<0.001	21	46	0.316	1.611	0.654-3.971	0.3	14	53	0.255	3.742	0.989-14.160	0.052
	>4 cm^3	10	54		1			29	35		1			27	37		1			17	47		1			7	57		1		
Total		32	99					58	73					77	54					38	93					21	110				

Abbreviation: Y yes, N no, OR odds ratio, CI confidential interval

Table 2: Relationship between preoperative neurological symptoms and new postoperative neurological deficits

		Postoperative deficits		X^2 test	Logistic analysis			Postoperative deficits (<4 cm^3)		X^2 test	Logistic analysis		
		Y	N	P-value	OR	95% CI	P-value	Y	N	P-value	OR	95% CI	P-value
Spontaneous pain	Y	5	27	0.943	0.923	0.293-2.910	0.891	4	16	1	0.944	0.217-4.106	0.938
	N	16	83		1			8	32		1		
Tenderness	Y	10	48	0.736	1.149	0.426-3.095	0.784	6	22	0.796	1.216	0.308-4.798	0.78
	N	11	62		1			6	26		1		
Tinel sign	Y	14	63	0.423	1.142	0.387-3.370	0.809	9	38	0.754	0.516	0.100-2.659	0.429
	N	7	47		1			3	10		1		
Numbness	Y	9	29	0.127	1.975	0.693-5.629	0.203	7	13	0.04	4.378	1.088-17.609	0.038
	N	12	81		1			5	35		1		

Abbreviation: Y yes, N no, OR odds ratio, CI confidential interval

402ml,17%,and 3 days , respectively. No significance was observed among these factors. However, concerning complication, the incidence of postoperative hematoma was significantly lower in LS group (p<0.02).

Conclusion: This new vessel sealing system is composed of an electrosurgical generator and a hand piece with a ratcheted scissor mechanism, and this item can offer consistent permanent autologous sealing of vessels without leaving foreign items within the body, such as clipping wire. Ligasure® could effectively prevent post-operative hematoma in surgery for malignant soft tissue tumors.

P2–Poster 080 2556005

MULTI-INSTITUTIONAL SOFT TISSUE SARCOMA REAL TIME PEER REVIEW RADIOTHERAPY QUALITY ASSURANCE ROUNDS

Charles Catton[1]; Colleen Dickie[1]; Simon Xie[1]; Anthony Griffin[3]; Peter Ferguson[3]; Jay Wunder[3]; Lyndon Morley[1]; Conrad Falkson[2]; Michael Sharpe[1]; Peter Chung[1]; David Shultz[1]; Ho Kit Tam[2]; Alex Hammond[4]; Samuel Appiah[1]; Brian O'Sullivan[1]
[1]Princess Margaret Cancer Centre, Toronto, ON, Canada;
[2]Kingston General Hospital, Kingston, ON, Canada;
[3]Mount Sinai Hospital, Toronto, ON, Canada;
[4]London Health Sciences Centre, London, ON, Canada

Objective: To determine the feasibility of multi-institutional Soft Tissue Sarcoma (STS) Real Time Radiotherapy Quality Assurance (RTQA) Rounds, standardize collected metrics and processes, and report our initial experience on the efficiency and effectiveness of these rounds.

Methods: Regional centres involved in multidisciplinary STS RT treatment were invited to attend biweekly RTQA rounds, which aligned with Provincial Sarcoma Services. Data was reviewed from July 2015-April 2016. Real time review was conducted according to provincial privacy regulations using a tele-videoconferencing network approved by all participating institutions. Radical and complex palliative cases were discussed. Metrics collected include number of cases reviewed, timeliness of review, case complexity (follows protocol or individualized plan), intent/management, prescription, target volumes, organs at risk (OARs), pre-tx and on-tx imaging, DVHs, and RT plan. 'Learning moments' were defined as significant discussion about an issue that led to improved team knowledge, standardization of practice, and/or contributed to practice improvement. Discussion included issues on practice/management, dose/fractionation, plan quality and DVHs, target volumes, and RT technique. The group must review, approve or suggest plan adjustments, and reach a consensus for each case reviewed. Plan changes were recorded.

Results: Three large provincial centres consistently attend RTQA rounds. 192 cases have been presented during the study timeframe (81% of all cases). 71% of cases were reviewed before the start of RT or within one week from the onset of RT. The remainder were reviewed greater than one week from the start of RT. The summary of peer review metrics and learning moments are shown in Figures 1 and 2 respectively. 9 plan adjustments have resulted; 6 contour modifications, 2 fractionation changes, and one addition of bolus.

Conclusion: Multi-institutional STS real time RTQA rounds increase the critical mass of specialists evaluating treatment plans for a rare disease. They are feasible and are now routine practice. Chosen quality metrics' effectiveness was demonstrated by discussion in 88-100% of cases, except for on-treatment imaging. 'Learning moments' discussion reflects successful knowledge translation and communication amongst centres engaged in this provincial initiative. 9 clinically important changes were made before the start of RT. Efficiency metrics are expected to improve with automated RT QA programs which are being explored.

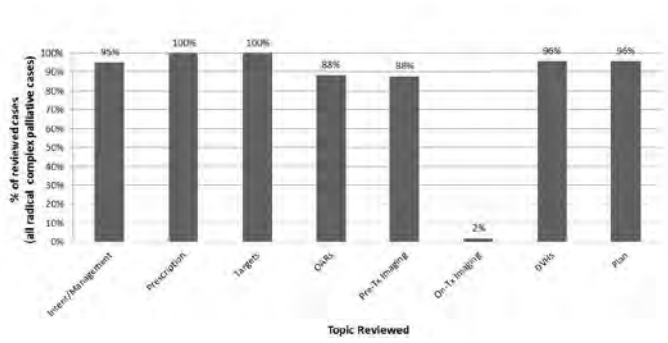


Fig 1: Metrics reviewed and collected during provincial Radiotherapy Quality Assurance Rounds, and the percentage of cases discussed. Radical and palliative cases included from July 2015 to April 2016 (n=192).

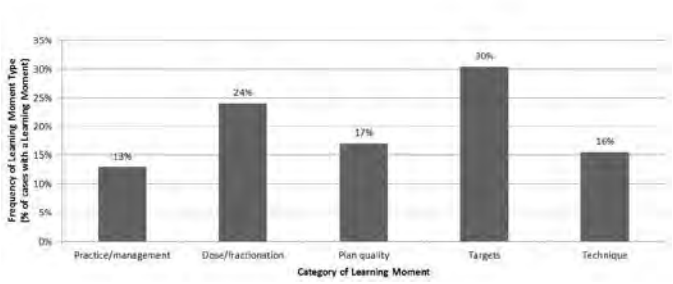


Fig 2: Types of learning moments and their frequency collected during provincial Radiotherapy Quality Assurance Rounds. Radical and palliative cases included from July 2015 to April 2016 (n=192).

P2–Poster 081 2565741

CLINICAL OUTCOMES OF LIMB SALVAGE SURGERY WITH POSTOPERATIVE INTENSITY-MODULATED RADIATION THERAPY FOR MALIGNANT TUMORS OF THE EXTREMITIES

Ryosuke Takahashi[1]; Toshihiro Matsuo[1]; Shintaro Yuki[3]; Shoji Shimose[3]; Katsuhisa Kawanami[1]; Masataka Deie[2]
[1]Orthopaedic Oncology, Aichi Medical University, Nagakute City, Japan; [2]Orthopaedic Surgery, Aichi Medical University, Nagakute City, Japan; [3]Kure Medical Center, Kure City, Japan

Objective: Recently, the standard of care for soft tissue sarcomas has changed from conventional radiotherapy to intensity-modulated radiation therapy (IMRT). IMRT has an ability to conform to the shape of the intended treatment target with a reduced dose to adjacent organs at risk compared to conventional radiation. Another advantage of IMRT is the opportunity to reduce overall treatment time using an integrated boost concept with simultaneously increased dose per fraction to the gross tumor volume.

We evaluated the outcomes and toxicities of adjuvant IMRT following function-preserving surgery in the treatment of patients with soft tissue sarcoma and metastasis of the extremities.

Methods: Between 2013 and 2015, 9 patients with soft tissue sarcoma were treated with limb salvage surgery followed by IMRT. There were 6 men and 3 women, with an average age of 69 years old (range:51 to 87 years). The average tumor size was 12 cm (range: 5-20 cm). Functional mobility of the limb was expressed according to the International Symposium on Limb salvage (ISOLS) scale, which is based on Enneking's criteria for all patients. Morbidity was assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. All patients with these tumors underwent marginal tumor resection and/or chemotherapy at our institute. After conservative surgery, we performed IMRT for all patient. The average duration of postoperative observation was 10 months (range: 3 to 19 months). The average total radiation was 46 Gy (range: 24-60 Gy). Treatments were given once a day over an average of 21 days (range:6-30 days).

Results: The oncological outcomes were: 3 patients were continuously disease-free, 2 patients had no evidence of disease, and 4 patients died from their disease. All patients had no local recurrence after surgery. The average functional score was 81% (range: 53-100). Among the 9 patients, 2 (22%) had grade 1–2 edema, and 1 (11%) had grade 2 joint stiffness. Another patient developed grade 2 acute dermatitis. There were no severe complications such as infection, tissue necrosis, fracture, or nerve palsy.

Conclusion: In this study, IMRT for malignant tumors of the extremities provide excellent local control and preserve good limb function. So far, there have been no neurotoxic or severe complications. Despite the small number of patients, our encouraging results are valuable for limb-preserving surgery of unmanageable tumors of the extremities involving critical neurovascular structures.

Clinical data								
age	gender	location	pathology	period (months)	prognosis	Gly/Fx	Enne king	size(cm)
70	F	hand	pleomorphic leiomyosarcoma	13	DOD	50/25	83	6
77	F	thigh	pleomorphic liposarcoma	12	DOD	60/30	53	15
75	M	forearm	clear cell carcinoma	24	NED	24.0/6	100	7
87	M	thigh	myxofibrosarcoma	3	DOD	50/25	90	15
84	M	upper arm	myxofibrosarcoma	20	CDF	42.5/16	90	5
62	M	thigh	synovial sarcoma	7	DOD	42.5/16	60	20
52	M	thigh	myxoid liposarcoma	16	CDF	50/25	93	20
51	M	thigh	epithelioid sarcoma	15	CDF	50/25	63	12
66	F	upper arm	myxofibrosarcoma	3	DOD	50/25	100	8

P2–Poster 082 2566725

U.S. RACIAL/ETHNIC DISPARITIES WITHIN MODERN TRENDS OF RADIATION TREATMENT OF SOFT-TISSUE SARCOMAS

Felix Chinea; Vivek N. Patel, MD; Deukwoo Kwon; Jonathan Trent; Raphael Yechieli
Radiation Oncology, University of Miami, Parkland, FL, USA

Objective: Equal access to multi-modality treatment options is crucial for proper management in patients with soft-tissue sarcomas. We aim to assess racial/ethnic inequalities in the use of radiotherapy across the United States.

Methods: A total of 17,584 patients diagnosed with soft-tissue sarcoma from 2004-2013 were collected from the Surveillance, Epidemiology, and End Results database. Patients were further evaluated by race/ethnicity: Non-Hispanic White (n= 11,846), Non-Hispanic Black (n= 1,820), Hispanic/Latino (n= 2,466), American Indian/Alaskan Native (n= 111), Asian American/Pacific Islander (n= 1,256), and Unknown (n= 85). Univariate and multivariate analyses were conducted for Non-Hispanic White, Non-Hispanic Black, Hispanic/Latino, and Asian American/Pacific Islander individuals in order to determine whether there were differences in treatment sequences (surgery only vs. adjuvant radiotherapy + surgery vs. neoadjuvant radiotherapy + surgery) over time. Multivariate analyses were adjusted for race, age at diagnosis, marital status, insurance status, T stage, N stage, M stage, and grade.

Results: In univariate analysis for Non-Hispanic White and Hispanic/Latino patients, significant trends were found in decreased adjuvant radiotherapy and increased neoadjuvant. For Non-Hispanic Black patients, significant trends for decreased surgery only and increased neoadjuvant radiotherapy were found. All trends for Asian American/Pacific Islander patients were insignificant. In the multivariate analysis, Non-Hispanic White patients showed significant trends toward decreased adjuvant radiotherapy (OR= 0.96, p< 0.001) and increased neoadjuvant radiotherapy (OR= 1.08, p< 0.001). Non-Hispanic Black patients showed no significant changes in treatment type. Hispanic/Latino patients showed a significant increase in neoadjuvant radiotherapy (OR= 1.20, p= 0.001) and a consequential decrease in adjuvant radiotherapy (OR=.96, P=0.009). Asian American/Pacific Islander patients showed insignificant trends for all treatment sequences.

Conclusion: Inequalities in treatment types exist on univariate and multivariate analysis within different racial and ethnic groups. Non-Hispanic white patients and Hispanic/Latino patients experience decreasing use of adjuvant in favor of neoadjuvant radiation therapy. This shift in treatment sequence has not been observed among non-Hispanic Black patients. Further studies exploring the etiologies for this disparity as well as the clinical impact of these inequalities are warranted.

P2–Poster 083 2567998

COMPLETE RESPONSE OF SOFT TISSUE SARCOMAS TO PREOPERATIVE RADIOTHERAPY

Jungo Imanishi, MD[1]; John Slavin[3]; Fiona Chan[3]; Lester W. Chan[2]; Samuel Y. Ngan[4]; Sarat Chander[4]; Stephen Sharp[5]; Peter F. Choong[2]
[1]Orthopaedic Oncology and Surgery, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [2]Orthopedics, St. Vincent's Hospital, Fitzroy, Victoria, Australia; [3]Pathology, St. Vincent's Hospital, Fitzroy, Victoria, Australia; [4]Radiation Oncology, Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia; [5]The University of Melbourne, Parkville, Victoria, Australia

Objective: The aim of this study was to determine whether complete response (CR) to preoperative radiotherapy (RT) predicts better clinical outcomes, and to reveal which subgroups benefit most from RT.

Methods: Extremity and trunk sarcomas treated with pre-operative RT and surgery at a single institution between 1996-2012 were retrospectively reviewed. Inclusion criteria were (1) non-metastatic sarcomas, (2) receipt of preoperative RT, 50.4Gy over 28 fractions, and (3) ≥2 years follow up for survivors. Exclusion criteria were (a) previous surgery, (b) receipt of preoperative chemotherapy, and (c) >12 weeks from RT completion to surgery. A total of 185 cases, aged 15–95 (mean, 56.9) years, were eligible. Histotypes were undifferentiated pleomorphic sarcoma (82 cases), myxoid liposarcoma (39 cases), myxofibrosarcoma (16 cases), leiomyosarcoma (13 cases), synovial sarcoma (12 cases) and others (23 cases).

Clinico-pathologic information, including patient gender and age, tumor location, size and depth, and follow up status were collected from medical records. Follow up status was updated by information from the state cancer council. Pathologic response was graded by two experienced pathologists according to the percentage of viable area on glass slides. CR was pre-determined prior to the study as no viable tumor cells with ≤5% of severely-altered, i.e. possibly viable area.

Categorial data was compared between CR and non-CR using Chi-Square test. Local-recurrence-free survival (LRFS) and disease-specific survival (DSS) were compared between CR and non-CR, using Kaplan-Meier method and Log-Rank test.

Results: CR was observed in 45 cases (24%). CR rates for undifferentiated pleomorphic sarcoma, myxoid liposarcoma, and other histotypes were 23/82 (28%), 20/39 (51%), and 2/64 (3%), respectively. Univariate analysis revealed the histotypes of undifferentiated pleomorphic sarcoma and myxoid liposarcoma as the only clinico-pathological factor associated with CR (Table 1). No local recurrence was observed in CR group, whereas 21 local recurrences

occurred in non-CR group (5-year LRFS: 100% vs. 84.4 (95% CI: 77.5–91.3)%, *P* = 0.007). Five-year DSS between CR and non-CR were 84.7 (73.1–96.3)% and 76.7 (69.2–84.2)% (*P* = 0.12).

Conclusion: CR can be a surrogate of good local control. Histotype is a strong predictor for radio-sensitivity, however tumour size and depth are not. Further investigation is required regarding what features of undifferentiated pleomorphic sarcomas are related to RT sensitivity.

Table 1. Correlation between clinico- pathologic factors and pathologic response to radiotherapy

Characteristic		CR (*N*)	non-CR (*N*)	*P* value
Histotype	UPS	23	59	<0.0001
	MLS	20	19	
	Others	2	62	
Patient age	≥80 years	3	16	0.34
	< 80 years	42	124	
Patient gender	Male	23	80	0.25
	Female	22	55	
Tumor location	Extremity	41	127	0.94
	Trunk	4	13	
Tumor size	>5 cm	35	101	0.46
	≤5 cm	10	39	
Tumor depth	Deep	42	118	0.12
	Superficial	3	22	

UPS undifferentiated pleomorphic sarcoma;
MLS myxoid liposarcoma

P2–Poster 084 2570435

TRENDS IN UTILIZATION OF RADIOTHERAPY FOR TREATMENT OF SOFT TISSUE SARCOMAS: A POPULATION-BASED ASSESSMENT

Vivek N. Patel, MD; Felix M. Chinea; Deukwoo Kwon; Jonathan Trent; Raphael Yechieli
Radiation Oncology, University of Miami, Parkland, FL, USA

Objective: Patients with soft-tissue sarcomas are often treated by a multimodality approach. Radiotherapy is utilized in the neoadjuvant setting as well as the adjuvant setting to improve local control and overall survival. Contemporary changes in the utilization of these treatments over time has not been evaluated. This study investigates the patterns of use for both surgery and radiotherapy over time in the treatment of patients with soft-tissue sarcomas.

Methods: This is a population-based study utilizing the Surveillance, Epidemiology, and End Result database. Data was extracted from the years 2004-2013 (documentation limitated prior to 2004). Data from a total of 17,584 patients diagnosed with soft-tissue sarcoma was collected. The purpose of this study was to compare the type and sequence of treatment received as follows: surgery alone, neoadjuvant radiotherapy followed by surgery, or surgery followed adjuvant radiotherapy in patient population with high probability of treatement including radiotherapy. A yearly time trend was evaluated using a univariate and multivariate regression model with year at diagnosis as a continuous variable. In the multivariate analysis, we utilized race, age at diagnosis, marital status, insurance status, T stage, N stage, M stage, and grade. Patients with T1 favorable disease, regional, or metastatic disease were not included.

Results: Comparing each year there was a constant utilization rate of surgery revealing no statistical difference in either the univariate and multivariate analyses. There was a decrease in the use of adjuvant radiotherapy from 2004 to 2013 which was statistically significant in both the univariate (OR= 0.97, p< 0.001) and multivariate analyses (OR= 0.97, p= 0.003). Conversely, there was an increase in the employment of neoadjuvant radiotherapy that was statistically significant in univariate (OR= 1.08, p< 0.001) and multivariate analysis (OR= 1.13, p< 0.001).

Conclusion: This population-based study shows that while the proportion of patients receiving surgery alone has not significantly changed, there has been an increase in patients receiving neoadjuvant radiotherapy and consequently a decrease in adjuvant radiotherapy for treatment of patients with soft-tissue sarcomas. This paradigm shift in treatment may have implications on disease outcome.

P2–Poster 085 2560692

COST EFFECTIVENESS ANALYSIS OF NEOADJUVANT VERSUS ADJUVANT RADIOTHERAPY TREATMENT FOR SOFT TISSUE SARCOMA OF THE LOWER EXTREMITIES

Megan Crosmer, Residency[1]; Richard Mather[1]; Perez Agaba[1]; Howard Levinson[2]; William Eward[1]
[1]Orthopaedic Surgery, Duke University, Durham, NC, USA; [2]Plastic Surgery, Duke University, Durham, NC, USA

Objective: Soft tissue sarcomas (STS) are rare, malignant soft tissue tumors that are commonly found in the extremities and are treated with wide local excision and either neoadjuvant or adjuvant radiotherapy (XRT). Neoadjuvant and adjuvant XRT provide equivalent outcomes in terms of local control and overall survival; however, neoadjuvant XRT is associated with increased rates of wound complications while adjuvant XRT is associated with increased risks of fibrosis and lymphedema. The purpose of this study was to compare economic costs and quality of life associated with the adverse events of neoadjuvant versus adjuvant XRT to determine the most cost effective treatment option.

Methods: A Markov decision model was constructed for a cost-utility analysis comparing neo- to adjuvant XRT for extremity STS. Outcome probabilities of fibrosis, lymphedema, and wound healing complications were derived from the literature for both neoadjuvant and adjuvant XRT. Costs of treatment for wound complications, lymphedema, and fibrosis were derived from the Medicare database. Utilities were measured in the form of quality-adjusted life years (QALYs) and were derived from the literature.

Results: The cost of treatments for wound complications, lymphedema, and fibrosis were $7,109.15 for neoadjuvant XRT versus $2,496.56 for adjuvant XRT. Neoadjuvant and adjuvant XRT produced 3.21 and 3.08 QALYs respectively. The incremental cost effectiveness ratio for neoadjuvant XRT was $35,214, making it the preferred therapy. Holding all other variables constant, adjuvant XRT is preferred if the rate of fibrosis is less than 43.8% or if the risk of wound complication is less than 2.4%. Neoadjuvant XRT is preferred if the rate of fibrosis is below 35.9% or if the rate of wound complication is less than 45%. At a fibrosis utility of 0.706 the impact of the complications from the treatment approach are balanced.

Conclusion: In patients receiving radiotherapy for lower extremity STS, neoadjuvant XRT is more costly in terms of treatments for adverse events (wound complications, lymphedema, and fibrosis) than adjuvant XRT. Patients who receive neoadjuvant XRT, however, have improved quality of life as compared to patients receiving adjuvant XRT. As long as willingness to pay exceeds $35,000, neoadjuvant XRT is the preferred cost effective treatment. Individual risks and costs should be taken into account, however, to determine the best treatment for each patient.

P2–Poster 086 2565663

OVARIES ARE IMPORTANT ORGANS AT RISK (OAR) FOR RADIATION THERAPY (RT) TREATMENT PLANNING FOR SOFT TISSUE SARCOMA (STS) OF THE THIGH, GROIN AND BUTTOCK

Konstantin A. Kovtun, MD[1]; Wee-Pin Yeo[1]; Catherine Philips[2]; Akila Viswanathan[1]; Elizabeth H. Baldini[1]
[1]Radiation Oncology, Dana-Farber/Brigham and Women's Hospital, Boston, MA, USA; [2]Diagnostic Radiology Department, Brigham and Women's Hospital, Boston, MA, USA

Objective: Since median age of cancer patients is 65, fertility and estrogen production are not relevant considerations for most women treated with RT. However, for pre-menopausal women and those of child-bearing age, it is crucial to keep dose to ovaries as low as possible. Ovaries are not generally discussed as OARs when planning RT for thigh and buttock STS. We performed a matched pair analysis for these sites to compare dosimetry from plans designed without regard for ovary dose (standard plans) to those with an ovary-sparing approach to assess for potential inadvertent dose delivery to ovaries in the former.

Methods: Standard sarcoma GTV, CTV, and PTV planning volumes and standard OARs (bone, bowel, bladder, rectum) were contoured by a sarcoma dedicated radiation oncologist on CT planning scans for 23 women with STS of the thigh, groin or buttock. In addition to CT, 14 patients had pelvic MRs. Ovaries were contoured and evaluated by 3 physicians. Comparative IMRT plans (50 Gy) were created by an expert sarcoma dosimetrist. Paired-T tests were used to determine dosimetric differences between planning approaches including conformity index (CI) defined as 100% isodose volume divided by target volume.

Table 1. Dosimetric comparisons for thigh and buttock Standard Plans and Ovary-Sparing Plans

	Standard Plan	Ovary-Sparing Plan	p-value
Mean bilateral ovary dose (MBOD)	652 cGy	483 cGy	0.005
Mean ipsilateral ovary dose	1072 cGy	888 cGy	0.03
Mean contralateral ovary dose	235 cGy	78 cGy	0.07
Conformity Index (CI)	1.11	1.19	0.01
Tumor < 10 cm from Pubic Symphysis (n=13) MBOD	809 cGy	533 cGy	0.0004
Tumor >= 10 cm from Pubic Symphysis (n=10) MBOD	527 cGy	460 cGy	0.32
Proximal Medial Thigh MBOD (n=13)	445 cGy	293 cGy	0.008
Other Thigh MBOD (n=6)	95 cGy	19 cGy	0.33
Buttock MBOD (n=4)	2161 cGy	1800 cGy	0.2

MBOD: mean bilateral ovary dose

Results: Median age was 61 years and median tumor size was 8 cm (range 2 – 17). Sites were: proximal medial thigh including groin (13), non-medial or distal thigh (6) and buttock (4). Ovaries were difficult to localize on planning and diagnostic CT scans and easier to identify on MR scans (n=14).

Compared to standard plans, ovary-sparing plans significantly decreased dose to ovaries at the expense of minimally reduced dose conformality, (Table 1). Doses to bone were not significantly different. In subgroup analysis, reduction of mean ovary dose was significant for proximal medial thigh subsites and for tumors < 10 cm from symphysis. Absolute ovary dose was also higher for tumors < 10 cm from symphysis, proximal medial thigh and buttock sites (Table 1). An example of comparative plans is shown in Fig. 1.

Conclusion: Ovary avoidance plans achieve significant ovary dose reduction at the expense of minimal reduction in dose conformality. For thigh, groin and buttock STS in pre-menopausal women, ovaries should always be contoured as an avoidance structure to prevent inadvertent delivery of excess dose to ovaries. This is particularly important for tumors close to the pelvis such as buttock, proximal medial thigh and groin sites. Pelvic MR should be obtained to optimally localize ovaries for contouring.

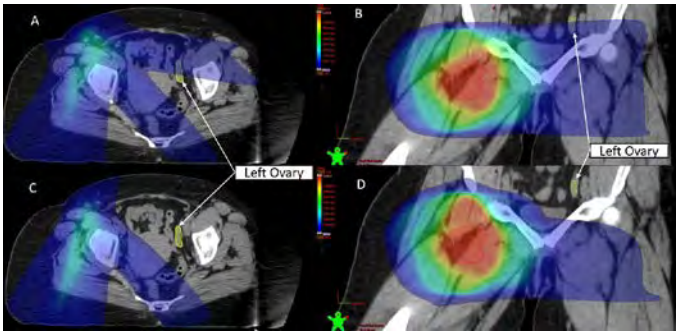


Figure 1. Comparison of a standard plan (A and B) and ovary-sparing plan (C and D) for a patient with a proximal medial thigh soft tissue sarcoma.

P2–Poster 087 2570315

PREGNANCY OUTCOMES AFTER RADIATION THERAPY

Karen De Amorim Bernstein, MD[3]; Saveli Goldberg[1]; Torunn Yock[1]; Yen-Lin Chen[1]; Joseph Schwab[2]; Francis Hornicek[2]; Alex Haynes[4]; John T. Mullen[4]; Gregory M. Cote[5]; Edwin Choy[5]; Jennifer Wo[3]; Thomas F. DeLaney[3]

[1]Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [2]Orthopedic Surgery, Massachusetts General Hospital, Boston, MA, USA; [3]Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [4]Surgery, Massachusetts General Hospital, Boston, MA, USA; [5]Hematology/Oncology, Massachusetts General Hospital, Boston, MA, USA

Objective: Fertility and the childbearing ability are of concern to patients and physicians after treatment with radiation therapy near the reproductive organs, as radiation can cause ovarian and uterine damage. Our goal was to report cases of successful pregnancies after RT.

Methods: This retrospective analysis includes 7 females who received radiation therapy and were able to carry on a pregnancy after RT. Three patients also received chemotherapy. Six patients received radiation therapy to the spine and one patient received radiation therapy to the retroperitoneum. Patients had the following histologies: 2 medulloblastomas, 2 chordomas, 1 osteosarcoma, 1 chondrosarcoma and 1 liposarcoma.

Results: Seven patients were able to carry a pregnancy after completion of radiation therapy. The median age at diagnosis was 24 (age range 19-34). The median radiation dose delivered was 60.3 Gy (range::23.4-71.8 Gy). Four patients received proton therapy only and 3 patients received a combination of photon and proton therapy. With a median follow up time of 7 years, all patients had local control of their primary tumors at the last follow up.

Conclusion: Fertility and future pregnancy were achieved by 7 patients after receiving radiation therapy near reproductive organs. We were not able to capture the number of patients who attempted pregnancy and were unsuccessful, due to lack of specific data clinical data reported on patients who received radiation therapy during child bearing age. Nonetheless, we consider it inspiring and hopeful to report cases of successful pregnancies after RT near reproductive organs to patients who may encounter themselves in the difficult situation of requiring a treatment for a malignant process that can potentially impact their ability to have children.

P2–Poster 088 2562317

A LIMITED INDICATION FOR ADJUVANT RADIOTHERAPY FOR HIGH-GRADE SOFT TISSUE SARCOMA

Shintaro Iwata, MD[1]; Takeshi Ishii[1]; Akira Kawai[2]
[1]Div.Orthopaedic Surgery, Chiba Cancer Center, Chiba, Japan; [2]Div. Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan

Objective: Recent guidelines have recommended adjuvant radiotherapy (aRT) for primary high-grade soft tissue sarcoma (STS), especially for cases with larger-diameter tumours or insufficient surgical margins. However, the specific subtype of high-grade STS that benefits from aRT is unclear. We conducted this retrospective cohort study to develop a better understanding of the indication for aRT in patients with high-grade STS.

Methods: This study was conducted using data from a Bone and Soft Tissue Tumor Registry in Japan run by the Japanese Orthopaedic Association Musculoskeletal Tumor Committee from 2006. Inclusion criteria were as follows: (1) histological diagnosis of high-grade STS , (2) definitive surgery for the primary tumour and (3) a minimum follow-up period of 12 months (for living patients). Overall survival (OAS) and local control rate (LCR) were calculated using the Kaplan–Meier product limit method. Differences in survival were assessed by the log-rank test and the Cox proportional hazard regression method.

Results: A total of 2,924 out of 63,931 all registered patients were enrolled in this study. The follow-up period ranged from 12 to 90 months (median 32 months). aRT was performed in 803 (27%) patients, and more frequently in patients diagnosed with myxofibrosarcoma, those having a trunk tumour with a maximum diameter of >5 cm, and those with insufficient surgical margins (all $p < 0.0001$). The 3-year OAS and LCR were 80.1% and 87.4%, respectively. Multivariate analysis revealed that tumour site (trunk, hazard ratio [HR] 1.75), maximum diameter (>5 cm, HR 1.53) and surgical margins (insufficient, HR 1.96) were statistically correlated with LCR. Surprisingly, aRT itself was a risk factor for local relapse (HR 1.56) in our study. In a subgroup analysis of cases with wide margins, no advantage was observed for aRT. In addition, subgroup analysis for each subtype with insufficient margins revealed that only leiomyosarcoma showed a trend towards better LCR with the addition of aRT (92% vs 61%, $p = 0.14$), whereas no prognostic advantage for aRT was observed for any other subtype.

Conclusion: Our study result showed an opposite effect on the local control of aRT, may be brought by our limited indication for aRT for patients with poorer prognosis. No benefit of aRT for cases with wide surgical margins was observed. Large tumours located in the trunk with insufficient surgical margins might be candidates for aRT, but the suitable subtype that will benefit from aRT remains unknown.

P2–Poster 089 2570319

MINIMALLY-INVASIVE SURGERY USING INTRAOPERATIVE ELECTRON-BEAM RADIOTHERAPY FOR THE SOFT TISSUE SARCOMA WITH TENDON INVOLVEMENT

Akihiko Matsumine, MD, PhD[1]; Masaya Tsujii[1]; Tomoki Nakamura[1]; Kunihiro Asanuma[1]; Takao Matsubara[1]; Takuya Kakimoto[1]; Yuki Yada[1]; Tomohito Hagi[1]; Akinori Takada[2]; Noriko Ii[2]; Yoshihito Nomoto[2]; Akihiro Sudo[1]
[1]Department of Orthopedic Surgery, Mie University Graduate School of Medicine, Tsu City, Mie, Japan; [2]Department of Radiology, Mie University Graduate School of Medicine, Tsu City, Mie, Japan

Objective: The surgical resection of soft tissue sarcoma (STS) with a wide margin sometimes causes functional disability of the affected limb, because a wide resection requires the excision of adjacent structures, including the bones, nerves, arteries, veins and tendons.

Intraoperative electron-beam radiotherapy (IOERT) is designed to provide a large radiation dose to a target tissue while sparing normal tissues. There is a large amount of published work on the use of IOERT in combination with surgery with/without external-beam radiation therapy in the treatment of soft tissue sarcomas.

Although these conventional IOERT has been used to achieve limb preservation without local recurrence, the limb-function has not usually been considered after treatment. We therefore developed a novel minimally-invasive surgical technique using IOERT to reduce the incidence post-operative functional disability in patients with peri-/intra-tendinous STS.

Methods: The study population included five patients who received treatment for distal extremity STSs. After elevating the tumor mass, including the tendon and nerve from the tumor bed with a wide margin, a lead board was inserted beneath the tumor mass to shield the normal tissue. IOERT (25-50 Gy) was then applied, and the tumor excised with care taken to maintain the continuity of the tendon.

Results: In a desmoid patient, local recurrence was observed at a region outside the irradiated field. No cases of neuropathy were observed. The mean limb function score was excellent in all patients. None of the high-grade sarcoma patients had local recurrence or distant metastasis.

Conclusion: In the current study, IOERT was delivered with a wide margin, and the surrounding tissue was completely shielded with a lead board and applicator; the tumor was then excised with a marginal or intralesional margin. Thus, the current surgical procedure should be distinguished from conventional IOERT, which is applied after the resection of the tumor with an aim of reducing local recurrence.

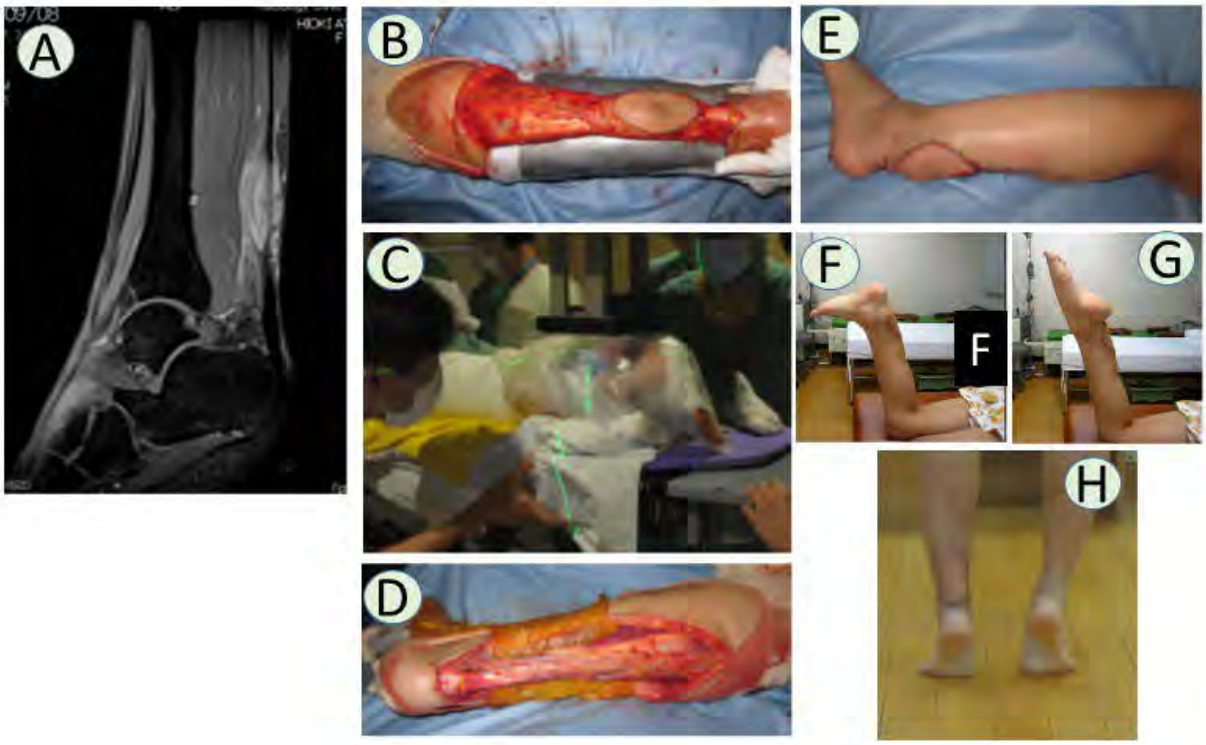
We showed the successful clinical outcomes of minimally-invasive surgery using IOERT in the treatment of extremity STS. Although the current study is only a pilot study with a small number of patients, it shows that this minimally-invasive procedure has the potential to become a standard treatment option for selected patients.

The Clinical Details of the Patients

no.	age	gender	diagnosis	location	condition at initial treatment	involved tendon	location	tumor size (cm)	histologic grade	metastasis	chemotherapy
1	14	f	desmoid	forearm	recurrence three times	FDS, FDP	intratendinous	4	intermediate	no	no
2	21	f	clear cell sarcoma	leg	primary	calcaneal tendon	intratendinous	4	high grade	no	yes
3	28	f	synovial sarcoma	leg	inadequate resection at initial hosp.	calcaneal tendon	peritendinous	0.7	high grade	no	no
4	36	f	clear cell sarcoma	ankle	primary	TP	intratendinous	3	high grade	no	yes
5	62	f	myxofi-bro-sarcoma	forearm	inadequate resection at initial hosp.	EDC	peritendinous	4	high grade	no	no

FDS: flexor digitorum superficialis, FDP: flexor digitorum profundus, TP: tibialis posterior, EDC: extensor digitorum communis

Fig. 1



Surgical procedure and postoperative limb function
(A) T2 weighted-MR image showing clear cell sarcoma located at calcaneal tendon. (B)After the elevation of the tumor mass, including the tendon and nerve from the tumor bed, two 3-mm-thick lead boards were inserted beneath the tumor mass to shield the normal tissue. (C) The patients were transferred to the radiotherapy department, and 35-50 Gy of 12 MeV electrons were delivered. (D) After irradiation, the patients were returned to the operation room, and underwent the marginal/intralesional resection of the tumor, preserving the tendon and nerve. (E) The soft tissue defect was reconstructed using a free musculocutaneous flap. The photographs at the final follow-up time showing the normal ankle movement (F and G) and ability of stand on toe (H).

P2–Poster 090 2567158

RESECTION OF SOFT TISSUE SARCOMA WITH ADEQUATE WIDE MARGIN CAN LEAD TO GOOD LOCAL CONTROL WITHOUT ADJUVANT RADIOTHERAPY

Toshiyuki Kunisada[1]; Tomohiro Fujiwara[1]; Joe Hasei[1]; Hiroyuki Yanai[2]; Toshifumi Ozaki[1]
[1]Orthopaedic Surgery, Okayama University Hospital, Okayama, Japan; [2]Pathology, Okayama University Hospital, Okayama, Japan

Objective: The concept of surgical margin in Japan was published in 1989 by Japanese Orthopaedic Association (JOA), and barrier concept was distinctive compared with Enneking's staging. Initially, 5cm-wide margin was planned to treat soft tissue sarcoma (STS). Lately, high-resolution MRI is available and provides good anatomical location, and 2cm-wide margin can be considered as adequate margin. We evaluated local control and prognosis following resection of STS using JOA surgical margin concept.

Methods: TREATMENT STRATEGY: The concept of JOA surgical margin was applied for all patients. Surgical resection with at least 2cm-wide margin was attempted whenever possible. Marginal or 1cm-wide margin are acceptable when preserving critical organs. Radiotherapy (RT) is conducted postoperatively only for marginal margin or R1 assessed in resected specimen. Chemotherapy is indicated for patients less than 60 years old with deep seated, high grade and large tumor.

PATIENTS: Inclusion criteria are localized STS in the extremities or trunk, intermediate to high grade, limb sparing surgery, primary complete resection at our institution, and minimum 3 years of follow-up. We excluded tumors arising from genetic disease such as NF1. We retrospectively analyzed 75 patients treated between 2007 and 2011 (13 UPS, 10 MFS, 9 myxoid LS, 8 SS, 7 MPNST and 28 others).

Results: Average follow-up was 67 (12-111) months. 21 (28%) patients received inadequate (whoops) resection before referring to our hospital. 10 patients underwent postoperative RT according to our treatment strategy. 21 (28%) patients received chemotherapy. There were 5 (7%) local recurrences with average 23 months after surgery (2 MFS, 2 myxoid LS, 1 pleomorphic LS). Only 1 (myxoid LS) of 10 patients treated with postoperative RT developed local recurrence. Distant metastasis was shown in 16 patients with average 27 months after surgery. 5 year overall survival was 84%.

Conclusion: Many papers demonstrated that resection in combination with RT improved local control rates. Historically in Japan, surgeons have treated STS by achieving safe surgical margin rather than by using adjuvant RT. In this series, resection alone with 2cm-wide margin led to good local control with limb sparing, which is identical to previous reports with surgery plus RT. Adjuvant RT should be given for resection with marginal margin or R1 margin of the resected specimen.

P2–Poster 091 2570753

SURGERY ALONE IS SUFFICIENT THERAPY FOR LOW-RISK SYNOVIAL SARCOMA PATIENTS

Andrea Ferrari[2]; Yueh-Yun Chi[4]; Gian Luca de Salvo[6]; R. L. Randall[5]; Douglas S. Hawkins[3]; Gianni Bisogno[7]; Sheri Spunt[1]
[1]Stanford University School of Medicine, Palo Alto, CA, USA; [2]Istituto Nazionale dei Tumori, Milano, Italy; [3]Seattle Children's Hospital, Seattle, WA, USA; [4]COG Data Center, Gainesville, FL, USA; [5]Huntsman Cancer Institute, Salt Lake City, UT, USA; [6]Istituto Oncologico Veneto, Padova, Italy; [7]Universita degli Studi di Padova, Padova, Italy

Objective: Retrospective analyses suggest that low-risk synovial sarcoma patients can be safely treated with surgery alone, but no prospective studies have confirmed the safety of this approach. We pooled outcome data from two prospective clinical trials utilizing surgery only for low-risk synovial sarcoma to assess outcomes with a surgery only approach and to identify predictors of treatment failure.

Methods: The European Paediatric Soft Tissue Sarcoma Study Group NRSTS2005 trial assigned patients with <= 5 cm grossly resected tumors, regardless of grade, to surgery only. Children's Oncology Group study ARST0332 used surgery only for non-metastatic, widely resected <=5 cm high-grade tumors and grossly resected intermediate-grade tumors of any size. A pooled analysis of outcomes for eligible and evaluable patients with synovial sarcoma was performed.

Results: From 2007 to 2012, 60 eligible and evaluable synovial sarcoma patients under 21 years of age were enrolled on NRSTS2005 (n=24) or ARST0332 (n=36). Most had extremity primary tumors (n=53), had documented SYT rearrangement (n=49), and had undergone primary re-excision (n=41). Median tumor size was 3 cm (range, 0.6-7.8 cm). FNCLCC grade was 1 (n=4), 2 (n=41), or 3 (n=9). Three-year event-free survival was 90.0% (95% CI 81.9%, 98%) and overall survival was 100% at a median follow-up of 5.3 yrs (range 1.9-12.9 yrs). All 8 events were local tumor recurrence. Histologic grade (low vs. high), tumor size (<= vs. > 3 cm), and presence or absence of primary re-excision did not predict tumor recurrence.

Conclusion: Patients with small, adequately resected synovial sarcoma, regardless of grade, can be safely treated with a surgery only approach. Avoiding the use of adjuvant chemotherapy and radiotherapy in this low-risk patient population may decrease both short- and long-term morbidity and mortality.

P2–Poster 092 2555378

MULTI-AGENT CHEMOTHERAPY IN ADVANCED SOFT TISSUE SARCOMA (STS): MORE IS NOT ALWAYS BETTER

Alona Zer, MD[2]; Rebecca Prince[1]; Eitan Amir[1]; Albiruni A. Razak[1]

[1]DMOH, Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Rabin Medical Center, Petach Tikva, Israel

Objective: Despite lack of overall survival (OS) benefit from doxorubicin-based combinations over doxorubicin alone in advanced STS, the role of multi-agent chemotherapy remains controversial.

Methods: We conducted a systematic review and meta-analysis to evaluate harms and benefits of multi-agent chemotherapy in advanced STS. The analysis comprised of all published chemotherapy RCTs in advanced STS comparing single agent to multi-agent therapy. Data from studies reporting a hazard ratio and 95% confidence intervals (CI) for OS and progression-free survival (PFS) were pooled in a meta-analysis. Meta-regression was utilized to explore the association between toxicity and dose intensity and both OS and PFS.

Results: 22 RCTs published between 1974-2015, comprising 5747 patients, met inclusion criteria. Overall, multi-agent chemotherapy was associated with improved OS (HR 0.79, p=0.02), and borderline improved PFS (HR 0.86, p=0.05). Compared to studies with anthracycline as controls, there was a non-significantly greater magnitude of effect among studies with non-anthracycline chemotherapy as controls (HR for OS 0.73 vs. 0.82, p for difference=0.63 and HR for PFS 0.73 vs. 0.91, p for difference=0.13). Similarly, compared to studies with cytotoxic therapy-based experimental groups, there was a non-significantly greater magnitude of effect among studies with biological therapy-based experimental groups (HR for OS 0.64 vs. 0.86, p for difference=0.37 and HR for PFS 0.79 vs. 0.87, p for difference=0.52). There was borderline significant association between dose reductions, which were more common in the combination arms, and worse PFS (beta=0.70, p=0.053).

Conclusion: Our series demonstrated that multi-agent chemotherapy was associated with improved outcomes. This finding may be driven by studies utilizing non-anthracycline-based controls as well as studies exploring the addition of biological agents to chemotherapy. Future studies of multi-agent chemotherapy should focus on these groups rather than on the addition of cytotoxic agents to anthracyclines.

P2–Poster 093 2565308

A PHASE 1/2 STUDY OF ALDOXORUBICIN AND 14 DAYS CONTINUOUS INFUSION OF IFOSFAMIDE/ MESNA IN METASTATIC OR LOCALLY ADVANCED SARCOMAS

Sant P. Chawla, MD[1]; K. Kumar Sankhala[1]; Shanta Chawla[2]; Victoria Chua[1]; Erlinda M. Gordon[1]; Neal Chawla[1]; Kelli Sung[2]; Doris Quon[1]; Katherine Kim[1]; Lita Fernandez[1]; Bryan Leong[1]; Scott Wieland[2]; Daniel Levitt[2]

[1]Sarcoma Oncology Center, Santa Monica, CA, USA; [2]CytRx Corporation, Los Angeles, CA, USA

Objective: Aldoxorubicin (A) has demonstrated superior anti-tumor efficacy and lack of cumulative cardiac toxicity in multiple studies. A is doxorubicin (D) with a linker which rapidly binds in vivo to albumin after iv. We studied the combination of A administered on Day 1 with continuous infusion (CI) of ifosfamide/Mesna (I-M) days 1-14, as first line therapy or second line therapy in patients with sarcomas to evaluate efficacy and toxicity.

Methods: 37 patients entered the study at one of 2 dose levels of A:170 or 250 mg/m2 (125 or 185 mg/m2 D equiv) administered on Day 1. I-M (1 g/m2 of each per day) was given up to 14 days as a CI via an out-patient portable pump. Chemotherapy cycles were repeated at 28 day interval. I-M was limited to a maximum of 6 cycles to avoid cumulative marrow toxicity, but A was continued in responding patients for clinical benefit. Subjects were followed for tumor response by CT scans and echocardiogram for cardiac toxicity every 8 weeks along with standard labs.

Results: Of the 37 patients enrolled as of June 16, 2016, the results of 24 evaluable patients are presented here. Twenty of the 24 patients had soft tissue sarcoma, 2 had metastatic osteosarcoma and 2 had dedifferentiated chondrosarcoma. Eight of 24 patients (33%) had a partial response (PR), 15/24 (62%) had stable disease (SD) and only 1/24 (5%) had progressive disease with over all disease control rate of 95% (PR+SD). Eleven of 24 (46%) patients had received at least 6 cycles of A (cumulative D equivalent more than 1000 mg/m2). Four patients were considered surgically resectable after 6 cycles of chemotherapy with percent of tumor necrosis of 95% and 90% in one patient each and 80% in two patients. Median duration of PFS was 6+ (2-19+) months.

The most prevalent toxicity was gr 3 or 4 neutropenia. Three patients had SAEs of febrile neutropenia. There was no clinical cardiac toxicity/ congestive heart failure. No patient had LVEF < 50% on echocardiograms at any time.

Conclusion: The combination of A + I-M appears to be superior in anti-tumor efficacy to D/I-M with durable responses. A + I-M combination is quite tolerable with expected reversible hematologic toxicity. Of the 46% patients who received more than 1000 mg/m2 of D equivalent; no cardiac toxicity was observed.

P2–Poster 094 2554705

RANDOMIZED PHASE 3, MULTICENTER, OPEN-LABEL STUDY COMPARING EVOFOSFAMIDE (EVO) IN COMBINATION WITH DOXORUBICIN (D) VS. D ALONE IN PATIENTS (PTS) WITH ADVANCED SOFT TISSUE SARCOMA (STS); STUDY TH-CR-406/SARC021

William Tap[1]; Zsuzsanna Papai[2]; Brian Van Tine[3]; Steven Attia[4]; Kristen Ganjoo[5]; Robin Jones[6]; Scott Schuetze[7]; Damon Reed[8]; Sant P. Chawla[9]; Richard Riedel[11]; Antoine Italiano[14]; Peter Hohenberger[10]; Thierry Alcindor[15]; Stewart Kroll[12]; Patrick Schöffski[13]
[1]Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [2]Allami Egeszsegugyi Kozpont, Budapest, Hungary; [3]Washington University St. Louis, St. Louis, MO, USA; [4]Mayo Clinic Florida, Jacksonville, FL, USA; [5]Stanford University, Stanford, CA, USA; [6]Royal Marsden, London, United Kingdom; [7]University of Michigan, Ann Arbor, MI, USA; [8]Moffitt Cancer Center, Tampa, FL, USA; [9]Sarcoma Oncology, Santa Monica, CA, USA; [10]Universitatsklinikum Mannheim, Mannheim, Germany; [11]Duke University, Durham, NC, USA; [12]Threshold Pharmaceuticals, South San Francisco, CA, USA; [13]Universitair Ziekenhuis Leuven - Gathuisberg, Leuven, Belgium; [14]Institut Bergonie, Bordeaux, France; [15]Canadian Clinical Trials Group, Kingston, ON, Canada

Objective: PRIMARY OBJECTIVES
1. To evaluate the efficacy of TH-302 in combination with doxorubicin as determined by overall survival in subjects with locally advanced unresectable or metastatic soft tissue sarcoma previously untreated with chemotherapy (neoadjuvant and adjuvant chemotherapy permitted) compared with doxorubicin alone
2. To assess the safety of TH-302 in combination with doxorubicin in subjects with locally advanced unresectable or metastatic soft tissue sarcoma compared with doxorubicin alone

Methods: This was a multi-national, open-label, randomized (1:1) Phase 3 study of Evo (300 mg/m^2) IV on Days 1 and 8 (21-day cycle) with D on Day 1 vs. D alone (75 mg/m^2, bolus or continuous). Pts on Evo plus D could receive Evo alone after Cycle 6. Key eligibility: locally advanced unresectable or metastatic STS, intermediate or high grade, no prior chemotherapy for advanced disease, ECOG 0/1, measurable disease (RECIST 1.1). The primary endpoint was overall survival (OS). The study had 85% power and one-sided alpha of 2.5% to detect 33% improvement in OS. Secondary endpoints were PFS, response rate (RR) and safety.

Results: From Sept 2011 to Jan 2014, 640 pts were randomized (317 Evo+D, 323 D); 621 pts were treated. Baseline characteristics were balanced. Median age: 59 years (range 18-89); 54% female; 57% ECOG 0; 36% leiomyosarcoma, 17% liposarcoma, 12% undifferentiated pleomorphic sarcoma; 89% metastatic, 11% locally advanced disease. Median cycles were 6 and D dose intensity was >90% through 6 cycles, in both arms. Single agent Evo was continued in 46% of pts on Evo+D after Cycle 6. OS endpoint was not reached (HR = 1.06 [95% CI: 0.88-1.29]) with median OS of 18.4 months with Evo + D vs 19.0 months with D. RR was 28.4% on Evo+D vs 18.3% for D (odds ratio of 1.77 [95% CI: 1.20 – 2.58, p=0.003]. Median PFS was 6.3 months on Evo+D vs 6.0 months on D, HR = 0.85 (95% CI: 0.70-1.03, p=0.099). Most common grade 3/4/5 AEs were anemia (35%), neutropenia (33%) and leucopenia (18%). Febrile neutropenia was noted in 18% of pts on Evo+D and 11% on D. AEs leading to death were 2.6% on Evo+D and 1.0% on D. AEs leading to discontinuation were 8.3% on Evo+D and 6.2% on D.

Conclusion: The combination of Evo+D did not improve OS compared to D. The safety profile was consistent with that previously reported.

P2–Poster 095 2530606

PROGNOSIS OF PATIENTS RECEIVING FIRST LINE CHEMOTHERAPY FOR ADVANCED SOFT TISSUE SARCOMAS WITH LOCALLY ADVANCED VS DISTANT METASTASIS VS BOTH: AN EORTC-STBSG DATABASE ANALYSIS

Arjan Verschoor[1]; Saskia Litiere[2]; Sandrine Marreaud[2]; Ian Judson[3]; Maud Toulmonde[4]; Eva Wardelmann[5]; Winette Van der Graaf[3]; Axel Le Cesne[6]; Alessandro Gronchi[7]; Hans Gelderblom[1]
[1]Medical Oncology, Leiden University Medical Center, Leiden, Netherlands; [2]European Organisation for Research and Treatment of Cancer, Brussels, Belgium; [3]Royal Marsden Hospital, London, United Kingdom; [4]Institut Bergonié, Bordeaux, France; [5]Gerhard Domagk Institute of Pathology, University Hospital Muenster, Muenster, Germany; [6]Institut Gustave Roussy, Villejuif, France; [7]Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

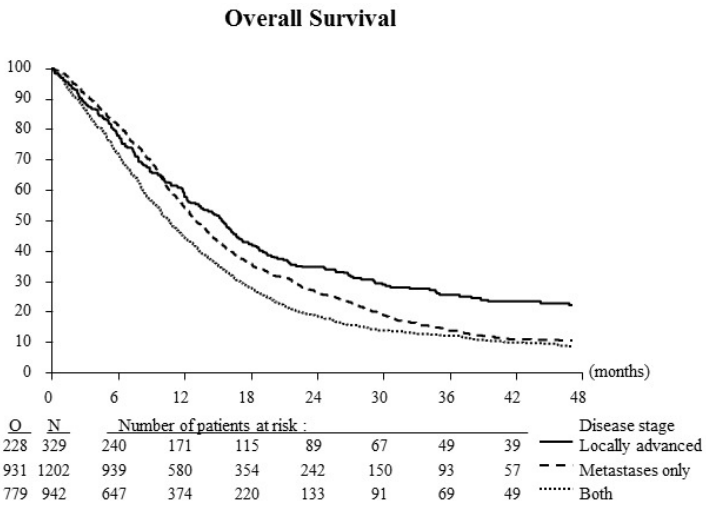
Objective: In patients with advanced soft tissue sarcoma treated with chemotherapy, WHO performance status, histologic subtype and histologic grade are known prognostic factors. Although the difference between the subgroups: local disease only, metastatic disease only and both local and metastatic disease is easily made, its prognostic relevance is thus far unknown. The aim of this EORTC database study was to study the difference in prognosis between these subgroups in patients receiving first line chemotherapy for advanced soft tissue sarcoma.

Methods: A retrospective database analysis was performed on 2473 patients receiving first line chemotherapy for advanced soft tissue sarcoma from 12 EORTC sarcoma trials in order to establish differences in prognosis and prognostic factors for the different disease stages. Endpoints were overall survival (OS), progression-free

survival (PFS) and overall response rate (RR). Factors studied were age, sex, histologic subtype, histologic grade, WHO performance status (PS), treatment and time since initial diagnosis.

Results: Compared to patients with locally advanced disease only, patients with metastatic disease only had a worse OS (hazard ratio (HR) = 1.25 (95% confidence interval (CI) 1.08-1.45)) and patients with both local and metastatic disease had the worst outcome (HR = 1.59 (95% CI 1.37-1.84). Median OS was 15.4 (95% CI 13.0-16.9), 12.9 (12.4-13.9) and 10.6 (9.8-11.3) months respectively. Similar differences were seen for PFS (5.8 months (95% CI 4.4-6.5), 4.3 months (3.9-4.7) and 3.2 months (2.9-3.5) respectively) and overall RR. For OS prognostic factors were PS and time since initial diagnosis. Tumour site, histological subtype, grade, age and gender were prognostic in some, but not all groups that were studied. For PFS and overall RR there were also differences in the prognostic factors between the studied groups.

Conclusion: This large retrospective database study shows that patients with advanced soft tissue sarcomas treated with first line chemotherapy with locally advanced disease, metastatic disease and both local and metastatic disease show markedly differences in survival. This should be accounted for in future study design, interpretation of study results and daily clinical practice.



Overall survival

P2–Poster 096 2570640

PROSPECTIVE VALIDATION OF A MOLECULAR SIGNATURE PREDICTIVE OF RESPONSE TO TRABECTEDIN IN SOFT- TISSUE SARCOMAS WITHIN EORTC 62091 TRIAL

Antoine Italiano[1]; Nathan Touati[2]; Saskia Litiere[2]; James Butrynski[11]; Nicolas Penel[3]; Jean Yves Blay[4]; Nicolas Isambert[5]; Mohammed Milhem[6]; Jan Kerst[7]; An Reyners[7]; Sandrine Marreaud[2]; Françoise Collin[5]; Winette Van der Graaf[8]; Hans Gelderblom[9]; Alessandro Gronchi[10]

[1]Institut Bergonie, Bordeaux, France; [2]EORTC, Bruxelles, Belgium; [3]Centre Oscar Lambret, Lille, France; [4]Centre Léon Bérard, Lyon, France; [5]Centre Georges François Leclerc, Dijon, France; [6]University of Iowa, Iowa, IA, USA; [7]Netherlands Cancer Institute, Groningen, Netherlands; [8]Royal Marsden Hospital, London, United Kingdom; [9]Leiden University, Leiden, Netherlands; [10]Istituto Nazionale dei Tumori, Milan, Italy; [11]Overlake Hospital, Bellevue, WA, USA

Objective: The aim of the EORTC 62091 trial was to compare the efficacy of trabectedin to doxorubicin in the first-line setting of advanced/metastatic soft tissue sarcoma. Although the trial was stopped early due to lack of efficacy of trabectedin as compared to doxorubicin, several patients experienced a long duration of benefit to trabectedin. BRCA1 genotype could be a potential predictive factor for trabectedin efficacy. Endpoints have been updated with more complete follow-up for the purpose of this study.

Methods: In this randomized multicentre prospective dose-selection phase IIb superiority trial, 133 patients were randomized between doxorubicin (n=43), trabectedin (3-hour infusion, n=47) and trabectedin (24-hour infusion, n=43). PFS was defined as time from random assignment until objective progression by response evaluation criteria in solid tumours (RECIST 1.1), global deterioration of the health status requiring discontinuation of the treatment, or death from any cause. Based on tumor samples availability, BRCA1 genotype status was available for 60 patients (doxo n=23, trab24hrs n=14, trab3hrs n=23). Patients with BRCA1 haplotype being at least one AAAG allele have been classified into the “favorable” group and the other into the “non-favorable” group.

Results: At the time of this analysis, 1 patient was still on protocol treatment. Major reasons for protocol treatment discontinuation were disease progression (12/40 doxo, 26/40 trab24hrs, 31/46 trab3hrs) and toxicity (1/40 doxo, 8/40 trab24hrs, 7/46 trab3hrs). No significant improvement was observed in the trabectedin arms as compared to the doxorubicin arm in PFS (trab24hrs vs doxo: HR 0.90, 95% CI 0.57-1.40, 1-sided p =0.317; trab3hrs vs doxo: HR 1.11, 95% CI 0.72-1.71, 1-sided p =0.687) and OS (trab24hrs vs doxo: HR 1.38, 95% CI 0.83-2.32, 1-sided p =0.892; trab3hrs vs doxo: HR 1.44, 95% CI 0.87-2.40, 1-sided p =0.921).

There was no statistically significant association between BRCA1 haplotype and PFS ("favorable" n=47 vs. "non-favorable" n=13: HR 0.81, 95% CI 0.43-1.52, p=0.509).

Conclusion: Trabectedin was not shown to be superior to doxorubicin in this setting and therefore, doxorubicin remains the standard 1st line treatment of advanced STS. The predictive value of BRCA1 haplotype for trabectedin efficacy suggested by retrospective studies could not be confirmed here but a major limitation was the small number of patients with available tumor samples.

P2–Poster 097 2558960

PHASE II STUDY OF PM01183 AS A SINGLE AGENT OR IN COMBINATION WITH CONVENTIONAL CHEMOTHERAPY IN METASTATIC AND/OR UNRESECTABLE SOFT TISSUE SARCOMAS

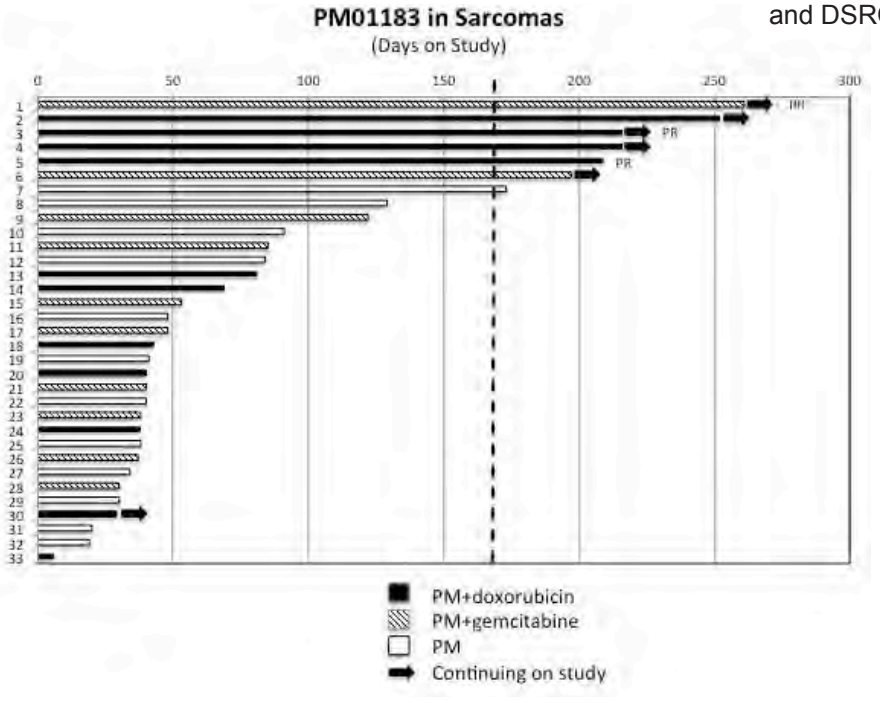
Gregory M. Cote, MD, PhD[1]; Edwin Choy[1]; Jeffrey A. Morgan[2]; Priscilla Merriam[2]; Andrew Wagner[2]; Katherine Thornton[2]; GD Demetri[2]; Suzanne George[2]
[1]Hematology/Oncology, Massachusetts General Hospital, Boston, MA, USA; [2]Hematology/Oncology, Dana-Farber Cancer Institute, Boston, MA, USA

Objective: In metastatic STS chemotherapy response rates are less than 50% and durability remains limited. PM01183 (lurbinectedin) is a new anticancer agent that blocks trans-activated transcription, induces DNA double-strand breaks and modulates tumor microenvironment. Preclinical and phase I data show potential activity in STS. In this multi-strata phase II study the primary objective was to determine disease control rate (DCR = ORR+SD) at 24 wks of PM01183 alone or in combination with chemotherapy in STS. Secondary objectives include ORR, PFS, OS at 2 yrs and the safety profile in these patients.

Methods: This is an open-label, 3 arm study including stratum A (stA, anthracycline-naive), PM01183+doxorubicin every 21d for 6 cycles followed by PM01183 alone; stratum B (stB, prior anthracycline or contraindication), PM01183+gemcitabine on d1 and d8 of a 21d cycle; stratum C (stC, prior anthracycline and gemcitabine) PM01183 on d1 of a 21d cycle. Eligibility includes metastatic/unresectable STS, RECIST 1.1 measurable, age 18-75 yo, ECOG PS <2 and normal organ function. Low-grade and bone sarcomas were excluded and patients were limited to no more than 2 prior cytotoxic therapies. Imaging was obtained every 6 wks for cycles 1-8 and then every 9 wks thereafter. Each stratum included 2-stages requiring 3/10 24-week DCR responses in stA and stB, 2/12 24-week DCR for stC, to accrue to 20 total patients per stratum.

Results: As of June 15, 2016 33 patients have been accrued (stA=11, stB=10, stC=12). Histologies include LMS (n=14), MPNST (n=3), synovial (n=3), DSRCT (n=2), DDLPS (n=1), myxLPS (n=1) and the remaining are unclassified or rare subtypes. The 24-week DCR endpoint responses include stA=4/11 (LMS n=2, myxLPS n=1, DDLPS n=1), stB 2/10 (LMS, DSRCT) and stC 1/12 (LMS). Only stA has opened to the second stage. Of the patients reaching the 24-week DCR endpoint 5 remain on study and 3 of these (all LMS) achieved PR. Median PFS and OS will be calculated when the study data matures. The therapies were well tolerated with most AE's being hematologic. These include 39 G3-4 events of which G3=9 and G4=21 were considered related to the study treatments (nausea G3=1; cytopenias G3=8, G4=21). There were no treatment-related deaths.

Conclusion: PM01183 as a single agent or with chemotherapy was well tolerated with primarily hematological toxicity. The combination of PM01183+doxorubicin reached the 24-week DCR endpoint and is now accruing to the second stage. Preliminary activity was seen in LMS, LPS and DSRCT.



P2–Poster 098 2565673

PHASE 2 TRIAL OF 5-IMINO-13-DEOXYDOXORUBICIN (GPX-150) IN METASTATIC AND NON-RESECTABLE SOFT TISSUE SARCOMAS

Brian Van Tine[1]; Mark Agulnik[2]; Richard D. Olsen[4]; Gerald M. Walsh[4]; Arthur Klausner[4]; Mohammed Milhem[3]
[1]Washington University in Saint Louis, St. Louis, MO, USA; [2]Northwestern University, Chicago, IL, USA; [3]University of Iowa, Iowa City, IA, USA; [4]Gem Pharmaceuticals, Birmingham, AL, USA

Objective: The primary objective was to determine the efficacy of GPX-150 administered intravenously every three weeks to patients with soft tissue sarcoma, as determined by Progression Free Rate (PFR) at 12 months of treatment. Secondary objectives were to describe (1) the effects of GPX-150 on soft tissue sarcoma using a range of secondary efficacy measures; and (2) the safety profile of GPX-150 under the conditions of this trial.

Methods: We performed a Phase 2 efficacy and safety study in 22 patients enrolled with locally advanced and/or metastatic intermediate or high grade soft tissue sarcoma (STS). The open-label, single-arm study of GPX-150 was performed in the front line setting. Patients who met all entry criteria received GPX-150 at a starting dose of 265 mg/m^2 along with pegfilgrastim every 21 days for up to 16 cycles or until death, disease progression, or unacceptable toxicity. Using RECIST 1.1, response evaluations were performed every 6 weeks for the first 24 weeks, then every 9 weeks for the remainder of the trial. Safety and toxicity data were obtained.

Results: Of 21 evaluable patients for efficacy, there was a 43% Clinical Benefit Rate at 16 weeks. One patient had a partial response and 8 patients had stable disease (SD) for at least 6 cycles. Two patients had grade 3-4 neutropenia (10%); 1 patient had grade 3 febrile neutropenia (5%); 3 patients (14%) had grade 3 anemia. All other toxicities including mucositis, nausea, vomiting, alopecia and fatigue were less than grade 3. A reversible, asymptomatic left ventricular ejection fraction fall to below 50% (MUGA) occurred in 3 patients.

Conclusion: Anticancer activity was demonstrated in patients with STS, and GPX-150 could be administered for up to 16+ cycles. There was no irreversible cardiotoxicity. GPX-150 was well tolerated. Other than hematological toxicity, no grade 3 or 4 toxicities occurred.

P2–Poster 099 2565733

TRABECTEDIN WITH PROPHYLACTIC N-ACETYLCYSTEINE (NAC) CO-TREATMENT IN PATIENTS WITH RECURRENT SOFT TISSUE SARCOMA (STS) AND REDUCED LIVER AND RENAL FUNCTION

Salvatore Grisanti[1]; Vittorio D. Ferrari[1]; Susanna Bianchi[1]; Vincenza Azzara[2]; Barbara P. Lazzari[1]; Francesca Consoli[1]; Elisa Roca[1]; Paola Rehmann[2]; Salvatore Golemi[1]; Cristina Gurizzan[1]; Carla Galloni[2]; Alfredo Berruti[1]
[1]Medical Oncology, University of Brescia, Brescia, Italy; [2]Clinical Pharmacology, Spedali Civili of Brescia, Brescia, Italy

Objective: Trabectedin [Yondelis®, PharmaMar, Spain] (T) is indicated for the treatment of adult patients with advanced STS, after failure of anthracycline-based chemotherapy or who are unsuited to receive these agents. The safety profile of T includes transient and self-limited all grade AST/ALT and creatinine elevation in up to 80% and 45% of patients (pts), respectively. Dexamethasone (D) premedication significantly reduces hepatotoxicity. However, pts with baseline liver and/or renal abnormalities can experience more severe organ damage leading to treatment discontinuation. N-Acetylcysteine (NAC) is a glutathione precursor which protects against the hepato- and nephro-toxicity induced by different drugs. We evaluated the effect of addition of NAC during T treatment of recurrent STS.

Methods: Pts with recurrent STS were treated with T 1.5 mg/m^2 given as a 24-h i.v.infusion every three weeks with D premedication. Pts with reduced baseline liver function (defined as Child-Pugh A) and/or renal function (defined as creatinine clearance [CrCl] <50) or ALT toxicity > grade (G) 1 after the first cycle, were treated with NAC in addition to standard T/D schedule from cycle 2. NAC was administered at the dose of 600 mg tid following the T infusion day for 7 days. Hepato- and nephro-toxicity was monitored in terms of ALT elevation and CrCl reduction from baseline levels, respectively. The effect of NAC was evaluated as number of T cycles administered and T dose intensity (DI). The difference between pts with or without NAC was evaluated with a Chi-square test.

Results: From October 2012 to May 2016, 18 pts were treated with T and 8 of them received NAC. Main results are summarized in Table 1. No statistically significant differences were observed in the median number of administered T cycles, T dose and DI in pts with liver/renal impairment treated with NAC, compared with patients with normal organ function (Table 2). In the 7 pts with ALT > G1 after the first cycle, NAC co-treatment obtained a median 62% ALT reduction from the highest ALT value. In parallel, NAC co-treatment obtained CrCl stabilization.

Conclusion: This series demonstrates that T can be safely administered to pts with baseline reduced liver and renal function or >G1 ALT increases after first cycle. Fur-

ther studies are warranted to additionally clarify the NAC co-adjuvant treatment with D and T in reducing hepato- and nephrotoxicity.

Table 1. Patients and treatment characteristics

ID	Age	STS	No. of previous CT lines	Liver impairment	Renal impairment (CrCl mL/min)	NAC (Y/N)	No. of T cycles	Median T dose/cycle (mg)	Median DI (%)	Reason of interruption
1	38	SS	2	None	None	N	8	2.1	95	PD
2	76	LMS	2	HBV+ hepatitis	<30	Y	7	1.75	67	PD
3	65	LPS	1	CLF	<50	Y	3	2.1	74	PD
4	58	LPS	1	M+	<50	N	2	2.0	77	PD
5	67	LPS	3	None	<50	N	4	1.85	76	Sepsis
6	35	MPNST	2	None	None	N	4	2.0	79	PD
7	41	HG	1	None	None	N	4	2.1	78	PD
8	67	LMS	2	M+	<30	Y	4	2.0	77	PD
9	31	LPS	1	None	None	N	4	1.62	64	Surgery
10	48	LMS	2	M+	<50	Y	4	2.0	90	On treatment
11	60	SS	1	CLF	None	Y	1	2.0	78	PD
12	57	LMS	2	M+	None	Y	5	2.16	86	PD
13	69	HG	2	HBV+ hepatitis	<50	Y	3	1.4	65	PD
14	60	HG	3	CLF	None	Y	11	2.2	96	PD
15	66	HG	2	CLF	None	Y	4	2.1	83	PD
16	50	LMS	2	None	None	N	12	2.4	80	PD
17	35	LPS	1	None	None	N	4	2.25	88	PD
18	71	LPS	1	None	<50	N	3	2.0	88	PD

Legend: CrCl: creatinine clearance; DI: dose intensity; SS: synovial sarcoma; HG: high-grade not otherwise specified; LMS: leiomyosarcoma; LPS: liposarcoma; FBS: fibrosarcoma; MPNST: malignant peripheral nerve sheath tumor; M+: metastases; HBV: hepatitis B virus; CLF: chronic liver failure; PD: progressive disease.

Table 2. Differences in treatment exposure between patients with or without NAC co-treatment

	NAC+	NAC-	p
Median no. T cycles	4	4	ns
Median T dose/cycle (mg)	1.95	2.0	ns
Median dose intensity (%)	80	82	ns

P2–Poster 100 2555443

PLATINUM-BASED REGIMENS IN ADVANCED PEDIATRIC TYPE RHABDOMYOSARCOMA IN ADULTS: EXPERIENCE OF TWO CENTERS

Nadia Hindi, MD[1]; Pablo Luna[2]; Jose Duran[2]; Pilar Sancho[1]; Roberto Lasso[1]; Alvaro Montaño[1]; Rafael Ramos[2]; Javier Martin- Broto[1]

[1]Medical Oncology, Virgen del Rocio University Hospital, Seville, Spain; [2]Medical Oncology, Son Espases University Hospital, Palma de Mallorca, Spain

Objective: Rhabdomyosarcoma (RMS) in adults is a rare and aggressive disease. Standard chemotherapy regimens developed in pediatric population fail to obtain similar results in adults. Metastatic RMS in adults is a fatal disease. The aim of this retrospective study is to describe the activity of alternative platinum-based regimes in adult patients (pts) with relapsed/metastatic RMS.

Methods: Pts diagnosed with RMS (excluding pleomorphic histology) from August 1994 to March 2016 and treated with platinum- based regimes, specifically BOMP/EPI (bleomycin, vincristine, methotrexate, cisplatin alternating with etoposide, cisplatin, and ifosfamide) in University Hospital Virgen del Rocio and University Hospital Son Espases were reviewed. Data regarding clinical and histopathological characteristics, therapy and survival were collected. Radiological responses were evaluated by RECIST. Kaplan-Meier method was used for overall survival (OS) and event-free survival (EFS).

Results: We identified eight pts with RMS treated with BOMP/EPI: Median age at diagnosis was 20.8y (17-42), F/M=4/4. Five pts had alveolar RMS and 3 pts embryonal RMS. Site of primary tumor was head and neck in 4 pts, limbs in 2 pts, pelvis in 1 pt, and heart in 1 pt. Three pts received BOMP/EPI as upfront therapy (all with metastatic disease at diagnosis) and 5 pts at relapse (3 metastatic, 2 locally advanced). Pts received a mean of 3.7 cycles (1-8). Best RECIST response was: partial response (PR) in 4/8 (50%), stable disease (SD) in 2/8 (25%), not evaluable in 2/8 (25%). 4/8 pts also underwent surgery and 3/8 underwent radiotherapy (RT). 4/8 pts experienced ≥grade 3 neutropenia, No toxic deaths occurred. With a median follow-up from start of therapy of 22 mos (1-258), 7/8 pts have progressed, with a median EFS of 8.9 mos (95% CI 7.7-10) and 4/8 pts have died, with a median OS of 35.4 mos (95% CI 19.2-51.5), and 2 and 5-year OS rates of 75% and 50% respectively. Three pts received again BOMP/EPI at progression after stopping therapy while in response: 2/3 obtained a new PR, with disease control after 10 mos and 229 mos.

Conclusion: BOMP/EPI is an active chemotherapy regimen in adults with pediatric type metastatic RMS, with outcomes in terms of survival clearly superior for what expected for this poor prognosis population. This encouraging results worth prospective validation.

P2–Poster 101 2569845

TRABECTEDIN IN WELL DIFFERENTIATED VERSUS DEDIFFERENTIATED LIPOSARCOMA

Roberta Sanfilippo[1]; Vittoria Colia[1]; Elena Fumagalli[1]; Rossella Bertulli[1]; Salvatore Provenzano[1]; Silvana Pilotti[1]; Angelo Paolo Dei Tos[2]; Carlo Morosi[1]; Alessandro Gronchi[1]; Paolo Casali[1]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [2]General Hospital of Treviso, Milan, Italy

Objective: To further understand the activity of Trabectedin (T) in well differentiated versus dedifferentiated liposarcoma.

Methods: From April 2003, 44 patients (M/F=24/20) with advanced well differentiated/dedifferentiated liposarcoma, previously treated with a median of 3 chemotherapy lines (range1 -6) received T. Clinical records were reviewed focusing on response and treatment outcome. Median age was 57 yrs (range 37-79).

Results: Thirteen patients had a predominantly well-differentiated morphology liposarcoma (11 arising from retroperitoneum, one from spermatic cord and one from mediastinum) and 31 a classic dedifferentiated liposarcoma (28 arising from retroperitoneum, one from mediastinum, two from limbs). In 12 out of the 31 DDLPS patients, we were able to analyze pathologically the dedifferentiated component. This was scored as G3 in 10 cases and G2 in 2. A total of 296 courses were delivered (median 4, range 1-32), and 34% of patients received more than 5 courses of T. Six partial responses, two minor responses and 17 stable disease were observed, for a PR rate of 13% and a SD (SD+MR) rate of 43%. All patients with PR or MR had a predominantly well differentiated liposarcoma. No responses were observed in classic “high grade” dedifferentiated liposarcoma. Overall median PFS was 3,5 months, with 34% of patients free from progression at 6 months. In patients with a predominantly well-differentiated morphology, PFS was 14 months, with 6 responders in 13 patients.

Conclusion: Sensitivity to T may be higher in liposarcomas with a predominantly well-differentiated morphology. Further series and prospective evidence would be needed.

P2–Poster 102 2534346

SAFETY PROFILE OF TRABECTEDIN THERAPY IN PATIENTS WITH ADVANCED SOFT TISSUE SARCOMAS (STS) FOLLOWING FAILURE OF PRIOR CHEMOTHERAPY: UPDATED RESULTS OF A GLOBAL EXPANDED ACCESS PROGRAM

R. Jones[1]; R.G. Maki[2]; S.R. Patel[3]; C.R. Shin[4]; T. McGowan[4]; L. Marquez[5]; T.V. Parekh[5]; M. von Mehren[6]; G.D. Demetri[7]
[1]Royal Marsden Hospital / Institute of Cancer Research, London, United Kingdom; [2]Mount Sinai Medical Center, New York, NY, USA; [3]The University of Texas, MD Anderson Cancer Center, Houston, TX, USA; [4]Janssen Scientific Affairs, LLC, Horsham, PA, USA; [5]Janssen Research & Development, LLC, Raritan, NJ, USA; [6]Fox Chase Cancer Center, Philadelphia, PA, USA; [7]Dana-Farber Cancer Institute and Ludwig Center at Harvard, Boston, MA, USA

Objective: To provide an updated safety profile of trabectedin therapy in patients with advanced soft tissue sarcomas. Study ET743-SAR-3002 was an expanded access program (EAP) to provide trabectedin to patients with incurable STS following progression of disease with standard therapy. This study represents one of the largest therapeutic experiences for pretreated STS patients to date. Prior efficacy and safety data accrued over approximately 5 years through October, 2010 were previously published. At this time all data collection, with the exception of serious adverse event (SAE) reporting, was stopped.

Methods: Adult patients (age >18 years) with advanced STS (mainly leiomyosarcoma and liposarcoma), following relapse or disease progression after standard-of-care chemotherapy, received trabectedin 1.5 mg/m^2 every 3 weeks [q3wk] administered as a 24-hour infusion until documented disease progression or unacceptable toxicity. Overall, 39 sites participated in the EAP: US (34), Canada (4), and Israel (1). SAEs were reported by investigators to the sponsor. Here we report an update on the cumulative SAEs collected in this study through April 2016.

Results: A total of 3253 patients were treated from 2005 until 2016. Overall, the incidence of patients experiencing SAEs (irrespective of investigator assigned causality) was 1383 (42.5%). The most common SAEs were: dyspnea 130 (4.0%), vomiting 126 (3.9%), nausea 124 (3.8%), pneumonia 103 (3.2%), dehydration 100 (3.1%), pyrexia 97 (3.0%), abdominal pain 86 (2.6%) thrombocytopenia 83 (2.6%) and anemia 79 (2.4%). Select SAEs of interest were: neutropenic sepsis 1 (0.03%), rhabdomyolysis 37 (1.1%), and cardiomyopathy 1 (0.03%). Fatal SAEs occurred in 330 (10.1%) advanced STS patients, the most common system organ class was neoplasms 115 (3.5%).

Conclusion: Safety data from this EAP is consistent with the known safety profile of trabectedin that has been previously reported in well controlled clinical trials.

P2–Poster 103 2554229

INCREMENTAL BENEFIT-COST RATIO OF TRABECTEDIN VS PAZOPANIB FOR THE TREATMENT OF ADVANCED, METASTATIC, SOFT TISSUE SARCOMA IN SPAIN

Jose Miguel Fernandez[1]; Roberto Diaz Beveridge[2]
[1]Health Economics, Pharmamar, Colmenar Viejo, Madrid, Spain; [2]Hospital Universitario La Fe, Valencia, Spain

Objective: To evaluate the Incremental Benefit Cost Ratio (BCR) of trabectedin (Yondelis®, Pharmamar) versus pazopanib (Votrient®, Novartis). Both are currently licensed for the treatment of advanced, metastatic Soft Tissue Sarcoma (mSTS), after failure to an initial chemotherapy line.

Methods: We developed a standard BCR model from the Spanish National Healthcare System's (NHS) costs prospective -including palliative care- .

The above model accrued costs and clinical outcomes within the longest Time to First Subsequent Therapy (TFST) timeframes.

All the clinical data was sourced from two independent Phase III trials comparing trabectedin vs. dacarbazine (ET743-SAR-3007) and pazopanib vs. placebo (PALETTE); after adjusting for imbalances on baseline population characteristics. From the costing standpoint, we took published reimbursement tariffs.

Deterministic and Probabilistic Sensitivity Analysis (PSA) -Montecarlo simulation- were also performed to test the robustness of the findings.

Results: TFST was significantly longer in the trabectedin arm –with an average (SE) of 9.6(0.5)1 vs. 6.9(0.3)2 months-; so, we took such period as reference for calculations. Incremental BCR was consistently above 1 (69.7% of PSA runs) with the most plausible value of 1.29, associated to a net monetary benefit (NMB) of 6,829.71 Euro per patient.

Therefore; from a NHS prospective, trabectedin was found very likely to provide with a higher BCR when compared with pazopanib for a similar cohort of advanced, mSTS patients.

Conclusion: To our knowledge; this is the first comparative analyses assessing the full range of costs and benefits whilst on treatment –and beyond the Progression Free Survival Interval-, within the mSTS setting. Findings reassure the advantage for patients, clinicians and payers of using trabectedin; arguably because its mechanism of action is translated into delaying following treatments 'administration, and, therefore, saving medical and monetary resources.

References

1 ET743-SAR-3007 Clinical Study Report (CSR).
2 PALETTE Clinical Study Report (CSR)

P2–Poster 104 2570688

TRABECTEDIN THERAPY FOR HIGH-GRADE SARCOMAS: A SINGLE INSTITUTION'S EXPERIENCE

Sandra Santos, Resident; Ruben Fonseca; João Freitas; Paulo F. Tavares; Jose M. Casanova
Ortopedia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

Objective: High grade sarcomas are a rare entity, whose treatment in the last decades, despite improvements in chemotherapy protocols, has translated in only moderate improvement of survival. In recent years, trabectedin has been approved for the treatment of these patients, mainly as a second line of treatment. However, there are few clinical studies with regards to its efficacy, and the main source of data has been institutional case series.

Methods: Patient charts were reviewed for patients with high-grade sarcomas treated with trabectedin at our institution, between December 2008 and June 2016. Trabectedin was administered at 3 to 4-week intervals, at the recommended dose of 1.5mg/m^2. Patients who underwent less than 3 trabectedin cycles were excluded. Descriptive statistical analysis was performed.

Results: A total of 71 patients were identified, of which 8 were excluded; of the remaining 63 patients, there were 31 female and 32 male. Mean age at the time of diagnosis was 52,4 (17-78) years. The most common histologic subtypes observed were leyomiossarcoma (n=14), lyposarcoma (n=11), synovial sarcoma (n=7), dedifferentiated sarcoma (n=6) and fibrossarcoma (n=5). 60,3% of patients presented with methastatic disease (either on initial presentation or as disease progression). Most common tumor location was the upper/lower limbs (55,6%), followed by peritoneal/retroperitoneal locations (22.2%), trunk and pelvis (14,3%) and viscera (7.9%). At the moment of chart review, 23 patients were alive, with a mean overall survival of 42 (12-108) months since diagnosis; in the deceased patient group, median overall survival was 24 (12-192) months. In patients presenting with ≥ 36 months overall survival (n=33), the most common histologic subtypes were lypossarcoma, leyomiossarcoma and synovial sarcoma. Median number of trabectedin cycles was 6,5 (3-40) in the deceased patient group, and 17,5 (3-61) cycles in the alive patient group; of these, 73,9% are still in treatment with trabectedin. Trabectedin was used as ≥ second-line chemotherapy in 88,9% of cases.

Conclusion: Trabectedin has shown encouraging results in our patient population, with a significant increase in overall survival, more apparent in patients with histologic subtypes of leyomiossarcoma, lypossarcoma and synovial sarcoma. Our results are comparable to those previously observed in the literature, and support the use of trabectedin in patients with high-grade sarcomas who have failed standard-of-care agents.

P2–Poster 105 2566640

RELATIONSHIP BETWEEN MONOCYTE REDUCTION AND RADIOLOGICAL TISSUE MODIFICATION IN STS PATIENTS TREATED WITH TRABECTEDIN

Bruno Vincenzi; Marianna Silletta; Grazia Armento; Mariella Spalato Ceruso; Giovanna Catania; Daniele Santini; Giuseppe Tonini
Medical Oncology, University Campus Bio Medico of Rome, Rome, Italy

Objective: Recent data suggest that Trabectedin (T) can modify the intratumoral inflammatory infiltrate by a selective modulation of the monocyte/macrophage system. This selective mechanism can justify partially the anticancer activity of T. Furthermore, biologic response evaluated through Choi criteria, provides more valuable prognostic information than size measurement only (RECIST criteria). We carried out a single centre, retrospective analysis to evaluate the correlation between circulating monocytes reduction and tissue density modification (defined as the decrease in tumour density ≥15%).

Methods: Contrast-enhanced CT-scans were independently reviewed by two radiologist. Inclusion criteria were the followings: diagnosis of locally advanced/metastatic soft tissue, at least 3 cycles of T after failure or intolerance to at least one prior treatment (containing anthracycline + ifosfamide), complete blood count available weekly for the first course of treatment and more, complete follow up data available, CT-scans available for revision.

Results: 38 patients (22 men and 16 women) fulfilling the inclusion criteria were evaluated. Median age was 54 years. Most frequent primary sites were limbs/trunk (12, 31.6%) and retroperitoneum (11, 28.9 %). Most frequent histologies were leiomyosarcoma (10, 36.3%), liposarcoma (8, 21%) and synovial sarcoma (7,18.4%). In 26 patients (68.4%) we observed a reduction of at least 40% of blood monocytes count compared with pre-treatment percentage. Independently by RECIST response, among those 26 patients, 21 showed a reduction of tissues density, according to Choi criteria, after treatment with T (P= 0.0086). Only in 4 cases we identified a reduction of at least 40% in monocytes count without a corresponding biologic response at CT scan. Conversely, no statistically significant difference was detected between RECIST response rate and monocytes blood count. Concordance between Choi and RECIST criteria was low (Kappa=0.189), both in the group of patients with and without the reduction of monocytes of least 40%.

Conclusion: Our data suggest, for the first time, that the well-recognized tissue modification induced by T could be at least in part justified by the modulation of monocytes, and consequently by the intratumoral macrophages infiltration.

A larger analysis and a confirmatory population study are required in order to validate this preliminary data.

P2–Poster 106 2556970

ANTI-TUMOR EFFECTS OF TRABECTEDIN ON CLEAR CELL SARCOMA CELL LINES

Takaaki Nakai[1]; Yoshinori Imura[2]; Shutaro Yamada[1]; Sho Nakai[1]; Hidetatsu Otani[2]; Satoshi Takenaka[1]; Kenichiro Hamada[1]; Akira Myoui[1]; Nobuhito Araki[2]; Kazuyuki Itoh[3]; Hideki Yoshikawa[1]; Norifumi Naka[1]
[1]Orthopedic Surgery, Osaka University Graduate School of Medicine, Osaka, Osaka, Japan; [2]Musculoskeletal Oncology Service, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan; [3]Department of Biology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan

Objective: Clear cell sarcoma (CCS) is an aggressive soft-tissue sarcoma characterized by melanocytic differentiation. CCS is defined by EWS-ATF1 fusion gene resulting from chromosomal translocation t(12;22)(q13;q12) and is generally resistant to conventional chemotherapy and radiation therapy. Trabectedin is a marine-derived natural product and is currently prepared synthetically. Previous studies reported its potent anti-tumor efficacy against several malignancies but not CCS. In the present study, we investigated anti-tumor effects of trabectedin on human CCS cell lines *in vitro* and *in vivo*.

Methods: We used 4 human CCS cell lines, SU-CCS1 (EWS-ATF1 type1), Senju-CCS (type1), Hewga-CCS (type2) and KAS (type3). Hewga-CCS and Senju-CCS were established in our laboratory. We examined effects of trabectedin on growth and survival of these CCS cell lines *in vitro* and *in vivo*. Cell cycle inhibition, apoptosis induction and melanocytic differentiation were evaluated by flow cytometry, immunoblotting, and *in vivo* xenograft models.

Results: Trabectedin suppressed proliferation of 4 CCS cell lines in a dose-dependent manner (IC_{50}: SU-CCS1: 0.30nM, Senju-CCS: 0.87nM, Hewga-CCS: 0.48nM, KAS: 0.42nM). By flow cytometric analysis, 1nM of trabectedin induced G2/M cell cycle arrest and more than 10nM of trabectedin increased number of cells in sub-G1 phase in all CCS cell lines. Cleavage of caspase-3 was enhanced dose-dependently after trabectedin exposure by immunoblotting. Interestingly, prior to cleavage of caspase-3, expression of melanocytic differentiation markers such as MITF, TYR and TRP2 was upregulated transiently by treatment with trabectedin. Administration of trabectedin notably abrogated growth of CCS xenograft tumors compared with that of vehicle control. Additionally, the rates of melanin-positive cells and cleaved caspase-3-positive cells were increased in trabectedin-treated CCS xenograft tumors.

Conclusion: Trabectedin exerted significant anti-tumor effects against CCS cell lines by inducing cell cycle arrest and apoptosis, and, at least in part, by promoting melanocytic differentiation. These findings suggested that trabectedin should be a novel effective treatment for human CCS.

P2–Poster 107 2567652

TRABECTEDIN AS FIRST LINE IN ADVANCED SOFT TISSUE SARCOMA (STS) PATIENTS UNFIT TO RECEIVE STANDARD CHEMOTHERAPY: SAFETY AND EFFICACY FROM TR1US STUDY

Federica Grosso[1]; Lorenzo D'Ambrosio[2]; Toni Ibrahim[4]; Stefano Tamberi[5]; Emanuela Palmerini[6]; Danila Comandini[9]; Giacomo Giulio Baldi[7]; Marina Bergaglio[8]; Andrea De Censi[10]; Massimo Zucchetti[11]; Emanuela Marchesi[3]; Matteo Puntoni[12]; Domenico Marra[10]; Maurizio D'Incalci[11]; Giovanni Grignani[2]
[1]SC Oncologia, ASO SS Antonio e Biagio e C Arrigo, Alessandria, Italy; [2]Division of Medical Oncology, Candiolo Cancer Institute - FPO, IRCCS, Candiolo (TO), Italy; [3]Italian Sarcoma Group, Bologna, Italy; [4]Osteoncology and Rare Tumors Center, IRST Meldola, Meldola (FC), Italy; [5]Oncology Unit, Ospedale per gli Infermi, Faenza (RA), Italy; [6]Chemotherpy Unit, Istituto Ortopedico Rizzoli, Bologna, Italy; [7]Medical Oncology Unit, Hospital of Prato, Prato, Italy; [8]Oncology Unit, Villa Scassi Hospital, ASL3 Genovese, Genova, Italy; [9]Divisione di Oncologia Medica, Ospedale San Martino, Genova, Italy; [10]Division of Medical Oncology Unit, EO Ospedali Galliera, Genova, Italy; [11]IRCCS-Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy; [12]E.O. Ospedali Galliera, Biostatistic Unit, Genova, Italy

Objective: About 50% of STS patients (pts) develop metastases within 3 years from diagnosis and die for disease. Trabectedin (T) has been registered for advanced STS pts who failed or are unsuitable for anthracycline-based chemotherapy (A-CT). Activity and toxicity of T is widely assessed in 2ndline, but few data are available for T as 1st line when medical conditions contraindicate A-CT. This study aimed at assessing the activity, tolerability and pharmacokinetic (PK) of 1st line T in advanced STS pts unfit to receive A-CT.

Methods: Pts received intravenous T 1.3-1.5 mg/m^2 as a 24-h infusion q3weeks until progression/unacceptable toxicity. Principal inclusion criteria were: unsuitability to receive A-CT (*i.e.*: stable arrhythmia, previous myocardial infarction [MI]; PS≥2, age≥80 years), ECOG 0-2, GFR ≥30 mL/min, adequate organ function. Sample size was calculated using the Bryant & Day design. T plasma concentrations were measured by HPLC-MS/MS and PK parameters calculated by the software NCPKA v.2.4. Response, progression-free survival (PFS) and overall survival (OS) were assessed according to RECIST 1.1 and Kaplan Meier method, respectively.

Results: From 2/2014 to 12/2015, 24 pts (12 female), median age 78 (range 64-89, IQR 74-82) entered the study. Histotypes were: leiomyosarcoma 11 (46%), liposarcoma 8 (33%), other STS 5 (21%). Only 2 pts had previously received adjuvant A-CT. Overall 114 courses of T were delivered with a median of 4 cycles (range 1-16, IQR 3-6).

All pts received steroid premedication. The steady-state plasma concentration and the clearance of T were 1.55 ng/mL and 39 ml/min/m^2. We observed 4 pts not evaluable for response (17%), 13 SD (54%), 2 PR (8%) and 5 PD (22%) for an overall disease control rate (DCR) of 62%. At a median follow-up of 14 months (mos), median PFS was 4 (IQR 2-25), and median OS 9 (IQR 4-25) mos. Drug related G3-4 adverse events (AEs) were neutropenia (37,5%), fatigue (21%) and transaminitis (12.5%), with 2 serious AEs deemed possibly related to T: thoracic pain with reversible heart failure in a pt with history of MI, and creatinine increase in a pt with huge abdominal mass. No T-related death was observed.

Conclusion: In this unfit pts population the DCR was 62% and median PFS 4 mos superimposable to that of previous studies. PK values were in the range of those reported for younger adult population. These findings confirm that T can be an appropriate option for both elderly pts and those unsuitable for A-CT.

P2–Poster 108 2542257

OVERCOMING PRIMARY RESISTANCE TO VEGF TARGETED AGENTS IN ANGIOSARCOMA BY TARGETING THE MITOGEN- ACTIVATED PROTEIN KINASE PATHWAY

Michael J. Wagner, MD[1]; Vinod Ravi[2]; Wei-Lien Wang[3]; Jean M. Hanson[4]; Yasmin Lyons[4]; Rebecca A. Previs[4]; Archana Nagaraja[4]; Kyunghee Noh[4]; Monika Haemmerle[4]; Selanere Mangala[4]; Sunila Pradeep[4]; Prahlad Ram[5]; Alexander Lazar[3]; Anil Sood[4]

[1]Cancer Medicine, M.D. Anderson Cancer Center, Houston, TX, USA; [2]Sarcoma Medical Oncology, M.D. Anderson Cancer Center, Houston, TX, USA; [3]Pathology, M.D. Anderson Cancer Center, Houston, TX, USA; [4]Gynecologic Oncology and Reproductive Medicine, M.D. Anderson Cancer Center, Houston, TX, USA; [5]Systems Biology, M.D. Anderson Cancer Center, Houston, TX, USA

Objective: Angiosarcomas are rare cancers of endothelial cell origin with a high mortality rate. Response rates to drugs targeting the VEGF pathway are low. We hypothesized that oncogenic mutations activate MAPK signaling in angiosarcoma, and targeting MAPK signaling with MEKi will increase the efficacy of anti-VEGF/VEGFR therapy.

Methods: Patient samples were evaluated for phospho-ERK1/2 (p-ERK) by immunohistochemistry (IHC). Multiple *in vitro* (cell viability, reverse phase protein arrays (RPPA)) and *in vivo* (mouse models) experiments were used to determine efficacy and underlying mechanisms of VEGFR and MEK-targeted agents.

Results: Using IHC in 60 angiosarcoma clinical samples, 26/60 (44%) had uniformly high expression of p-ERK, and another 7 (12%) had focal areas with high p-ERK staining. In the HAMON angiosarcoma cell line, RPPA and network analysis showed that both the MAPK and PI3K/AKT pathways are activated compared to normal endothelial cells. Trametinib and cediranib individually had IC50 levels in the nanomolar range in the 3 angiosarcoma cell lines (SVR, HAMON, and ASM5) tested, but no synergy was observed *in vitro*. In contrast, *in vivo* tumor size was reduced by >90% in the combination compared to vehicle or either agent alone (vehicle 913 mm^3, trametinib 242 mm^3, cediranib 466 mm^3, and trametinib+cediranib 14.5 mm^3; p=0.01) and tumor weight (vehicle 0.39g, trametinib 0.21g, cediranib 0.30g, and trametinib+cediranib 0.03g; p<0.01), with a significant decrease in proliferation in the combination group compared with either treatment alone.

Conclusion: Our results show that >50% of clinical angiosarcoma samples have high levels of MAPK activation. Although there is no clear synergy *in vitro* with VEGFRi and MEKi in angiosarcoma cell lines, there is a robust combinatorial effect *in vivo*. Combination of VEGFRi and MEKi represents a promising therapeutic strategy for angiosarcoma.

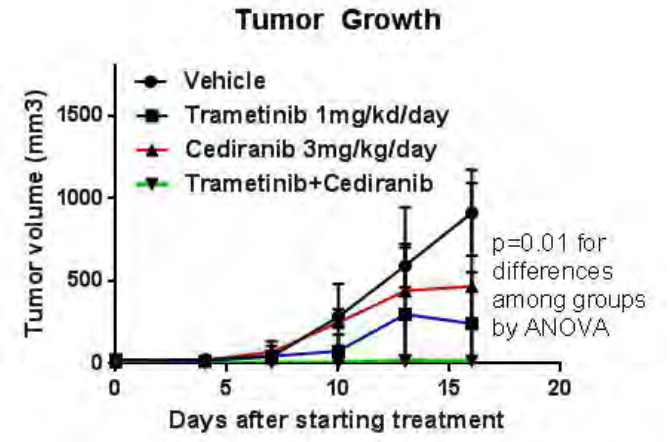


Figure 1. There was a significant combinatorial effect (ANOVA p=0.01 for difference between groups) on tumor growth with VEGFRi+MEKi in a SVR xenograft model.

P2–Poster 109 2570651

A PHASE I / II STUDY OF THE SAFETY AND EFFICACY OF THE COMBINATION OF GEMCITABINE AND DOCETAXEL WTIH MORAB-004 IN METASTATIC SOFT TISSUE SARCOMA

Robin L. Jones[3]; Sant P. Chawla[2]; Steven Attia[6]; Patrick Schöffski[4]; Hans Gelderblom[5]; Bartosz Chmielowski[7]; Axel LeCesne[13]; Brian Van Tine[8]; Jonathan C. Trent[9]; Shreyaskumar Patel[10]; Andrew J. Wagner[11]; Rashmi Chugh[12]; John W. Heyburn[1]; Susan C. Weil[1]; Robert G. Maki[14]
[1]Clinical, Morphotek, Inc., Exton, PA, USA; [2]Sarcoma Oncology Research Center, Santa Monica, CA, USA; [3]Seattle Cancer Care Alliance, Seattle, WA, USA; [4]UZ Leuven Medical Hematology Oncology, Leuven, Belgium; [5]Leiden University Medical Center, Leiden, Netherlands; [6]Mayo Clinic – Jacksonville, Jacksonville, FL, USA; [7]Hematology/Oncology, UCLA Department of Medicine, Los Angeles, CA, USA; [8]Washington University School of Medicine, St. Louis, MO, USA; [9]University of Miami School of Medicine – Sylvester Comprehensive Cancer Center, Miami, FL, USA; [10]MD Anderson Cancer Center, Houston, TX, USA; [11]Dana-Farber Cancer Institute, Boston, MA, USA; [12]Division of Hematology / Oncology, University of Michigan, Ann Arbor, MI, USA; [13]Department of Medicine, Institut Gustave Roussy, Villejuif, France; [14]Mount Sinai School of Medicine, New York, NY, USA

Objective: To evaluate the progression-free survival (PFS) of subjects treated with the combination of gemcitabine/docetaxel (G/D) plus MORAb-004 (M4) versus G/D plus placebo in subjects with metastatic soft tissue sarcoma (mSTS) in 4 defined histological subgroups.

Methods: In the first stage of the study, patients were evaluated for safety and tolerability of a dose of 8mg/kg was established and used for ph 2. In the ph 2 efficacy stage which included an adaptive design, Patients were randomized on a 2:1 basis to receive either G/D + M4 or G/D + placebo. The primary objective was to evaluate progression-free survival (PFS) in 4 STS subgroups (liposarcoma, leiomyosarcoma, pleomorphic and "other"). Secondary objectives included overall survival (OS), overall response rate (ORR), progression free rate (PFR) at 12, 24, 48 and 52 weeks and safety of M4 in combination with G/D. Exploratory objectives included the analysis of putative biomarkers of response.

Results: 209 patients were randomized, 139 to the M4 arm and 70 to the placebo arm. There was no significant difference in PFS, median PFS for the M4 arm 18.7 weeks (11.6-27.4) compared to the placebo arm 24.1 weeks (11.1-36.1), HR 1.08 (95%CI, 0.77-1.50), p=0.6562. There was no significant difference in OS, median OS in the M4 arm 17.5 months (14.8-19.4) and not reached in the placebo arm, HR 1.15 (95%CI, 0.74-1.78), p=0.5389. The ORR was 27 (19.4%) in the M4 arm and 14 (20%) in the placebo arm, p=1.0. No new safety issues were identified and adverse events were generally well balanced across the 2 arms, with fatigue, anemia and nausea being the most common.

Conclusion: M4 combined with G/D did not demonstrate improvements in PFS or OS in advanced STS when compared to placebo. Overall tolerability between the m4 and placebo arms appeared comparable. Subgroup analysis and exploratory biomarker evaluation are ongoing.

P2–Poster 110 2569989

TRC105 (ENDOGLIN ANTIBODY) IN COMBINATION WITH PAZOPANIB (P) IN PATIENTS (PTS) WITH ADVANCED ANGIOSARCOMA (AS)

K. Kumar Sankhala[1]; Steven Attia[2]; Minal A. Barve[3]; Jennifer Wright[4]; Richard Riedel[5]; Steven I. Robinson[6]; Robert M. Conry[7]; Patrick M. Boland[8]; Ben K. Seon[8]; Delia Alvarez[9]; Bonne J. Adams[9]; Ronald L. Shazer[9]; Charles P. Theuer[9]; Robert G. Maki[10]
[1]Sarcoma Oncology Research Center, Santa Monica, CA, USA; [2]Mayo Clinic, Jacksonville, Jacksonville, FL, USA; [3]Mary Crowley Cancer Research, Dallas, TX, USA; [4]University of Utah, Salt Lake City, UT, USA; [5]Duke University, Durham, NC, USA; [6]Mayo Clinic, Rochester, Rochester, MN, USA; [7]University of Alabama at Birmingham, Birmingham, AL, USA; [8]Roswell Park Cancer Institute, Buffalo, NY, USA; [9]TRACON Pharmaceuticals, San Diego, CA, USA; [10]Icahn School of Medicine at Mount Sinai, New York, NY, USA

Objective: P is approved for the treatment of advanced angiosarcoma (AS), but activity is modest, with median PFS of 3.0 months and median OS of 9.9 months in a recent study of 30 AS patients, of whom none achieved complete response (CR). Endoglin is a surface receptor expressed on activated endothelium, including tumor vasculature, that is also expressed on AS tumor tissue and may be a fundamental driver of this endothelial malignancy. Endoglin is upregulated following VEGF inhibition and may mediate resistance to P. A Phase 1B/2A study of TRC105, an endoglin antibody, in combination with P in pts with advanced STS, was reported previously (ASCO 2016). Following the demonstration of activity in AS, additional patients have been recruited into the trial in an AS expansion cohort.

Methods: Ph1B (N=18) was a dose escalation trial to determine the TRC105 RP2D with P at 800 mg/day. Ph2A (n=63) was a single arm evaluation of TRC105 at the RP2D of 10 mg/kg weeklywith P at 800 mg/day in STS. The AS expansion cohort (N=13) included two groups of pts: Group A received TRC105 at the RP2D concurrently with P at 800 mg/day; Group B received single agent TRC105 at the RP2D, with P added at progression.

Results: Five AS patients were treated in the original Ph1B/2A study, and all five demonstrated tumor reductions by RECIST 1.1, of whom two remain on study with durable

CR (14 and 21 months), with median PFS > 12.9 months (95% CI 2.1, NA). All AS pts (N=16): median age=59, M:11 F:5, median prior lines of systemic therapy=1. Eleven of 13 AS pts have enrolled in the AS cohort (4 in Group A and 7 in Group B). Three of 4 Group A patients demonstrated clinical or radiographic evidence of tumor reduction, and two remain on study. Four of seven Group B patients have added P following progression on single agent TRC105, and five remain on study. Adverse events (AEs) characteristic of each drug were not increased in frequency or severity. Common TRC105 related AEs in AS patients included grade (G) ≤ 2 telangiectasia (with epistaxis and gingival bleeding) and G≤3 anemia and headache, common P related AEs included G≤3 fatigue, diarrhea, and hypertension.

Conclusion: TRC105 was well tolerated when combined with P and the combination was active in AS, including durable CR. A global Phase 3 study in AS of P ± TRC105 is planned.

P2–Poster 111 2570725

SAFETY, TOXICITY, AND ACTIVITY OF MULTI-KINASE VEGFR TKI VANDETANIB COMBINED WITH MTOR INHIBITOR EVEROLIMUS IN AN ADVANCED SARCOMAS COHORT OF A PHASE I STUDY

Anthony P. Conley, MD; Vinod Ravi; Neeta Somaiah; SR Patel; Robert S. Benjamin; Maria A. Zarzour; Joseph A. Ludwig; Dejka Araujo; Winston Huh; Vivek Subbiah

Sarcoma Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA

Objective: Advanced/metastatic sarcomas refractory to standard therapy represent an area of unmet need. Multi-kinase VEGFR tyrosine receptor kinase inhibitors such as pazopanib have efficacy in advanced/metastatic soft tissue sarcomas. Pre-clinical studies have shown that mTOR inhibitors overcome primary and/or acquired resistance to VEGFR inhibitor monotherapy. We hypothesized that Vandetanib (V), a multi-kinase inhibitor of VEGFR/RET, combined with everolimus (E), an mTOR inhibitor, could overcome resistance to monotherapy so we designed a phase 1 trial.

Methods: A standard 3+3 dose escalation/expansion trial was designed to determine safety, maximum tolerated dose, recommended Phase II dose (RP2D), dose-limiting toxicities (DLTs) and activity of V+E in advanced/refractory solid tumors including a sarcoma cohort. Response was assessed by RECIST 1.1. Progression-Free Survival (PFS) and Overall Survival (OS) was evaluated.

Results: Among 22 pts with advanced sarcoma, 18 pts (82%) with soft tissue sarcomas (STS) and 4 pts (18%) with bone sarcoma were enrolled. Alveolar soft part sarcoma was the most common STS (4 pts, 18%). Ewings sarcoma was the most common bone sarcoma (2 pts, 9%). Median age was 40 y (18y – 82 y). Median ECOG PS was 1 (0 – 3). Median number of prior therapies was 3 (1 – 9). For V dosing, 3 pts (14%) were at 200 mg/day dose level and 19 pts (86%) were at 300 mg/day. For E dosing, 1 pt (5%) was at 2.5 mg/day, 3 pts (14%) at 5 mg/day, and 18 pts (82%) at 10 mg/day. Dose reductions occurred in 7 pts (32%). DLTs were noted in 3 pts (diarrhea, thrombocytopenia, QTc prolongation); 2 pts at V 300 mg/day- E 10 mg/day dose level and 1 pt at V 300 mg/day- E 5 mg/day dose level. No G5 toxicities were noted. Thrombocytopenia was the most common G3 toxicity (27%) and G4 toxicity (9%). Median number of cycles received was 4 (1 – 14). 21 pts (96%) were evaluable for response, which included 2 PR (epithelioid sarcoma, pleomorphic sarcoma) (9.5%), 11 SD (52%), and 8 PD (38%). Of note 1 pt with ewings sarcoma has SD and associated PFS of 9.9 months. Median PFS was 4.5 months (0.8 – 12.7 months), and median OS was 13.9 months (2.2 - 32.3 months).

Conclusion: The combination did not have any unexpected toxicities from either monotherapy. V+E was reasonably tolerated and appears to exert activity in in this heavily pre-treated sarcoma population. Further evaluation of the multi-VEGF TKI and mTOR inhibition in a formal phase 2 strategy should be considered for selected sarcoma subtypes.

P2–Poster 112 2541028

THE REAL-LIFE CLINICAL OUTCOME OF PAZOPANIB TREATMENT IN PATIENTS WITH SOFT TISSUE SARCOMA: A JAPANESE MUSCULOSKELETAL ONCOLOGY GROUP STUDY

Tomoki Nakamura, MD, PhD[1]; Akihiko Matsumine[1]; Eisuke Kobayashi[11]; Nobuhito Araki[2]; Takahiro Goto[3]; Tsukasa Yonemoto[4]; Hideshi Sugiura[5]; Yoshihiro Nishida[6]; Hiroaki Hiraga[12]; Kanya Honoki[7]; Taketoshi Yasuda[8]; Shogen Boku[9]; Akihiro Sudo[1]; Takafumi Ueda[10]

[1]Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Tsu, Mie, Japan; [2]Department of Orthopaedic Surgery, Osaka General Medical Center, Osaka, Japan; [3]of Orthopedic Surgery and Musculoskeletal Oncology, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan; [4]Division of Orthopedic Surgery, Chiba Cancer Center, Chiba, Japan; [5]Department of Orthopedic Surgery, Aichi Cancer Center, Nagoya, Japan; [6]Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan; [7]Department of Orthopaedic Surgery, Nara Medical University, Kashihara, Japan; [8]Departmemt of Orthopaedic Surgery, University of Toyama, Toyama, Japan; [9]Department of Medical Oncology, Hyogo Cancer Center, Akashi, Japan; [10]Department of Orthopaedic Surgery, Osaka National Hospital, Osaka, Japan; [11]Department of Orthopaedic Surgery, National Cancer Center Hospital, Tokyo, Japan; [12]Department of Orthopaedic Surgery, Hokkaido Cancer Center, Sapporo, Japan

Objective: We investigate the efficacy and safety of pazopanib in 156 Japanese patients with relapsed soft tissue sarcoma (STS). This was a retrospective study based on the collection of postmarketing surveillance (PMS) data.

Methods: We retrospectively reviewed the PMS data and an independent questionnaire was administered to Japanese Musculoskeletal Oncology Group (JMOG) members. The inclusion criteria were as follows: 1) the primary tumor was an STS that arose at the extremities/trunk; and 2) patients had received pazopanib for an unresectable local recurrence and/or a metastatic lesion. Patients received pazopanib with the objective of treating local recurrence (n=20), metastasis (n=104), and both (n =32). The patient median age was 53.8 years. The primary objective of this study was to clarify the efficacy of pazopanib for patients with STS.

Results: The median treatment duration was 28.7 weeks, and the average dose intensity of pazopanib was 609 mg. Adverse events occurred in 127 patients (81.4%). In addition to the main common toxicities, such as hypertension and liver disorder, pneumothorax (n=11) and thrombocytopenia (n=16) also were observed. Among all 156 patients in the study population, an evaluable tumor response (according to RECIST) occurred in125 patients. Thirteen patients achieved a partial response (PR). Seventy-four patients achieved stable disease (SD), which was maintained for a period of >6 months (long SD) in 32 of 74 patients. Histologically, a PR or long SD was achieved in patients with alveolar soft part sarcoma (ASPS) (78%), leiomyosarcoma (LMS) (44%), and synovial sarcoma (SS) (44%). The median progression-free survival for all patients was 15.4 weeks. The median progression-free survival for patients with LMS, SS, undifferentiated pleomorphic sarcoma (UPS), and LPS was 18.6 weeks, 16.4 weeks, 15.3 weeks, and 8 weeks, respectively. The median survival for all patients was 11.2 months. The median survival for patients with LMS, SS, UPS, and LPS was 20.1 months, 10.6 months, 9.5 months, and 7.3 months, respectively.

Conclusion: There were apparent differences in the radiographic efficacy of pazopanib treatment among the histologic types of STS. A PR or long SD may be expected in patients with ASPS, LMS, SS, and UPS who receive pazopanib. Pazopanib treatment is a new, tolerable treatment option; however, adverse events, such as pneumothorax and thrombocytopenia, which did not occur frequently in the PALETTE study, should be taken into consideration.

P2–Poster 113 2562838

IMPACT ON OUTCOME OF CONCOMITANT ADMINISTRATION OF GASTRIC ACID SUPPRESSION (GAS) THERAPY AND PAZOPANIB IN SOFT TISSUE SARCOMA (STS) PATIENTS TREATED WITHIN EORTC 62043/62072 TRIALS

Olivier Mir, MD, PhD[1]; Nathan Touati[2]; Michela Lia[2]; Saskia Litiere[2]; Axel Le Cesne[1]; Stefan Sleijfer[3]; Michael Leahy[4]; Robin Young[5]; Jean-Yves Blay[6]; Zsuzsanna Papai[7]; Ron Mathijssen[3]; Nielka Van Erp[8]; Hans Gelderblom[9]; Winette Van der Graaf[10]; Alessandro Gronchi[11]

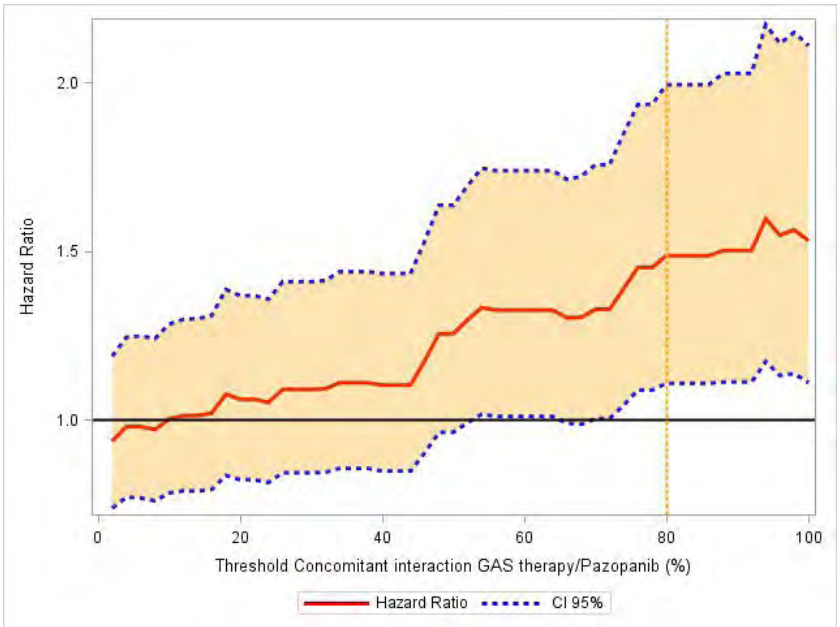
[1]Sarcoma Group, Gustave Roussy Cancer Campus, Villejuif, France; [2]European Organization for Research and Treatment of Cancer, Brussels, Belgium; [3]Erasmus MC - Cancer Institute, Rotterdam, Netherlands; [4]The Christie NHS Foundation Trust, Manchester, United Kingdom; [5]Weston Park Hospital, Sheffield, United Kingdom; [6]Centre Leon Berard, Lyon, France; [7]National Medical Canter, Budapest, Hungary; [8]Radboud University Medical Centre, Nijmegen, Netherlands; [9]Leiden University Medical Center, Leiden, Netherlands; [10]The Institute of Cancer Research and the Royal Marsden NHS Foundation Trust, London, United Kingdom; [11]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy

Objective: Pazopanib is an oral tyrosine-kinase inhibitor indicated for the treatment of patients with advanced STS. Its absorption is pH-dependent, which makes patients potentially susceptible to drug-drug interaction when pazopanib is co-administered with gastric acid suppressive

agents (GAS) such as proton pump inhibitors and Histamine type-2 receptor antagonists. Co-administration could reduce the systemic exposure of pazopanib, and lead to a decrease in therapeutic benefit.

Methods: The EORTC 62043 and 62072 studies, were single-arm phase II and placebo-controlled phase III studies respectively of pazopanib for patients with advanced STS. We compared the outcome of patients reported to receive GAS therapy for ≥80% of pazopanib treatment duration with patients that received pazopanib but did not meet this GAS therapy criteria. The impact of concomitant GAS therapy was assessed on progression free survival (PFS) and overall survival (OS) using a multivariate Cox model adjusting for performance status (0/1), gender, tumour grade (low/intermediate/high) and age (≤50/>50). Multivariate (adjusting for GAS therapy administration before pazopanib) and univariate Cox models were performed as secondary analyses. Finally, sensitivity analyses using different thresholds on the overlapping administration period were considered.

Results: Of 333 eligible patients, 117 (35%) used GAS therapy at some time during pazopanib treatment. Fifty-nine patients (17.7%) received it concomitantly for >80% of pazopanib treatment duration. Median PFS was shorter in GAS users versus no-users: 2.8 months vs. 4.6 months respectively (HR 1.49 (95%CI 1.11-1.99), p = 0.008). Concomitant administration of GAS therapy was also associated with a worse OS: 8.0 months vs. 12.6 months (HR 1.81 (95% CI 1.31-2.49), p < 0.001). A similar trend was observed from the other models performed as secondary analyses. A longer period of overlap of GAS therapy with the administration of pazopanib had a detrimental effect on the outcome of the patients (see figure).



Evolution of the Hazard Ratio (Concomitant Administration of GAS therapy/pazopanib and PFS) according to the selected threshold value

Conclusion: In the EORTC 62043 and 62072 trials, almost 1 out of 3 patients took GAS therapy during pazopanib treatment. Administration of GAS therapy for at least 80% of the time with pazopanib was associated with a significantly decreased PFS and OS. Withdrawal of GAS therapy must be considered whenever possible. Therapeutic drug monitoring of pazopanib plasma concentrations could be helpful for patients on pazopanib and GAS therapy.

P2–Poster 114 2529585

MECHANISM OF PAZOPANIB RESISTANCE IN SYNOVIAL SARCOMA

Yoshihiro Matsumoto, MD, PhD[1]; Nobuhiko Yokoyama[1]; Tomoya Matsunobu[2]; Makoto Endo[3]; Setsu Nokitaka[1]; Kiichiro Iida[1]; Fukushima Suguru[1]; Yukihide Iwamoto[2]
[1]Orhopaedic Surgery, Kyushu University School of Medicine, Fukuoka, Fukuoka, Japan; [2]Kyushu Rosai Hospital, Fukuoka, Japan; [3]National Cancer Center Hospital, Tokyo, Japan

Objective: Synovial sarcoma (SS) is a rare high-grade malignant mesenchymal tumour with a relatively poor prognosis despite intensive multimodal therapy. Although pazopanib, a multi-kinase inhibitor, is often used for advanced SS, most cases of SS eventually become resistant to pazopanib. In the present study, we investigated the mechanisms of acquired pazopanib resistance in SS.

Methods: To examine acquired pazopanib resistance, three SS cell lines, SYO-1, YaFuss, and HS-SY-II, were isolated after multiple selection steps with increasing concentrations of pazopanib, up to 20 mM. SYO-1 was also used in vivo. Then, pazopanib-resistant clones were investigated to assess potential mechanisms of acquired pazopanib resistance.

Results: Stable pazopanib-resistant clones were established and exhibited enhanced cell cycle progression and cell growth with increased ERK1/2 phosphorylation. Pazopanib-resistant cells were more sensitive than parental cells to a MEK-inhibitor, trametinib, both in vitro and in vivo. Furthermore, addition of low-dose trametinib partially reversed the pazopanib resistance. In two of three pazopanib-resistant clones, dual specificity phosphatase 6 (*DUSP6*) was downregulated. Inhibition of *DUSP6* expression in parental YaFuss cells caused enhanced cell growth and resistance to pazopanib, which recapitulated acquired pazopanib resistance.

Conclusion: Acquired pazopanib resistance in SS was associated with activation of ERK1/2 through downregulation of *DUSP6* expression. Simultaneous treatment with pazopanib and a MEK inhibitor could be a promising strategy to overcome pazopanib resistance in SS.

P2–Poster 115 2531913

BODY COMPOSITION VARIATION IN DOXORUBICIN-REFRACTORY SOFT TISSUE SARCOMA (STS) PATIENTS (PTS) TREATED WITH REGORAFENIB VERSUS PLACEBO: AN ANCILLARY ANALYSIS OF REGOSARC TRIAL

Nicolas Penel, MD, PhD[1]; Aurélien Carnot[1]; Thomas Brodowicz[2]; Axel Le Cesne[3]; Blay Jean-Yves[4]; Sophie Taieb[5]; Emilie Decoupigny[6]; Jennifer Wallet[7]; Emmanuelle Tresch-Bruneel[7]; Stéphanie Clisant-Delaine[6]; Olivier Mir[3]
[1]Medical Oncology, Centre Oscar Lambret, Lille, France; [2]Medical Oncology, Wien University Hospital, Wien, Austria; [3]Medical Oncology, Gustave Roussy, Villejuif, France; [4]Medical Oncology, Centre Léon Bérard, Lyon, France; [5]Imaging Department, Centre Oscar Lambret, Lille, France; [6]Clinical Research Unit, Centre Oscar Lambret, Lille, France; [7]Biostatistics and Methodology Unit, Centre Oscar Lambret, Lille, France

Objective: REGOSARC trial is a double-blinded placebo-controlled phase II trial assessing the activity and safety of regorafenib in advanced STS pts. This trial showed a significant improvement of progression-free survival (PFS) in non-adipocyctic STS treated with regorafenib: 4.0 (2.6-5.5) vs 1.0 months (1.0-1.8); HR = 0.36 [0.26-0.53], p<0.0001. The purpose of the present analysis is to measure the body composition changes and to determine if they could be prognostic factors of outcome or predictive of toxicity.

Methods: Collected variables were weight (W), body mass index (BMI), and normalized total adipose tissue (nTAT), normalized total lean mass (nTLM) and normalized skeletal muscle (nSM) at the 3rd lumbar vertebra were measured by computed tomography (CT) at baseline and after 1 month of treatment. Prognostic factors were identified using univariate Cox Model. Factors associated with toxicity were identified using Student's t tests.

Results: CT-scans of 104 pts were assessable for this analysis (51 pts receiving regorafenib and 53 placebo). We observed a statistically significant decrease in all parameters i.e., W, BMI, nTAT, nTLM and nSM, in both arms. The changes were significantly more marked with regorafenib for nSM (p=0.04) and for nTLM (p=0.04). Baseline W, BMI, nTAT, nTLM, and nSM and their changes after one month of treatment were not prognostic of either PFS or OS. None of these parameters was associated with 90-day mortality. Change in nTLM was associated with occurrence of Grade 3 arterial hypertension (p=0.045). Changes in W (p=0.002), in BMI (p=0.027), in nSM (p=0.045) and in nTLM (p=0.045) were associated with occurrence of Grade 3 diarrhea. None of these parameters was associated with hand foot skin reaction. None of these parameters were associated with regorafenib dose reduction during the 1st month or the 6 first months of treatment.

Conclusion: Regorafenib significantly modifies nSM and nTLM. Body composition parameters were not prognostic of either PFS or OS. Change in some body composition parameters were associated with Grade 3 arterial hypertension and Grade 3 diarrhea occurrence.

P2–Poster 116 2531836

REGOSARC: REGORAFENIB VERSUS PLACEBO IN DOXORUBICIN-REFRACTORY SOFT TISSUE SARCOMA: A QUALITY- ADJUSTED TIME WITHOUT SYMPTOMS OF PROGRESSION OR TOXICTY (Q-TWIST)

Vincent Berry[1]; Laurent Basson[2]; Emilie Bogart[2]; Olivier Mir[3]; Blay Jean-Yves[4]; Antoine Italiano[5]; François Bertucci[6]; Christine Chevreau[10]; Bernadette Liegl-Antzager[7]; Stéphanie Clisant-Delaine[8]; Emmanuelle Tresch-Bruneel[2]; Emilie Decoupigny[8]; Axel Le Cesne[3]; Thomas Brodowicz[9]; Nicolas Penel[1]
[1]Medical Oncology, Centre Oscar Lambret, Lille, France; [2]Biostatistics and Methodology Unit, Centre Oscar Lambret, Lille, France; [3]Medical Oncology, Gustave Roussy, Villejuif, France; [4]Medical Oncology, Centre Leon Beard, Lyon, France; [5]Medical Oncology, Institut Bergonie, Bordeaux, France; [6]Medical Oncology, Institut Paoli Calmette, Marseille, France; [7]Pathology Department, Graz University Hospital, Graz, Austria; [8]Clinical Research Unit, Centre Oscar Lambret, Lille, France; [9]Medical Oncology, Wien University Hospital, Wien, Austria; [10]Medical Oncology, Institut Universitaire du Cancer Toulouse - Oncopole, Toulouse, France

Objective/Introduction: REGOSARC is a double-blind randomized phase II trial with 4 parallel cohorts (liposarcoma, leiomyosarcoma, synovial sarcoma and other sarcoma) comparing the activity and safety of regorafenib versus placebo. We report here an ancillary study assessing the risk-benefit ratio using Q-TWiST.

Patients and Method: Overall survival was partitioned into 3 distinct health states: time with unacceptable toxicity (TOX), time after progression according to RECIST 1.1 (REL) and time without symptoms of progression or toxicity (TWiST). Utilities were set up at 1 for TWiST and 0.5 for REL or TOX. Then, to take into account the point of view of pts, we interviewed 30 pts, not included in REGOSARC trial but treated with tyrosine kinase inhibitors and 30 pts suffering from metastatic sarcoma for defining "unacceptable toxicity" according to the nature, grade and duration of events. Using the point of view of the patients, we have conducted a sensitivity analysis with 9 alternative scenarios of what is an unacceptable toxicity.

Results: In non-adipocytic sarcoma, the PFS was 4.0 months (2.6-5.5) versus 1.0 month (1.0-1.8) with regorafenib and placebo, respectively; and OS were 13.4 (8.6-17.3) versus 9.0 (6.8-12.5), respectively. Principal

component analysis shows that both groups of interviewed pts similarly assessed toxicity with a very high concordance for anorexia (Crombach Alpha=0.92), asthenia (0.87), arterial hypertension (0.86), diarrhea (0.87), mucositis (0.88), hand foot skin reaction (0.87). Using classical definition of unacceptable toxicity (including all grade 3 and 4 clinical toxicities), the Q-TWiST were 8.0 months (7.0-9.0) with regorafenib versus 5.7 months (4.9-6.4) with placebo; the difference was statistically (p<0.001) and clinically significant (2.3 months [1.0-3.6]). Sensitivity analysis showed that whatever the definition of unacceptable toxicity, the Q-TWiST was always significantly better with regorafenib (range, 1.1 to 2.4 months).

Conclusion: Regorafenib significantly improves the **quality**-adjusted time without symptoms of progression or toxicity in doxorubicin-refractory sarcoma, whatever the definition of "unacceptable toxicity".

P2–Poster 117 2570680

SYSTEMATIC REVIEW AND META-ANALYSIS OF PAZOPANIB (PZB) VERSUS OTHER ANTI-ANGIOGENIC, TYROSINE KINASE INHIBITORS (AATKI) IN ADVANCED SARCOMAS

Lee D. Cranmer, MD PhD FACP[1]; Elizabeth T. Loggers[2]; Seth M. Pollack[2]; Ivo Abraham[3]
[1]Division of Medical Oncology, University of Washington, Seattle, WA, USA; [2]Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [3]Department of Pharmacy Practice and Science, University of Arizona, Tucson, AZ, USA

Objective: Pzb is an aaTKI approved in the U.S. for advanced, non-adipocytic soft-tissue sarcomas after failure of prior systemic therapy. Other mechanistically similar aaTKIs have also been explored in sarcomas. While Pzb may possess unique properties enhancing its anti-sarcoma activity, its activity may, instead, be a general anti-angiogenic TKI (aaTKI) property or a reflection of how Pzbwas studied clinically. This meta-analysis aimed to distinguish these possibilities.

Methods: We searched MEDLINE and Web of Science for phase 2/3 trials prior to 5/1/2016 using either Pzb or other aaTKI as monotherapy in ≥1 trial arm or stratum to treat sarcomas. Excluded were case reports/series and named use of drugs; and studies in gastrointestinal stromal tumor, Kaposi's sarcoma, carcinosarcoma, or Wilms' tumor. Outcomes included median progression free (PFS) and overall survival (OS) with specified 95%CI; and overall response rate (ORR) with 95%CI specified or, alternately, calculated via exact Clopper-Pearson method 95%CI. A random effects meta-analysis was conducted with pre-specified strata considered as distinct trials.

Results: From 253 search-yielded references, 5 Pzb treatment strata in 2 trials and 31 other aaTKI strata in 17 trials met inclusion criteria. Meta-analyses comparing Pzb vs other aaTKIs yielded, respectively, ORR of 5.2% (95%CI=2.5-8.7) vs 5.6% (95%CI=3.5-7.8); median PFS of 3.7 m (95%CI=2.6-4.7) for vs 3.2 m (95%CI=2.4-4.0); and median OS 11.4 m (95%CI=9.9-12.9) vs 13.8 m (95%CI=9.3-18.3). Median PFS (Pzb>other aaTKI) and OS (aaTKI>Pzb), but not ORR, differed significantly (p<0.05) by drug treatment group.

Conclusion: PFS was longer but OS shorter in Pzb vs other aaTKI-treated pts. The PFS vs OS discordance may reflect differences in the biology of pts in Pzb studies vs drugs in other studies, with Pzb studies demonstrating less heterogeneity than non-Pzb studies. ORR was similar and low in the two groups. Further studies to clarify Pzb's activity may be useful in targeting it as monotherapy and in selecting companion drugs for combination therapy.

P2–Poster 118 2537944

THE ANTI-PLATELET-DERIVED GROWTH FACTOR RECEPTOR α ANTIBODY OLARATUMAB (LY3012207/IMC-3G3) DEMONSTRATES ANTI-TUMOR ACTIVITY IN MODELS OF PEDIATRIC BONE AND SOFT TISSUE SARCOMA

Caitlin May; Nick Loizos; Ruslan Novosiadly; Wayne Blosser; Michele Dowless; Gerard Oakley; Christophe Marchal; Amelie Forest; Robert Iliaria; Louis F. Stancato
Eli Lilly and Company, Indianapolis, IN, USA

Objective: Platelet-derived growth factor receptor alpha (PDGFRα) is implicated in several types of carcinoma and sarcoma, where its aberrant expression and/or activation promote primary tumor growth and metastasis. In addition, PDGF signaling has been identified in tumor-associated stromal cells, where it facilitates both angiogenesis and fibroblast activation in order to support local tumor growth. Therefore, PDGFRα signaling may mitigate disease progression via autocrine and paracrine modes of activation, facilitating crosstalk between the tumor and stroma. Olaratumab is a fully humanized monoclonal antibody that selectively binds human PDGFRα and blocks signaling initiated by PDGF ligand binding. We evaluated the efficacy of olaratumab and 1E10, a high affinity anti-mouse PDGFRα antibody, alone and in combination with standard-of-care (SOC) in models of pediatric bone and soft tissue sarcoma; furthermore, we examined the effects of SOC on receptor expression in pediatric cell lines and patient-derived xenografts (PDXs).

Methods: Olaratumab/1E10 were evaluated for their anti-tumor activity alone and in combination with SOC in patient-derived and cell-derived mouse models of pediatric bone and soft tissue sarcoma. Immunohistochemical analysis was performed on control and treated tumor samples.

Gene expression of PDGF pathway components in cell lines as well as in tumor samples was determined using the Modaplex platform.

Results: A PK/PD relationship was established in the HuO9 human osteosarcoma model whereby olaratumab inhibited PDGFRα-driven signaling in a dose-dependent fashion. In addition, olaratumab/1E10-containing treatment regimens delayed primary tumor growth in mouse models of pediatric malignancies including osteosarcoma and rhabdoid tumors. Interestingly, expression of pathway components did not necessarily predict sensitivity to treatment indicating that PDGFRα and ligand expression was *necessary but not sufficient* for olaratumab sensitivity. In addition, treatment of bone and soft tissue sarcoma cells with SOC decreased mRNA expression of *PDGFRA* and other pathway components.

Conclusion: PDGFRα signaling is blocked by olaratumab/1E10 in mouse models of pediatric sarcoma, resulting in tumor growth inhibition. Furthermore, SOC reduces *PDGFRA* expression in bone and soft tissue sarcoma cell and tumor models.

P2–Poster 119 2550045

PHOSPHOPROTEOMIC PROFILING IN SARCOMAS REVEALS ALK AND MET AS NOVEL ACTIONABLE TARGETS IN SYNOVIAL SARCOMAS

Emmy Fleuren[1]; Myrella Vlenterie[2]; Winette Van der Graaf[1]; Melissa H. Hillebrandt-Roeffen[2]; Sabri Cebeci[2]; Amy van de Ven[2]; Uta E. Flucke[2]; Jianmin Wu[3]; Yvonne M. Versleijen-Jonkers[2]; Roger Daly[4]
[1]Institute of Cancer Research, London, United Kingdom;
[2]Radboud UMC, Nijmegen, Netherlands;
[3]Center for Cancer Bioinformatics, Being, China;
[4]Monash University, Melbourne, Victoria, Australia

Objective: Despite multimodal treatments, the survival of most advanced sarcoma patients has not improved significantly during the last decades. Though novel therapies are high on the agenda, candidate-based targeted treatments have met with limited clinical success, stressing the need for an unbiased and comprehensive analysis of oncogenic signaling networks to reveal therapeutic targets and personalized treatment strategies.

Methods: We utilized a mass-spectrometry (MS)-based phosphoproteomics screening approach to profile the largest and most heterogeneous set of sarcoma cell lines (*n=20*) to date, including both adult and pediatric/adolescent and young adult (AYA) sarcomas as well as soft-tissue sarcomas (STS) and bone sarcomas. For the four included synovial sarcoma (SS) cell lines, tyrosine phosphorylation data was validated by functional *in vitro* and *in vivo* assays using clinically available inhibitors, as well as validating target expression by immunohistochemistry on a tissue microarray (TMA) of 43 clinical SS tumor specimens.

Results: The MS-based phosphoproteomics screen provided a novel subclassification of sarcoma based on tyrosine phosphorylation patterns, demonstrated that particular tyrosine kinases exhibit enhanced phosphorylation in particular histological subtypes, and identified driver kinases with outlier levels of activation. ALK was identified as a novel driver in the Aska-SS SS cell line, which was explained by an underlying ALK translocation. Functional ALK dependency was confirmed *in vitro* with high sensitivity for the ALK inhibitor TAE684 (IC_{50} 26±3 nM) and the ALK/MET inhibitor crizotinib (IC_{50} 46±5 nM). Importantly, a panel of 43 clinical SS specimens displayed similar characteristics, with ALK immunopositivity in 14% of patients and one harboring an ALK translocation. Other SS cell lines and sarcoma subtypes exhibited multiple activated tyrosine kinases, providing a rationale for combined targeting approaches. Indeed, high MET and PDGFRA phosphorylation in Yamato-SS cells predicted sensitivity to crizotinib and pazopanib (PDGFR) *in vitro* and *in vivo*. Clinically, immunohistochemical MET or PDGFRA expression was detected in 58% and 84% of SS patients, respectively, with co-expression in 56%.

Conclusion: Our integrated approach has led to the identification of ALK, MET and PDGFRA as novel and actionable therapeutic targets in SS *in vitro.*

P2–Poster 120 2570512

REGORAFENIB IN PATIENTS WITH METASTATIC SOFT TISSUE SARCOMAS (STS): PRELIMINARY RESULTS FROM AN OPEN-LABEL PHASE II STUDY (RESOUND)

Rita De Sanctis, MD; Silvia Bozzarelli; Andrea Marrari; Lorenza Rimassa; Simona Sala; Vittorio Quagliuolo; Armando Santoro
Humanitas Cancer Center, Rozzano (Milan), Italy

Objective: Regorafenib is an oral multikinase inhibitor indicated in GIST after imatinib and sunitinib failure. Angiogenesis plays a key-role in sarcoma biology, especially in leiomyosarcoma (LMS), synovial sarcoma (SS) and vascular sarcoma (VS).

Methods: RESOUND is a single-stage, phase II trial enrolling patients (pts) with various types of metastatic tumors refractory to standard treatments, including LMS, SS and VS. Here we present the results of the STS cohort. Main inclusion criteria: ≥1 measurable lesion, ECOG PS <2, adequate hematological, hepatic and renal functions. Pts received oral regorafenib 160 mg once daily in cycles of 3 weeks on/1 week off until disease progression or unacceptable toxicity. Response was assessed by CT scan every 8 weeks according to RECIST 1.1 criteria. Safety was assessed every 14 days for the first 8 weeks, then every 28 days. Primary endpoint was progression-free rate (PFR) at 2 months (8/19 pts, 42% required). Secondary

end-points were safety, progression free survival (PFS) and overall survival (OS).

Results: From April 2015 to June 2016, 15 STS pts (11 LMS, 3 SS, 1 VS) were enrolled. Male/female ratio was 4/11, median age was 61 (range, 20-80) and median number of previous chemotherapy regimens 4 (range, 1-7). 12 patients underwent the first post baseline CT assessment and were evaluable for the primary endpoint. At 8 weeks, 9 stable disease and 3 progressive disease were observed. The 2–month PFR was 75%.

The most common drug-related CTC-AE Grade (G) 3 adverse events (AEs) were hypertension (26%), fatigue (13%) and rash/desquamation (6%). Main G1-2 AEs were fatigue (53%), diarrhea, anorexia, hand-foot skin reaction and hypertension (13%). Dose reductions and delays were required in 53% and 13% pts, respectively. At a median follow-up of 5.8 months , median PFS and OS were not reached.

Conclusion: Regorafenib is well-tolerated and manageable and appears to be effective in metastatic, pretreated LMS, SS and VS.

P2–Poster 121 2565555

TEMOZOLOMIDE POST PAZOPANIB TREATMENT FAILURE MAY EXTENT PROGRESSION FREE SURVIVAL IN PATIENTS WITH ADVANCED SARCOMA: A CASE SERIES

Manojkumar Bupathi[2]; James Chen[1]
[1]Department of Biomedical Informatics and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA; [2]Department of Medical Oncology, The Ohio State University, Columbus, OH, USA

Objective: Soft tissue sarcomas (STS) are rare and heterogeneous mesenchymal tumors where the prognosis remains abysmal in advanced disease. Pazopanib (paz), a multi-tyrosine kinase inhibitor, is standard of care for patients who fail cytotoxic chemotherapy with modest efficacy. Thus, there is increasing interest in combining paz with existing therapeutic modalities. As paz is cytostatic rather than cytoreductive, combinations involving conventional cytotoxic chemotherapies may be useful for improving therapeutic activity. The cytotoxic agent, temozolomide (tem), has some activity in patients with advanced STS. We therefore hypothesized that their combination may demonstrate increased activity in STS as compared to single agents.

Methods: A retrospective study was done to determine the clinical benefit of tem with paz (OSU IRB:2014E0450), in patients who previously derived benefit from single-agent paz. Patients with metastatic soft tissue or bone sarcomas who progressed on paz were continued on paz with the addition of tem. Progression free survival (PFS) was measured from start of paz to disease progression on single-agent paz and from the addition of tem therapy to disease progression.

Results: A total of 10 patients were evaluated. The mean age at diagnosis was 48 (50% M: 50% F). Except one, all patients had progressive disease on at least 1 line of therapy prior to starting on combination therapy. Subtypes included spindle cell sarcoma, leiomyosarcoma, extraskeletal myxoid chondrosaroma, dedifferentiated chondrosarcoma, small blue cell round tumor, epithelioid sarcoma and myxoid chondrosarcoma. The progression free survival (PFS) for single agent VEGFRi, was 8 months in 9 patients. One patient who received single agent paz was censored as their paz start date was unclear. The clinical benefit rate at 4 months (PR+CR+SD) of combination therapy was seen in 6 out of 10 patients. The PFS was 6 months for combination therapy ranging from 0 to 17 months, with four patients still on therapy. Two patients on combination therapy did not receive complete at least one cycle of therapy due to other medical complications. Of the remaining eight patients, six had either stable disease or partial response at 4 months. At the time of data evaluation, 4 patients are still on combination therapy.

Conclusion: In this advanced sarcoma population, the addition of tem to paz may greatly benefit a subset of patients compared to paz alone. Future prospective trials are needed to validate these findings.

Table 1:

Response to pazopanib therapy and VEGFi + temozolomide therapy

Patient ID	Subtype	Prior therapies (excluding pazopanib)	Response at 4 months	Total Duration on combination therapy
1*	Sarcoma NOS	Surgery	SD	15 months
2	Extraskeletal myxoid chondrosarcoma	sunitinib, XRT, nivolumab	PD	2 months
3	Non-uterine leiomyosarcoma	AIM, XRT, denosumab, gemcitabine/docetaxel	SD	7 months
4*	Spindle cell sarcoma	none	PR	17 months
5*	Dedifferentiated chondrosarcoma	everolimus	SD	9 months
6	Non-uterine leiomyosarcoma	gemcitabine/docetaxel +/-morab004, doxorubicin	PD	1 month
7	Small blue round cell tumor	VAC/IE, XRT with irinotecan	PD	<1 month
8	Epithelioid sarcoma	AIM, XRT with paclitaxel, gemcitabine/docetaxel,	PD	2 months
9*	Spindle cell sarcoma	XRT	SD	5 months
10	Myxoid chondrosarcoma	none	SD	13 months

PD: Progressive disease * Patient still on therapy
SD: Stable disease
PR: Partial Response
AIM: doxorubicin, ifosfamide, mesna
VAC/IE: vincristine, doxorubicin, cyclophosphamide alternating with ifosfamide and etoposide
Morab004: Ontuxizumab

P2–Poster 122 2556482

SIROLIMUS AND ZOLEDRONIC ACID FOR MULTIOSTEOTIC PSEUDOMYOGENIC HEMANGIOENDOTHELIOMA OF THE BONE IN A CHILD: CASE REPORT AND REVIEW OF LITERATURE

Olivia M. Danforth, BS; Caleb Oh; Paul Kent
Rush Medical College, Chicago, IL, USA

Objective: Pseudomyogenic hemangioendothelioma (PMH) is a rare neoplasm with morphologic and immunohistochemical features of both vascular and sarcomatous tumors first described in 1992. PMH typically presents as slow-growing multifocal nodules of tissue planes of the extremities in young adults, with male predominance. Surgery is the mainstay of treatment, including amputation when necessary to achieve margins. Local recurrence is common with associated morbidity and rare mortality. Lung metastasis and transformation to a more aggressive Ewing Sarcoma-like neoplasm is described. Chemotherapy (including doxorubicin, cisplatin, and vincristine) has been reported with variable efficacy. Inhibitors of the Mammalian Targets of Rapamycin drugs (mTOR) show promise in sarcomas, including other hemangioendotheliomas and everolimus has been reported in one PMH case. The bis-phosphonate zoledronic acid (ZA) inhibits osteoclast-mediated bone resorption, has effectiveness in osteosarcoma, and is used for bony metastasis prevention in other cancers.

Table 1 - Selected Cases

Paper	Patient	Presentation	Features	Treatment	Outcome	LOF
Amary 2012	22yo F	Finger mass +Pn Local invasion, ulceration	Multifocal; skin, subq fat, bone	PE	Alive and NED	10 wks
Friel 2014	8yo F	Pn w/ ambulation Dx and Tx as SCFE, abnl XR	Solitary; bone	WLE(-), endoprosthetic reconstruction	Alive and NED	11 mos
Sheng 2013	22yo M	Leg nodule + Pn w/ local recurrences	Multifocal; skin, subq fat, muscle, lung mets	AKA, chemo	Alive w/ mets	3 mos
Davis 2015	20yo M	1yr hx LE skin lesions + Pn	Multifocal; skin, subq fat, bone	Toe amputation, WLE(-), RFA	Alive and NED	2 yrs
Requena 2013	20yo F	1yr hx calf nodule	Multifocal; skin, subq fat, muscle	SE”	Alive w/ possible mets	2 yrs
Requena 2013	27yo M	5mo hx perioral lesions	Multifocal; skin, mucosa	SE	Alive and NED	1 yr
Righi 2015	25yo M	3mo hx wrist Pn	Multifocal; skin, bone, subq fat, muscle	SE”, hand amputation	Alive and NED	19 yrs
Stuart 2013	30yo M	6mo hx LE nodules +Pn	Multifocal; skin, subq fat, bone	Amputation declined, (Oral CPM + Pred)	Responded but lost to F/U	10 mos
UC Path	22yo M	6mo hx ulcerating UE plaques +Pn	Multifocal; skin, subq fat	WLE	Alive and NED	4 mos
Mirra 1992	21yo M	Heel Pn, Dx and Tx as DJD, nodules on cast removal	Multifocal; skin, subq fat, bone	SE, (DOX + CPM + VCR + MTX)	Alive and NED	13 yrs
Mirra 1992	18yo M	Exertional UE Pn	Multifocal; skin, soft tissue, bone, lung, pericardium	(CPM + VCR + DOX), SE”, 6Gy RT, pulmonectomy	Died 2/2 malignant hypercalcemia	7 yrs
Mirra 1992	20yo F	Toe mass	Multifocal; skin, bone	R hemipelvectomy	Alive and NED	1 yr
Mirra 1992	21yo M	Foot mass	Multifocal; skin, subq fat	WLE + LN dissection, nitrogen mustard perfusion	Alive and NED	2.75 yrs
Joseph 2015	22yo M	Thigh nodule	Multifocal; bone	(CISPT + DOX + GCB), WLE, everolimus	Alive	5 mos

Table 1. Selected cases of PMH in children and AYA patients from review of literature. Treatments listed in order provided where specified. Treatment information listed in order provided where available. WLE = wide local excision, (-) indicates negative margins specified, SE = simple excision, SE”= 2 or more serial excisions, PE = partial excision, XRT = x-ray therapy, XR = x-ray, RFA = radiofrequency ablation, Chemo = systemic chemotherapy, unspecified, Pn = pain, NED = no evidence of disease, Subq = subcutaneous, CPM = cyclophosphamide, DOX = doxorubicin, Pred = prednisone, GCB = gemcitabine, VCR = vincristine, CISPT = cisplatin, SCFE = Slipped Capital Femoral Epiphysis, DJD = Degenerative Joint Disease.

Case Report: A 6-year old boy presented with multifocal PMH of the bones of the right leg. Amputation was recommended by several experts. After family and multidisciplinary meetings and second opinions, the family chose a recommended course of ZA and sirolimus (SIR) as initial therapy with the goal of avoiding amputation. We report clinical improvement supported by PET-CT at 6 months. PET-CT of our patient at 6 months shows markedly improved metabolic activity. Treatment was associated with mild and manageable adverse effects including bone pain, fever, and rash following ZA infusion, mucositis, and polyuria with enuresis. Patient reported improved mobility, decreased pain and discontinuation of opioid pain medication.

We review previous case series on PMH in children and adolescents and young adults (AYA.)

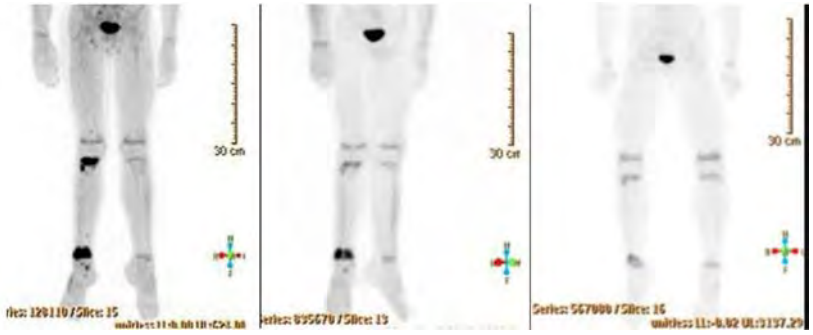


Figure 2. PET-CT series at presentation, 4 months, and 6 months (left to right.) At presentation, hypermetabolic activity in the right distal and proximal tibular and fibular metaphyses, posterior calcaneus, right inguinal lymph nodes, and right popliteal lymph node are seen with sclerotic lesions involving the talus, cuboid, and medial cuneiform bones. Follow-up imaging shows significant improvement in hypermetabolic activity.

Methods: We searched PubMed/Google Scholar, keywords: “pseudomyogenic hemangioendothelioma,” “epithelioid sarcoma-like hemangioendothelioma.”

Results: We found 20 children and AYA with PMH. Variable response to conventional chemotherapy was described in several cases, and one pediatric case was treated with endoprosthetic reconstruction but did not require systemic therapy. Ours was the youngest case and the only one using immune therapy.

Conclusion: Systemic therapy has an unclear role in treatment of PMH. In select cases it may reduce or eliminate the need for radical surgery. Increasing knowledge and identifying non-surgical strategies for PMH is imperative.

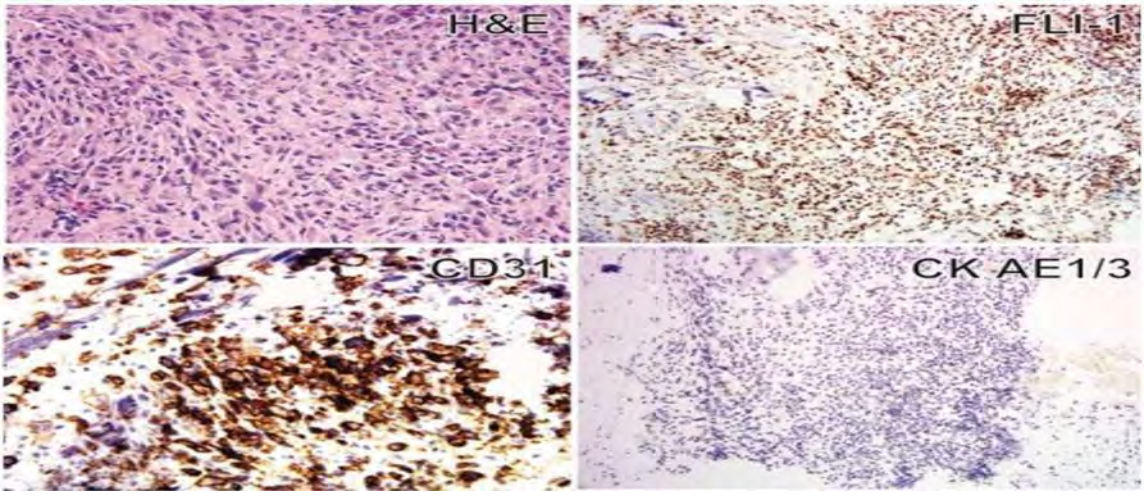


Figure 1. Hematoxylin and eosin (H&E) stain of the tumor showing plump spindle cells with eccentric nuclei with vescicular chromatin, conspicuous nucleoli, and abundant eosinophilic cytoplasm (top left) in a background of inflammatory cells. Mitotic figures are readily identified. These features make this tumor rhabdomyoblast-like or similar to an epithelioid sarcoma. Immunohistochemistry shows the tumor cells are positive for FL-1 (top right) and CD31 (bottom left) and negative for Cytokeratin AE1/AE3 (bottom right.) CK AE1/3 was positive in the previous biopsies.

P2–Poster 123 2536123

PAZOPANIB IN ADVANCED VASCULAR SARCOMAS: AN EORTC SOFT TISSUE AND BONE SARCOMA GROUP RETROSPECTIVE ANALYSIS

Attila Kollár[1]; R Jones[3]; Silvia Stacchiotti[4]; Hans Gelderblom[5]; Michele Guida[2]; Giovanni Grignani[6]; Neeltje Steeghs[7]; Akmal Safwat[8]; Daniela Katz[9]; Florence Duffaud[10]; Stefan Sleijfer[11]; Winette Van der Graaf[12]; Nathan Touati[13]; Saskia Litiere[13]; Bernd Kasper[14]

[1]Medical Oncology, University Hospital Bern, Inselspital, Bern, Switzerland; [2]National Cancer Institute "Giovanni Paolo II", Bari, Italy; [3]Royal Marsden Hospital, London, United Kingdom; [4]Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy; [5]University Medical Center, Leiden, Netherlands; [6]Institute of Cancer Research and Treatment, Torino, Italy; [7]The Netherlands Cancer Institute, Amsterdam, Netherlands; [8]Aarhus University Hospital, Aarhus, Denmark; [9]Hadassah-Hebrew University Medical Center, Jerusalem, Israel; [10]La Timone University Hospital & Aix-Marseille University, Marseille, France; [11]Erasmus MC - Cancer Institute, Rotterdam, Netherlands; [12]The Institute of Cancer Research and the Royal Marsden NHS Foundation Trust, London, United Kingdom; [13]European Organisation for Research and Treatment of Cancer (EORTC), Bruxelles, Belgium; [14]Mannheim University Medical Center, Mannheim, Germany

Objective: Pazopanib is a multitargeted tyrosine kinase inhibitor approved for the treatment of adult patients with selective subtypes of advanced soft-tissue sarcoma who have previously received standard chemotherapy including anthracyclines or were unfit for anthracyclines. Data on its efficacy in vascular sarcomas are limited. The main objective of this study was to investigate the activity of pazopanib in vascular sarcomas.

Methods: Clinical data of patients with advanced vascular sarcomas, including angiosarcoma (AS), hemangioendothelioma (HE) and intimal sarcoma (IS) treated with pazopanib in a real-life setting were retrospectively collected from EORTC center records. Additionally, patients treated within the EORTC 62043 and 62072 trials were included in the analysis. Patient and tumor characteristics were documented. Response was assessed according to RECIST 1.1. and survival analysis was performed. Disease control rate was the total rate of: complete response, partial response and stable disease.

Results: Out of 52 patients, 40 (76.9%), 10 (19.2%) and 2 (3.8%) patients suffered from AS, HE, IS, respectively. Patient and tumor characteristics are illustrated in Table 1. The response rate was 8 (20%), 2 (20%) and 2 (100%) in the AS, HE and IS subtypes, respectively. Disease control rate was 37.5% and 60% in AS and HE, respectively. There was no difference in response rate of cutaneous AS and non-cutaneous AS (p=0.86) and radiation-associated vs non-radiation-associated AS (p=0.81). Median PFS and median OS (from commencing pazopanib) were 3 months (95% CI: 2.1-4.4) and 9.9 months (95% CI: 6.5-11.3) in AS, respectively.

Conclusion: Pazopanib demonstrated a degree of clinical efficacy in angiosarcoma, HE and IS. In AS patients, no difference in response rate was observed between cutaneous/ non-cutaneous and radiation-associated/ non radiation-associated tumors. The role of pazopanib in combination with other agents in vascular sarcomas should be explored.

Patient and Tumor Characteristics of Vascular Tumors

	Angiosarcoma N=40 N (%)	Hemangioendothelioma N=10 n (%)	Intimal sarcoma N=2 N (%)
Median age (years)	62.4 yrs	47.2 yrs	67.2 yrs
Gender Female Male	 15 (37.5%) 20 (62.5%)	 4 (40%) 6 (60%)	 1 (50%) 1 (50%)
Disease stage Locally advanced Metastatic	8 (20%) 32 (80%)	2 (20%) 8 (80%)	1 (50%) 1 (50%)
Site of primary tumor Breast Scalp/Head Abdomen Thorax Extremity	15 (37.5%) 6 (15%) 8 (20%) 7 (17.5%) 4 (10%)	0 (0%) 1 (10%) 4 (40%) 4 (40%) 1 (10%)	0 (0%) 0 (0%) 0 (0%) 1 (50%) 1 (50%)
Localization Skin Non-skin unknown	15 (37.5%) 24 (60%) 1 (2.5%)	0 (0%) 10 (100%) 0 (0%)	0 (0%) 2 (100%) 0 (0%)

P2–Poster 124 2554618

AXI-STS: A UK NCRI SARCOMA CLINICAL STUDIES GROUP PHASE II TRIAL OF THE VEGFR INHIBITOR AXITINIB IN ADVANCED SOFT TISSUE SARCOMA (STS)

Penella Woll[2]; Piers Gaunt[1]; Ian Judson[3]; Sandra Strauss[4]; Jeremy Whelan[4]; Michael Leahy[5]; Ana Hughes[1]; Penny Goodby[1]; Christine Ingram[6]; David Hughes[6]; Lucinda Billingham[1]
[1]University of Birmingham, Birmingham, United Kingdom; [2]University of Sheffield, Sheffield, United Kingdom; [3]The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom; [4]University College Hospital, London, United Kingdom; [5]The Christie Hospital NHS Foundation Trust, Manchester, United Kingdom; [6]Royal Hallamshire Hospital, Sheffield, United Kingdom

Objective: This open-label, multicentre, stratified phase II trial assessed the activity, safety and tolerability of the VEGFR inhibitor axitinib 5mg PO BD in patients with advanced STS unsuitable for or relapsed after standard chemotherapy. The treatment was separately assessed in four strata: angiosarcoma, synovial sarcoma, leiomyosarcoma (LMS) and other sarcoma. Results for LMS and other sarcoma have been reported previously. This report is of the final two strata (angiosarcoma and synovial sarcoma).

Methods: The primary outcome measure was RECIST progression-free survival (PFS) rate at 12 weeks. Patients with stable or responding disease at 12 weeks were defined as a success. Simon's two-stage minimax design (p_0=20%, p_1=40%, α=0.05, Power=80%) was applied separately to each stratum. If 5 or more successes were seen in the first 18 patients, then 33 were to be recruited in total. The primary outcome measure was met if ≥ 11 successes were observed from 33. Patients were only assessable if they had at least 4 weeks of treatment. Secondary outcome measures included tumour response rate, PFS time, overall survival time and toxicity.

Results: 38 angiosarcoma and 36 synovial sarcoma patients were recruited from 13 UK centres. Table 1 reports baseline characteristics. Both strata passed the interim stopping criteria with 9 (angiosarcoma) and 10 (synovial sarcoma) successes out of 18. Preliminary results indicate that the 12-week PFS rate was 12/31 (39%; 90% Wilson's CI, 26 to 53%) for angiosarcoma and 17/30 (57%; 90% Wilson's CI, 42 to 70%) for synovial sarcoma. Both these confidence intervals exclude the lower critical value of 20% and the upper confidence interval includes or exceeds the upper critical value of 40%. The 12-week PFS rate for the synovial sarcoma stratum was similar to the rate of 49% (18/37) reported in a phase II trial in sarcoma with another TKI, pazopanib. The commonest toxicities were diarrhoea, mucositis, nausea, fatigue, anorexia, arthralgia, cough, dyspnea, voice alterations and hypertension. The commonest grade 3 and 4 toxicities were hypertension and fatigue. Toxicities were comparable to other studies with axitinib. There was one grade 4 dyspnea event in the synovial stratum. Data on response rate, PFS time and overall survival time will be presented.

Conclusion: The VEGFR inhibitor axitinib has activity in patients with angiosarcoma and synovial sarcoma. The drug is well tolerated and merits further investigation in a phase III setting for this patient population.

A Summary of Baseline Characteristics for the Patients

Parameter	Angiosarcoma (n=38)	Synovial sarcoma (n=36)
Age Median Range	 65 28-82	 44 21-73
Sex Male Female	 13 (34) 25 (66)	 18 (50) 18 (50)
WHO PS 0 1 2	 17 (45) 18 (47) 3 (8)	 16 (44) 18 (50) 2 (6)
Tumour Trojani Grade 1 2 3 Not Known	 3 (8) 9 (24) 20 (51) 6 (16)	 0 (0) 11 (31) 18 (50) 7 (19)
Weight (kg) Median Range	 77 46-127	 75 47-124

Numbers are N (%) unless specified

P2–Poster 125 2566345

ASSESSMENT OF PATIENT-SPECIFIC T CELL RESPONSES AMONGTHE SARCOMA SPECTRUM

Jessica Thaxton, PhD, MsCR; Lee Leddy
Orthopaedics, Medical University of South Carolina, Charleston, SC, USA

Objective: Immunotherapy holds great promise as an avenue for novel therapeutic intervention among the sarcoma spectrum. In order to aptly develop appropriate immunotherapeutic strategies it is necessary to define differential lymphocyte populations drawn to particular microenvironments of sarcoma subtypes. The objective of this work was to survey T cell subsets among the spectrum of sarcomas with autologous PBMC as control.

Methods: We collected primary tumor on the day of surgery and patient-matched peripheral blood cells (PBMC) for control. We did not include patient samples that had received radiation or samples from patients that had received chemotherapy within 12 days prior to surgery. Necrotic tissue from tumor was removed and tumors were dissociated to

single cell suspension. Autologous PBMC sample was prepared over ficoll gradient. Flow cytometric analysis was performed on tumor infitrating lymphocytes (TIL) and PBMC to quantify CD45+/CD4+/CD8+ populations and to further differentiate phenotypes of such subsets (Treg: CD45/CD4/CD127/CD25) (CD4/CD8/CD45RO/CD62L/PD1+) (CD4/CD8/CD45RO/PD1+/DR5+) (CD4/CD8/CD45RO/PD1+/KLRG1+).

Results: Of sarcomas surveyed >50% display more than 5% CD45+ cells within tumor. We find that high-grade deep pleiomorphic undifferentiated sarcomas (PUS) tend toward elevated proportions of CD4+ T cells above other sarcoma subtypes. Strikingly, regardless of sarcoma subtype, all CD8+ T cells within tumor microenvironments were driven toward an effector memory cell phenotype (CD8/CD45RO+/CD62L-) and depleted of naïve subset when compared to autologous matched PBMC, *p=0.0054 and *p=0.0135, respectively. Survey of effector memory CD8+ TIL among sarcoma subtypes demonstrated >50% were PD1+ and this elevation was highly significant compared to autologous PBMC as control (*p=0.0083).

Conclusion: Our initial assessment shows that microenvironments of particular sarcoma subtypes may attract differential lymphocyte lineages. This is critical to decipher further in order to develop immunotherapeutic strategies that aim to regress sarcomas. We are able to demonstrate that across sarcoma subtypes CD8+ T cells are driven toward the effector memory phenotype and demonstrate exhaustion characterized by PD1+. Taken together, this work begins to paint a picture of varied TIL infiltrates specific to sarcoma subtypes, but unified by the common denominator of immune cell exhaustion.

P2–Poster 126 2537288

A PHASE I TRIAL OF DENDRITIC CELL VACCINATION WITH AND WITHOUT INHIBITION OF MYELOID DERIVED SUPPRESSOR CELLS BY GEMCITABINE PRE-TREATMENT FOR CHILDREN AND ADULTS WITH SARCOMA

Gabriel Tinoco, MD[2]; John M. Goldberg[1]; Edward Ziga[1]; Emil Kamar[2]; Georges Tahhan[2]; Eric Wieder[2]; Despina Kolonias[2]; Eli Gilboa[3]; Geoffrey Stone[3]; Jonathan Trent II[2]; Julio Barredo[1]; Krishna Komanduri [2]; Breelyn A. Wilky[2]

[1]Pediatric Hematology/Oncology, University of Miami, Miami, FL, USA; [2]University of Miami Miller School of Medicine and Sylvester Comprehensive Cancer Center, Miami, FL, USA; [3]Department of Immunology, University of Miami, Miami, FL, USA

Objective: Sarcomas are rare, heterogeneous bone and soft tissue neoplasms that tend to affect children and young adults. Few therapies have proven to significantly improve overall survival in metastatic and advanced sarcomas refractory to standard chemotherapy. Autologous dendritic cell (DC) vaccination has shown promising anti-tumor effects in breast, prostate, and colon cancers. Antigen-loaded DCs intensify the adaptive immune response, by enhancing T-cell activity within the lymph nodes and inducing tumor cell death through apoptosis and cytolysis. However, the activity of DCs may be limited by native immunosuppressive cells including myeloid derived suppressor cells (MDSC). Administration of concurrent therapy to suppress MDSC, such as gemcitabine, may enhance the activity of autologous DCs leading to improved anti-tumor immune activity.

Methods: We report an ongoing phase I dose-escalation study of autologous DC vaccination in children and adults with advanced or metastatic sarcomas who undergo surgical resection of a metastatic tumor. The study is a 5+3 design, modified from the conventional 3+3 dose escalation schema to determine safety and recommended phase 2 dose (Table 1). Endpoints include safety and toxicity as well as progression-free survival. There are three intended dose levels - 3, 6, and 12 million DCs per treatment - followed by an additional cohort of patients who will receive the RP2D of DCs plus gemcitabine therapy to abrogate MDSC. Patient monocytes are collected by standard pheresis, and incubated with GM-CSF and IL-4 to generate immature DCs which are loaded with autologous tumor lysates from the patient's surgical resection. The DC product is administered to the patient intradermally in imiquimod-treated skin to complete in situ maturation. Treatment consists of four weekly injections of autologous DCs, followed by four monthly "boosters" of tumor lysate. Peripheral blood samples are collected for immunoprofiling of MDSC and T-cells. Patients are monitored radiographically for recurrence or progression.

Results: At this time, 11 of the 20 planned patients have been enrolled on the protocol; including 6 patients at dose level 1 and 5 patients at dose level 2. There have been no DLTs.

Conclusion: Autologous Dendritic Cell Vaccination in sarcomas demonstrates safety and feasibility when used as adjuvant therapy for patients after resection of metastatic sarcoma.

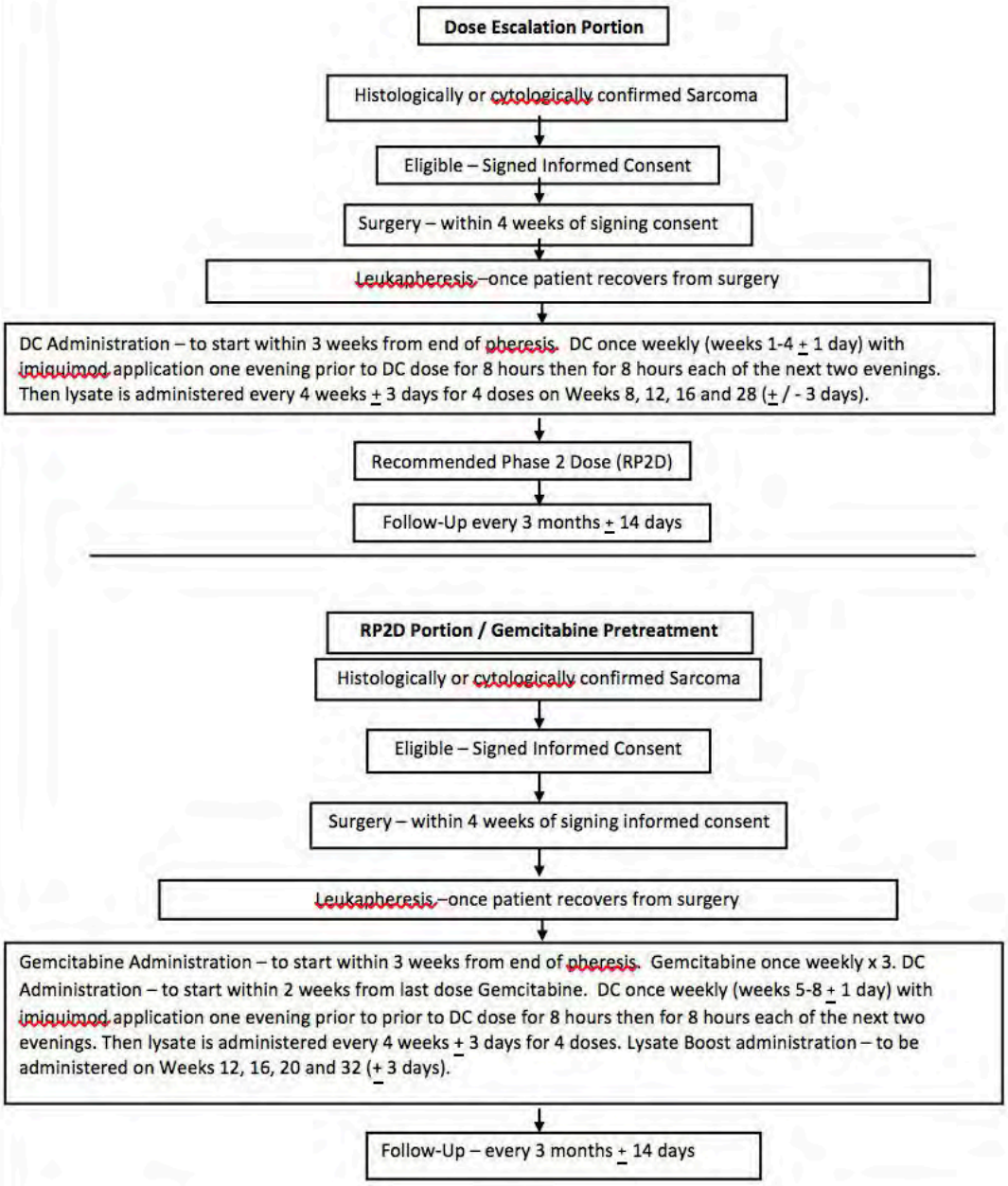


Table 1. Study design.

P2–Poster 127 2563651

HIGH PDL1 EXPRESSION IN TREATED SARCOMAS MAY BE ALTERED BY NEOADJUVANT TREATMENT AND CORRELATE WITH DECREASED OVERALL SURVIVAL

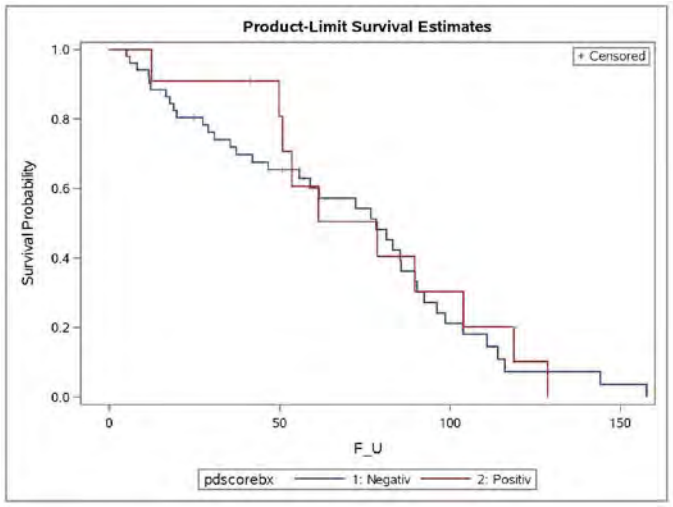
Matthew J. Lasowski, MS; Matthew Stemm; Manpreet Bedi; John Charlson; Craig Mackinnon
Cancer Center, Medical College of Wisconsin, Milwaukee, WI, USA

Objective: Ascertain the incidence of PDL1 positivity in sarcomas. Investigate the expression of PDL1 in heterogeneous sarcoma samples at time of biopsy and at time of resection after neoadjuvant treatment to determine if changes in expression levels occur. Determine if PDL1 expression impacts overall survival.

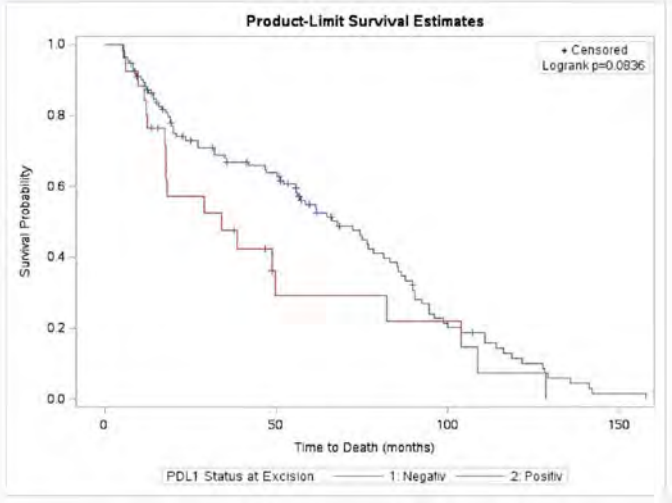
Methods: Tumor specimens were obtained from 63 patients at initial diagnosis and 137 patients at time of resection after neoadjuvant treatment. 52 cases had paired samples with both a biopsy sample prior to neoadjuvant treatment and an excision sample after treatment. PDL1 expression was analyzed blindly using qIHC and interpreted as either negative or positive for PDL1 expression. Overall survival (OS) was determined by retrospective review of patient records. Kaplan-Meier and log-rank analysis was performed in regards to PDL1 expression status.

Results: 11 of 63 patients had tumors with PDL1 positivity at time of initial biopsy. At resection 26 of 137 had PDL1 positivity of their post-treatment STS. 52 cases had paired biopsy and resection samples. 9 of 52 patients were PDL1 positive at biopsy and 11 of 52 patients were positive at time of resection. Of the 11 positive at resection, 7 were negative at biopsy and of the 9 PDL1 biopsy samples that were positive, 5 lost positivity at resection.. The populations were evenly distributed with regards to treatment, stage, Karnofsky Performance Status, smoking status, sex, and age. Kaplan-Meier curves showed no significant difference in OS between negative or positive PDL1 expression at time of biopsy (p=0.7988). There was a trend toward worse 5-year OS with positive PDL1 expression in the post-treatment resected tumors (36 mo vs. 55 mo, respectively, p=0.0836). Of the 52 paired cases, 9 were positive at biopsy and 22 positive resection. 7 cases were negative at biopsy but positive at resection and 5 were positve at biopsy and negative at resection.

Conclusion: Quantitative analysis of PDL1 expression in resected STS after neoadjuvant treatment may be associated with worse 5-year overall survival. The paired biopsy and resected STS from 52 patients suggests that PDL1 expression may be altered by neoadjuvant treatment with cases both losing or gaining PDL1 positivity. However, further studies with larger sample size are warranted in order to detect the true correlation with survival and other factors influencing outcomes.



Overall survival based on PDL1 expression on treatment naive STS biopsy samples



Overall survival based on PDL1 expression on post neo-adjuvant treatment STS resection samples

P2–Poster 128 2555232

A PILOT FEASIBILITY STUDY OF IMMUNOTHERAPY WITH COMBINATION TRABECTEDIN AND NIVOLUMAB IN ADVANCED SOFT TISSUE SARCOMA

William W. Tseng, MD[2]; K. Kumar Sankhala[1]; Erlinda M. Gordon[1]; Suzan Arasheben[1]; Justin Daneshrad[1]; Sant P. Chawla[1]
[1]Sarcoma Oncology Center, Santa Monica, CA, USA; [2]Surgery, Section of Surgical Oncology, University of Southern California, Keck School of Medicine, Los Angeles, CA, USA

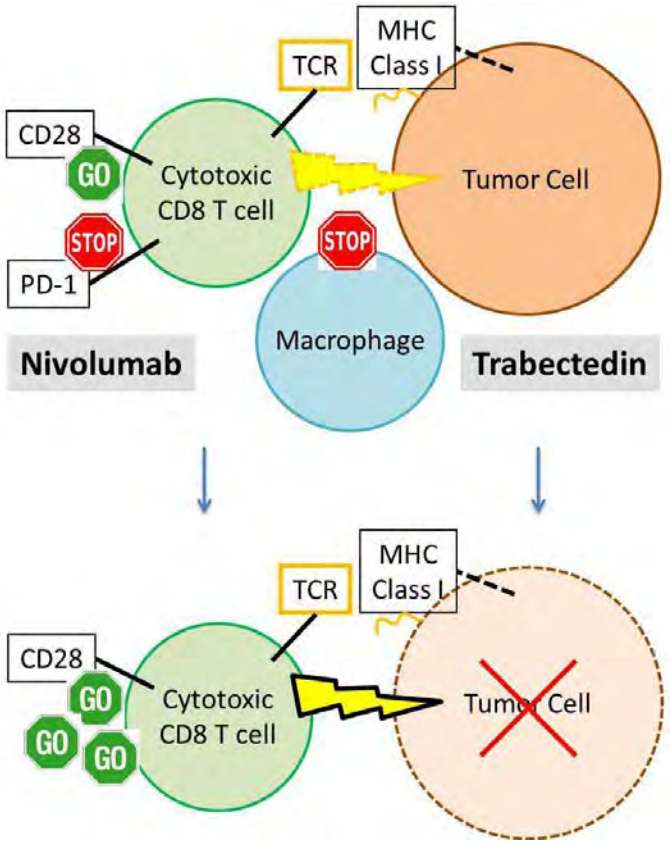
Objective: Trabectedin has direct cytotoxic activity in tumor cells and has also been shown to deplete pro-tumor macrophages in the tumor microenvironment (Germano et al., Cancer Cell 2013). Nivolumab inhibits the immune

checkpoint molecule, PD-1, which restores anti-tumor activity in tumor-infiltrating T cells. We hypothesize that the combination of trabectedin and anti-PD-1 therapy will synergistically attack tumor cells and promote anti-tumor immunity. Greater efficacy of both agents together compared to single agent alone has been demonstrated in preclinical mouse models of cancer (Guo et al., J Transl Med 2015). We sought to evaluate the safety, toxicity, and efficacy of this combination therapy in patients with advanced soft tissue sarcoma (STS).

Methods: Patients with locally-advanced and/or metastatic STS are eligible for this ongoing study. Each patient receives 1 dose of single-agent trabectedin (1.5 mg/kg continuous intravenous infusion, CIV, for 24 hours), followed by trabectedin CIV in combination with nivolumab (3 mg/kg IV over 30 minutes) every 3 weeks, starting 3 weeks after the first trabectedin dose. Baseline and follow-up cross sectional imaging are performed after every 2 cycles of combination therapy. Tumor response is assessed by RECIST v1.1 and immune-related response criteria (irRC).

Results: At the time of abstract submission, 14 patients have been enrolled. Histologic subtypes include malignant fibrous histiocytoma / undifferentiated pleomorphic sarcoma (n = 6), leiomyosarcoma (n = 3), synovial sarcoma (n = 2), myxoid liposarcoma (n = 2) and chondrosarcoma (n = 1). All patients have metastatic disease and have had a median of 4 lines of prior systemic therapy. To date, 8 patients have received at least 1 cycle of combination therapy with no limiting toxicity.

Conclusion: Immunotherapy has great potential in the treatment of STS (Tseng et al., Hum Vaccin Immunother 2014). To our knowledge, our study is the first to explore this combination immunotherapy in patients with advanced STS. Early data suggest that the safety profile is acceptable with no limiting toxicity. Updated data including tumor response rates will be presented. The combination of trabectedin and anti-PD-1 therapy is expected to have synergistic effects based on their mechanism of action on the tumor-immune microenvironment.



Combination Immunotherapy in STS: In the tumor microenvironment, trabectedin and nivolumab (anti-PD-1) have synergistic mechanisms of action to attack tumor cells and promote anti-tumor immunity.

P2–Poster 129 2570652

RADIOTHERAPY ENHANCES NATURAL KILLER HOMING AND FUNCTION IN CANINE BONE AND SOFT TISSUE SARCOMAS

Jiwon S. Park[1]; Steven K. Grossenbacher[2]; Jaime F. Modiano[3]; Erik Ames[2]; Arta M. Monjazeb[4]; William T. Culp[5]; Mingyi Chen[6]; Michael S. Kent[5]; William J. Murphy[2]; Robert J. Canter[1]
[1]Surgery, UC Davis, Sacramento, CA, USA; [2]Dermatology, UC Davis, Sacramento, CA, USA; [3]Veterinary Clinical Sciences, University of Minnesota, Minneapolis, MN, USA; [4]Radiation Oncology, UC Davis, Sacramento, CA, USA; [5]School of Veterinary Medicine, UC Davis, Davis, CA, USA; [6]Pathology, UC Davis, Sacramento, CA, USA

Objective: Although effective in hematologic malignancies, natural killer (NK) cells have been less successful in solid cancers. We have previously shown that radiotherapy (RT) plus NK therapy is effective in pre-clinical models of human sarcomas. Because sarcomas are common in dogs and are an excellent resource for immunotherapy, we hypothesized that dog PBMC-derived NK cells could be expanded and activated ex vivo for combination radioimmunotherapy in canine models of sarcoma.

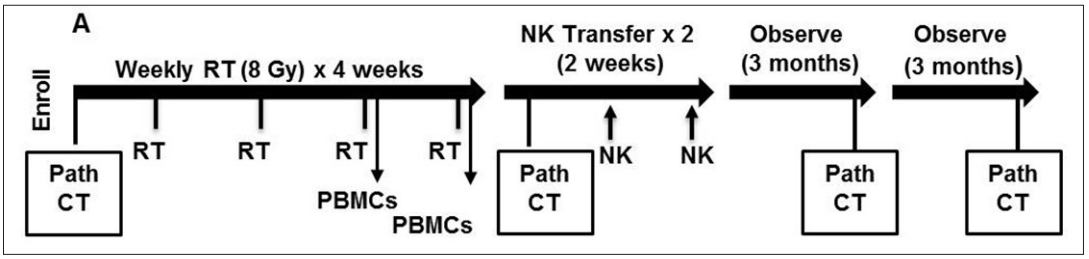


Figure 1. UC Davis School of Veterinary Medicine Treatment Schema (IACUC #18857) for Combined RT/NK Immunotherapy Clinical Trial in Canines with Osteosarcoma.

Methods: Canine NK cells were isolated from 10 mls of fresh whole blood using Ficoll separation and CD5 depletion. Isolated NK cells were then expanded in co-culture with irradiated human K562c9IL21 for 2-3 weeks. Canine osteosarcoma (OS) tumor lines and fresh dog primary sarcomas were evaluated for NK killing before or after RT in vitro and in xenograft experiments. NK cytotoxicity was measured using 7AAD or chromium release killing assays. Using 6-month metastasis-free survival as the primary endpoint, a canine clinical trial is underway evaluating RT and adoptive intratumoral NK immunotherapy as a novel therapeutic strategy.

Results: NK expansion was successful in 17/23 donors from baseline 6.5(±1.9) $x10^6$ cells to 258.9(±76.1) $x10^6$, mean increase 46.2X (±12.7). Canine NK cells were also responsive to human cytokines (IL-2, IL-12, and IL-18), but expansions were lower (1.6-3.5 fold expansion over 14 days). NK cytotoxicity to OS and NK-sensitive CTAC cells in vitro increased in a dose-dependent fashion reaching 74 – 88% cytotoxicity at effector:target ratios of 10–20:1 ($P<0.001$). RT augmented NK cytotoxicity with greatest synergy at 10 Gy RT in 4-hour killing assays (1.3-3.4X increased killing, $P<0.01$). Similar results were observed with RT sensitization to NK killing in primary canine sarcomas. In a dog sarcoma PDX model using focal RT, intravenous NK transfer, and human IL-15 for in vivo NK support, focal RT increased NK homing to tumors by 3.8X±0.3 ($P<0.001$). Simultaneously, we have treated 7 of planned 14 dogs with spontaneous osteosarcoma in a canine clinical trial. Of 3 evaluable dogs, there was 1 partial response and 2 are metastasis-free at the 6- month primary endpoint (which compares favorably to a historical metastasis rate of 80% with RT alone).

Conclusion: Canine NK cells can be successfully expanded and activated ex-vivo, and canine NK cytotoxicity and homing is increased following RT. Preliminary results from a canine clinical trial of palliative RT and autologous NK transfer for osteosarcoma are promising.

P2–Poster 130 2561280

M1 MACROPHAGES AS PREDICTOR OF POOR RESPONSE TO TRABECTEDIN TREATMENT IN MYXOID LIPOSARCOMA

Marco Fioramonti; Michele Iuliani; Giulia Ribelli; Francesco Pantano; Daniele Santini; Giuseppe Tonini; Bruno Vincenzi

Campus Bio-Medico University of Rome, Rome, Italy

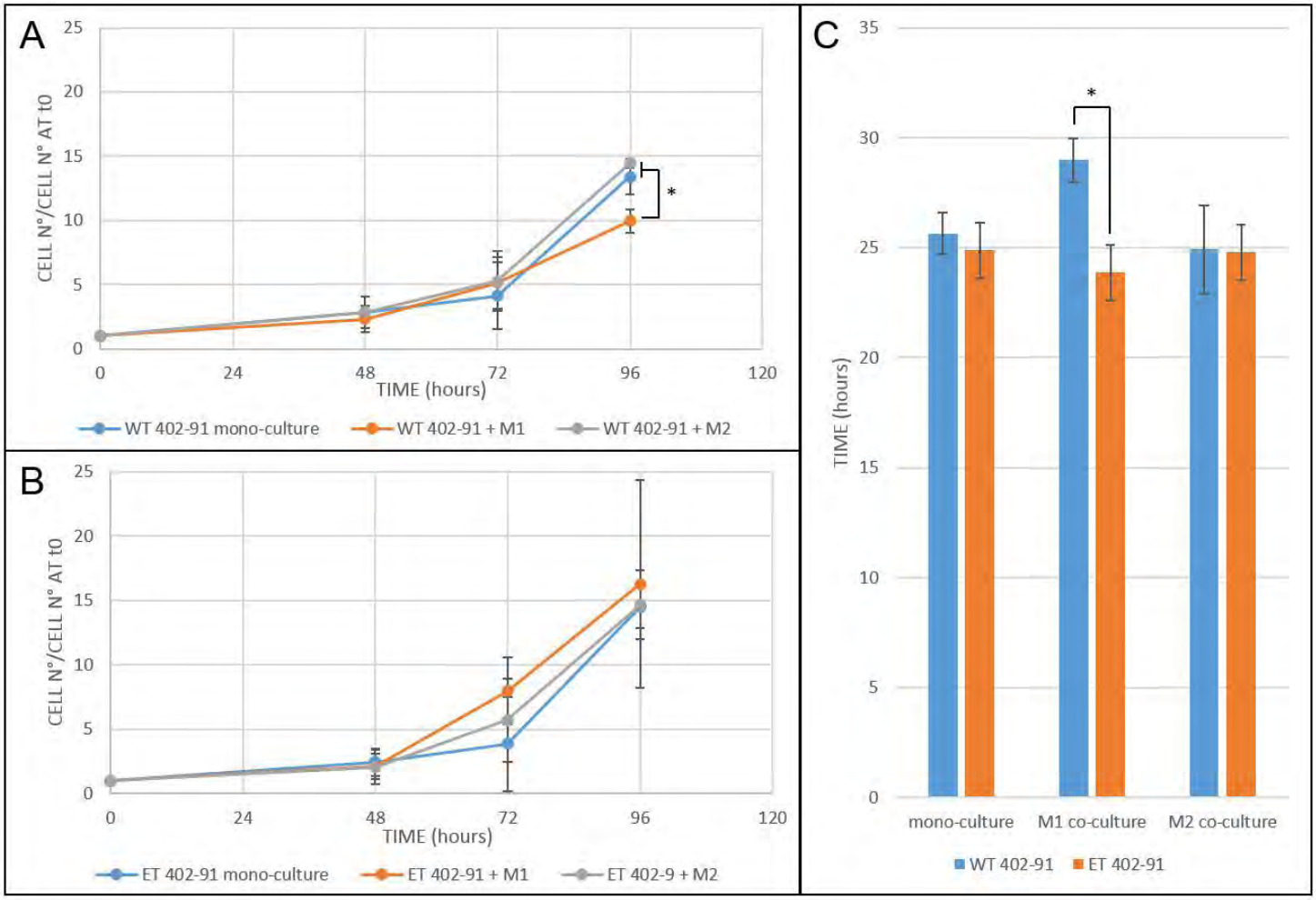
Objective: Myxoid liposarcoma (MLS) represents a specific subtype of liposarcoma, one of the most common malignant soft tissue tumors affecting adults. Trabectedin is a DNA-binding agent interfering with gene transcription, regulation, and DNA repair machinery and it is able to induce cell cycle perturbation. Although an high sensitivity of MLS to trabectedin has been reported, most patients become resistant. A well-established model to study this phenomenon is the trabectedin-resistant (ET) 402-91 cell line and its counterpart wild type (WT). The aim of this study is to understand the key role of M1/M2 polarized macrophages in the selection and acquisition of trabectedin-resistant phenotype in MLS.

Methods: Both WT and ET 402-91 cell lines were cultured in RPMI culture media supplemented with 10% of fetal bovine serum. GFP+ WT 402-91 and RFP+ ET 402-91 cell lines were obtained by stable transfections with lentiviral particles. CD14+ monocytes were isolated from buffy coats of healthy donors and differentiated into macrophages with MCSF. M1 polarization was performed using interferon-γ and LPS, whereas M2 polarization with interleukin-4. Co-culture experiments between MLP cell lines and M1/M2 macrophages were performed using transwell system.

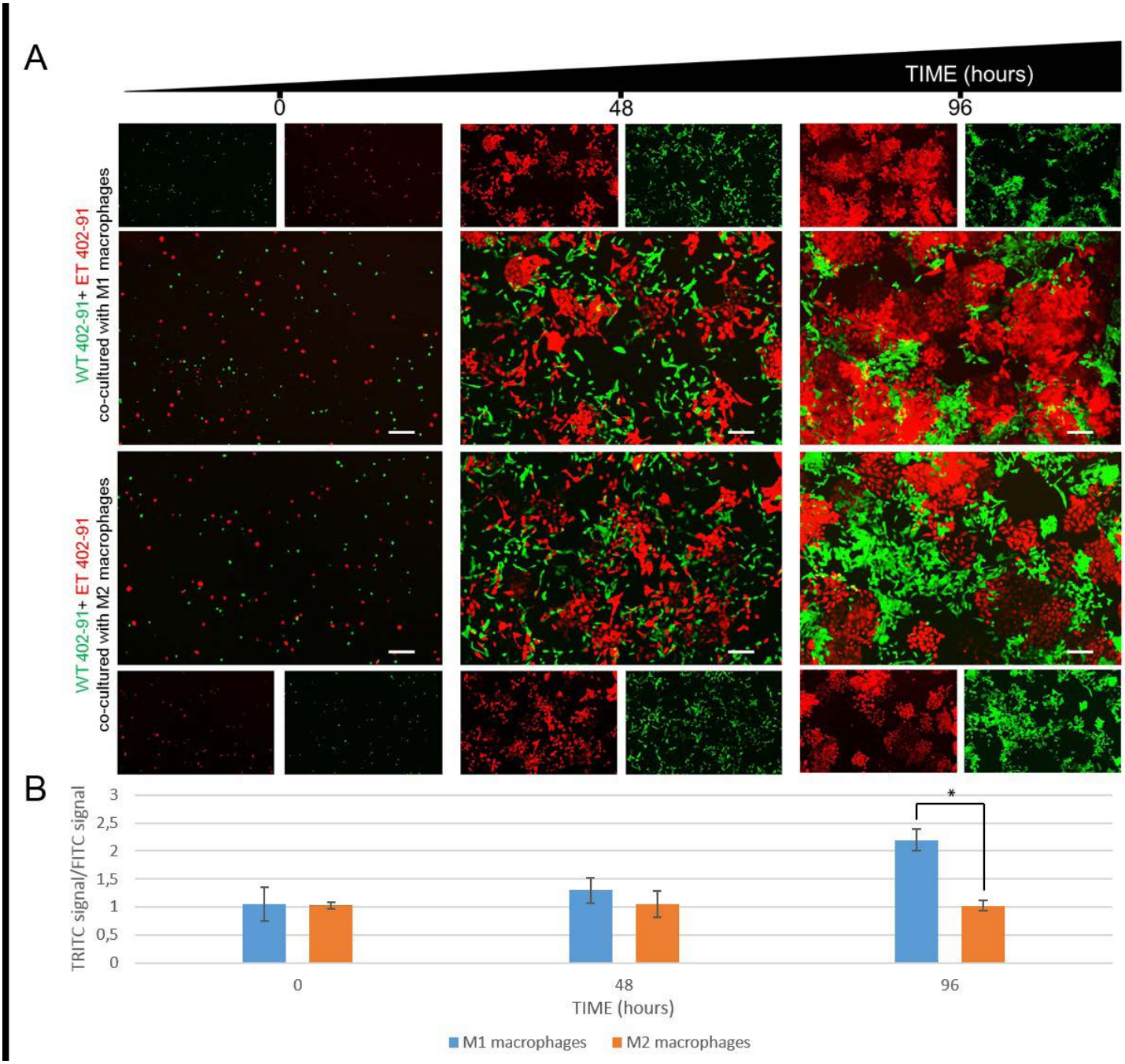
Results: M1 macrophages inhibit WT 402-91 proliferation at 96 hours of co-culture compared to WT 402-91-M2 co-culture and to control (mono-culture). Conversely, M1 and M2 macrophages have no impact on proliferation of ET 402-91 cells. Population doubling time (PDT) of M1 co-cultured WT 402-91 is 5.11 hours higher than PDT of M1 co-cultured ET 402-91 (28.97 hours vs 23.86; $P = 0.036$). This data is confirmed co-culturing GFP+ WT 402-91 and RFP+ ET 402-91, cell-to-cell contact, under influence of M1/M2 macrophages in transwell; indeed RFP+ ET 402-91 percentage become progressively higher than GFP+ WT 402-91 after 96 hours in presence of M1 macrophages

but not with M2 macrophages (75%-35% vs 52%-48%; P = 0.04).

Conclusion: These data show that the presence of M1 macrophages could promote the selection of trabectedin-resistant phenotype in MLS. Our findings suggest that M1 macrophages may predict a poor response to trabectedin treatment in MLS patients but further analyses are warranted to confirm this hypothesis.



A) Proliferation curves of WT 402-91 in mono-culture, cultured with M1 macrophages and M2 macrophages; WT 402-91 cells show a decreased proliferation rate at 96 hours of co-culture with M1 macrophages compared to WT 402-91-M2 co-culture and to control (mono-culture). B) Proliferation curves of ET 402-91 cells in mono-culture, cultured with M1 macrophages and M2 macrophages; neither M1 or M2 macrophages show any effect on ET 402-91 proliferation. C) PDT of WT 402-91 and ET 402-91 in mono-culture, cultured with M1 macrophages and M2 macrophages; M1 macrophages induce a significant increase of WT 402-91 PDT.
* = P < 0.05



A) Representative images of direct co-culture experiments between GFP+ WT 402-91 and RFP+ ET 402-91 under the influence of M1/M2 macrophages; the presence of M1 macrophages leads to a progressive increase of percentage of RFP+ ET 402-91. B) Ratio between TRITC (RFP+ ET 402-91) and FITC (GFP+ WT 402-91) signals; the TRITC signal becomes 2.2 times higher compared to FITC signal at 96 hours of co-culture with M1 macrophages.
* = $P < 0.05$
Bar scale = 200 μm

P2–Poster 131 2537146

NEOADJUVANT INTRALESIONAL INJECTION OF TALIMOGENE LAHERPAREPVEC WITH CONCURRENT PREOPERATIVE RADIATION IN PATIENTS WITH LOCALLY ADVANCED SOFT TISSUE SARCOMAS: PHASE 1B/2 TRIAL

Varun Monga, MBBS[1]; Benjamin Miller[2]; Carryn Anderson[6]; Bryan Allen[6]; Monzer Abu-Yousef[7]; Catherine Metz [7]; Maheen Rajput[7]; Eve Clark[7]; David Kuehn[7]; Munir Tanas[3]; Sarah Mott[4]; Zuhair Ballas[8]; Chinemerem Abanonu[5]; Sudershan Bhatia[6]; Mohammed Milhem[1]

[1]Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [2]Department of Orthopedics and Rehabilitation, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [3]Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [4]Biostatistics, Holden Comprehensive Cancer Center, Iowa City, IA, USA; [5]DaVita HealthCare Partners of Nevada, Las Vegas, NV, USA; [6]Radiation Oncology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [7]Radiology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [8]Immunology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA

Objective: Local disease control is of prime importance in management of locally advanced high grade soft tissue sarcoma (STS). Preoperative external beam radiotherapy (EBRT) has been shown to significantly improve local disease control, functional outcomes and survival in patients with locally advanced STS. Talimogene laherparepvec (TVEC) is an immune-enhanced, oncolytic herpes simplex virus type 1 (HSV-1) designed for intratumoral injection and is currently approved to treat locally advanced melanoma. We proposed a novel approach using neoadjuvant oncolytic immunotherapy with TVEC in combination with EBRT and report the incidence of dose-limiting toxicities (DLT) in subjects with locally advanced high grade STS.

Methods: Patients with histologically confirmed diagnosis of locally advanced high grade STS that is unresectable with clear wide margins, for which preoperative radiotherapy is considered appropriate were enrolled after receiving informed consent. Patients with retroperitoneal, bone, Ewing, Kaposi and visceral sarcomas or any history of prior or current autoimmune diseases or on any immunosuppressant medications were excluded. TVEC was injected intra-tumoraly with or without ultrasound guidance at initial dose of up to 4.0 ml of 10^6 PFU/ml 3 weeks prior to starting radiation therapy and then injected 10^8 PFU/ml weekly concurrently with standard dose radiation therapy of 50 Gy over 5 weeks as per NCCN guidelines. Weekly injections of TVEC were continued until 4-6 weeks following which the patient is taken for surgery. Patient is followed every 12 weeks with imaging through 24 months. DLTs were assessed using CTCAE v 4.0.

Results: 7 patients were enrolled on the study. None required dose de-escalation. Most adverse events were expected and were grade 1. Fatigue (100%), flu like symptoms (71.4%), fevers (71.4%) and nausea (57.1%) were managed with supportive care. Anemia (85.7%) and elevation in alanine aminotransferase (57.1%) were self-limited. Radiation related dermatitis was seen in 6 out of 7 patients but none developed infectious complications. There were no serious adverse events including treatment related deaths noted.

Conclusion: Neoadjuvant immunotherapy treatment with TVEC concurrently with radiation therapy for locally advanced soft tissue sarcoma is safe and well tolerated. No DLT were observed. Phase 2 trial (NCT02453191) evaluating efficacy and planned correlative studies is ongoing.

P2–Poster 132 2556856

PAX3-FOXO1 KNOCKDOWN REDUCES PD-L1 EXPRESSION IN AN ALVEOLAR RHABDOMYOSARCOMA CELL LINES

Yoshihiro Nitta; Mitsuru Miyachi; Kazutaka Ouchi; Hideki Yoshida; Shigeki Yagyu; Ken Kikuchi; Kunihiko Tsuchiya; Tomoko Iehara; Hajime Hosoi

Pediatrics, Kyoto Pref. Univ. Med., Kyoto, Japan

Objective: Novel therapeutic strategy is required to cure patients with *PAX3-FOXO1* positive metastatic rhabdomyosarcoma (RMS). Programmed cell death 1 ligand 1 (PD-L1) plays a major role in suppressing the immune system. Here, we examined the relationship between *PAX3-FOXO1* fusion gene and PD-L1 expression to explore the possibility of using anti-PD-1 antibody as treatment for metastatic RMS.

Methods: Four *PAX3-FOXO1*-positive RMS cell lines (RM2, Rh4, Rh30, Rh41) were used. The PD-L1 expression was determined by flow cytometry. Peripheral blood mononuclear cells were stained with carboxyfluorescein succinimidyl ester (CFSE) and co-cultured with RM2 cells. Dilution of the CFSE signal was evaluated for proliferation by flow cytometry.

Results: Two of the four cell lines (Rh30 and RM2) showed higher expression of PD-L1. *PAX3-FOXO1* knockdown resulted in 35.6% and 37.3% decrease in cell-surface expression of PD-L1 in the two cell lines. In HLA-A24 matched allogenic RM2 cells, *PAX3-FOXO1* knockdown enhanced the proportion of proliferating CD8-positive T-cells in co-culture experiments.

Conclusion: Our results show that *PAX3-FOXO1* plays a role in PD-L1 mediated immune escape. Anti-PD-1 antibody can be a novel therapeutic strategy against *PAX3-FOXO1*-positive RMS with high PD-L1 expression.

P2–Poster 133 2557919

INTRATUMORAL IMMUNE-RESPONSE AND MISMATCH REPAIR STATUS IN LEIOMYOSARCOMA: A PILOT STUDY

Jonathan E. Cohen[1]; Eli Pikarsky[2]; Feras Eleyan[1]; Tamar Hamburger[1]; Adi Levi[1]; Tamar Peretz[1]; Daniela Katz, MD[1]
[1]Oncology, Hadassah Hebrew University Medical Center, Jerusalem, Israel; [2]Pathology Department, Hadassah Hebrew University Medical Center, Jerusalem, Israel

Objective: Leiomyosarcoma (LMS) is the second most frequent soft tissue sarcoma. DNA mismatch repair deficiency (MMR-D), mutational load and tumor lymphocytic infiltration (TIL) have been associated with response to immune checkpoint inhibitors (ICIs) in different malignancies. The immunologic landscape of leiomyosarcoma is ill-defined; here, we set out to characterize the genomic-immunologic interaction of this disease.

Methods: Archived primary LMS-tissues from 11 patients (7 uterine LMS (ULMS) + 4 LMS) were retrospectively analyzed for expression of MMR genes (MSH2, MLH1, MSH6 and PSM2), PDL-1 expression by tumor cells and various T cell subpopulations expressing PD-1, CD3 or CD8. Slides were examined by a certified pathologist and immune-stains were graded on a scale from 0-3, for PDL-1 percentage of positive cells was also recorded. Positive staining was considered 1-3 or ≥1%.

Results: Loss of expression of MMR proteins was detected in tumor tissue from 2/11 LMS patients (1 ULMS, 1 LMS). T cells were present in all samples (CD3+) whereas CD8 staining was positive in all but one. PDL-1 was positive in 4/11 and PD-1 in 6/11. Interestingly, the MMR-deficient LMSs have CD8 infiltration but lack PDL-1 expression.

Conclusion: Our pilot results indicating that MMR-loss was associated with a lymphocytic infiltration is in line with previous reports suggesting that the associated high mutational load leads to neoantigen generation and invokes an immune response. Lack of PDL-1 expression in these tumors may indicate other mechanisms for immune tolerance in these cases. This could help refine future trials testing immune check point drugs in LMS.

Interaction between intra-tumoral CD8 and PDL-1.

	PDL-1 positive	PDL-1 negative
CD8 positive	4	4+2 MMR-D
CD8 negaitive	0	1

Mismatch repair deficient (MMR-D) LMSs have CD8 infiltration but lack PDL-1 expression

P2–Poster 134 2570678

SPLIT ANERGY OF NATURAL KILLER CELLS IN RECURRENT OR REFRACTORY SOFT TISSUE SARCOMA

Paulo Rodrigues-Santos[1]; Jani Sofia Almeida[2]; Patrícia Couceiro[2]; José Rui Simplício[2]; Vera Alves[1]; Manuel Santos-Rosa[1]; Paulo F. Tavares[3]
[1]Instituto de Imunologia, Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal; [2]Laboratório de Imunologia e Oncologia, Centro de Neurociências e Biologia Celular, Coimbra, Portugal; [3]Unidade de Tumores do Aparelho Locomotor, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

Objective: The aim of the present study was to analyze Natural Killer cells in recurrent or refractory STS patients and the effect of therapy on receptor repertoire and functional capacity of these cells.

Methods: We analyzed peripheral blood samples from STS patients (osteosarcoma, myxoid liposarcoma, liposarcoma, clear cell sarcoma, high-grade pleomorphic sarcoma, leiomyosarcoma, epithelioid leiomyosarcoma and giant cell tumor of the bone) treated with high-dose methotrexate (MTX), Cisplatin (CDDP), Cyclophosphamide/Bortezomib/Dexamethasone (CyBorD), etoposide (VP16), denosumab (anti-RANKL) and/or trabectedin and healthy blood donors as controls. Extended analysis of NK-cell receptor repertoire and functional properties was performed by target cell visualization assay (TCVA), multiparametric flow cytometry, cell sorting, Luminex xMAP technology (45-plex cytokine and chemokine panel) and real-time quantitative PCR (gene expression analysis).

Results: Relative frequency of NK cells was found significantly reduced in refractory or recurrent STS patients with poor cytolytic capacity and normal IFN-γ production, defining a split anergy status. NK cells exhibited a mature status (increased CD57) and deficient activation (decreased CD69), although CD62L NK cells were found similar to controls, meaning untouched capacity of migration to secondary lymphoid organs. NK receptor repertoire was found altered with significant upregulation of NKp44, NKG2A, NKG2D, PD-1 and CD137 (4-1BB) and downregulation of CD226 (DNAM-1). Analysis of a large panel of 45 cytokines and chemokines revealed an increase of IL-10, TGF-β, IL-4 and normal production of IFN-γ by STS NK cells.

Conclusion: NK cells are significantly affected in recurrent or refractory STS with a split anergy phenotype - decrease cytotoxicity and normal production of IFN-γ. Combination of NK cell-based immunotherapy with pharmacological interventions should be investigated in order to reduce metastatic potential and to eradicate cancer cells.

Financial Support: FEDER (Programa Operacional Factores de Competitividade – COMPETE) and FCT (Fundação para a Ciência e a Tecnologia) through project PEst-C/SAU/LA0001/2013-2014.

P2–Poster 135 2558611

BIOINFORMATIC IDENTIFICATION OF NOVEL TARGETS FOR SARCOMA IMMUNOTHERAPY

Micheala Baldauf[1]; Franziska Blaeschke[2]; Andreas Kirschner[3]; Merve M. Kiran[1]; Marlene Dallmayer[1]; Martin F. Orth[1]; Julia S. Gerke[1]; Julian Musa[1]; Rebeca Alba Rubio[1]; Aruna Marchetto[1]; Giuseppina Sannino[1]; Thomas Kirchner[1]; Uwe Thiel[3]; Tobias Feuchtinger[2]; Thomas G. Grünewald, Group-Leader[1]

[1]Laboratory for Pediatric Sarcoma Biology, Institute of Pathology, LMU Munich, Munich, Bavaria, Germany; [2]Pediatric Hematology, Oncology and Stem Cell Transplantation, Dr. von Hauner University Children's Hospital, LMU Munich, Munich, Germany; [3]Children's Cancer Research Center, Klinikum rechts der Isar, Technische Universität München, Munich, Germany

Objective: Conventional sarcoma therapies often have limited effect despite high toxicity. Thus, more specific and less toxic therapies are required to improve outcome. Due to its specificity, adoptive T cell therapy emerged as a promising therapeutic option.

Methods: We combined bioinformatic analysis of gene expression microarrays with *in vitro* and *in situ* experiments to identify novel and highly specific immunogenic targets for multiple cancer entities, focusing on human sarcoma and pediatric cancers.

Publicly available gene expression data generated on the same microarray platform for >2,700 samples comprising 50 tumor entities and 71 normal tissue types were rigorously quality-checked, clinically annotated and normalized simultaneously. An in-house algorithm was used to scan transcriptome-wide in each cancer entity for highly and specifically expressed genes that are virtually not expressed in normal tissues.

Results: As a proof-of-concept we identified known tumor-associated antigens like LIPI for Ewing sarcoma or PRAME in neuroblastoma, but also many novel candidates of which some appear suitable for targeting multiple tumor types. The specific expression of these proteins is currently being validated in a tissue microarray. Subsequently, we identified immunogenic peptides encoded by the most specific transcripts by predicting the strength of their peptide-MHC-binding to HLA-A02:01. Next, the peptides with the highest affinity were crosschecked with protein-databases to exclude sequence similarity with otherwise abundantly expressed proteins. The high affinity of the identified peptides was validated in T2-cell peptide-binding assays. The four most effective peptides, which are potentially suitable as specific immunotherapeutic target for 7 tumor entities, are currently screened for naturally occurring specific T cells in peripheral blood, from which the corresponding T cell receptor shall be cloned. In addition, we developed a user-friendly web-browser to make our transcriptomic data and immunogenic peptide libraries easily accessible to other researchers.

Conclusion: Collectively, we provide a comprehensive, exquisitely curated and validated catalogue of cancer-specific, immunogenic and high-affinity peptides across 50 cancer entities. We anticipate that our data will constitute a rich resource for further immunotherapy-development, ultimately helping to improve patient outcome.

P2–Poster 136 2558012

TRABECTEDIN IN ADVANCES UTERINE SARCOMAS: A FIVE-YEARS EXPERIENCE OF A CANCER CENTER

Ana S. Patrão, MD; Miguel Henriques Abreu; Susana Sousa; Deolinda Pereira

Oncologia Médica, Instituto Português de Oncologia do Porto, Barcelos, Portugal

Objective: Trabectedin (TD) has shown to be a useful drug in the management of advanced pretreated leiomyosarcomas. In uterine leiomyosarcomas, it showed an overall survival(OS) benefit of 2.5 months when compared with dacarbazine. Now, this drug could also be considered in selected non L-subtype sarcomas.

In this work, we report five-years experience of a single cancer center with TD in the management of uterine sarcomas.

Methods: Review of clinical data.

Results: We've identified 8 patients treated between 2011-2016. Most cases were leiomyosarcomas (87.5%) and one patient had an endometrial stromal sarcoma, ESS, (12.5%). Two patients (25%) were diagnosed with stage IV disease. All patients had undergone previous hysterectomy and four out of the six patients (67%) with localized disease received also adjuvant radiotherapy and one (16%) adjuvant chemotherapy (with gemcitabine and docetaxel). Most patients received TD in third or fourth line (n=6, 75%), usually after doxorubicin, ifosfamide and gemcitabine/docetaxel, with the exception of the patient with the ESS that performed the treatment in eighth line (12%). By the time they were treated with TD, the median patients age was 58 years (range: 52-76) and all of them had performance status (PS) of 0 or 1 and visceral metastasis, with a median of 3 sites involved most frequently the lung (n=6, 75%). The median number of cycles of TD performed was 3.0 (range: 1 –13). The best response was stable disease in 33.3% of patients and progressive disease in 66.7% of patients. The most common toxicity was fatigue in four patients (50%), and three patients experienced grade 3 toxicity (fatigue, anaemia and thrombocytopenia and dyspnoea). Progression free survival (PFS) and OS after TD were 2 (CI: 0.8 – 3.1) and 15 months (CI: 4.7-25.3) respectively. Four patients (50%) received more lines af-

ter this treatment. OS after recurrence diagnosis was 50 months (CI: 25.0-74.9).

Conclusion: In our series, we did not document objective responses to TD and the PFS was 2 months. The toxicity profile was similar to the described in the literature. Nevertheless, the OS was better than reported, likely related with the good performance status and the ability to receive posterior treatments in this particular group of patients.

P2–Poster 137 2565754

THE ROLE OF ESTROGEN AND PROGESTERONE AS PROGNOSTIC FACTORS FOR ADENOSARCOMA OF THE UTERUS

Michael J. Nathenson, MD; Vinod Ravi; Heather Y. Lin; Wei-Lien Wang; Alexander Lazar; Dejka Araujo; Neeta Somaiah; Maria A. Zarzour; Ravin Ratan; SR Patel; Robert S. Benjamin; Anthony P. Conley
Sarcoma, MD Anderson, Houston, TX, USA

Objective: Uterine adenosarcoma is the rarest of sarcomas that characteristically involve the uterus. Standard treatment involves surgical resection with hysterectomy and BSO, resulting in a 50-70% 5-yr overall survival (OS). Hormonal therapy, including leuprolide, anastrozole, and megestrol acetate, is occasionally used to treat these patients with varying, though generally poor results. Data regarding the prognostic role of the estrogen receptor (ER) and progesterone receptor (PR) in this rare uterine sarcoma is lacking. The objective of this study was to retrospectively examine the prognostic significance of estrogen and progesterone receptor nuclear reactivity by immunohistochemistry (IHC) in the MDACC uterine adenosarcoma experience.

Methods: The institutional tumor registry identified 165 patients with uterine adenosarcoma seen in consultation between 1982 and 2014. Clinical data was collected retrospectively. The Kaplan-Meier method estimated OS and disease-free survival (DFS). The Log-rank test probed the difference in survival between groups. ER and PR positivity on IHC was defined as ≥10% of tumor cell nuclei.

Results: ER expression was tested in 46 pts and PR expression in 45 pts. IHC staining for ER was positive in 70% of pts. IHC staining for PR was positive in 69% of pts. There was a 84% concordance between positive ER and PR staining. Of 34 pts with sarcomatous overgrowth (SO), ER was positive in 62%. Of 11 pts without SO, ER was positive in 91%. Of 32 pts with SO, PR was positive in 63%. Of 12 pts without SO, PR was positive in 83%. The SO status of 1 pt was unknown. The median OS and DFS was significantly improved for ER positive pts compared to ER negative pts, Table 1. The median OS (significant) and DFS (trend) was improved for pts with SO comparing ER positive pts to ER negative pts, Table 1. The median OS and DFS was significantly improved for PR positive pts compared to PR negative pts, Table 2. Pts with adenosarcoma without SO with positive ER or PR did not achieve median OS or DFS, Table 1,2.

Conclusion: Uterine adenosarcoma patients with positive ER or PR had a statistically significant improvement in median OS and DFS compared to those patients with negative ER or PR, suggesting a possible role of ER and PR as prognostic factors for uterine adenosarcomas. The benefit of ER and PR as prognostic factors was most apparent in the absence of SO, a known favorable prognostic factor. Nonetheless, ER status was still a prognostic factor for patients with SO.

Median OS and DFS by ER and sarcomatous overgrowth status

	ER positive	ER negative	p value
OS for all patients	8.5 yrs	8.2 yrs	0.017
OS for SO patients	9.9 yrs	8.2 yrs	0.045
OS for non-SO patients	NR	1.9 yrs	-
DFS for all patients	6.3 yrs	3.9 yrs	0.002
DFS for SO patients	5.7 yrs	3.9 yrs	0.052
DFS for non-SO patients	NR	1.1 yrs	-

NR-not reached

Median OS and DFS by PR and sarcomatous overgrowth status

	PR positive	PR negative	p value
OS for all patients	8.9 yrs	6.8 yrs	0.048
OS for SO patients	9.9 yrs	6.8 yrs	0.067
OS for non-SO patients	NR	1.9 yrs	-
DFS for all patients	6.3 yrs	4.3 yrs	0.031
DFS for SO patients	5.7 yrs	4.3 yrs	0.33
DFS for non-SO patients	NR	1.1 yrs	-

NR-not reached

P2–Poster 138 2542471

SELECTIVE MARGINAL RESECTIONS IN THE MANAGEMENT OF AGGRESSVE ANGIOMYXOMAS

Henry G. Smith, MRCS[1]; Khin Thway[1]; Christina Messiou[1]; Desmond Barton[2]; Joseph Meirion Thomas[1]; Andrew J. Hayes[1]; Dirk C. Strauss[1]; Myles J. Smith[1]
[1]The Sarcoma Unit, The Royal Marsden Hospital, London, United Kingdom; [2]The Gynaecology Unit, The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom

Objective: Aggressive angiomyxomas are rare tumours that most commonly present in the pelvis of women of childbearing age. This study presents the results of selective marginal resection of this disease in patients managed at a single institution.

Methods: Patients diagnosed with an aggressive angiomyxoma from July 2001 to July 2015 were identified from a prospectively maintained histopathology database. Electronic patient records, imaging and pathology reports were retrieved and reviewed.

Results: Seventeen patients were diagnosed with aggressive angiomyxoma in the study period. The median age at diagnosis was 48 years. Females were more commonly affected with a M:F of 1:8.5. Fourteen patients presented with a primary lesion. The remaining three had recurrent disease, having undergone a single previous excision. The most common differential diagnoses were an ischiorectal abscess or Bartholin's cyst. Fifteen tumours occurred in the pelvis, with two tumours at other sites. The median maximum tumour diameter was 10 cm (range 1.2 to 20 cm). Pre-operative cross sectional imaging demonstrated the tumour approximated to the vagina in 9 patients, the anal sphincters in 6 patients, the rectum in 6 patients, the bladder in 4 patients and the urethra in 3 patients. A supralevator component was present in 10 patients and in 3 patients the tumour extended into the abdominal cavity exerting a mass effect on intra-abdominal structures. Of the patients with pelvic tumours, 12 were managed operatively via perineal (8/12), abdominal (1/12) or abdominoperineal (3/12) approaches. Excision was performed in a marginal fashion with minimal morbidity. Local recurrence developed in 58.3% (7/12) with a median local recurrence free survival of 25 months. Of the seven patients with recurrent disease, five were asymptomatic and managed non-operatively. Salavage surgery was performed in the remaining 2 patients. No patients developed metastatic disease and all were alive at the time of writing.

Conclusion: Aggressive angiomyxomas are rare tumours with a propensity for local recurrence. Atypical presentations of other perineal pathologies should prompt further investigation. Surgery should be reserved for symptomatic patients and is associated with minimal morbidity with radical surgery reserved for symptomatic recurrences.

P2–Poster 139 2569998

TREATMENT OF RETROPERITONEAL LIPOSARCOMAS AT A REFERAL CENTER: RETROSPECTIVE ANALYSIS OF PROGNOSTIC FACTORS

Alexandre M. Sousa, Resident; Ana Isabel Ferreira; Catia Ribeiro; Ana Ferreira; Sofia Conde; Marta Soares; Mariana Afonso; Flavio Videira; Jorge Guimaraes; Augusto Moreira; Joaquim Abreu de Sousa
Surgical Oncology, IPO PORTO, Vila Nova de Gaia, Portugal

Objective: Liposarcomas are a common form of retroperitoneal soft tissue malignant tumors. Struggle to optimize treatment is mainly due to difficulty in translating big data from global retroperitoneal tumors into the specific retroperitoneal liposarcoma patient. We've reviewed a cohort of retroperitoneal liposarcoma patients from a referral center to establish demographic and therapeutic aspects affecting prognosis.

Methods: A retrospective analysis of a single-center data base of retroperitoneal sarcoma was performed. Adult surgical patients diagnosed with retroperitoneal liposarcoma between 2007 and 2013 were included.

Results: Fifty-five patients were included. Thirty-two were female (58%). Median age of 62 years old (range 19-84). The majority were symptomatic at diagnosis (76.4%) with a median size of 20.5 cm. Histology results were the following: 28 well differentiated, 11 dedifferentiated, 9 myxoid and 7 high grade liposarcoma. Well differentiated tumors were more common in women and occurred at a more advanced age. After a median follow up of 48 months, 5 years' disease specific survival was 63%.

Well differentiated sarcomas and female gender were associated with a better prognosis (both $p<0.001$). Involvement of adjacent organs and high grade tumors had worse prognosis. Specific histology impacted survival outcome. After the first surgery, no difference on survival was observed between R0 and R1 resections. Thirty-seven patients were reoperated out of 38 who had recurrence.

At reoperation, R1 margins performed worse than R0 margins. No difference on survival was observed when comparing patients who underwent one, two or more than two procedures. Dedifferentiation at recurrence was not associated with a worse outcome. Regarding adjuvant treatment, no difference was observed on survival between adriamycin, ifosfamide or trabectadin.

Conclusion: This group presents with large volume lesions and attempting an early diagnosis does not seem likely. Female gender had better survival and less cases of high grade lesions suggesting a role of fat tissue-hormone interaction on outcome.

As surgical therapy is concern, macroscopic clearance seems to be the most relevant aspect during the first operation (resecting adjacent organs if necessary). At a reoperation, an effort should be made to achieve complete R0 margins.

These findings, at least, supports our current strategy of surgical resection with multiple re-interventions if necessary, but new approaches are necessary in order to improve treatment results.

P2–Poster 140 2569963

NATIONAL TREATMENT PATTERNS OF RETROPERITONEAL SARCOMA IN IRELAND

Meagan E. Wiebe[1]; Gerry Kelliher[2]; Una Hayden[1]; Charles Gillham[1]; Gary O'Toole[1]; Amy Gillis[1]; Paul F. Ridgway[2]
[1]Irish Sarcoma Group, at St. Vincent's University, St Luke's and Tallaght Hospitals, Dublin, Ireland; [2]National Clinical Programme in Surgery, RCSI, Dublin, Ireland

Objective: Soft tissue sarcoma specific overall survival in Ireland approximates the UK and lags behind North America[1]. Centralisation of services for this rare tumour group is underway. 10-15 retroperitoneal and peritoneal soft tissue sarcomas are expected in the population each year. The use of perioperative radiation remains controversial. This study aims to define the clinical incidence of retroperitoneal sarcoma in Ireland, the number of cases receiving surgical management, and the subgroup of cases provided with multimodal therapy.

Methods: NQAIS, a national surgical and medical data tool, was interrogated to determine the number of cases of retroperitoneal sarcoma diagnosed between January 2011 and March 2016. Data was decoded, and analysed in terms of demographic, hospital admission, diagnostic, and procedural variables. Ethical approval was obtained.

Results: Eighty-two patients were identified with an ICD-10 diagnosis of 'malignant neoplasm of retroperitoneum' (C48.0). It was the primary diagnosis in 95.1% of the cohort (78/82). Slight male preponderance was noted (51.2%). The highest rate was seen between the ages of 61-80 years old (51.2%). Most had low co-morbidity (Charlson index of 0-1; 60%), remained in hospital for 4-10 days (53.6%), and were treated at four of the Irish university hospitals (51.2%). Surgery was the primary procedure used to manage 58.5% of the patients (48/82), followed by biopsy (19.5%, 16/82), and chemotherapy (14.6%, 12/82).

Conclusion: The number of retroperitoneal sarcoma cases identified corresponds with the expected incidence of primary retroperitoneal sarcoma in Ireland. Surgery, as the primary procedure in 58%, implies that the slight majority of retroperitoneal sarcoma undergo resection without preoperative biopsy, which is against current guidelines.

Reference:

[1]Bhatt N, Deady S, Gillis A, Bertuzzi A, Fabre A, Heffernan E, Gillham C, O'Toole G, Ridgway PF. *Epidemiological study of soft-tissue sarcomas in Ireland.* Cancer Med. 2016; 5(1): 129-135.

P2–Poster 141 2540926

DOES EXTENDED SURGICAL RESECTION IMPROVE OUTCOMES IN PRIMARY RETROPERITONEAL WELL- DIFFERENTIATED LIPOSARCOMA?

Naruhiko Ikoma, MD; Christina Roland; Keila E. Torres; Gary Mann; Kelly K. Hunt; Janice Cormier; Barry W. Feig
Surgical Oncology, MD Anderson Cancer Center, Houston, TX, USA

Objective: Recurrence after surgical resection of retroperitoneal well-differentiated liposarcoma (RP WDLPS) is common, and is a treatment challenge. We aimed to investigate whether en-bloc organ removal as part of the primary resection of RP WDLPS confers an outcome advantage in patients treated at a major sarcoma center.

Methods: After receiving Institutional Review Board approval, the departmental sarcoma database was reviewed to identify patients with RP WDLPS who underwent initial surgical resection for primary disease at the MD Anderson Cancer Center (MDACC) during the study period 1994-2010. Medical records were retrospectively reviewed to identify patient/tumor/treatment factors. Associations between clinicopathologic variables and overall survival (OS) as well as disease free survival (DFS) were examined.

Results: We identified 54 patients who underwent surgical resection of primary RP WDLPS; 52 patients (96%) had complete (R0, R1) resection. Median tumor size was 30 cm (range 8.5-78), and 19% (10/54) had multifocal tumors. En-bloc organ resections were performed in 52% of patients (28/54). Organs most commonly resected were kidney (n=20), followed by adrenal (n=14) and spleen (n=7). Of those patients who underwent en-bloc resections, 21% of patients (6/28) had pathologic confirmation of tumor invasion of resected organs (5 kidneys and 1 small bowel). Five patients (9%) developed post-operative complications (grade 3, 4), and there was no post-operative mortality. Median survival time was 11.3 years, and 5-year survival rate was 82.7%. Five-year local recurrence rate was 42%, and a total of 29 patients (56%) developed local recurrence during follow up. Median time to recurrence was 3.0 years (range 0.2-10.2). Multivariate analysis revealed that multifocality of the primary tumor (hazard ratio [HR] 3.75, 95% confidence interval [CI] 1.32-10.65; p=0.013) and organ invasion (HR 3.75, 95%CI. 1.309-11.17; p=0.036) were associated with shorter OS. En-bloc organ resection was not associated

with improved OS (HR 1.44, 95% CI 0.56-3.67; p=0.448) or DFS (HR 1.06, 95% CI 0.54-2.08; p=0.877).

Conclusion: In patients with primary RP WDLPS operated on at our institution, tumor invasion of contiguous organs was rare, and en-bloc organ resection was not associated with improved OS or DFS. In patients with primary RP WDLPS, we recommend selective resection of contiguous organs if there is clinical suspicion for invasion at the time of surgical resection.

P2–Poster 142 2561942

PHASE I TRIAL OF PRE-OPERATIVE IMAGE-GUIDED INTENSITY MODULATED PROTON RADIATION THERAPY (IMPT) WITH SIMULTANEOUSLY INTEGRATED BOOST TO THE HIGH RISK MARGIN FOR RETROPERITONEAL SARCOMAS

Thomas F. DeLaney, MD[1]; Yen-Lin Chen[1]; Judith Adams[1]; Shea Hickey[2]; Dian Wang[3]; Elizabeth H. Baldini[4]; Karen De Amorim Bernstein[1]; Beow Yeap[2]; Stephen M. Hahn[5]; Petur Nielsen[6]; Edwin Choy[7]; John T. Mullen[8]; Sam S. Yoon[9]

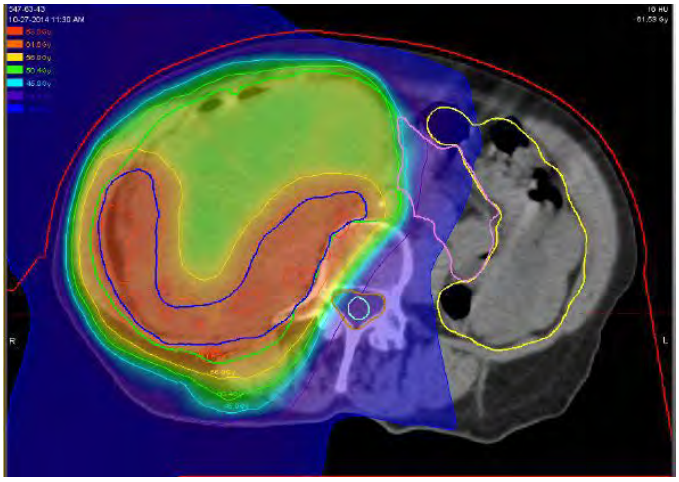
[1]Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [2]Cancer Center, Massachusetts General Hospital, Boston, MA, USA; [3]Radiation Oncology, Rush University Medical Center, Chicago, IL, USA; [4]Radiation Oncology, Brigham and Women's Hospital, Dana Farber Cancer Institute, Boston, MA, USA; [5]Radiation Oncology, M.D. Anderson Cancer Center, Houston, TX, USA; [6]Pathology, Massachusetts General Hospital, Boston, MA, USA; [7]Medical Oncology, Massachusetts General Hospital, Boston, MA, USA; [8]Surgical Oncology, Massachusetts General Hospital, Boston, MA, USA; [9]Surgical Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Objective: To conduct a phase I/II trial with photon IMRT and proton IMPT arms to selectively escalate retroperitoneal sarcoma (RPS) preoperative radiation dose to a clinical target volume (CTV2) judged by the treating surgeon and radiation oncologist to be at high risk for positive margins, aiming to reduce the risk of LR. We report the proton IMPT phase I study arm.

Methods: Patients > 18 years with primary or locally recurrent RPS were entered on study and treated with preoperative IMPT. 50.4 GyRBE in 28 fractions of 1.8 GyRBE was delivered to the average risk clinical target volume (CTV1) encompassing the GTV and adjacent tissues at risk of subclinical disease. A simultaneous integrated boost was delivered to CTV2 to doses that were sequentially escalated from 60.2 GyRBE to 61.6 GyRBE and 63.0 GyRBE in 28 fractions of 2.15, 2.20, and 2.25 GyRBE respectively. Phase I study primary objective was determination of the MTD of radiation to CTV2, which would then be further tested in the follow-on phase II study.

Results: Eleven patients were accrued to increasing protocol IMPT dose levels without acute dose limiting toxicities (DLTs) preventing dose escalation to MTD. Acute toxicity was generally mild with no radiation interruptions. No unexpected perioperative morbidity was noted. Eight months postoperatively, one patient developed hydronephrosis treated by stent; that ureter, dissected off tumor, had received 57.5 GyRBE preoperatively. Retained ureters were subsequently constrained to 50.4 GyRBE without further problem. With 18-month median follow-up, there were no LRs.

Conclusion: IMPT dose escalation to CTV2 to 63 GyRBE was achieved without acute DLT; phase II IMPT study will accrue to that dose. Parallel IMRT phase I arm is currently accruing. Ureters undergoing high dose radiation and surgical manipulation are at risk for hydroureter; our future studies will constrain retained ureter(s) to 50.4 GyRBE to avoid ureteral stricture.



Radiation plan for patient with a dedifferentiated liposarcoma, treated to CTV1 to 50.4 GyRBE and CTV2 to 61.6 GyRBE in 28 fractions .

P2–Poster 143 2562787

A COMPARISON OF RADIOTHERAPY TARGET VOLUMES DELINEATED WITH MRI AND CT IN PATIENTS HAVING PRE- OPERATIVE RADIOTHERAPY FOR RETROPERITONEAL SARCOMA IN THE PIRS STUDY

Daniel R. Henderson, FRCR[1]; Gabriele Poillucci[2]; Jessica Winfield[2]; Dirk C. Strauss[3]; Shane Zaidi[1]; Christina Messiou[2]; Aisha Miah[1]

[1]Radiotherapy, Royal Marsden Hospital, London, United Kingdom; [2]Radiology, Royal Marsden Hospital, London, United Kingdom; [3]Surgery, Royal Marsden Hospital, London, United Kingdom

Objective: The relatively poor soft-tissue contrast of CT imaging used for radiotherapy contouring may result in

geographical miss of tumours, or include excess normal tissue. The superior soft tissue contrast of MRI is likely to produce a more accurate target volume, potentially improving local control and reducing normal tissue toxicity. In this study we compared volumes delineated using CT with MRI.

Methods: Twenty patients in the PIRS study (NCT01902667) had gross tumour volumes (GTVs) contoured by a radiologist and oncologist on CT and MRI imaging (T1- and T2-weighted) using the Eclipse planning system. CT and MRI were contoured independently. To assess intra-observer variability, contouring was repeated on both CT and MRI two months after the initial session, without reference to previous contours.

Results: Mean GTV for CT was 1513 cc vs. 1634 cc for MRI (p = 0.83; paired t-test). The range of volumes was 21.1 cc to 4873 cc and 36.6 cc to 5424 cc for CT and MRI, respectively. The mean difference in volumes between CT- and MRI-based contours was 11.8% (range 1.0-32.6%). Intra-observer variability was 6.0% (0.0-7.6%) and 5.0% (0.5-15.6%), for CT and MRI, respectively. Example images showing the significant differences between MRI and CT contours will be shown.

Conclusion: CT and MRI target volumes can vary significantly. If MRI is taken as the gold standard, this implies that it produces more accurate volumes than CT. Further work is required to determine how best to incorporate MRI into radiotherapy work flow (such as accurate MRI fusion or MRI-based planning).

P2–Poster 144 2569916

TREATMENT OF RETROPERITONEAL SARCOMA IN GERMANY - RESULTS OF A SURVEY OF THE GERMAN INTERDISCIPLINARY SARCOMA STUDY GROUP AND THE GERMAN SOCIETY OF GENERAL AND VISCERAL SURGERY

Jens Jakob, MD[1]; Anna Gerres[1]; Bernd Kasper[4]; Markus Wartenberg[2]; Ulrich Ronellenfitsch[1]; Hans-Rudolf Raab[3]; Peter Hohenberger[1]
[1]Department of Surgery, University Medical Center Mannheim, University of Heidelberg, Germany, Mannheim, Germany; [2]Das Lebenshaus, Wölfershausen, Germany; [3]Department of Surgery, University Hospital Oldenburg, Oldenburg, Germany; [4]Interdisciplinary Tumor Center Mannheim, University Medical Center Mannheim, Mannheim, Germany

Objective: Retroperitoneal sarcomas (RPS) are rare cancers with some variability in clinical and histopathological presentation. In Germany, general treatment strategies of retroperitoneal sarcoma are unknown since centralized registers do not exist. The objective of this survery was to access the medical care of RPS patients in Germany.

Methods: In cooperation with the German Society of general and visceral surgery, the german interdisciplinary sarcoma study group and the patient advocacy group “Das Lebenshaus” we designed an online survey assessing diagnostic and treatment strategies (e.g. performance of tumor biopsies, discussion in multidisciplinary tumor boards, adminitration of multimodal therapies, surgical strategy) as well as the expectations on short and long term outcome (e.g. postoperative complications, disease specific survival, long term complications). From December 2015 to June 2016, all German surgical departments (n=962) were invited to take part in the survey and reminders were sent every second month.

Results: 146/962 (15%) surgical departments participated in the survey. University hospitals and tertiary care centers were more likely to answer the survey than others. Seven departments treat more than 10 RPS patients per year. A sarcoma board exists in nineteen hospitals. Local staging is generally performed by abdominal MRI or CT imaging, chest CT is used by 89% of the respondents. Preoperative biopsies are taken regularly in 51% of the participating departments. In 67%, retroperitoneal compartment (i.e. multivisceral) resection represents the standard surgical strategy for RPS; 33% of the surgeons generally perform a systemic lymphadenectomy. Pre- or postoperative irradiation or chemotherapy are administered in more than 50% of the cases in 28% and 23%, respectively. Estimates on 5-year local-recurrence-free and overall survival varied between 2 – 100% (median 28%) and 1 - 100% (median 52%). 84% of the respondents would appreciate workshops on the treatment of RPS and 94% a nationwide RPS register to improve the treatment of RPS patients.

Conclusion: The survey demonstrates a large heterogeneity in RPS treatment strategies in Germany. Dedicated education programs and centralized treatment strategies are warranted to improve the standard of care.

P2–Poster 145 2529180

SURGERY FOR RETROPERITONEAL SARCOMAS IN THE ELDERLY

Henry G. Smith, MRCS; Joseph Meirion Thomas; Myles J. Smith; Andrew J. Hayes; Dirk C. Strauss
Sarcoma Unit, Academic Surgery, The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom

Background: Retroperitoneal sarcomas occur in an anatomically complex location often involving several adjacent organs. Surgery with multi-visceral resection constitutes the mainstay of curative therapy. This study sought to characterise the morbidity and oncological outcomes of surgery for retroperitoneal sarcoma in an elderly population.

Methods: Patients with primary, localised retroperitoneal sarcoma referred between 1/1/08 - 31/12/14 were identified

from multidisciplinary meeting records. The proportion of patients proceeding to surgery and oncological outcomes were compared between two groups – those aged >65 years and <65 years.

Results: A total of 385 patients were identified. The most common histological subtypes were de-differentiated liposarcoma (40.3%), well-differentiated liposarcoma (19.5%) and leiomyosarcoma (18.2%). A greater proportion of patients aged > 65 years did not undergo surgery (41.8% vs 12.0%). The rates of irresectable tumours were similar between cohorts (17.5% vs 11.0%). However, non-operative management due to comorbidities (13.4% vs 0.5%) or patient choice (8.2% vs 0.5%) was more common in patients aged >65 years. 281 patients (73.0%) proceeded to surgery. Patients aged >65 years had a higher rate of peri-operative morbidity (28.3% vs 9.5%), although no difference in peri-operative mortality or oncological outcomes was noted between age groups. The survival of patients managed non-operatively was significantly shorter than those undergoing surgery (median survival 15 vs 91 months, $p < 0.001$).

Conclusion: Extended resections for primary retroperitoneal sarcoma in the elderly achieve comparable oncological outcomes but with increased rates of morbidity when compared with younger patients. The outcomes of patients unsuitable for surgery are poor regardless of age.

P2–Poster 146 2567751

IS RESECTION INDICATED FOR SCHWANNOMA OF THE RETROPERITONEUM/PELVIS?

Sally M. Burtenshaw[1]; Rebecca Gladdy[1]; Brendan C. Dickson[2]; Peter Ferguson[1]; Carol Swallow[1]
[1]General Surgery, Mount Sinai Hospital, Toronto, ON, Canada; [2]Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada

Objective: Approximately 5-10% of patients who present with a soft tissue mass in the retroperitoneum or pelvis (RP/P) will be diagnosed with a benign peripheral nerve sheath tumour, the majority being schwannomas. While resection has often been recommended as the optimal management of schwannoma, this can be technically challenging and functionally morbid for tumours in the RP/P. Over the past 15 years, we have adopted an initially non-operative approach to these tumours, and herein describe the outcomes.

Methods: Patients diagnosed with schwannoma of the RP/P at our centre from 2000-2015 were identified from a prospective abdominal sarcoma database. Diagnosis was based on histomorphologic and immunophenotypic criteria outlined in the WHO Classification, together with compatible imaging (CT and/or MRI). Resection was recommended for severe symptoms, suspicious growth on imaging and/or diagnostic uncertainty.

Results: 63 patients (36F/27M) with schwannoma of the RP(n=38) or P(n=25) form the study cohort. At presentation, median age was 46(20 -78), median tumour size was 6.1cm(1.8-14.3), and the majority of patients (68%) were symptomatic.

Six patients underwent resection shortly after presentation, due to untenable symptoms and/or uncertain pathology. Fifty-seven patients were initially observed with serial imaging; four of these underwent resection at 1, 9, 44 and 53 mos for progressive symptoms/tumor size. Thus, the overall non-operative management rate was 84%. Median follow-up in the non-operative group (n=53) was 34 mos (1-157). Some degree of tumour growth over time was observed in the majority of patients (60%). In those with follow-up times of ≥2yrs(n=46) and ≥5 yrs(n=19), median change in tumour size was +9% (-17% - +46%) and +26% (-33% - +82%) over baseline, respectively. No evidence of MPNST or other malignancy developed in any of the 63 patients.

Although the majority of patients who underwent resection reported some degree of symptom relief, two of ten reported worsening. Patients who were managed non-operatively reported no worsening of symptoms over time.

Conclusion: The natural history of schwannoma of the RP/P managed non-operatively was to grow, albeit slowly. Patients adapted to the growth without significant increase in symptoms. Identification of predictors of significant growth could assist with initial decision-making regarding resection.

P2–Poster 147 2565613

PRIMARY RADIATION THERAPY FOR ABDOMINO-PELVIC SOFT-TISSUE SARCOMA ACHIEVES GOOD RESULTS IN PATIENTS WITH INOPERABLE DISEASE

Priyanka Patel; Natalie Nobar; Shane Zaidi; Dirk C. Strauss; Andrew J. Hayes; Myles J. Smith; Christina Messiou; Charlotte Benson; Ian Judson; Aisha Miah
Sarcoma Unit, The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom

Objective: Surgery remains the primary radical treatment option for abdomino-pelvic soft tissue sarcoma, with the addition of radiotherapy potentially improving local control rates. We report outcomes of patients who initially presented with inoperable primary or recurrent abdomino-pelvic soft tissue sarcoma receiving primary radiotherapy alone.

Methods: Retrospective analysis of patients identified from a prospective sarcoma database between 2012 and

2015. Patients with inoperable solitary sites of disease receiving high dose palliative or radical dose radiotherapy were identified. Survival outcomes were calculated from time of completion of radiotherapy to date of relapse (local/distant) or last follow up.

Results: Between 2012-2015, 32 patients (median age 59 years, range 24-85 years) received primary radiotherapy to an inoperable or recurrent abdomino-pelvic sarcoma. Histological subtypes: pleomorphic (6), leiomyosarcoma (5), liposarcoma (13), low grade fibromyxoid sarcoma (2), MPNST (3) and other (4). Commonest fractionation schedules were: 50.4 Gy/28# (15), 60-65 Gy/30# (6) and 30 Gy/10# (6) using IMRT (25) or conformal radiotherapy technique. One patient received SBRT (30Gy/3#).

All patients completed radiotherapy without delays, 1 patient did not complete planned treatment due to grade 3 anorexia and fatigue. Nine patients suffered with grade 1 toxicities primarily nausea, diarrhoea, fatigue, 3 patients experienced grade 2 toxicities including constipation, diarrhoea, anorexia and fatigue; 2 patients had grade 3 toxicities with fatigue and sepsis.

Following first radiological response assessment at 4 weeks after RT: 1 patient had a complete response, 12 patients showed partial response, 9 patients had stable disease and 10 demonstrated progression at the irradiated site. At a median follow-up of 19 months (0.7- 51.7 months), median local relapse free survival was 17.3 months (0.9- 51.7 months), median progression free survival 13.7 months (0.9-51.7) and median overall survival 26.6 months (6.2- 51.7). Eight patients went on to have palliative chemotherapy, 3 patients had further palliative radiotherapy and 3 proceeded to surgical resection.

Conclusion: Primary radiotherapy achieves good local control rates and should be considered in patients with inoperable solitary sites of disease.

P2–Poster 148 2570592

OUTCOMES IN PRIMARY ABDOMINAL OR RETROPERITONEAL LEIOMYOSARCOMA MANAGED WITH A MULTIDISCIPLINARY APPROACH

Fernando A. Angarita, MD, MSc[1]; Ana Olteanu[1]; Brendan C. Dickson[2]; Martin E. Blackstein[3]; Charles Catton[3]; Ian McGilvray[4]; Peter Chung[5]; Abha Gupta[6]; Rebecca Gladdy[1]

[1]Department of Surgery, Mount Sinai Hospital, Toronto, ON, Canada; [2]Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada; [3]Department of Medical Oncology, Mount Sinai Hospital, Toronto, ON, Canada; [4]Department of Surgery, University Health Network, Toronto, ON, Canada; [5]Department of Radiation Oncology, University Health Network, Toronto, ON, Canada; [6]Department of Medical Oncology, University Health Network, Toronto, ON, Canada

Objective: We report the outcomes and recurrence patterns of patients with primary abdominal/retroperitoneal leiomyosarcoma (LMS) treated with a multimodality approach at a high volume sarcoma center.

Methods: Patients with LMS considered for curative intent treatment were identified from a sarcoma database (1997-2014). Patients with extra-abdominal/retroperitoneal LMS, unresectable/metastatic LMS on presentation, or who had surgery performed elsewhere were excluded. Clinicopathological and treatment details were extracted. Primary outcomes were disease free (DFS) and overall (OS) survival. Secondary outcome was recurrence patterns. Survival analyses were calculated by Kaplan-Meier curves and compared by log-rank.

Results: Fifty patients met the inclusion criteria. Median follow-up time was 45m (IQR: 27-70m). Median age at presentation was 59y (IQR: 51-70y). Patients were mainly female (68%). Thirty-eight (76%) had retroperitoneal LMS of which 20 arose from or invaded the inferior vena cava. Twelve (24%) had abdominal LMS arising from the rectum, small bowel mesentery, or portal vein. Neoadjuvant radiation therapy (RT) was administered to 31 (62%). Nine (18%) received neoadjuvant chemotherapy (CT) with doxorubicin/ifosfamide (n=8) or doxorubicin (n=1). Treatments were RT+surgery (SX) (42%), SX (24%), RT+CT+SX (20%), RT and/or CT (8%), or observation (6%). Seven (14%) did not have SX due to progression in tumor size and/or location post-neoadjuvant treatment (n=5), development of metastasis during neoadjuvant treatment (n=1), or patient preference (n=1). Forty-three (86%) had SX. Median resected tumor size was 8.8cm (IQR: 6.2-15.5cm). Margins were R0 (88%) or R1 (12%). Of patients who had SX 40% developed recurrences, which were solely distant and mainly single-site (77%). Recurrences involved bone (26%), lung (22%), liver (16%), and other organs (36%). Median DFS was 16m (IQR: 8-22m), independent of primary site and multimodality treatment. Recurrences were treated with CT

and/or RT (29%), SX + CT and/or RT (29%), observation (24%), or SX (18%). Median OS was 83m (IQR: 46-111m), independent of primary site or multimodality treatment.

Conclusion: Patients with abdominal/retroperitoneal LMS who undergo surgery at our center frequently receive neoadjuvant RT/CT. Despite the approach recurrences are frequent and exclusively distant thus suggesting biological factors likely play a role in the DFS of LMS, especially because our results were independent of primary tumour site and multimodality treatment.

P2–Poster 149 2558023

A PHASE II CLINICAL TRIAL OF CONCURRENT AXITINIB AND PEMBROLIZUMAB IN SUBJECTS WITH ADVANCED ALVEOLAR SOFT PART SARCOMA AND OTHER SOFT TISSUE SARCOMAS

Breelyn A. Wilky, MD[1]; Jonathan Trent II[1]; Rosenberg Andrew[2]; Ty K. Subhawong[3]; Eric Wieder[1]; Despina Kolonias[1]; Deukwoo Kwon[4]; Efrosyni Sfakianaki[3]; Krishna Komanduri[1]

[1]Hematology/Oncology, Sylvester Comprehensive Cancer Center, Miami, FL, USA; [2]Pathology, University of Miami, Miami, FL, USA; [3]Radiology, University of Miami, Miami, FL, USA; [4]Biostatistics, Sylvester Comprehensive Cancer Center, Miami, FL, USA

Objective: Immune checkpoint inhibitors block tumor-mediated suppression of the immune system and have produced remarkable, durable responses in a variety of solid tumors refractory to traditional chemotherapy. Recent results from a phase II trial of single-agent pembrolizumab in soft tissue sarcomas reported an overall response rate of 19%. Previous combinations of checkpoint inhibitors with anti-VEGF therapy increased immune cell infiltration and improved tumor response in melanoma and renal cell carcinoma. Axitinib, a pan-VEGFR tyrosine kinase inhibitor has shown anti-tumor activity in soft tissue sarcomas, with acceptable toxicity in combination with pembrolizumab in renal cell carcinoma. This abstract reports a phase II **trial in progress** of combination axitinib plus pembrolizumab for soft tissue sarcomas (NCT02636725).

Methods: The study is a single-arm, single-institution open-label phase II trial of oral axitinib administered twice daily with concurrent pembrolizumab 200 mg IV every three weeks. Eligible patients include those with metastatic or unresectable soft tissue sarcomas, or bone sarcomas with evaluable soft tissue lesions with adequate end-organ function and no curative treatment options. The primary endpoint is progression-free rate at 12 weeks by RECIST 1.1, with secondary endpoints including toxicity, overall response rate and PFS. Axitinib will be dose-escalated according to toxicity. Correlative studies include blood and tumor samples collected pre-treatment, on-treatment and at progression. We will measure the association between PFS and the following endpoints: T cell infiltration, T cell subtype and activation status, and expression of various checkpoint proteins. Radiographic response will also be assessed according to alternative measures of response including Choi criteria, immune-related response criteria, MRI volumetrics, and PERCIST 1.0 using correlative PET scans. We will also measure changes in circulating tumor cells in patients treated on the regimen and associate this with radiographic response and PFS.

Results: At the time of this abstract, 7 of the planned 30 patients have been enrolled on the protocol and received at least one dose of both study drugs. There have been no DLTs.

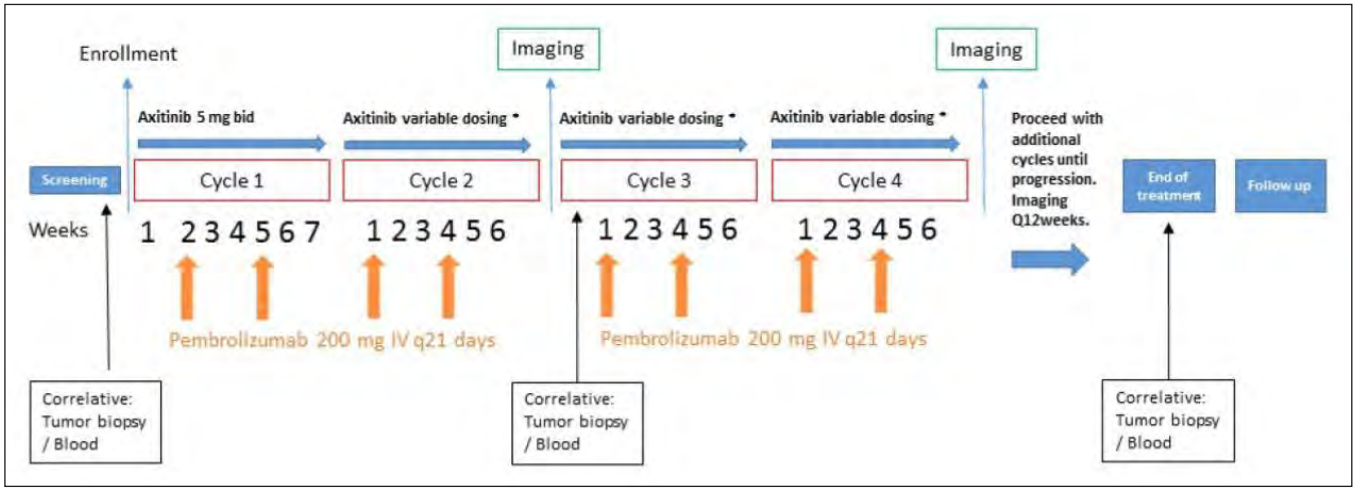


Figure 1. Treatment schema. The first cycle of treatment will be seven weeks, with one week of axitinib alone prior to initiation of pembrolizumab. Subsequently, six-week cycles of treatment consist of twice daily oral doses of axitinib administered continuously with intravenous (I.V.) administration of pembrolizumab on day 1 and 22. The first five evaluable patients will be considered a safety lead-in, and will not have axitinib dose escalation above 5 mg PO bid. In subsequent cycles, patients will begin cycle 1 with axitinib 5 mg PO twice daily (BID) and be monitored for DLT; these patients may then have axitinib dose-escalated as tolerated for the individual patient starting with cycle 2. Dose de-escalations may occur at any time for toxicity.

Conclusion: The use of concurrent axitinib and pembrolizumab in patients with advanced soft tissue sarcoma is feasible and has not demonstrated intolerable toxicity in an ongoing phase II trial.

P2–Poster 150 2570389

ALVEOLAR SOFT PART SARCOMA (ASPS) DISPLAYS A STRUCTURALLY ORGANIZED INFILRATING MYELOID CELLS

Silvia Stacchiotti, MD[1]; Marcella Tazzari[2]; Tiziana Negri[3]; Paolo Casali[1]; Silvia Brich[3]; Silvana Pilotti[3]; Chiara Castelli[2]
[1]Cancer Medicine, Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy; [2]Unit of Immunotherapy of Human Tumors, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [3]Laboratory of Experimental Molecular Pathology, Department of Diagnostic Pathology and Laboratory, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Objective: ASPS is a very rare sarcoma that expresses angiogenesis-related molecules and has a distinctive angiogenic phenotype with a peculiar tumor-associated vasculature. The role of tumor-infiltrating myeloid cells in the formation and maintenance of abnormal blood vessels in tumors is known. We report on the presence of cells expressing myeloid markers in the inflammatory infiltrate of a small series of ASPS. We also evaluated the in situ adaptive immunity by checking the presence of T cells at the tumor site.

Methods: The naïve tumor tissues of 5 pts treated at our institution were examined by IHC and confocal immunoflourescence. The following myeloid (CD14, CD163, CSFR1) and angiogenic related markers (VEGFR2, CD31) were examined together with the markers for T cells (CD3, CD8, CD4). Presence of T regulatory cells was assessed by Foxp3 staining. Expression of PDL-1/PD-1 checkpoint molecules was also evaluated.

Results: A sizeable population of CD163+CD14+ tumor-associated macrophages was clearly detectable in all cases, in 2 distinct areas: interspersed within nest tumor and in the perivascular region where they were aligned to VEGFR2+ cells of endothelial nature (CD31+). These CD31+ cells were encircling the distinctive nests/alveolar structures of ASPS. CSFR-1 immunoreactivity displayed a distribution similar to that of CD163. The pattern of PDL1/PD1 expression recapitulates in terms of shape and distribution what observed for macrophage markers. Immunofluorescence and confocal analyses, are ongoing to evaluate the precise nature the PDL-1/PD1 immunolabeled cells. In all samples the staining for CD3 defining infiltrating T cells was highly heterogeneous with two cases displaying a high frequency of CD3+ cells inside the tumor nests.

Conclusion: In this small series of ASPS, we found that CD14+ and CD163+ myeloid cells constitute the prominent cells in the inflammatory infiltrate and define the presence of M2-like macrophages. These myeloid cells are active inflammatory components that may promote VEGF-mediated vasculogenesis and may provide trophic support to ASPS vascular network. This immunophenotypic ASPS signature strongly suggests that the myeloid immune component may directly influence the response to anti-angiogenic therapies. In addition, the PDL-1/PD-1 positivity, if confirmed on a larger series, suggests a rationale for regimens with PD pathway blockade. An international effort is planned to corroborate these observations and to better define the immunoprofile of ASPS.

P2–Poster 151 2556593

ALVEOLAR SOFT PART SARCOMA IN CHILDREN AND YOUNG ADULTS

Ricardo J. Flores[1]; Douglas J. Harrison[2]; Noah Federman[3]; Winston Huh[2]; Murali Chintagumpala[1]; Rajkumar Venkatramani[1]
[1]Pediatrics, Baylor College of Medicine, Houston, TX, USA; [2]Pediatrics, MD Anderson Cancer Center, Houston, TX, USA; [3]Pediatrics, Ronald Reagan UCLA Medical Center, Los Angeles, CA, USA

Objective: Alveolar soft part sarcoma (ASPS) is a rare mesenchymal tumor characterized by ASPL-TFE3 translocation. Apart from complete surgical resection, there is no standardized management strategy. We describe the clinical presentation, treatment, and outcome of patients diagnosed with ASPS at less than 30 years of age.

Methods: Clinical data of 50 children and young adults with ASPS between 1980 and 2014 was retrospectively collected from three major institutions.

Results: Median age at diagnosis was 20 (1.5–30) years. 32 (64%) patients (pts) were female. Median follow-up was 28 (1– 228) months (mo). Primary sites included mostly limbs (63%) and trunk/retroperitoneum/pelvis (25%). ASPL-TFE3 translocation was positive in the 23 pts tested. IRS post-surgical staging was I in 11 (22%), II in 7 (14%), III in 3 (6%), and IV in 29 (58%) pts.

Of the 11 IRS-I pts, 7 were observed after surgery; one relapsed at 12 mo, treated with imatinib and remained alive with disease at 23 mo. Four pts received XRT; one relapsed distally (lungs) at 41 mo, treated with doxorubicin/ifosfamide and died at 46 mo.

Of the 7 IRS-II pts, 4 received adjuvant XRT to tumor bed, one received XRT and chemotherapy, one received imatinib only, and one observed. Five pts relapsed and 2 had died at last follow-up at 11 and 95 mo.

Of the 3 IRS-III pts, 2 had tongue tumors, and received

sunitinib with partial response followed by resection with negative margins. Both were alive at last follow up at 27 and 28 mo. The third pt received doxorubicin/ifosfamide without response and died.

Of the 29 IRS-IV pts, 8 pts were observed initially without treatment, 6 received cytotoxic chemotherapy (no objective response), and 11 received targeted therapy that included tyrosine-kinase inhibitors in 6 pts, and angiogenesis or VEGF inhibitors in 5 pts. Treatment information was not available in 4 pts. Overall, 14 pts received targeted therapy (upfront or at progression); 3 had partial response and 6 stable disease.

For all pts, 5-year event-free survival (EFS) and overall survival (OS) were 28% and 67% respectively. For pts with localized tumors (IRS I-III), 5-year EFS and OS were 61% and 76% respectively. For pts with metastatic tumors, 5-year EFS and OS were 9% and 61% respectively.

Conclusion: Localized ASPS has a good prognosis after gross total resection. ASPS is resistant to cytotoxic chemotherapy. Although there are no curative therapies for pts with metastatic disease, prolonged disease stabilization may be achieved with targeted therapies.

P2–Poster 152 2570365

EPITHELOID SARCOMA IN CHILDREN AND YOUNG ADULTS: RESULTS OF THE COOPERATIVE SOFT TISSUE SARCOMA (CWS) STUDIES

Ewa Koscielniak, MD, PhD[1]; Erika Hallmen[1]; Ivo Leuschner[2]; Monika Sparber-Sauer[1]; Monika Scheer[1]; Marc Münter[3]; Thekla von Kalle[4]; Steffan Loff[5]; Stefan Bielack[1]; Thomas Klingebiel[6]

[1]Ped. Oncology and Haematology, Klinikum Stuttgart, Olgahospital, Stuttgart, Baden-Württemberg, Germany; [2]Paidopathology, University Kiel, Kiel, Germany; [3]Radiation Oncology, Klinikum Stuttgart, Stuttgart, Germany; [4]Pediatric Radiology, Klinikum Stuttgart, Stuttgart, Germany; [5]Pediatric Surgery, Klinikum Stuttgart, Stuttgart, Germany; [6]Pediatric Oncology/Hematology and Hemostasis, University Children's Hospital, Frankfurt, Germany

Objective: Epitheloid Sarcoma (ES) is a rare, high grade malignancy, representing 4 to 8 % of childhood non-rhabdomyosarcomatous soft tissue sarcoma (NRSTS). It belongs to the SMARCB1 deficient tumor family. We report on therapy and outcome of the patients with ES registered in the 6 consecutive CWS studies -81, -86, -91, -96, -2002P and CWS-registry SoTiSaR.

Methods: The series includes 63 patients (age 1-27 yrs, median 14). Diagnosis was confirmed by central pathology review for each study but was not repeated for this analysis. Patients were treated according to the corresponding CWS-recommendation for NRSTS. Surgery with/without radiotherapy (depending on postsurgical status) was the mainstay of treatment. Chemotherapy (vincristine, cyclophosphamide or ifosfamid, actinomycin D, doxorubicin and etoposide (in the CWS-91)) was recommended for patients with non-resectable and metastatic tumors.

Results: Most tumors occurred in extremities (63 %), 30 were initially excised (21 complete - IRS Group I, 9 marginal - IRS Group II), 33 patients (21 with localized disease - IRS Group III and 12 with metastases - IRS Group IV) received incomplete excision or biopsy only as first surgical approach. In the IRS Group IV most metastases occurred in the lung (67%). Regional nodes were involved in 6 (12%) patients with localized and 6 (50%) with metastatic tumors. Five years EFS and OS for 51 patients with localized disease were 43 % ± 13 and 68 % ± 21 (CI 95 %) respectively. In 45 patients a CR was achieved, 19 relapsed subsequently (locally in 11(22%) and metastatic or combined in 8(16 %)). In 6 patients a primary progression occurred. Response to neoadjuvant chemotherapy was evaluable in 12 cases (1 good and 2 objective responses). No significant difference in EFS and OS in the IRS II and IRS III depending on radiotherapy (RT) was seen. For the IRS Group IV, 5 years EFS and OS were 0% and 8% ± 18, CI 95 % respectively. IRS Group, tumor size (< vs. > 5 cm) and tumor invasiveness (T-status) correlated significantly with outcome.

Conclusion: Only patients with primary completely resected tumors had a good chance for surviving. Nevertheless a small proportion of patients with advanced localized tumor can be cured with multimodal therapy. Molecular profiling is needed to better understand the differences in clinical behavior. The majority of patients with advanced ES have no real chance for a cure and are candidates for innovative biologically based therapies.

P2–Poster 153 2522194

LONG-TERM RESULTS OF TREATMENT OF ADVANCED DERMATOFIBROSARCOMA PROTUBERANS (DFSP) WITH IMATINIB MESYLATE

Piotr Rutkowski, MD, PhD[1]; Anna Klimczak[1]; Tomasz Switaj[1]; Iwona Lugowska[1]; Beata Jagielska[2]; Michal Wagrodzki[3]; Renata Woroniecka[3]; Barbara Pienkowska-Grela[3]; Maria Debiec-Rychter[4]
[1]Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland, Warszawa, Poland; [2]Department of Oncology, Cardiooncology and Internal Medicine, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland, Warszawa, Poland; [3]Department of Pathology, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland, Warszawa, Poland; [4]Department of Human Genetics, KU Leuven and University Hospitals Leuven, Leuven, Belgium

Objective: Dermatofibrosarcoma protuberans (DFSP) is rare, infiltrating dermal neoplasm, characterized by indolent growth and low probability of metastases**.** The first effective systemic therapy in DFSP introduced into clinical practice was imatinib, demonstrating high activity in advanced cases. The aim of the study was to perform an analysis of patients with advanced DFSP treated with imatinib, with or without surgery, in routine clinical practice with long-term follow-up.

Methods: We analyzed the data of 31 Caucasian patients (14 male, 17 female; median age 56 years) with locally advanced/initially inoperable and/or metastatic DFSP, who started therapy with imatinib at initial dose 800 mg daily between 12/2004 and 07/2014. All diagnoses were confirmed by FISH for the presence of specific *COL1A1-PDGFB* fusion using Dual Color Dual Fusion Probe, Abbott (CE-IVD) . Median follow-up time was 5.3 years.

Results: Fibrosarcomatous transformation (FS-DFSP) was confirmed in 16 patients (52%). Metastases were present in 15 cases (8– lungs, 5 – soft tissues, 2 – lymph nodes). 5-year progression-free survival (PFS) rate was 58% (median 6.8 years), 5-year overall survival (OS) rate was 64% (median time for OS was not reached). The shorter PFS and OS correlated with FS-DFSP and presence of metastatic disease. 5-year PFS rate was 93% for classic DFSP and 33% for FS-DFSP. The best overall responses were: 21 partial responses (68%, including 8 FS-DFSP, but the responses were shorter than for classic DFSP), 6 stable disease (19%) and 4 progressive diseases (13%). Thirteen patients (47%) underwent resection of residual disease and nine of them remained free of disease, although imatinib was discontinued. Median survival after progression on imatinib was 19 months, and longer survivals were observed only in cases where rescue surgery/radiotherapy was possible.

Conclusion: Our results indicate the long-term activity of imatinib in therapy of inoperable and/or metastatic cases of DFSP. Some DFSP patient initially evaluated as un-resectable/metastatic or demanding mutilating surgery turned resectable after imatinib therapy and this rational approach leading to complete remission is potentially curative.

P2–Poster 154 2570392

INSIGHTS ON THE BIOLOGY OF EWSR1 AND TAF15-POSITIVE EXTRASKELETAL MYXOID CHONDROSARCOMA

Monica Brenca[1]; Maurizio Polano[1]; Tiziana Negri[2]; Gian Paolo Dagrada[2]; Dominga Racanelli[1]; Sabrina Rossi[3]; Silvia Brich[2]; Kelly Fassetta[1]; Angelo Paolo Dei Tos[3]; Maria A. Pantaleo[4]; Alessandro Gronchi[2]; Paolo Casali[2]; Silvia Stacchiotti[2]; Silvana Pilotti[2]; Roberta Maestro[1]
[1]Experimantal Oncology 1, National Cancer Institute CRO Aviano, Aviano, Italy; [2]National Cancer Institute INT Milano, Milano, Italy; [3]Treviso General Hospital, Treviso, Italy; [4]University of Bologna, Bologna, Italy

Objective: Extraskeletal myxoid chondrosarcoma (EMC) is a rare soft tissue sarcoma with uncertain differentiation. A distinct genetic feature of this tumor is the translocation of the NR4A3 gene that fuses with either EWSR1 or TAF15. Less frequently with other partners (TCF12 or TFG). Although EMC with non-EWSR1 fusions have been reported to correlate with rhabdoid phenotype and high-grade morphology, how the type of NR4A3 chimera impinges upon EMC biology is still poorly defined. To shed light on this issue we analyzed the transcriptional profile of a set of 10 EMC tumor samples.

Methods: Ten Formalin-Fixed, Paraffin-Embedded EMC samples (7 EWSR1-NR4A3 and 3 TAF15-NR4A3) were transcriptionally profiled by RNA-seq. An average of 50 million reads per sample were obtained. STAR, HTseqcount and DESEQ2 were used for reads mapping, quantification and differential expression analysis, respectively.

Results: The gene expression profile was computed from transcriptome data and compared between EWSR1-NR4A3 and TAF15-NR4A3 positive EMC. Most EWSR1-positive tumors tended to cluster separately to TAF15-positive EMC. Pathway analysis highlighted an enrichment in GO-terms related to neurogenesis, axon guidance and angiogenesis in TAF15-positive EMC.

Conclusion: Our data suggest that EWSR1-NR4A3 and TAF15-NR4A3 chimeras differently affect EMC transcriptional profile, with a peculiar activation of pathways related to axon guidance and angiogenesis in TAF15-positive EMC. We previously reported that EWSR1-positive tumors seem to respond better to the antiangiogenetic drug sunitinib compared to TAF15-positive tumors. Overall our results,

beside highlighting a link between axon guidance and angiogenesis, suggests that the transcriptional program elicited by the NR4A3 chimeras likely accounts for the differential response to sunitinib.

P2–Poster 155 2560514

OUTCOMES AND SURVEILLANCE IMAGING (SI) PATTERNS FOLLOWING DEFINITIVE TREATMENT OF LOCALIZED EXTREMITY/TRUNK SOFT TISSUE SARCOMA (STS) WITH RADIATION THERAPY (RT) AND LIMB-SPARING SURGERY (LSS)

Sagar A. Patel[1]; Trevor J. Royce[1]; Constance M. Barysauskas[2]; Katherine Thornton[3]; Chandrajit Raut[4]; Elizabeth H. Baldini[1]

[1]Department of Radiation Oncology, Dana-Farber/ Brigham and Women's Cancer Center, Boston, MA, USA; [2]Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Boston, MA, USA; [3]Department of Medical Oncology, Dana- Farber/ Brigham and Women's Cancer Center, Boston, MA, USA; [4]Department of Surgery, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA, USA

Objective: Optimal SI following RT and LSS for localized extremity/trunk STS is unknown and practice patterns vary. We reviewed local (LR) and distant recurrence (DR) outcomes in relation to SI to help define appropriate SI algorithms.

Methods: Timing of LR, DR, and SI was recorded for 94 patients with localized STS of the extremity/trunk treated with preoperative RT (50Gy) and LSS from 2006-2014. Method of recurrence detection (SI or symptoms prompting imaging) was analyzed. LR, DR, recurrence-free (RFS) and overall survival (OS) rates were determined by Kaplan-Meier.

Results: Median tumor size was 7.5cm; 92% were high/ intermediate grade. Most common histologies were unclassified (34%), myxofibrosarcoma (25%), and leiomyosarcoma (9%). Median follow up was 60 months (range 13.4 – 119.1). Thirty patients (32%) recurred including 5 LR, 26 DR. Median time to LR was 36.2 months (14.4-65.7) and to DR was 10.4 months (5.2 – 76.9). 5-year LRF, RFS, and OS were 95%, 68%, 76%.

90% of patients underwent local SI, mostly MR (91%). Intervals between SI increased over time; median interval overall was 4.8 months (Table 1). Of 5 LRs, 3 were detected by SI (one had a palpable mass), and 2 had symptoms prompting imaging.

All patients underwent distant SI composed mostly of Chest CT (44%) and Chest/Abdomen/Pelvis CT (54%). Median interval between scans was 4.1 months (Table 2). Of 26 DRs, 23 (88%) were in lung, (19 lung only). The other 3 patients with DR (bone, liver, retroperitoneum and soft tissue) had disease visible on SI Chest CTs. 22 (85%) DRs were detected by SI (only one of whom had symptoms); 4 (15%) had symptoms prompting a scan. Among 19 lung only DRs, number of lung nodules was 1 for 5 patients, 2 for 4 patients, and >4 for 10 patients. Median OS from time of DR for all patients was 16.7 months; median OS for those with one lung nodule was 27.5 months, for two lung nodules was 17.9 months, and for multiple was 10.3 months.

Conclusion: RT and LSS achieves excellent local control in patients with intermediate/high grade STS. Our high use of local SI is costly and likely not necessary. It may be more appropriate to use local SI for select patients at high risk for LR or those with deep tumors unlikely to be palpable at recurrence. Conversely, DRs were more common, mostly asymptomatic, and primarily occurred in lung. Periodic lung SI is likely justified and further study is needed to determine optimal imaging scans and intervals. For most histologies, routine abdomen/pelvic SI may not be indicated.

Table 1. Patterns of Local Surveillance Imaging

Years Since Surgery	Median Scan Interval	MR	CT	X-ray
0 - 1	3.4 months	92%	8%	0%
1 - 3	5.1 months	91%	8%	1%
3 - 5	7.2 months	93%	5%	2%
5 - 10	12.2 months	81%	6%	13%
Total	4.8 months	91%	7%	2%

Table 2. Patterns of Distant Surveillance Imaging

Years Since Surgery	Median Scan Interval	Chest-Abdomen-Pelvis CT	Chest CT	PET	MR
0 - 1	3.2 months	58%	41%	1%	0%
1 - 3	4.0 months	52%	46%	1%	1%
3 - 5	6.2 months	59%	36%	3%	2%
5 - 10	11.0 months	40%	60%	0%	0%
Total	4.1 months	54%	44%	1%	1%

P2–Poster 156 2554411

WHAT MARGIN CLASSIFICATION SYSTEM BEST DISCRIMINATES THE RISK OF LOCAL RECURRENCE AFTER SOFT TISSUE SARCOMA RESECTION?

Kenneth R. Gundle, MD[1]; Lisa Kafchinski[2]; Sanjay Gupta[2]; Anthony Griffin[2]; Rita Kandel[3]; Brendan C. Dickson[3]; Peter Chung[4]; Charles Catton[4]; Brian O'Sullivan[4]; Jay Wunder[2]; Peter Ferguson[2]

[1]Orthopaedics & Rehabilitation, Oregon Health & Science University, Portland, OR, USA; [2]Dept of Surgery, University of Toronto, Mount Sinai Hospital, Toronto, ON, Canada; [3]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada; [4]Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada

Objective: The surgical margin after soft tissue sarcoma (STS) resection predicts local recurrence (LR). Our goal was to compare margin classification systems based on ability to discriminate LR risk.

Methods: A STS database was retrospectively reviewed from 1989 to 2014, excluding retroperitoneum tumors, DFSP, well-differentiated liposarcoma or metastases at presentation.

Three margin systems were compared:
1. R-classification: R0 is a negative margin (no tumor cells at inked margin); microscopic tumor cells at ink define R1; R2 is gross positive.
2. International Union against Cancer (UICC): R0 is no tumor cells within 1mm of ink; microscopic tumor cells within 1mm of ink define R1; and R2 is gross positive.
3. Margin context classification(MCC), where positive margins are separated into three categories: planned close but positive at critical structure (eg, major nerve); positive after whoops re-excision; inadvertent positive margins.

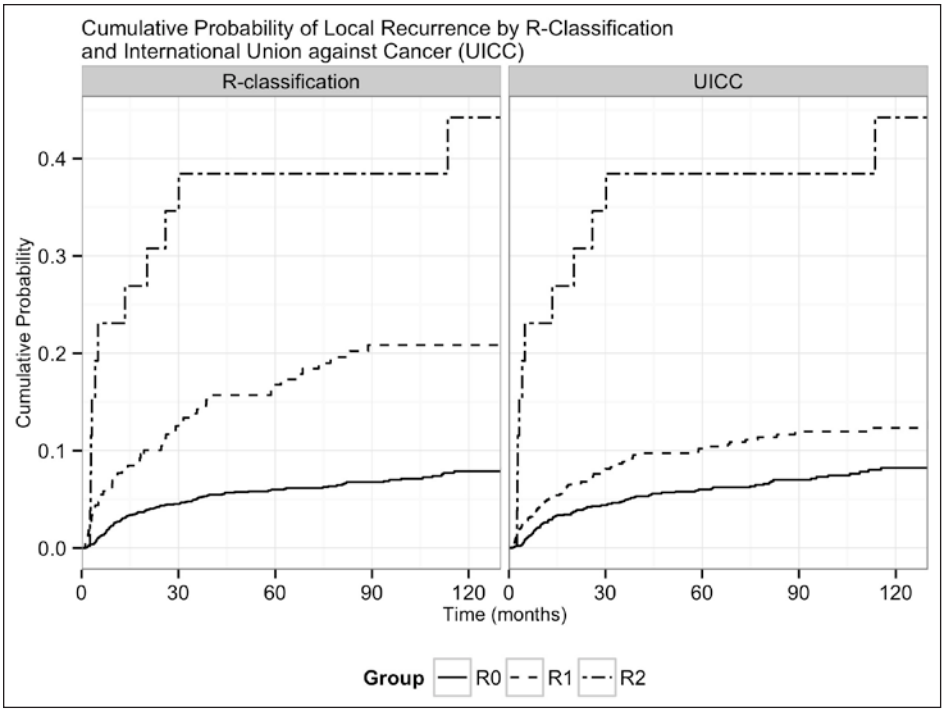
Fine & Gray competing risk regression model assessed each level from the margin systems, with an overall Wald test.

Results: 2,217 STS patients were eligible, mean follow-up 65 months (95%CI 63-68) and mean age was 56 (95%CI 55-57). Most tumors were deep (68%) and high grade (54%); mean maximum diameter was 8.3 cm (95%CI 8-8.6).

The R-classification had distinct LR risk among its three tiers (subdistribution hazards each p<0.001). LR rate was lower in R0 (5yr 6%[5-7]; 10yr 8%[7-9]) than R1 (5yr 17%[12-21]; 10yr 21%[16-26]). R2 LR rate was high (5yr 38%[20-57]; 10yr 44%[23-64]) but uncommon (1%, 26/2217).

The UICC system classified more resections as R1 than the R-classification (721 vs 277, p<0.001) without changing R2. This resulted in less LR in R1 with no change in LR for R0: 5-year LR was 6% (95%CI 5-7) for R0 and 10% (7-13) for R1; at 10 years R0 was 8%(7-10) and R1 was 12%(10-15). There was no LR difference between UICC R0 and R1 (p=0.07).

The MCC showed varying LR among its tiers (p<0.001). LR rates for positive margin on critical structures were not different than R0 (5yr LR 10%[5-17] vs 6%[5-7], p=0.6), but inadvertent positive margin had higher LR (5yr 28%[19-37], p<0.001).



Conclusion: The R-classification system was able to identify three distinct LR risk stratifications. The UICC system narrowed the difference in probability of LR between R1 and R0 (Figure), suggesting a less than 1mm margin may be adequate with adjuvant radiation. The MCC provides additional risk stratification that may aid in surgical planning and patient education.

P2–Poster 157 2569559

PREDICTION OF LOCAL AND METASTATIC RECURRENCE IN SOLITARY FIBROUS TUMOR: CONSTRUCTION OF A RISK CALCULATOR IN A MULTICENTER COHORT FROM THE FRENCH SARCOMA GROUP DATABASE

Corinne Bouvier, MD, PhD[1]; Noemie Resseguier[3]; Jean Yves Blay[4]; Axel Le Cesne[5]; Antoine Italiano[6]; Christine Chevreau[7]; Philippe Rosset[8]; Nicolas Isambert[9]; Dominique Ranchère-Vince[10]; Philippe Terrier[5]; Sylvie Bonvalot[5]; Nicolas Macagno[1]; Coralie Lemoine[3]; Jean Michel Coindre[6]; Sebastien Salas[2]
[1]Pathology, Timone Hospital, Marseille, France; [2]Oncology, Timone Hospital, Marseille, France; [3]Support unit for Clinical Research and Economic Evaluation, Faculty of Medecine Timone, Marseille, France; [4]Centre Léon Bérard, Lyon, France; [5]Institut Curie, Paris, France; [6]Institut Bergonié, Bordeaux, France; [7]IUCT Oncopole, Toulouse, France; [8]Orthopedic Surgery, CHU Tours, Tours, France; [9]Oncology, Centre Georges-François Leclerc, Dijon, France; [10]Pathology, Centre Léon Bérard, Lyon, France

Objective: Solitary fibrous tumors (SFT) are rare unusual ubiquitous soft tissue tumors which are presumed to be of fibroblastic differentiation characterized by a NAB2-STAT6 fusion transcript. Actually, the challenge is to establish accurate prognostic factors.

Methods: 214 consecutive patients with SFT were diagnosed for their first tumoral event in 24 participating cancer centers and were entered into the European database (www.conticabase.org). We performed univariate and multivariate analysis for Overall survival (OS), local recurrence incidence (LRI) and metastatic recurrence incidence (MRI) by taking competing risks into account. A prognostic model was constructed for LRI and MRI based on the variables that were selected for the multivariate models. The predictive accuracy of these prognostic models was assessed by studying discrimination (adapted C-index and Royston and Sauerbrei's measure D with bootstrap 95% CI).

Results: We restricted our analysis to 162 patients with local disease and absence of residual tumor after local treatment. Twenty patients (12.3%) were deceased at the time of analysis and the median OS was not reached. The LRI rates at 10 and 20 years were 19.2% and 38.6%, respectively. The MRI rates at 10 and 20 years were 31.4% and 49.8%, respectively. Multivariate analysis retained age and mitotic count for predicting OS. The factors influencing LRI were viscera localization, radiotherapy and age. Mitotic count, tumor localization other than limb and age has independent values for MRI. A 4-tiered score stratifying our population by risk of local and metastatic recurrence. Furthermore, 3 prognostic groups for OS were defined based on the number of unfavorable prognostics factors. Finally, calculations were performed to predict the risk of local and metastatic recurrence for individual patients.

Conclusion: LRI and MRI rates increased between 10 and 20 years so relapses were delayed. This suggests that long-term monitoring is useful. Moreover, our results suggest that radiotherapy should be part of the therapeutic strategy and confirm that mitotic activity is the best histological prognostic factor for SFTs whatever their localization. This study clearly also shows that different prognostic SFT sub-groups could benefit from different therapeutic strategies and that survival calculator could become standard practice in SFTs to individualize treatment based on the clinical situation.

P2–Poster 158 2565708

MALIGNANT PEROPHERAL NERVE SHEET TUMORS (MPNST) IN CHILDREN AND ADOLESCENTS: REPORT OF THE EUROPEAN PEDIATRIC SOFT TISSUE SARCOMA GROUP (EPSSG) STUDY NRSTS-2005

Max M. van Noesel[1]; Bernadette Brennan[2]; Gian Luca de Salvo[4]; Ilaria Zanetti[4]; Nadine Francotte[5]; Rita Alaggio[6]; Daniel Orbach[7]; Anna Kelsey[3]; Gianni Bisogno[8]; Michela Casanova[9]; Andrea Ferrari[9]
[1]Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands; [2]Pediatric Oncology, Royal Manchester Children's Hospital, Manchester, United Kingdom; [3]Department of Pathology, Royal Manchester Children's Hospital, Manchester, United Kingdom; [4]EpSSG Data Centre Istituto Oncologico Veneto IRCCS, Padova, Italy; [5]Department of Pediatrics, CHC-Clinique Esperance, Montegnée, Belgium; [6]Pathology Department, Padova University, Padova, Italy; [7]Pediatric Adolescent Young Adult Department, Institut Curie, Paris, France; [8]Pediatric Hematology and Oncology Division, Padova University, Padova, Italy; [9]Pediatric Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

Objective: MPNST are aggressive tumors of Schwann cells and in 50% associated with Neurofibromatosis type 1 (NF-1). MPNST are the second most frequent pediatric sarcoma (23%; Ferrari, Spunt 2011). Retrospective pediatric studies have shown a poor 5-year overall survival (OS) and progression-free survival (PFS) of 51% and 37%, respectively (Carli, 2005). Response to primary chemotherapy was estimated at 17-45%. Here, we analysed the results for localized MPNST patients in the prospective EpSSG NRSTS-2005 study.

Methods: A cohort of 59 localized MPNST patients from 8 European countries were treated in 3 treatment groups: 1. Surgical group (R0 ≤5 cm; R0 >5cm G1 and R1/N0 G1) (n=14). 2. Radiotherapy group (R0 >5cm G2 and R1/N0 G2-G3 ≤5cm and R1/N0 G2 >5cm) (n=4) with 50,4 Gy for R0 tumors and 54 Gy for R1 tumors. 3. (Neo-)adjuvant chemotherapy group (R0-1/N0 G3 >5cm; N=8) and R2 + N1; n=33). Chemotherapy: 6 courses ifosfamide 3 g/m2/day, for 3 days + doxorubicin 37.5 mg/m2/day, for 2 days. No doxorubicin during radiotherapy. Radiation fields were based

on initial tumor volume and positive, non-resected nodes. Relative low radiation doses of 50.4-54 Gy are based on higher post-radioation morbidity in growing children.

Results: Post-surgical staging : 24% R0, 20% R1, 56 R2 in 58 T1 and 42 T2 tumors. In 28/33 evaluable neo-adjuvant patients, the chemotherapy response was complete in 2 (6,9%); partial in 3 (10,3%); minor in 9 (31%); stable in 10 (34,5%). Total response to chemotherapy (CR + PR + MR) 47,2%. The 3-yrs EFS for surgical group was 100%; radiation group 67%; adjuvant group 37%; neoadjuvant group 40%. Outcome of 55/59 evaluable patients with a median follow-up of 39,5 months: 27 alive in 1st CR and 19 died of diease. The 3-yrs EFS was 56.1 (95%CI 41.0-68.7) and 3-yrs OS was 66.5 (95%CI 50.9-78.2).

Conclusion: Prospective International cooperative treatment protoocls on MPNST with local treatment and adjuvant chemotherapy are feasible. However, the outcome is comparable to historic, retrospective studies. Novel treatment strategies are necessary to improve outcome in pediatric MPNST

P2–Poster 159 2558414

NEUROPATHIC PAIN AFTER SURGERY FOR EXTREMITY SARCOMA: PREVALENCE AND PREDISPOSING FACTORS

Jong Woong Park; Han-Soo Kim; Ilkyu Han, MD, PhD
Orthopedic Surgery, Seoul National University Hospital, Seoul, Korea (the Republic of)

Objective: Neuropathic pain (NP) arises after injury to the nerves or to sensory transmitting systems in the spinal cord and brain. NP has been implicated as the most important cause of chronic post-operative pain. One of the major pathophysiological mechanisms of chronic post-operative NP is the damage to the nerves during surgery. Surgery for sarcoma of the extremities or pelvis often requires extensive tissue dissection to achieve adequate surgical margins for good oncologic outcome. In order to achieve adequate surgical margins, violation of inter-nervous plane is not uncommon. Because of these features, patients who undergo surgery for sarcoma of the extremities or pelvis may be prone to developing post-operative NP. To the authors' knowledge, no study has been published regarding the post-operative NP in extremity sarcoma surgery. With this regard, this study aimed to examine the prevalence of NP and to identify preoperative factors associated with development of NP, in patients who underwent surgery for sarcoma of the extremity or pelvis.

Methods: 149 Patients who underwent curative surgery at least 6 months prior to the visit for histologically confirmed extremity sarcoma were enrolled. The presence of NP was assessed by administering PainDetect, a widely used questionnaire for detecting NP. Patients with PainDetect scores≥13 were considered to have NP. Possible factors that might be associated with the development of NP were investigated; patients demographics, treatment modality, oncologic outcome and extent of surgery.

Results: Out of the 144 patients, 36 patients (25%) had NP. Patients with NP had significantly worse VAS ($p<0.001$), TESS score ($p<0.001$) and MSTS score ($p<0.001$) than patients without NP. Among the possible factors associated with NP, patients with persistent neuropathic pain were more likely to undergo pelvic surgery ($p=0.002$) and more than two times of surgeries ($p=0.014$). On univariate logistic regression analysis of associated factors of neuropathic pain after sarcoma surgery, revision surgery by any reasons ($p=0.016$) and surgery in pelvic area ($p=0.002$) were significant. On multivariate analysis, surgery in pelvic area (OR=5.05, $p=0.005$) and revision surgery by any reasons (OR=2.33, $p=0.038$) remained as independent factors associated with NP in extremity sarcoma surgery.

Conclusion: Our study suggests that the prevalence of NP after extremity sarcoma is considerable. Pelvic surgery and revision surgery can cause postoperative persistent neuropathic pain independently.

P2–Poster 160 2557340

CONDITIONAL SURVIVAL OF PATIENTS WITH SOFT TISSUE SARCOMA (STS) AFTER CURATIVE SURGERY

Florian Posch[1]; Lukas Leitner[3]; Michael Stotz[1]; Bernadette Liegl-Antzager[2]; Angelika Bezan[1]; Martin Pichler[1]; Joerg Friesenbichler[3]; Armin Gerger[1]; Herbert Stoeger[1]; Andreas Leithner[3]; Joanna Szkandera[1]
[1]Clinical Division of Oncology, Department of Medicine, Medical University of Graz, Graz, Austria; [2]Institute of Pathology, Medical University of Graz, Graz, Austria; [3]Department of Orthopaedics and Orthopaedic Surgery, Medical University of Graz, Graz, Austria

Objective: Risk factors can stratify soft tissue sarcoma (STS) patients according to their probability of disease recurrence and survival, and thus inform immediate treatment decisions. However, it is currently unclear how the initial risk changes in STS survivors after primary therapy. In this study, we apply the concept of conditional survival to prognosticate long-term outcome in STS survivors who underwent curative surgical treatment.

Methods: In this single-center historical cohort study, we explored the clinical course of 444 patients with localized STS who were operated in curtive intent between 1995 and 2015 (Table 1). After a median follow-up period of 5.5 years, we observed 44 (9.9%) local recurrences, 74 (16.7%) occurrences of distant metastasis, 65 (14.6%) STS-related deaths, and 59 (13.3%) deaths adjudicated to other causes. The 2-year conditional disease-free (CDFS) and 2-year conditional overall survival (COS) were defined as

the probability of surviving and remaining disease-free, or surviving, respectively, for an additional 2 years at a given time point after surgery.

Results: The 2-yr CDFS improved from 75.9% (95%CI: 71.2-80.0) at baseline, to 82.4% (77.5-86.3), 88.4% (83.4-91.9), and 90.3% (85.1-93.8) in patients who had survived disease-free for at least 1, 2, and 3 years, respectively. The 2-yr COS improved more modestly from 85.4% (81.4-88.7) at baseline, to 86.5% (82.2-89.8), 90.3% (85.9-93.4), and 91.5% (86.8-94.6) after 1, 2, and 3 years after baseline, respectively. At baseline, tumor grade G3 (Hazard ratio (HR)=3.3, 95%CI: 2.0-5.6, p<0.0001), AJCC stage III (HR=3.3, 95%CI: 2.2-5.1, p<0.0001), and a higher age (HR per 5 years increase above 60 years=1.2 (95%CI: 1.1-1.3, p<0.0001) were the strongest predictors of a worse 2-yr CDFS. At 3 year after baseline, the 2-year CDFS was neither associated with tumor grade G3 ((HR=3.3, 95%CI: 2.2-5.1, p<0.0001), nor with AJCC stage III (HR=3.3, 95%CI: 2.2-5.1, p<0.0001), and patients with G3 (89.3% vs. 91.3%) or stage III disease (88.0% vs. 91.1%) had a comparable 2-year CDFS than patients without these high risk features, respectively.

Conclusion: In patients with localized STS undergoing curative surgery, 2-year CDFS continuously improves over time. However, 2-year CDFS does not appear to increase above 90%. Patients harboring poor risk features at tumor diagnosis such as tumor grade G3 or AJCC stage III do not do worse than good risk patients after having survived for at least 3 years.

Table 1. Baseline characteristics of the study population

Variable	Median or n (%)
Age (years)	62 (47-73)
Grade G3	264 (59.6%)
Tumor size >5cm	284 (64.1%)
Adjuvant chemotherapy	40 (9.0%)
Adjuvant radiotherapy	261 (58.8%)

P2–Poster 161 2570657

PATTERNS OF CARE AND OUTCOME OF METATASTIC SOFT-TISSUE SARCOMA PATIENTS (PTS) ACCORDING TO HISTOLOGICAL SUBTYPE AND TREATMENT SETTING: THE METASARC STUDY

Antoine Italiano[1]; Axel Le Cesne[2]; Jean Yves Blay[3]; Isabelle Ray-Coquard[3]; Olivier Mir[2]; Maud Toulmonde[1]; Philippe Terrier[2]; Marion Savina[1]; Jean Michel Coindre[1]
[1]Institut Bergonie, Bordeaux, France;
[2]Institut Gustave Roussy, Villejuif, France;
[3]Centre Léon Bérard, Lyon, France

Objective: There are only limited data on the outcome of pts with metastatic STS according to the histological subtype and the treatment setting.

Methods: Data from 2225 pts with metastatic STS and included in the CONTICANET database were analyzed. Histological diagnosis was centrally reviewed in all the cases. Time to next treatment (TNT) was defined time from systemic treatment onset to next treatment or death of any cause, whichever comes first. Overall survival (OS) was defined time from systemic treatment onset to last patient contact or death of any cause.

Results: Median follow-up was 58 months. Median age was 56 yrs (range 18-93). The five most frequent histological subtypes were: leiomyosarcoma/LMS (22.4%), UPS (19.4%), dedifferentiated liposarcoma/DDLPS (9.3%), synovial sarcoma/SS (8.7%), and MPNST (3.7%). 1600 (72%), 950, 650, 496, 232, 134 received 1, 2, 3, 4, 5 or ≥6 lines of treatment respectively. Age > 75 yrs (11.5% of all patients) was significantly associated with a lower probability to receive a treatment. The 1st line regimen contained anthracycline and more than one drug in 56% and 46% of cases respectively. Inclusion in a clinical trial, use of off-label-drugs (gemcitabine, paclitaxel…) and locoregional treatment of metastases were associated with improved OS on multivariate analysis. TTNT and OS according to the treatment line setting for the 5 five most frequent histological subtypes are described in Figure 1. TTNT was highly correlated with OS.

Conclusion: A significant proporiton of patients (16.8%) do not receive any treatment (systemic or locoregional) in the metastatic setting. Leiomyosarcoma (LMS) represents clearly a distinct STS subgroup with a significantly better outcome. Benefit of systemic therapy beyond the 2nd line setting is limited except for LMS. Use of off-label-drugs (gemcitabine, paclitaxel…) is associated with improved outcome. Inclusion in a clinical trial and locoregional treatment of metastases should always be considered when feasible. Time to next treatment is highly correlated with overall survival and may represent an useful surrogate endpoint in clinical trials

	TTNT/OS (months)			
	TTNT1/OS1	TTNT2	TTNT3	TTNT4
LMS	7.6/24.4	5.7/17	4.6/12	4.3/9
UPS	4.2/9.3	3.5/6.2	2.5/5.2	2.5/5.2
DDLPS	4.3/11.7	5.6/9.5	2.4/6.5	3.2/3.9
SS	8.3/18.6	5.7/11.7	3.4/7.7	2.3/5.9
MPNST	3.9/12.2	2.8/6.8	3.3/7.9	2.7/5.4

P2–Poster 162 2528187

SARCOMA TUMOR SIZE (T) STAGING: HOW MUCH DO TUMORS DEFORM BETWEEN RADIOLOGY AND SURGERY?

Angela Pang, MBBS, MRCP[1]; Mariana Carbini[2]; Robert G. Maki[2]

[1]Medical Oncology, National University Hospital of Singapore, Singapore, Singapore; [2]Tisch Cancer Institute, Mount Sinai Medical Center, New York, NY, USA

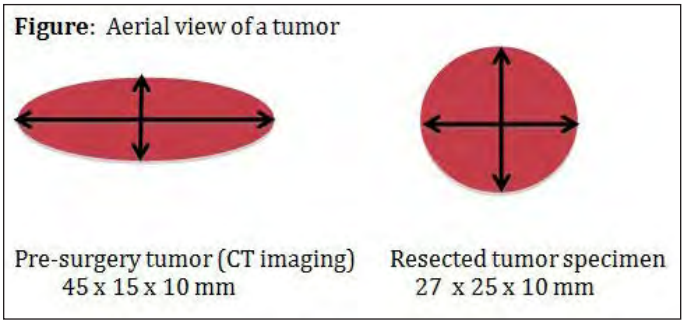
Objective: In the American Joint Committee of Cancer (AJCC) TNMG staging of soft tissue sarcomas, the longest dimension (1D) of the primary tumor at time of pathology analysis is the gold standard for Tumor (T) staging. Outside the situation of tumor rupture, tumor volume remains constant. However, after surgical resection, the dimensions of a sarcoma may be different compared to pre-operative imaging (Figure).

Because of shape changes, should we define T stage by imaging or by pathology measurement? To start to answer this question, we examine the variability of the measurements between radiology and pathology data. We examined 1D, cross sectional area (2D), and tumor volume (3D) variability in their possible use to determine T stage.

Methods: We reviewed imaging of patients with extremity sarcomas in our institution from 2010- 2015. Complete MRI or CT data were available for 79 patients' correlative comparison to sizes of resected specimens. After eliminating 10 samples that were grossly irregular (e.g. bilobate/dumbbell shape) and 11 samples with incomplete data, 58 samples had complete 3D measurements.

Pearson correlation coefficients were calculated for the paired variables (radiology vs pathology size in 1D, 2D and 3D). To compare variability, we reduced the dimensionality of the 2D and 3D data by taking the square root and cube root of the products of the dimensions, respectively.

Results: There was linear correlation between 1D, 2D or 3D imaging measures and actual tumor measurements. Pearson correlation coefficients (r^2) for 1D, 2D and 3D measurements were 0.93, 0.72 and 0.78, respectively, all $p<0.01$. The SEM (radiological sizes/pathology sizes) = 0.13, or 13% for 1D measurements. Thus, T stage could be incorrectly assigned in as many as 13% of samples near 5 cm in size; however, this proportion decreases the further the tumor is from the staging size cutoff.



Conclusion: 1D measures provided the smallest variability between radiology and pathology measurements. It is not clear how the 10-15% of primary sarcomas with irregular shapes should best be staged. 3D volume may be more relevant when assessing responses to therapy, rather than staging primary tumors.

P2–Poster 163 2566439

DEVELOPING A PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH 4 SUBTYPES OF SOFT TISSUE SARCOMA

Anne Skalicky[1]; Sameer Ghate[2]; Jose Perez[2]; Anne Rentz[1]

[1]Evidera, Seattle, WA, USA; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA

Objective: Soft tissue sarcomas (STS) are a heterogeneous group of rare and often malignant tumors that originate from mesenchymal tissue. More than 50% of STSs develop in an upper or lower extremity. The objective of this research was to examine the literature to identify patient-reported outcome (PRO) symptom measures used in STS patients and, if needed, to develop a disease-specific symptom inventory for STS subtypes: leiomyosarcoma, synovial sarcoma, liposarcoma, and undifferentiated sarcoma.

Methods: Literature review and clinical expert and patient interviews were conducted to determine disease-specific symptoms important to patients with 1 of the 4 STS subtypes. Very few PRO symptom instruments (n=5) were found in the STS clinical trial literature. Clinical experts identified the most relevant STS symptom items from the EORTC QLQ-C30, MDASI, MSAS, PRO-CTCAE, and 3-item STS symptom measure. STS patients were recruited from patient registries, panels, and advocacy groups. A symptom list was presented to patients in qualitative interviews and via Web survey to identify items for the STS-specific symptom inventory.

Results: Ninety symptom items were compiled and discussed with 3 clinical experts who identified 24 symptoms specific to the 4 STS subtypes. An electronic survey was created for patient review. Ten patients (with a goal of 12) were interviewed, and an additional 26 patients completed the electronic survey, to provide information for selection of symptoms for and development of the STS-specific symptom inventory.

Conclusion: No disease-specific PROs and very little information on symptoms relevant to STS patients exist. PROs can be used as a valuable tool in randomized controlled trials (RCTs) and by physicians to assess issues associated with STS. Next steps include collecting additional item pool

data from patients with STS and using the draft STS item pool in an RCT.

This research was funded by Novartis Oncology.

P2–Poster 164 2566592

A NEW SYMPTOM-SPECIFIC PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH SOFT TISSUE SARCOMA

Anne Rentz[1]; Anne Skalicky[1]; Sameer Ghate[2]; Sant P. Chawla[3]; Anthony P. Conley[4]; Victor M. Villalobos[5]; Jose Perez[2]

[1]Evidera, Seattle, WA, USA; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [3]Sarcoma Oncology Center, Santa Monica, CA, USA; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]University of Colorado School of Medicine, Aurora, CO, USA

Objective: Soft tissue sarcomas (STS) are a heterogeneous group of rare tumors that originate from mesenchymal/connective tissue. Very few patient-reported outcome (PRO) measures which meet the FDA PRO guidelines have been reported in randomized clinical trials with STS patients since 2000 (n=5) and none are available for the 4 STS subgroups of interest: leiomyosarcoma, synovial sarcoma, liposarcoma, and undifferentiated sarcoma. The objective of this research was to develop a disease-specific symptom inventory for these STS subtypes.

Methods: Literature review and clinical expert and patient interviews were conducted to determine disease-specific symptoms important to patients with the STS subtype of interest. Clinical experts reviewed a list of the symptom items from the EORTC, QLQ-C30, MDASI, MSAS, PRO-CTCAE and a 3-item symptom measure found during the literature review. STS patients, recruited from patient registries, panels, and advocacy groups, participated in a telephone interview to identify tumor symptoms or completed an electronic survey of STS-specific symptom items.

Results: Ten patients took part in qualitative interviews, and an additional 17 completed the electronic survey to provide information for the STS-specific symptom inventory. Participants were primarily female (96%) and 54 ± 8 years of age: 81% (n=22) with resected primary tumor and 96% (n=26) with metastasized tumor. Thirteen participants (48%) had metastases to the lungs. Most participants (74%) reported leiomyosarcoma, 15% reported undifferentiated sarcoma, 7% reported synovial sarcoma, and 4% (just 1 participant) reported liposarcoma. Most frequently reported tumor-specific symptoms were abdominal pain (n=12, 44%), pressure in the abdomen (n=9, 33%), and early satiety (n=7, 26%). Fatigue, anxiety, depression, and bloating were the most frequently reported tumor or treatment symptoms. Based on the results, the STS-specific symptom inventory conceptual framework includes 4 domains that capture symptoms of breathing (2 items), pain (6 items), eating and digestion (2 items), and menstrual cycle (2 female-only items) and assesses frequency and severity with a recall period of 7 days.

Conclusion: A number of symptoms are common across STS-subtypes and may form a single symptom inventory for specific patients with STS. This disease-specific PRO tool may prove beneficial for physicians to accurately and reproducibly assess symptoms in STS patients.

This research was funded by Novartis Oncology.

	A. How <u>often</u> did you have this symptom?	B. How <u>severe</u> was this symptom?
1. In the past 7 days, did you feel pain in your abdomen?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
2. In the past 7 days, did you feel full after you ate a small amount of food?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
3. In the past 7 days, did you feel pressure in your abdomen?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
4. In the past 7 days, did you feel bloated?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
5. In the past 7 days, did you feel pain in your stomach or intestines?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
6. In the past 7 days, did you have chest pain?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
7. In the past 7 days, did you have a cough?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
8. In the past 7 days, did you have shortness of breath?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
9. In the past 7 days, did you have muscle pain?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
10. In the past 7 days, did you have bone pain?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
11. [female only item]: In the past 7 days did you have menstrual flow?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe
12. [female only item]: In the past 7 days did you have menstrual pain?	☐ Never ☐ Rarely ☐ Occasionally ☐ Frequently ☐ Almost constantly	☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe

P2–Poster 165 2565362

THE PROGNOSTIC VALUE OF LYMPHOVASCULAR INVASION IN TRUNCAL AND EXTREMITY SOFT TISSUE SARCOMAS: A U.S. ANALYSIS FROM THE NATIONAL CANCER DATA BASE (NCDB)

Cecilia G. Ethun, MD[1]; Alexandra G. Lopez-Aguiar[1]; Jeffery M. Switchenko[2]; Theresa W. Gillespie[1]; Keith Delman[1]; Charles Staley[1]; Shishir K. Maithel[1]; Kenneth Cardona[1]

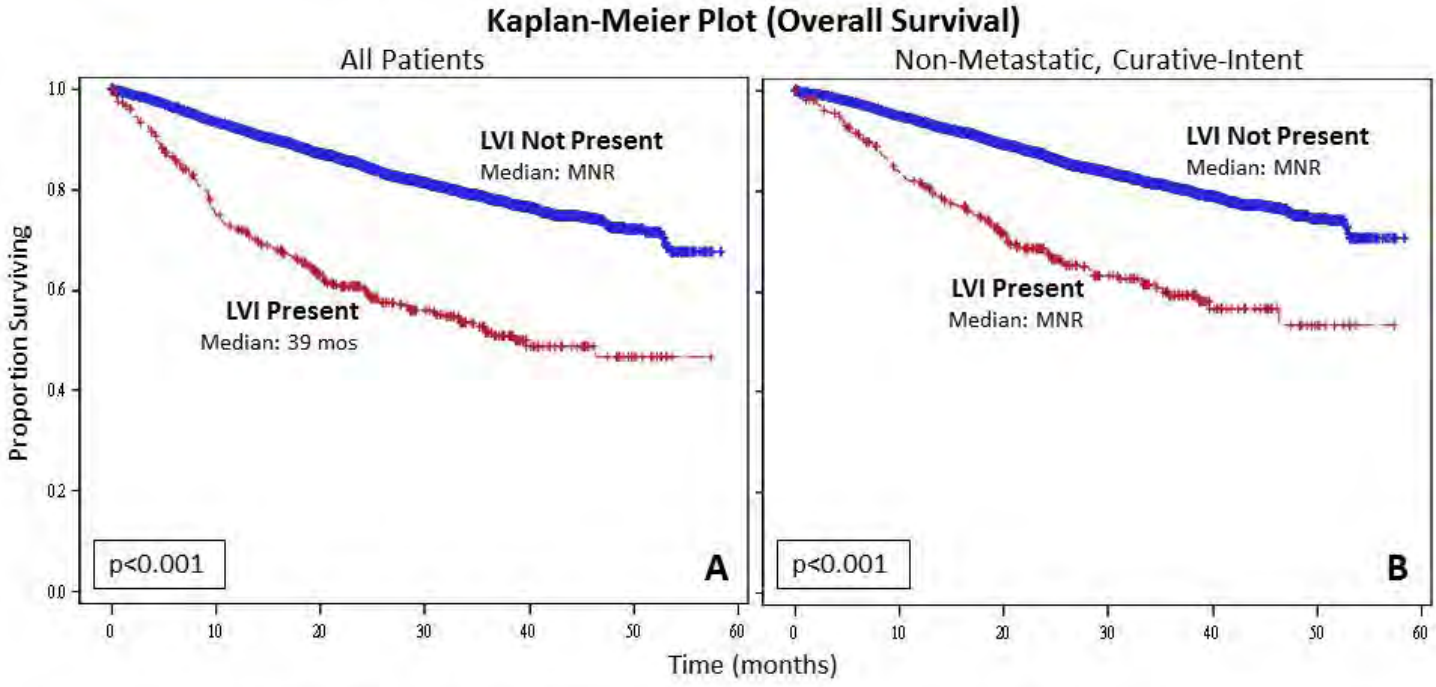
[1]Division of Surgical Oncology, Department of Surgery, Emory University, Winship Cancer Institute, Atlanta, GA, USA; [2]Department of Biostatistics, Rollins School of Public Health, Emory University, Winship Cancer Institute, Atlanta, GA, USA

Objective: To determine the association between lymphovascular invasion (LVI) and overall survival (OS) in primary soft tissue sarcomas (STS).

Methods: The National Cancer Data Base (NCDB) was queried for all patients, ages 18-85yrs, diagnosed with primary truncal and extremity STS from 2010-2012, who underwent resection and had LVI data. Primary endpoint was OS.

Results: Of 6,169 patients, the mean age was 56yrs and 55% were male. The most common location was extremity (65%) and most common histology groups were: (i) liposarcoma (LPS, 24%), (ii) MFH/UPS (19%), and (iii) leiomyosarcoma (LMS, 15%). 449 (7%) patients were LVI positive, half of whom were among the LPS, MFH/UPS, and LMS histologies. There were no differences in demographics or comorbidities between LVI positive and negative groups. Compared to LVI negative, LVI positive patients were more likely to have large (>5cm: 80% vs 66%; p<0.001), deep (80% vs 68%; p<0.001), and high-grade tumors (82% vs 57%; p<0.001). LVI positive patients were also more likely to have positive resection margins (27% vs 17%; p<0.001), have nodal (16% vs 2%; p<0.001) and metastatic disease (21% vs 4%; p<0.001), and receive chemotherapy (37% vs 18%; p<0.001). The presence of LVI was associated with worse median OS (39mos) compared to no LVI (MNR; p<0.001; Fig.1a), which persisted on stratum-specific UV analyses for all tumor grades, T-stages, and overall Stages I-III, but not Stage IV. On MV Cox regression analysis, LVI was associated with worse OS (HR 1.84; 95%CI, 1.39-2.43), while accounting for age, Charlson-Deyo score, histology group, tumor grade, size, depth, margin status, nodal and metastatic disease, and receipt of chemotherapy. Among patients with localized, non-metastatic disease who underwent curative-intent resections (n=5,696), the presence of LVI was still associated with worse OS on Kaplan-Meier (Fig.1b) and MV analyses (HR 1.86; 95%CI, 1.34-2.59; p<0.001).

Conclusion: Lymphovascular invasion appears to be an important adverse pathologic factor in truncal and extremity soft tissue sarcomas. Even when taking into account other



Lymphovascular Invasion	1-year Survival	3-year Survival
Not Present (n=5,647)	92%	78%
Present (n=442)	72%	51%

Lymphovascular Invasion	1-year Survival	3-year Survival
Not Present (n=5,360)	94%	81%
Present (n=336)	81%	59%

Figure 1. Lymphovascular invasion was associated with worse overall survival among A) all patients, and B) only patients with localized, non-metastatic disease who underwent curative-intent resections.

previously established prognostic factors, such as age, histology, grade, size, depth, and margin status, the presence of lymphovascular invasion was predictive of worse overall survival. Knowledge of lymphovascular invasion status may help better risk-stratify patients and guide management strategies, and should be considered in future prognostic classification schemes and nomograms.

Funded in part by NIH/NCI (P30CA138292)

P2–Poster 166 2570200

COMORBIDITY IN SARCOMA PATIENTS: A NATIONWIDE POPULATION-BASED STUDY

Mathias Raedkjaer[1]; Katja Maretty-Kongsted[1]; Michael M. Petersen[3]; Peter Vedsted[2]; Johnny Keller[1]
[1]Dept. of Orthopedic Surgery, Aarhus University Hospital, Aarhus C, Denmark; [2]Aarhus University, Aarhus, Denmark; [3]Dept. of Orthopedic Surgery, Copenhagen University Hospital, Copenhagen, Denmark

Objective: Comorbidity is an important prognostic factor for survival in cancers. The aims of this study were to examine the prevalence of comorbidity in sarcoma patients, and estimate the prognostic impact of comorbidity on overall and disease-specific mortality, and individual diseases within the Charlson Comorbidity Index (CCI) and in that way, point towards a more sarcoma-specific comorbidity index.

Methods: Through the validated national clinical database, Danish Sarcoma Registry (DSR), 2184 adult patients diagnosed with sarcoma in extremities and trunk between 1.1.2000-31.12.2013 was identified. Via the unique Danish possibility of linking patients on an individual level, the CCI-score was calculated from the Danish National Patient Registry (NPR) via the Civil Registration System (CRS). We obtained all recorded information on all hospital contacts and given diagnoses 10 years prior to the date of sarcoma diagnosis. We excluded the sarcoma diagnosis from the CCI calculation, but previous cancers, except non-melanoma skin cancer, were included. Data on date and cause of death was obtained from the DSR, CRS and the Cause of Death Registry (CDR).

Results: The overall prevalence of comorbidity was 20%. Patients with moderate/severe comorbidity had a significantly greater risk of dying from their sarcoma, than that of patients without any comorbidity, hazard ratio (HR): 1.61 (95% CI 1.14-2.26), p=0.006. Patients with localized stage at diagnosis and moderate/severe comorbidity had a significantly greater risk of dying from sarcoma, than that of patients without any comorbidity, HR: 2.10 (95% CI 1.37-3.22), p=0.001. Patients with moderate/severe comorbidity and metastatic stage at time of diagnosis however did not have greater risks of dying from sarcoma compared to patients without comorbidity. Among patients with comorbidity, moderate/severe renal disease (n=24, HR: 1.85 (95% CI 1.03-3.33), p=0,039) and any solid tumor (n=153, HR: 1,42, (95% CI 1,07-1,88), p=0.015) was significantly increased disease-specific mortality compared to the rest of the CCI-groups.

Conclusion: The prevalence of comorbidity in sarcoma patients is relatively low. Patients with moderate/severe comorbidity and localized stage at diagnosis had significantly increased disease-specific mortality compared to patients without comorbidity, even when adjusting for important factors such as age. Improved knowledge and awareness of comorbid diseases is important to prevent complications and improve treatment.

P2–Poster 167 2561892

THE INFLUENCE OF CLINICOPATHOLOGICAL FACTORS ON RECURRENCE PATTERN AND SURVIVAL OF EXTREMITY LIPOSARCOMA PATIENTS IN A LARGE SINGLE CENTER STUDY COHORT

Melissa Vos, MD[1]; Kees Verhoef[2]; Arno van Leenders[3]; Stefan Sleijfer[4]; Dirk Grünhagen[2]
[1]Medical Oncology/Surgical Oncology, Erasmus MC, Rotterdam, Netherlands; [2]Surgical Oncology, Erasmus MC, Rotterdam, Netherlands; [3]Pathology, Erasmus MC, Rotterdam, Netherlands; [4]Medical Oncology, Erasmus MC, Rotterdam, Netherlands

Objective: In 2015 approximately 43.5% of all (n=685) soft tissue sarcomas (STS) in the Netherlands were localized in the extremities, thereby making it the most common localization. Liposarcoma (LPS) is the most frequent subtype of extremity STS with frequent recurrence, but unfortunately there is not much known on how often, when and why LPS located in the extremities recurs. We investigated the recurrence and survival patterns of different subtypes of extremity LPS in the largest known single-center series of LPS patients.

Methods: A retrospective database of patients treated for LPS from 1985-2015 in a tertiary referral center was used to identify patients with LPS primary located in the extremities. Recurrence pattern (local/distant), survival and clinicopathological factors were analyzed in multivariate analyses.

Results: We identified 197 patients treated for LPS primary located in the extremities. Median follow-up was 45.5 months (interquartile range 18-96). Ninety-seven patients had a well differentiated LPS (WDLPS)(49.2%), 72 myxoid LPS (36.5%), 16 pleomorphic LPS (8.1%), 9 dedifferentiated LPS (DDLPS)(4.6%), and 3 other subtypes of LPS (1.5%, left out from further analysis). Of these 197 patients, 42 developed a local recurrence (LR)(21.3%), 26 distant metastasis (DM)(13.2%), 13 patients both LR and DM (6.6%) and 116 patients had no recurrence at the

latest control (58.9%). Pattern of recurrence differed between subtypes: LR was observed most frequently in DDLPS with a 5-year LR-free survival of 51.4%, followed by WDLPS (63.1%), pleomorphic LPS (73.3%) and myxoid LPS (86.7%, *P*=0.078). By contrast, DM occurred most frequent in pleomorphic LPS with a 5-year DM-free survival of 40.2%, followed by myxoid LPS (75.7%), WDLPS (95.3%) and DDLPS (100%, *P*<0.001). Overall survival at 5 years was 79.6%. Multivariate analysis showed that age (HR 1.025, *P*=0.012) and adjuvant radiotherapy (HR 0.268, *P*=0.001) affect the risk for LR, while subtype does not. For DM, the subtypes myxoid LPS (HR 8.131, *P*=0.001) and pleomorphic LPS (HR 17.791, *P*<0.001) were the most important prognostic factors. Tumor size and (positive) resection margins were no significant predictors in this cohort.

Conclusion: LPS subtypes have very distinct patterns of recurrence. DDLPS and WDLPS recur locally most frequently, while myxoid and pleomorphic LPS result in DM more regularly. These prognostic characteristics may be used to further tailor treatment of LPS patients.

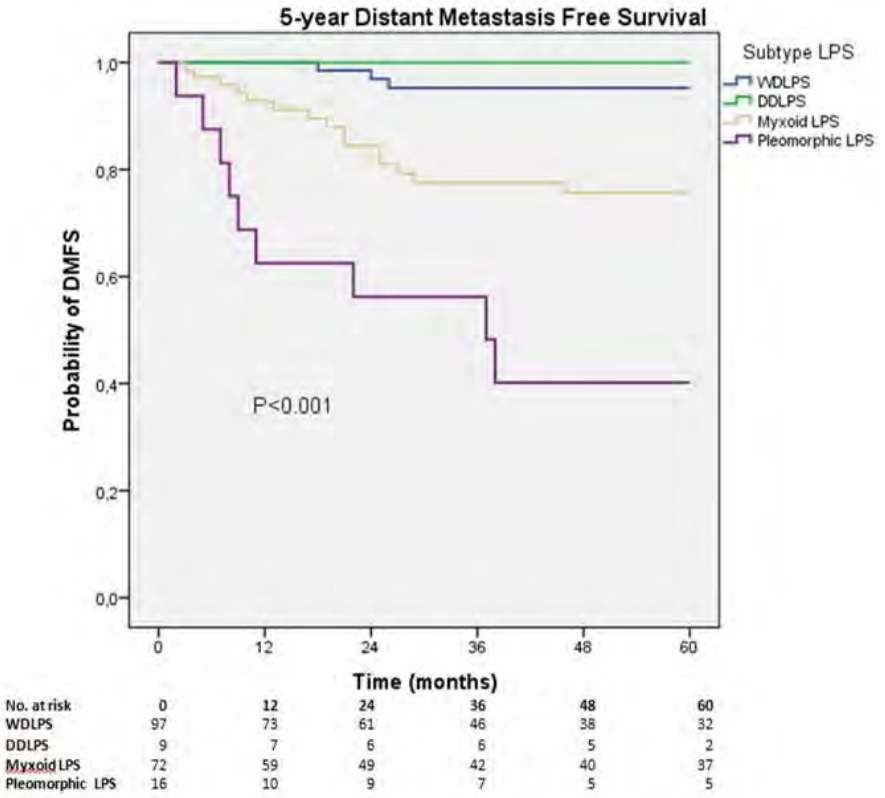


Figure 2. 5-year Distant Metastasis Free Survival (DMFS) by LPS subtype. Log-rank test was used to calculate p-value.

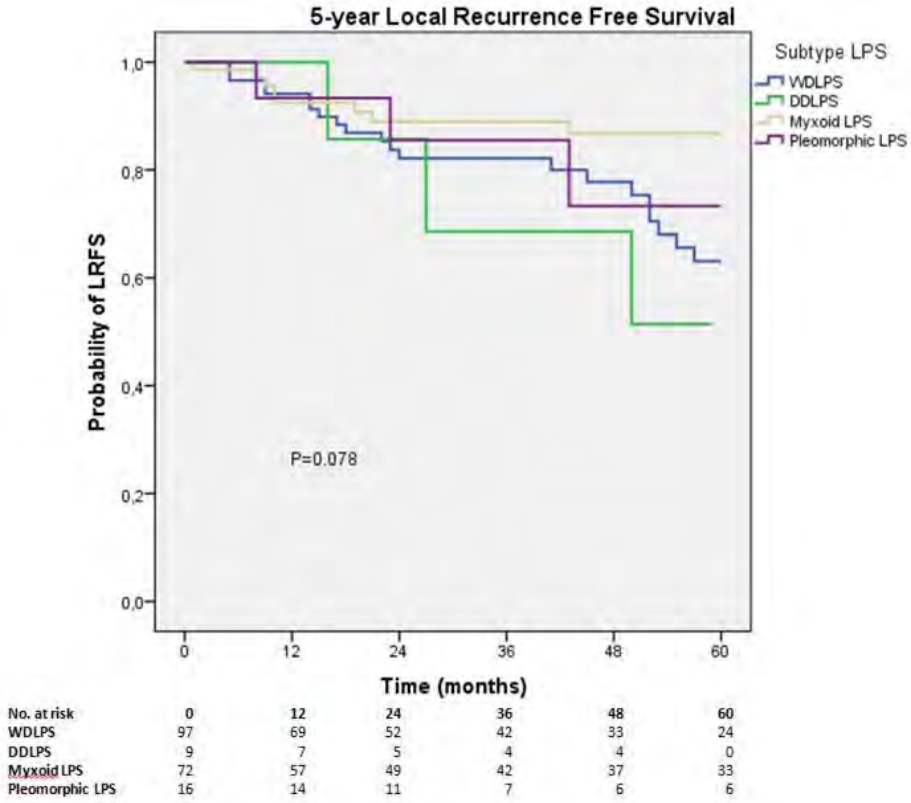


Figure 1. 5-year Local Recurrence Free Survival (LRFS) by liposarcoma subtype. Log-rank test was used to calculate p-value.

P2–Poster 168 2570491

PATTERNS OF RELAPSE OR DISEASE PROGRESSION IN PATIENTS WITH METASTATIC RHABDOMYOSARCOMA: A SINGLE INSTITUTION EXPERIENCE

Beatriz Rozo[1]; Hatel Moonat[1]; Andrea Hayes-Jordan[2]; Anthony P. Conley[3]; Dejka Araujo[3]; Douglas J. Harrison[1]; Anita Mahajan[4]; Lianchun Xiao[5]; Winston Huh[1]
[1]Pediatrics, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Medical Sarcoma, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]Biostatistics, University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children and adolescents. Patients with metastatic disease at diagnosis have a poor prognosis, but the patterns of treatment failure in these patients is not well described. The purpose of this study is to describe the patterns of relapse or disease progression in our cohort which may provide valuable information for improved multimodal therapy.

Methods: Retrospective medical record review of RMS patients with metastasis at diagnosis and relapse or disease progression treated at the University of Texas MD Anderson Cancer Center from 2000 to 2013.

Results: There were 64 evaluable patients with mean age at diagnosis of 25.2 years (range 0.8 to 71.6 years) and 36 were males. Alveolar RMS (ARMS) was most common subtype (n=29; 45%) then embryonal (ERMS; n=13) and RMS not otherwise specified (RMS NOS; n=13). Fusion status was known in 18 patients and 13 were FOXO1 translocation positive. Most common primary tumor sites were the abdomen/pelvis (non-bladder; n=18) and extremities (n=17). Multiple sites of metastases were noted in 40 patients (63%), and most common metastatic sites were distant lymph node (n=33; 52%), bone (n=30; 47%) and lung (n=26; 41%). Local control methods included radiation therapy (RT) alone (n=24), surgery (n=10), surgery + RT (n=10) and none (n=19). Progression on therapy was noted in 30 patients (47%) while relapse was seen in 34 patients at mean duration of 8.9 months after end of therapy (range 1-53 months). Multisite failure was noted in 27 patients (42%) and most common sites were lung (n=26), local (n=22) and bone (n=14). For local failures, most were progression on systemic therapy without receiving local control (n=13/22; 59%). Vincristine, doxorubicin, and ifosfamide (n=24) and vincristine, dactinomycin, and cyclophosphamide (n=16) were most common regimens, but only patients treated with vincristine, doxorubicin, cyclophosphamide, ifosfamide, etoposide-based regimen (VDC/IE) did not have progression on therapy observed (n=11). Median follow up was 24.6 months (1-91 months) and 48 patients died of disease, while 14 were lost to follow up with disease. Only 2 are alive without disease, and both are paratesticular ERMS.

Conclusion: The prognosis for metastatic RMS patients that have failed primary therapy is very poor, and improved systemic therapies beyond conventional cytotoxic chemotherapy are needed. Further study is needed to see if the VDC/IE backbone can serve as a template for future therapy.

P2–Poster 169 2570488

PULMONARY METASTASECTOMY IN SARCOMA PATIENTS: OUTCOMES AND PROGNOSTIC FACTORS

Umberto Cariboni; Rita De Sanctis, MD; Marta Giaretta; Emanuele Voulaz; Pierluigi Novellis; Piergiuseppe Colombo; Emanuela Morenghi; Chiara Mussi; Andrea Marrari; Luca Balzarini; Vittorio Quagliuolo; Armando Santoro; Marco Alloisio
Humanitas Cancer Center, Rozzano (Milan), Italy

Objective: Metastatic STS patients have poor prognosis with 3-year survival rate of 20–30%. Despite adequate treatment of localized disease, up to 50% of the patients develop local/distant relapse. About 30% of them present isolated lung metastases for which one therapeutic option is represented by pulmonary metastasectomy (PM). We aimed to analyze the clinical outcome of patients undergoing PM and prognostic factors associated to post-PM disease-free survival are analyzed.

Methods: All patients undergoing pulmonary metastasectomy at Humanitas Cancer Center were retrospectively reviewed. Analyzed variables included clinico-pathological, surgical and survival data. Exclusion criteria comprised a follow-up period inferior to one year. These parameters were evaluated by univariate and multivariate Cox regression analysis (significance level $p<0.05$).

Results: One hundred fifty-four patients underwent pulmonary metastasectomy (unilateral in 86, bilateral in 68 cases) from June 1997 to June 2015. Total complication rate was 7.1%. The median follow-up was 24 months (range, 0.23†-283 months). The median overall survival from diagnosis of pulmonary metastasis for all patients was 35.4 months. The 1-, 3-, 5- year disease-free survival rate were 32%, 20% and 17%, respectively.

In univariate analyses, the Disease-Free Interval (DFI) from primary tumor resection to pulmonary metastases < 18 months ($p= 0.004$), male gender ($p= 0.014$), grading G3 ($p= 0.024$) and bilateral metastases ($p= 0.032$) were identified as significant negative prognostic factors. Three histology risk groups were defined according to overall survival: high risk (mixofibrosarcoma, MPNST, Ewing sar-

coma), intermediate risk (leiomyosarcoma, liposarcoma and undifferentiated pleomorphic sarcoma) and low risk group (synovial and chondrosarcoma) with a 3-yr OS of 25%, 45% and 74%, respectively.

In multivariate analysis, male gender (p= 0.042), bilateral metastases (p= 0.004) and histology (intermediate vs low-risk group, p= 0.021; high respect low-risk group, p< 0.001) were identified as independent predictors of survival.

† Deceased patient.

Conclusion: Pulmonary metastasectomy for sarcoma is a valid therapeutic option in selected patients. High-risk histologies and bilaterality of lung metastases are independent prognostic factors associated with poor prognosis.

P2–Poster 170 2558648

ANALYSIS OF METASTASIS IN PATIENTS WITH SOFT TISSUE SARCOMA: IS EXTRA-PULMONARY METASTSIS RARE?

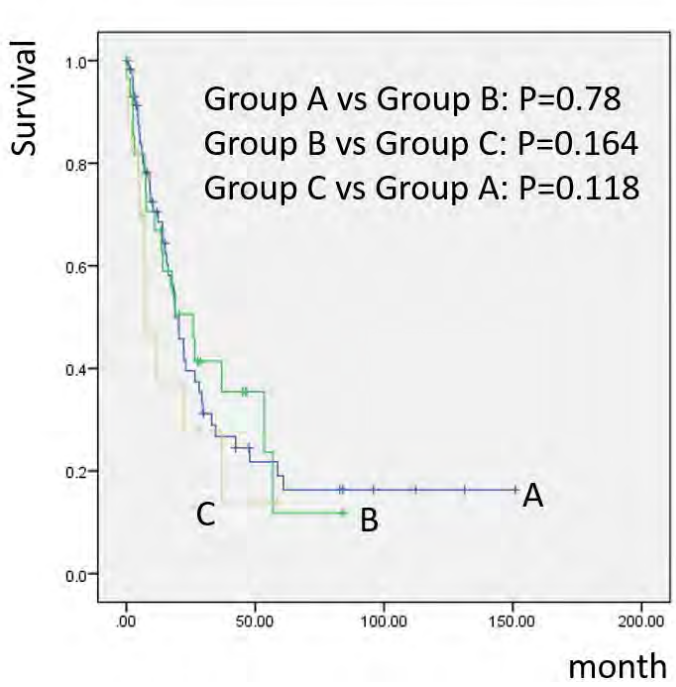
Yuki Yada; Tomoki Nakamura; Kazuma Okuno; Tomohito Hagi; Takao Matsubara; Kunihiro Asanuma; Akihiko Matsumine; Akihiro Sudo
Orthpeadic Surgery, Mie University, Tsu, Mie, Japan

Objective: Of patients with soft tissue sarcoma (STS), 10-38% of patients present with clinically detectable metastasis. Regarding the location of metastasis, 62-83% of sarcoma patients had lung metastasis. However, metastasis may appear in a variety of extra-pulmonary locations. The aim of this study was to analyze patterns of metastasis and post-metastatic survival in patients with STS.

Methods: Between 1995 and 2014, we evaluated 508 patients with primary STS who were treated at our institution and 109 patients (21.5%) developed metastasis. There were 68 males and 41 females with an average age of 57 years. Average follow-up period after initial metastasis was 35 months. 22 patients had metastases at presentation. The remaining 87 patients developed initial metastasis after the treatment of primary tumor.

Results: At initial metastatic site, lung metastasis developed in 78 of the 109 patients (71.6%), lung metastasis developed and extra-pulmonary metastasis in 49 patients (45.0%). The occurrence of lung and extra-pulmonary metastasis was observed in 18 patients (16.5%). 31 patients (28.4%) had only extra-pulmonary metastasis without any co-existing lung metastasis in the following sites: bone (n=16), lymph node (n=13), liver (n=12), muscle (n=8), subcutaneous tissue (n=8), brain (n=5), heart (n=3), digestive tract (n=3), retroperitoneum (n=3) and others (n=3). Histologically, patients with myxoid liposarcoma, UPS, clear cell sarcoma, and epithelioid sarcoma tend to develop extra-pulmonary metastasis. At final follow-up, 35 of the 109 patients were alive, but 75 had died of their disease. Three patients died of other cause. The post-metastatic survival was 29.2% at 3 years in 109 patients. The post-metastatic survival estimates at 3 years were 25.9% for 60 patients with isolated lung metastasis (Group A) vs. 35.5% for 35 patients with only extra-pulmonary metastasis (Group B). The post-metastatic survival was 12.7% at 3 years in patients with both lung and extra-pulmonary metastasis (Group C). There was no significant different in survival between the three groups (Figure.1). Of 109 patients, 48 patients had received metastasectomy. The prognosis of 48 patients had significantly better than that of the remaining 61 patients without metastasectomy (p<0.0001).

Figure.1



Conclusion: Extra-pulmonary metastasis is not rare event. We suggest that we should take care of extra-pulmonary sites as a possible metastasis and, if possible, metastasectomy should be considered to improve the post-metastatic survival.

P2–Poster 171 2544812

PATTERNS OF DISEASE RELAPSE IN PRIMARY EXTREMITY SOFT TISSUE SARCOMA

Henry G. Smith, MRCS; Nikolaos Memos; Joseph Meirion Thomas; Myles J. Smith; Dirk C. Strauss; Andrew J. Hayes
Academic Surgery, The Royal Marsden Hospital, Ashford, United Kingdom

Objective: Extremity soft tissue sarcomas comprise a range of distinct histological subtypes. This study aimed to characterise the patterns of disease relapse in patients un-

dergoing resection of primary extremity soft tissue sarcoma.

Methods: All patients undergoing resection of primary extremity soft tissue sarcoma at the Royal Marsden Hospital between January 2004 and January 2014 were identified from an institutional database.

Results: In the period examined, 556 patients underwent resection. The median age was 63 years with a M:F ratio of 1.3. The most common histological subtypes were undifferentiated pleomorphic sarcoma (169 patients, 30.4 per cent), well-differentiated liposarcoma (63 patients, 11.3 per cent), myxoid liposarcoma (62 patients, 11.2 per cent), myxofibrosarcoma (54 patients, 9.7 per cent) and leiomyosarcoma (39 patients, 7.0 per cent). The median maximum tumour diameter was 9 cm, with the majority of tumours being of intermediate or high grade (65.1%). The most common site was the thigh, accounting for 50.4% of cases.

Local recurrence free survival (LRFS) did not differ significantly between histological subtypes (p=0.222). Distant metastases free survival and disease specific survival did differ significantly between subtypes (DMFS, p<0.001; DSS p<0.001), with the worst outcomes seen in undifferentiated pleomorphic sarcoma 56% (95 % CI 52.5 to 61.1) and 60.1% (95% CI 55.6 to 64.6), respectively. However, on multivariable analysis, histological subtype was not found to be independently prognostic of LRFS, DMFS or DSS. Metastatic disease developed in 149 patients with the most common site of first metastasis being the lungs (120 patients, 80.5 per cent). The site of first metastasis differed between subtypes with extrapulmonary metastases predominant in myxoid liposarcoma (11 of 13 patients, 84.6 per cent, p<0.001).

Conclusion: Although histological subtype was not found to be an independent prognostic factor for oncological outcomes, the site of first metastasis differs significantly between subtypes.

P2–Poster 172 2570133

SERUM BIOMARKERS AS PROGNOSTIC FACTORS FOR METASTATIC SARCOMA

Ninna Aggerholm-Pedersen, MSc, MD, PhD; Katja Maretty-Kongsted; Steen Baerentzen; Johnny Keller; Akmal Safwat
Aarhus University Hospital, Aarhus, Denmark

Objective: We have previously shown that serum C-reactive protein (CRP), albumin, haemoglobin lymphocytes, and neutrophils combined in a biomarker scores (Aarhus composite biomarker score: ACBS) is prognostic for patients with localized bone and localized soft tissue sarcomas, even when adjusted for confounders such as comorbidity and patients age. The aim of this study was to assess the prognostic value of the ACBS in patients with metastatic disease.

Methods: All patients diagnosed with metastatic (bone and soft tissue) sarcomas during 1993-2008 were extracted from Aarhus sarcoma database. The pre-treatment levels of albumin, CRP, haemoglobin, neutrophils, and lymphocytes were collected. ACBS was calculated and patients stratified into 3 groups; low risk group with no abnormal biomarkers, intermediate risk group with only one abnormal biomarker and high risk group with more than one abnormal biomarker. The prognostic importance of ACBS on disease-specific mortality (DSM) was analysed. Adjustments were made for age, comorbidity, histological type using the cox proportional hazard model.

Results: A total of 239 patients with metastatic sarcoma were included. There were 173 patients with soft tissue sarcoma (STS) and 66 with bone sarcoma. The median age was 57 (2-90) years and 30 (3-82) years for STS and bone respectively. The 2-year DSM was 85% (95%CI:79-90) and 91% (95% CI:82-96) for STS and bone sarcoma respectively. Comorbidity was present in 36 % of STS patients and 27% of the bone sarcoma patients. The median DSM was 22 months (95%CI:11-36) for patient with low ACBS, 10 months (95%CI:8-13) for patient with intermediate ACBS, and 6 months (95%CI:4-7) for patients with high ACBS. After adjustment for comorbidity, patients' age at time of metastatic disease and histology, the hazard ratio for patients with an intermediate ACBS was 2.1 (95% CI:1.3-3.4), a high ACBS 3.4 (95% CI:2.1-5.5) compared to patient with a low ACBS score

Conclusion: The ACBS is an independent prognostic factor for disease-specific mortality. It may be used to stratify treatment strategy for patients with metastatic disease according to their risk.

P2–Poster 173 2569961

ADVANCED SOFT-TISSUE SARCOMA–RELATED TREATMENT PATTERNS AND OUTCOMES IN ELDERLY PATIENTS IN THE UNITED STATES

Maria Lorenzo[1]; Lisa Hess[2]; Steven Nicol[2]; Rohan Parikh[3]; Sean D. Candrilli[3]; James A. Kaye[4]
[1]Eli Lilly and Company Limited, Windlesham, Surrey, United Kingdom; [2]Eli Lilly and Company, Indianapolis, IN, USA; [3]RTI Health Solutions, Research Triangle Park, NC, USA; [4]RTI Health Solutions, Waltham, MA, USA

Objective: To describe patient and clinical characteristics as well as treatment patterns and outcomes of patients with advanced soft tissue sarcoma (STS) among patients over age 65 in the United States.

Methods: A retrospective cohort analysis was conducted using the Surveillance Epidemiology and End Results (SEER)-Medicare linked database. Patients ≥65 years of age with advanced STS (excluding cases of Kaposi's sarcoma or gastrointestinal stromal tumors) diagnosed from

Jan 1, 2001 to December 31, 2011 were eligible. Continuous enrollment in Medicare (without health maintenance organization enrollment) was required for ≥6 months prior to initial STS diagnosis. Patients with bone sarcomas were not included. Demographic and clinical characteristics as well as treatment patterns and overall survival (OS) data were summarized.

Results: Of the 4274 eligible pts, 2103 (49.2%) were male. Mean (standard deviation) age was 77.8 (7.3) years. At diagnosis, most patients had localized (1731 [40.5%]) or distant disease (1539 [36.0%]). The most common histological subtypes were leiomyosarcoma (922[21.6%]), undifferentiated pleomorphic sarcoma (519[19%]), and liposarcoma (440[16.1%]). Over 85% of patients had at least one reported comorbidity prior to diagnosis (784[18.3%] had congestive heart failure). Of the 1227 patients receiving first-line therapy, 325 (26.56%) received docetaxel plus gemcitabine and 231(18.8%) received doxorubicin monotherapy. Only 476 (38.8%) received second-line therapy; the most common regimen was doxorubicin monotherapy (101[21.2%]). Median OS (95%CI) from the start of first-line therapy was 13.6 months (12.9, 14.6) for those patients receiving any cancer directed treatment (n=2656) and 2.8 months (2.6, 3.4) for patients receiving supportive care only (n=1618).

Conclusion: STS is a heterogeneous disease with multiple histological subtypes and treatment patterns. Patients receiving active treatment for their disease demonstrated survival outcomes of only about a year. There is a need for more effective treatment to improve outcomes from this complex disease.

P2–Poster 174 2570650

CLINICAL FEATURES, TREATMENT AND PROGNOSIS OF ANGIOSARCOMA INVOLVING THE SPINE

Takeshi Hirose; Makoto Endo; Akihiko Yoshida; Rie Nakano; Shunichi Toki; Takenori Uehara; Masato Sugawara; Yoshihiro Araki; Tomoaki Mori; Koki Shimizu; Eisuke Kobayashi; Yoshikazu Tanzawa; Fumihiko Nakatani; Hirokazu Chuman
Akira Kawai National Cancer Center, Tokyo, Japan

Objective: Angiosarcoma is a rare high-grade malignancy accounting for less than 1% of all sarcomas. Angiosarcoma occurs most frequently in the skin, however, it can arise at any anatomical sites including breast, soft tissue, heart, and bone. Also, angiosarcoma can metastasize to the distal sites including lung, liver, lymph node, and bone. Thus, angiosarcoma sometimes affects bones including the spine, however, little is known about the clinical characteristics of those patients. The objective of this study is to clarify the clinical features, treatment and prognosis of angiosarcoma involving the spine.

Methods: We retrospectively reviewed the medical charts of patients with angiosarcoma who visited at our hospital between November 2001 and April 2016. We picked up the patients with angiosarcoma involving the spine and analyzed the clinical information of them.

Results: Among 101 patients who were pathologically diagnosed as angiosarcoma, 14 patients (14%) had spinal lesions. Seven patients showed spinal involvement at the initial visit, whereas the remaining 7 patients were found during the follow-up period. The primary tumor site included bone (n=5), heart (n=2), skin of the head (n=2), spleen (n=2), breast (n=1), soft tissue (n=1), and intestine (n=1). All patients had multiple bone lesions when spinal involvement was identified. The involved spine was cervical (n=1), thoracic (n=12) and lumber (n=11), and sacrum (n=3); some cases were overlapped. Two of the 14 patients developed paraplegia, which was treated by radiotherapy. The therapeutic modality included chemotherapy alone (n=8), a combination of radiotherapy and chemotherapy (n=3), radiotherapy with or without bone modifying agents (n=2), and best supportive care (n=1). No surgery was performed for the spinal lesion. The most frequently used regimen of chemotherapy was paclitaxel (n=9). The median overall survival time was 171 days from the detection of spinal involvement.

Conclusion: The frequency of spinal involvement of angiosarcoma was 17% in our series. Chemotherapy and/or radiotherapy were generally applied for these patients. Even though paraplegia was associated, surgery was difficult to perform because in most cases spinal lesions were multiple and destructive, and additionally patient's general status was too bad for an invasive surgery. Prognosis of patients with angiosarcoma involving the spine was poor. The further investigations are warranted to find the appropriate medical management for these patients.

P2–Poster 175 2570518

AYA PATIENT AND PROVIDER PERCEPTIONS OF FERTILITY PRESERVATION

Holly Spraker-Perlman[3]; Jennifer Wright[2]; Samantha Pannier[1]; Brynn Fowler[1]; Echo L. Warner[1]; Douglas Fair[3]; William Sause[4]; Jeffrey Yancey[2]; R. L. Randall[2]; Anne C. Kirchhoff[1]
[1]Cancer Control and Population Sciences, Huntsman Cancer Institute, Salt Lake City, UT, USA;
[2]Huntsman Cancer Institute, Salt Lake City, UT, USA;
[3]Primary Children's Hospital, Salt Lake City, UT, USA;
[4]Intermountain Healthcare, Salt Lake City, UT, USA

Objective: Adolescent and young adult (AYA) cancer patients diagnosed between the ages of 15-39 may not fit a pediatric or adult oncology profile. Approximately 1,000 AYAs are diagnosed with cancer in Utah every year and 6.4% of those are sarcomas. The Huntsman-Intermountain

Adolescent and Young Adult (HI-AYA) Cancer Study is an initiative to improve access to age-specific care for AYAs. Fertility preservation has been documented as a major concern for patients and survivors, and sarcoma patients specifically may be affected due to high dose alkylator and radiation therapies. This analysis aims to understand and compare the perceptions of fertility issues within the Utah AYA population with a special emphasis on sarcoma.

Methods: We completed AYA patient interviews (N=39) and a statewide oncology provider survey (N=92). Questions related to fertility preservation were asked of all participants. Descriptive statistics and qualitative content analysis identified barriers to fertility preservation.

Results: Almost 1/4 (N=9) of the AYA interviews were with sarcoma patients and 25% (N=23) of the oncology providers surveyed specialized in sarcoma. Of the overall AYA patient sample, 53.8% (N=21) expressed concerns related to fertility but only 17.9% (N=7) utilized fertility preservation services. Barriers to fertility preservation reported in the AYA interviews included cost, lack of information, and need to begin treatment immediately. Oncology providers echoed these findings with 63.0% (N=58) responding that AYAs need assistance with fertility information. Over half (54.4%, N=50) of oncology providers reported that they always/often discuss fertility preservation with newly diagnosed AYA cancer patients. The top three barriers to referring patients to fertility services included the necessity of starting cancer treatment as soon as possible, concerns about the financial cost of fertility services for patients, and feeling that patients do not want to discuss fertility preservation.

Conclusion: Despite the majority of AYA patients/survivors expressing concerns about fertility, utilization of fertility preservation services was low. Financial support for fertility preservation is needed and future research that explores awareness of financial resources may help ameliorate some barriers to fertility preservation. Additionally, improved patient provider communication may reduce lack of information about fertility services among AYA patients and provider discomfort with discussing fertility preservation.

P2–Poster 176 2570502

PATIENTS' PERSPECTIVES OF SARCOMA TREATMENT: RESULTS FROM A NATIONAL SARCOMA SURVEY IN ENGLAND

Eugenie Younger[3]; Jeremy Whelan[2]; Robin Jones[3]; Lindsey Bennister[1]; Winette Van der Graaf[3]
[1]Sarcoma UK, London, United Kingdom;
[2]UCLH, London, United Kingdom;
[3]Royal Marsden Hospital, London, United Kingdom

Objective: Sarcomas are rare and heterogeneous malignancies that can occur at any age and arise at any anatomic site. In comparison with commoner cancers, patients with sarcoma report a significantly poorer experience of their patient journey. Understanding the patients' perspectives of diagnosis, treatment and follow-up may influence management and outcomes for future sarcoma patients.

Methods: Questionnaires were designed by Quality Health in conjunction with Sarcoma UK, (an all sarcoma charity in the UK) patient advocates and sarcoma clinicians. In England, questionnaires were dispatched by post to a sample of 900 patients drawn from respondents to the NHS National Cancer Patient Experience Surveys 2010-14 (fieldwork January-March 2015). Here we focus on patient experience of treatment.

Results: Response rate was 64% (558 respondents; 418 soft tissue, 140 bone). 87% of patients were treated by a sarcoma specialist team; 66% attended >1 hospital for treatment and half travelled >20 miles for surgical treatment. Most patients (90%) did not mind travelling for surgery and 87% patients felt well informed to make decisions regarding their care and treatment. A written treatment plan was indicated as the key driver for good patient experience. 67% patients were not offered participation in a clinical trial, however in those who were, uptake was only 22%. Most patients (90%) had a designated clinical nurse specialist; 1/3 felt emotional support was inadequate. Only 28% were made aware of a national sarcoma charity. Most patients (87%) felt their follow-up pathway and who to contact for advice was clear. However almost half did not have a positive experience of rehabilitation. All treatment-related side effects with the greatest impact on daily life were pain, fatigue, dry/painful mouth, loss of nerve sensation.

Conclusion: Most patients in this survey were treated by sarcoma specialists and were prepared to travel to access best treatment and care. A written treatment plan encouraged a more positive experience. For those patients offered it, clinical trial participation rates were low. Although clinical support from a nurse specialist was good, access to additional emotional support services may help patients cope with the impact of sarcoma.

P2–Poster 177 2542312

IMPACT OF GERIATRIC FACTORS ON SURGICAL AND PROGNOSTIC OUTCOMES IN ELDERLY PATIENTS WITH SOFT- TISSUE SARCOMA

Yusuke Tsuda, MD[1]; Koichi Ogura[1]; Eisuke Kobayashi[2]; Toru Hiruma[3]; Shintaro Iwata[4]; Naofumi Asano[5]; Akira Kawai[2]; Hirokazu Chuman[2]; Takeshi Ishii[4]; Hideo Morioka[5]; Hiroshi Kobayashi[1]; Yusuke Shinoda[1]; Hirotaka Kawano[6]

[1]Orthopaedic Surgery, The University of Tokyo, Tokyo, Japan; [2]Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [3]Musculoskeletal Tumor Surgery, Kanagawa Cancer Center, Kanagawa, Japan; [4]Orthopedic Surgery, Chiba Cancer Center, Chiba, Japan; [5]Orthopedic Surgery, Keio University, Tokyo, Japan; [6]Orthopedic Surgery, The University of Teikyo, Tokyo, Japan

Objective: Patients aged ≥65 years requiring surgery for soft-tissue sarcoma (STS) are a concern in an aging society. We aimed to reveal the association of clinical/geriatric factors with survival period or postoperative events in such patients who underwent surgery.

Methods: We enrolled patients aged ≥65 years who underwent surgery for localized STS at five institutions. We retrospectively collected clinical/geriatric factors and laboratory data, and analyzed their association with outcomes using univariate and multivariate analyses.

Results: Among the 202 patients included, mean age at presentation was 73 years. Surgical margin was R0 in 139 patients (69%). The Eastern Cooperative Oncology Group Performance Status (ECOG PS) was ≥2 in 15 (7%). Thirty patients (15%) showed thinness (body mass index [BMI] <18.49 kg/cm2). High-sensitivity–modified Glasgow prognostic score ≥1 (Hs-mGPS) was seen in 52 patients (26%). Multivariate analysis showed that R1 surgical margin was significantly correlated with poor sarcoma-specific survival (SSS) (hazard ratio [HR] for R1 vs. R0, 3.17; P = 0.001) and event-free survival (EFS) (HR for R1 vs. R0, 2.56; P <0.001). Higher ECOG PS was significantly associated with poor SSS (HR for ≥2 vs. 0 or 1, 2.15; P = 0.038), and higher Hs-mGPS was significantly associated with poor EFS (HR for ≥1 vs. 0, 1.74; P = 0.046). Severe thinness (BMI <16.00) was a risk factor for postoperative events (OR for BMI <16.00 vs. ≥16.00, 8.15, P = 0.010).

Conclusion: Negative surgical margin is essential for improved survival. Modifying coexisting conditions could improve outcomes in elderly STS patients.

P2–Poster 178 2535716

BALANCING PROLONGED SURVIVAL WITH QUALITY OF LIFE USING LOW-DOSE PAZOPANIB MAINTENANCE: A COMPARISON WITH THE PALETTE STUDY

Kensaku Abe; Norio Yamamoto; Katsuhiro Hayashi; Akihiko Takeuchi; Takashi Higuchi; Yuta Taniguchi; Hisaki Aiba; Hiroyuki Tsuchiya

Orthopaedic Surgery, Kanazawa University, Kanazawa, Ishikawa, Japan

Objective: Currently, pazopanib is used as a second- or third-line adjuvant chemotherapeutic in patients with soft tissue sarcoma, given at a fixed dose of 800 mg once a day. However, pazopanib has many side effects, and there is no consensus on the optimal dosing schedule of pazopanib. In this study, we evaluated the dose and side effects as well as treatment outcomes of pazopanib in patients treated at our institution.

Methods: Twenty-five patients that were prescribed pazopanib between 2012 and 2015 were included in this retrospective analysis. All patients had distant metastases and had previously undergone treatment. Initial pazopanib doses were 800, 600, 400, 200, and 100 mg in 3, 3, 8, 7, and 4 patients, respectively (Table 1). Dose-dependent side effects of pazopanib were determined.

Results: The mean treatment duration was 7.6 (1.3-21.6) months, and the pazopanib dose was decreased in 72% of the cases. The maintenance pazopanib doses of 600, 400, 200, and 100 mg were administered to 3, 10, 8, and 4 patients, respectively (Table 1). The median progression-free survival (PFS) time was 7.7 months (95% confidence interval, 4.2-13.3) (Figure 1). The log-rank test revealed that there were no significant differences in the PFS times between the low and high-dose pazopanib groups during the initial (P = 0.79) or maintenance (P = 0.19) periods (Figure 2A, 2B). Moreover, PFS time in our study (various dose) was similar to that achieved by high-dose pazopanib in the PALETTE study. Of a total of 21 patients in whom the outcomes were evaluated, partial response, stable disease, and progressive disease were achieved in 4, 12, and 5 patients, respectively (Table 2). Moreover, majority of patients received a maintenance dose of 400 mg, and there were no significant differences in the PFS time between the low- and high-dose pazopanib groups, indicating that controlling the side effects might be more critical than administering higher doses.

Conclusion: Pazopanib has in fact provided benefits. However, patients on pazopanib suffer from many associated side effects that significantly impact their quality of life (QoL). Thus, it is critical to provide a balance between the life-prolonging effects of pazopanib and QoL. This study suggested that pazopanib should be started from a low dose with careful increase to avoid pazopanib-related side effects, which is necessary to provide a balance between

the life-prolonging effects of pazopanib and quality of life of patients.

Table 1. Distribution of patients taking different doses of pazopanib for initial and maintenance periods of the study.

	Initial dose	Maintenance dose
100 mg	4	4
200 mg	7	8
400 mg	8	10
600 mg	3	3
800 mg	3	0

Table 2. Radiographic assessment after pazopanib treatment.

Effect	first time	last time
Partial Response	4 (19%)	1 (5%)
Stable Disease	12 (57%)	4 (19%)
Progressive Disease	5 (24%)	16 (76%)

Figure 1

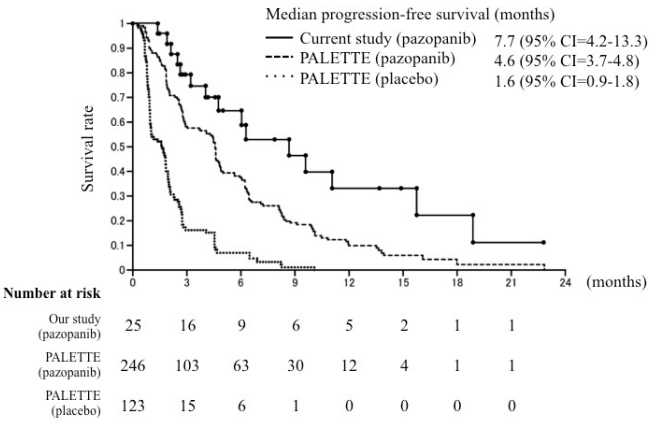


Figure 2A

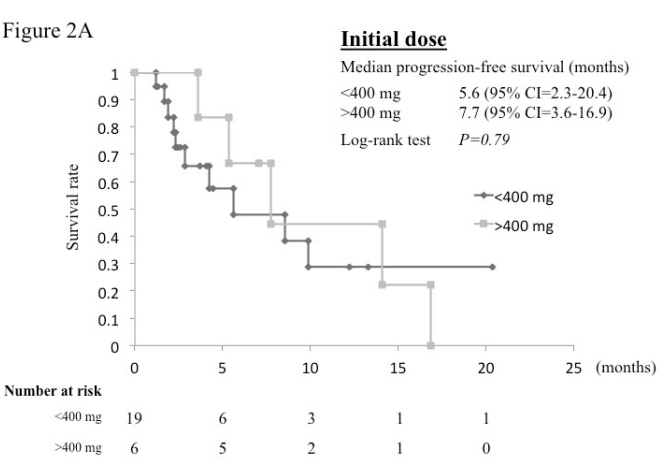
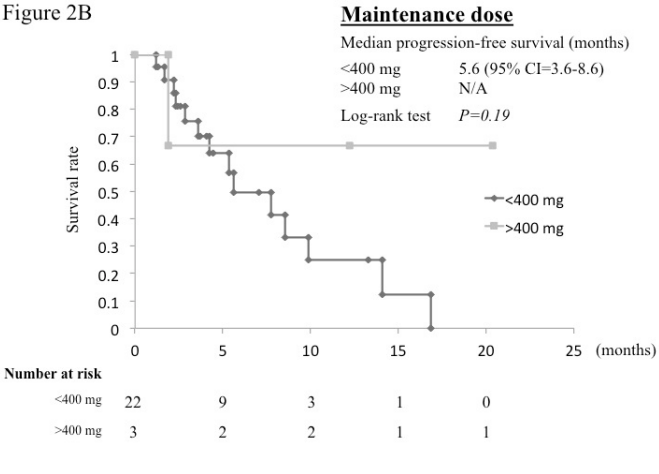


Figure 2B



P2–Poster 179 2529114

WELL DIFFERENTIATED / DEDIFFERENTIATED LIPOSARCOMA: ARE SOME PATIENTS AT RISK OF DEVELOPING A SECOND CANCER?

Eric E. Jung[1]; Shefali Chopra[2]; Ann Hamilton[3]; William W. Tseng[1]

[1]Surgery, Surgical Oncology, Keck School of Medicine, University of Southern Calfiornia, Los Angeles, CA, USA; [2]Pathology, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; [3]Preventative Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

Objective: Well differentiated / dedifferentiated (WD / DD) liposarcoma is one of the most common subtypes of soft tissue sarcomas. There are no known risk factors and a genetic predisposition has never been reported. We examined a case series of patients at our institution with WD / DD liposarcoma to determine the occurrence of a concurrent or subsequent second cancer and also determined the risk of second cancers among WD/DD liposarcoma cases included in the large, population-based National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database.

Methods: For the case series, patient demographics and clinicopathologic data were collected from the available medical records at our institution from June 2014 to June 2016 . For the SEER database analysis, we selected all adult patients from 9 combined registries who were diagnosed with WD / DD liposarcoma between 1973-2012. Observed/expected (O/E) ratios of concurrent or subsequent primary malignancies were calculated by comparing to the age-adjusted cancer incidence in the general population using the multiple primary standardized incidence ratio session of SEER*stat software.

Results: At our institution, 6 out of 32 consecutive patients (19%) with WD / DD liposarcoma had a concurrent second cancer: T cell lymphoma, papillary thyroid cancer,

renal cell carcinoma, gallbladder cancer, colon cancer and prostate cancer. Genetic testing was completed in 3 of these patients without identification of any known hereditary cancer syndromes. In the SEER database, among 1,845 patients diagnosed with WD / DD liposarcoma, 269 patients (14.6%) had 314 concurrent or subsequent second cancers with an O/E ratio of 1.33 (99% CI =1.15-1.54). In 69 patients (3.7%), this event occurred within 2 years of the liposarcoma diagnosis with an O/E ratio of 1.81 (99% CI = 1.33-2.40).

Conclusion: In some patients with WD / DD liposarcoma, there appears to be an increased risk of developing a second cancer compared to the general population. The etiology of this novel observation is unclear, however close screening for additional cancers may be beneficial in these patients. Further studies, including whole genome sequencing, are ongoing.

P2–Poster 180 2533243

ONCOLOGIC OUTCOMES IN PATIENTS WITH EXTREMITY MYXOFIBROSARCOMA AND UNDIFFERENTIATED PLEOMORPHIC SARCOMA: A MATCHED CASE-CONTROL STUDY

Christina Roland, MD[1]; Kelsey Watson[1]; Yi-Ju Chiang[1]; Yu Liang[2]; Nicole de Rosa[1]; Gary Mann[1]; Janice Cormier[1]; Kelly K. Hunt[1]; Barry W. Feig[1]; Wei-Lien Wang[2]; Alexander Lazar[2]; Keila E. Torres[1]

[1]Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA;

[2]Pathology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: Given the relatively recent recognition of myxofibrosarcoma (MFS) as a distinct pathologic entity from undifferentiated pleomorphic sarcoma (UPS), the clinical behavior and outcomes for patients with this disease are uncertain. The aim of this study was to compare the outcomes of patients with primary MFS with a matched cohort of UPS of the extremity.

Methods: The institutional tumor registry was queried for patients with primary MFS of the extremity with ≥ 20 % myxoid stroma that underwent macroscopically negative surgical resection (n=73). A 2:1 matched cohort (based on age, tumor size, margin status and administration of radiation) of patients with UPS were identified from a prospectively collected database (n=146). Patient, tumor and treatment variables were analyzed for associations with oncologic outcomes.

Results: Median tumor size was 6.5 cm and the majority of tumors were deep. 183 patients (84%) underwent R0 resection and 117 (81%) were treated with radiation. Thirty-one percent of patients were treated with chemotherapy and there was no difference between MFS (34%) and UPS (29%) patients. At a median follow-up of 4.4 years, 5-year overall survival (OS) was 75.8%. Although the incidence of first local recurrence was similar between both cohorts [UPS (18%) and MFS (27%) patients (p=0.1)], patients with MFS developed multiple local recurrences more often (n= 12/20, 60%) when compared to the UPS cohort (n= 7/26, 27%; p=0.036). Patients with UPS were twice as likely to develop distant recurrences compared to MFS patients (41% vs. 19%; p<0.01, respectively). Multivariate analysis of factors associated with recurrence and death demonstrated that deep tumors were associated with an increased risk of distant recurrence, which translated into reduced OS and disease-specific survival (Figure). Patients with microscopically positive margins had an increased risk of local recurrence (HR 2.22, 95%CI 1.16-4.24; p=0.016). UPS tumors were associated with increased risk of distant recurrence at 5-yrs (42%) compared to MFS (21%) on univariate (p<0.01) and multivariate analysis (Figure; HR 2.08, 95%CI 1.18-3.67; p=0.012).

Conclusion: Patients with MFS of the extremity are more likely to develop multiple recurrences when compared to UPS patients. Conversely, the UPS cohort has an increased risk of distant recurrence. Further understanding of this disease will guide clinicians in optimal management.

Multivariate Cox Regression Models (Recurrence)

	Local Recurrence			Distant Recurrence		
	HR	95% CI	P value	HR	95% CI	P value
Age at diagnosis						
≥ 60 v. < 60	0.93	0.52-1.68	0.81	0.92	0.58-1.47	0.734
Gender						
Male v. Female	0.87	0.48-1.56	0.636	0.76	0.48-1.19	0.236
Depth						
Superficial v. Deep	0.80	0.38-1.68	0.554	**0.26**	**0.10-0.64**	**0.003**
Resection margin						
R1 v. R0	**2.22**	**1.16-4.24**	**0.016**	1.09	0.60-2.01	0.759
Histology						
UPS v. MFS	0.67	0.37-1.22	0.188	**2.08**	**1.18-3.67**	**0.012**

Multivariate Survival Models

	OS			DSS		
	HR	95% CI	P value	HR	95% CI	P value
Age at diagnosis						
≥ 60 v. < 60	**1.94**	**1.12-3.37**	**0.019**	1.33	0.72-2.43	0.361
Gender						
Male v. Female	0.91	0.55-1.51	0.726	0.93	0.52-1.67	0.817
Depth						
Superficial v. Deep	**0.40**	**0.18-0.88**	**0.023**	**0.24**	**0.07-0.77**	**0.017**
Resection margin						
R1 v. R0	**1.85**	**1.85-1.04**	**0.036**	1.56	0.77-3.16	0.215
Histology						
UPS v. MFS	1.49	0.84-2.65	0.169	1.56	0.79-3.10	0.199

P2–Poster 181 2570714

ADHERENCE TO EXTREMITY SARCOMA STANDARDS OF CARE VARIES BY CASE VOLUME: A NATIONAL CANCER DATABASE (NCDB) ANALYSIS

John Charlson, MD[1]; Manpreet Bedi[1]; Rahul Rajeev[1]; David M. King[1]; John Neilson[1]; T. Clark Gamblin[1]; Kiran Turaga[2]
[1]Medical College of Wisconsin, Wauwatosa, WI, USA; [2]University of Chicago, Chicago, IL, USA

Objective: While it has been demonstrated for multiple cancers that centers with higher case volume have better outcomes, the underlying reasons for improved outcomes, while useful to understand, are not always clear.

We hypothesized that patients with extremity sarcomas treated at high volume (HV) centers were more likely to be treated according to consensus guidelines. Our aim was to analyze whether center volume was associated with three recommended components of sarcoma care - complete (margin negative) resection, radiotherapy for large high grade tumors, and chemotherapy for large high grade tumors.

Methods: Using the National Cancer Database (NCDB) PUF 2003-12, patients with extremity locoregional sarcomas were identified. Volume quartiles were created using total center volume for the time period. Propensity matching was performed using coarsened exact matching to create balanced cohorts with similar likelihood for treatment at a high volume center. Chi square and Kruskal Wallis tests were used to assess the relationship between volume quartile and the various aspects of care.

Results: The cohort of 87,533 patients were treated in 1358 institutions. A majority of patients (92%) were treated at comprehensive cancer centers (42%) and academic centers (49%) but the highest volume centers were mostly academic centers ($p<0.001$). The lowest volume (LV) centers saw older patients (63 yrs vs. 57, $p<0.001$), with government insurance (51% vs 41%, $p<0.001$), and higher Charlson Deyo scores (2.89 vs. 1.9, $p<0.001$). High volume (HV) centers saw patients with larger tumors (7.5cm vs. 6.0cm, $p<0.001$). Patients received neoadjuvant radiation (33%) in HV centers compared with 10% in LV ($p<0.001$), and were more likely to receive radiation and chemotherapy for large (>5cm), high grade tumors (56 vs 51% & 32 vs. 21% respectively, $p<0.001$). Patients treated at HV centers were less likely to have margin positive resections (16 vs. 28%, $p<0.001$). These effects persisted in matched cohorts ($p<0.001$ for all).

Conclusion: Higher volume centers are more likely to adhere to prescribed processes of care for patients with extremity sarcomas in in regard to surgery, radiation and chemotherapy. In addition, there may be disparity in utilization of HV centers related to insurance coverage, among other factors.

P2–Poster 182 2570699

FAMILY HISTORY OF CANCER AND ITS INCIDENCE ON ADULT ALVEOLAR RHABDOMYOSARCOMA (ARMS): AN MD ANDERSON CANCER CENTER (MDACC) SERIES

Branko Cuglievan, MD[1]; April DePombo[1]; Winston Huh[2]; Douglas J. Harrison[2]; Andrea Hayes-Jordan[3]; Joseph A. Ludwig[4]; Dejka Araujo[4]; Vinod Ravi[4]; SR Patel[4]; Cindy L. Schwartz[2]; Robert S. Benjamin[4]; Anthony P. Conley[4]
[1]Pediatric Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Sarcoma Pediatric Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Pediatric Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Sarcoma Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective: ARMS is considered to be one of the most aggressive pediatric malignancies. Adults with ARMS notoriously experience inferior outcomes. Our goal was to describe the different types of malignancies found in primary relatives of this population, reveal its frequencies and attempt to determine potential associations.

Methods: Adult ARMS patients (pts) over the age of 18 years (y) treated at MDACC from 2004 to 2015 were identified from our registry. Descriptive statistics and survival analysis were performed via multivariate analysis. All statistical analyses were performed using SAS 9.3 for Windows.

Results: 43 pts were identified. Median age at diagnosis was 31 y (range (R) 18 to 69 y). Median OS was 32 months (R: 2 to 97 months). 31 pts were younger than 40 y. From them, FOXO1 fusions were positive in 23 pts (74%), negative in 2 pts (6%) and not evaluated in 6 pts (19%). 12 pts were older than 40 y. From them, FOXO1 fusions were positive in 7 pts (58%), negative in 2 pts (17%) and not evaluated in 3 pts (25%). 34 pts had family history of cancer (79%); 18 male (53%) and 16 female (47%). Within this group the most common primary site for ARMS was the parameningeal space (21pts; 62%). 21 pts (62%) with intermediate risk disease and 13 pts (38%) with high risk disease had family history of malignancy. 11 pts (32%) had primary relatives with cancer (median of 1; R: 1-4). The median number of family members with malignant diseases was 2 (R: 1-5) and the median number of cancers in the family was 2 (R: 1-4). 27 different types of neoplasms were noted in this cohort. 9 pts had family history of prostate cancer (26%), 8 of breast cancer (24%) and 7 of colon cancer (20%).

Conclusion: The high incidence of family history of malignancy in our cohort suggests that a more comprehensive review of family history and genetic analysis should be considered. Further research is needed to help us elucidate other possible factors that could affect outcomes for this rare population of patients.

P2–Poster 183 2570265

INCIDENCE OF SARCOMAS AND HISTOLOGICAL SUBTYPES IN GERMANY – FIRST NATIONAL SURVEY

Meike Ressing[2]; Eva Wardelmann[3]; Peter Hohenberger, MD, PhD[1]; Jens Jakob[1]; Bernd Kasper[4]; Katharina Emrich[2]; Andrea Eberle[5]; Maria Blettner[2]; Sylke Zeisig[2]

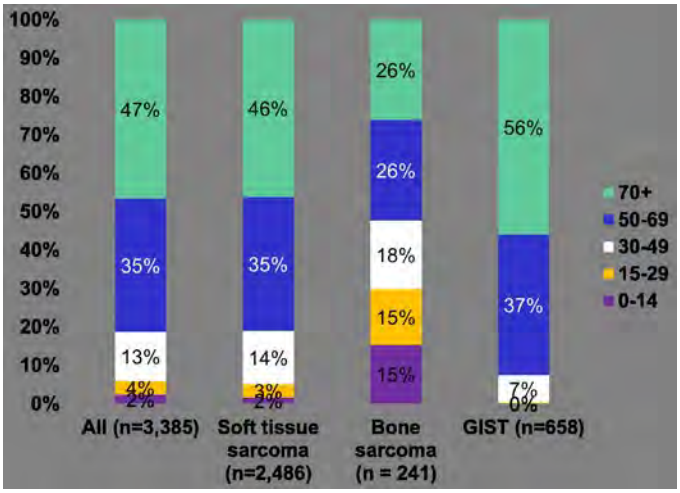
[1]Division of Surgical Oncology and Thoracic Surgery, Department of Surgery, University Medical Center Mannheim, University of Heidelberg, Mannheim, Germany; [2]Institute for Medical Biostatistics, Epidemiology and Informatics, University Medical Center, Johannes Gutenberg University, Mainz, Mainz, Germany; [3]Gerhard-Domagk-Institute for Pathology, University Hospital Münster, Münster, Germany; [4]Interdisciplinary Tumor Center Mannheim, University Medical Center Mannheim, University of Heidelberg, Mannheim, Germany; [5]Cancer Registry Bremen, Bremen, Germany

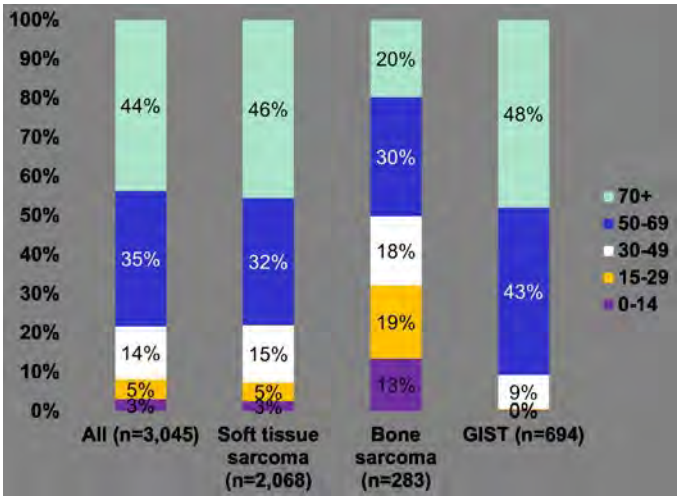
Objective: The population-based incidence of sarcoma and its histological subtypes in Germany is unknown due to the fact that the ICD codes C45-C49 were not centrally evaluated in a state-based health care system with multiple epidemiological cancer registries. The aim was to determine this incidence by pooling the data from the German epidemiological cancer registries.

Methods: Pooled data from the German Centre for Cancer Registry Data for the year 2012 of primary diagnosis were used. All German cancer registries with sufficient completeness and with no objection because of reasons of data protection were included (10 out of 11), covering a population of 69.8 Million people representing 87% of the German population. All malignant soft tissue tumors and bone tumors (sarcomas) according to the RARECARE Project [1] and to the WHO classification were considered for analysis and, gastrointestinal stromal tumours. Sensitivity analysis was performed excluding certain histologieswhich did not fulfill the criteria according to the WHO classification.

Results: The analysis included 3.045 cases in men and 3.385 cases in women diagnosed in 2012. The age adjusted incidence of sarcomas (European standard) was 6.8 (men) and 6.4 (women) per 100.000 inhabitants. About 71% of sarcomas were soft tissue sarcomas, about 21% GIST (gastrointestinal stromal tumours) and about 8% bone sarcomas. The most common histology subtypes besides GIST were fibrosarcomas (15%) and liposarcomas (11%) in men and complex neoplasia (21%) and fibrosarcomas (9%) in women. Interestingly sarcoma incidence was not different between genders, however the age distribution showed signficant differences (see figures)

Conclusion: Sarcomas as a heterogeneous group of neoplasia arising from diverse sites (e.g. connective tissue, skin, uterus, retroperitoneum, bones) and analysis of different subtypes of histologies are not part of routine reports on cancer incidence in Germany. This study is the first detailed analysis of a German wide population-based incidence of sarcomas being comparable to the incidence detected in the RARECARE Project.





P2–Poster 184 2566255

LOCAL RECURRENCE, DISTANT METASTASIS, AND DEATH IN PATIENTS WITH SOFT TISSUE SARCOMA AFTER CURATIVE RESECTION: A MULTI-STATE MODEL

Florian Posch[1]; Lukas Leitner[2]; Michael Stotz[1]; Bernadette Liegl-Antzager[3]; Angelika Bezan[1]; Martin Pichler[1]; Armin Gerger[1]; Marko Bergovec[2]; Herbert Stoeger[1]; Andreas Leithner[2]; Joanna Szkandera[1]

[1]Clinical Division of Oncology, Department of Medicine, Medical University of Graz, Graz, Austria; [2]Department of Orthopaedics and Orthopaedic Surgery, Medical University of Graz, Graz, Austria; [3]Institute of Pathology, Medical University of Graz, Graz, Austria

Objective: Baseline risk factors inform the prognosis of patients with soft tissue sarcoma (STS) undergoing cu-

rative surgery. However, the long-term survival outcome of these patients may also be influenced by intermediate events occurring during follow-up, such as local recurrence and distant metastasis. In this study, we use multi-state modeling to statistically dissect the complex epidemiologic relationship between local recurrence, distant metastasis and death due to STS or other causes.

Methods: In this study, we followed 444 patients with localized STS after curative surgery (Table 1). The association between clinical events occurring during follow-up were analyzed with unidirectional, semi-Markov, "clock-forward" multistate models.

Results: In competing risk analysis accounting for overall mortality, the 15-year cumulative incidences of local recurrence, distant metastasis, and overall recurrence were 15.9% (95%CI: 10.9-21.9), 21.1% (95%CI: 16.9-25.7), and 31.8% (95%CI: 25.6-38.1), respectively. In multi-state analysis, the onset of local recurrence was associated with a 3.6-fold increase in the risk of distant metastasis (Transition hazard ratio (THR)=3.59, 95%CI: 1.62-7.95, p=0.002), and a 2.9-fold increase in the risk of death (THR=2.85, 95%CI: 1.73-4.69, p<0.0001). The occurrence of distant metastasis was associated with a 12.6-fold increase in the risk of death (THR=12.65, 95%CI: 8.73-18.33, p<0.0001). Distant metastasis occurring after a long tumor-free interval did not exhibit a more favorable prognosis with respect to mortality than distant metastasis occurring early after surgery (p=0.28). In multi-state analysis, tumor grade G3 emerged as a significant predictor of both a higher risk of recurrence (THR=3.39, 95%CI: 2.11-5.43, p<0.0001), and a higher risk of death after developing recurrence (THR=1.84, 95%CI: 1.04-3.26,p=0.04).

Table 1. Baseline patients characteristics

Variable	Median or n (%)
Age (years)	62 (47-73)
Grade G3	264 (59.6%)
Tumor size >5cm	316 (71.2%)
Adjuvant chemotherapy	40 (9.0%)
Adjuvant radiotherapy	261 (58.8%)
Median follow-up	5.5 years
Local recurrence	74 (16.7%)
Distant failure	74 (16.7%)
Death due to STS	65 (14.6%)
Death due to other causes	59 (13.3%)

Conclusion: In patients with localized STS undergoing curative surgery, the occurrence of local recurrence and distant metastasis contributes to a dramatically impaired long-term survival experience. Furthermore, local recurrences represent a significant risk factor for distant metastasis. Distant metastasis after a long tumor-free interval harbors an equally dismal prognosis than early onset metastasis. Higher tumor stages at baseline not only associate with a higher risk of recurrence but also accelerate the time-to-death after the onset of recurrence.

P2–Poster 185 2566492

THERAPY AND OUTCOME OF PATIENTS FOLLOWING UNPLANNED EXCISIONS IN SOFT TISSUE SARCOMA: A MULTI- CENTRE EXPERIENCE

Maria A. Smolle, Medical Student[1]; Elisabeth Goldenitsch[2]; Felix Machacek[2]; Marko Bergovec[1]; Bernadette Liegl-Antzager[3]; Florian Posch[4]; Joanna Szkandera[4]; Andreas Leithner[1]
[1]Department of Orthopaedic Surgery, Medical University of Graz, Graz, Austria; [2]Orthopaedic Hospital Gersthof Vienna, Vienna, Austria; [3]Institute of Pathology, Medical University of Graz, Graz, Austria; [4]Division of Clinical Oncology, Internal Medicine, Medical University of Graz, Graz, Austria

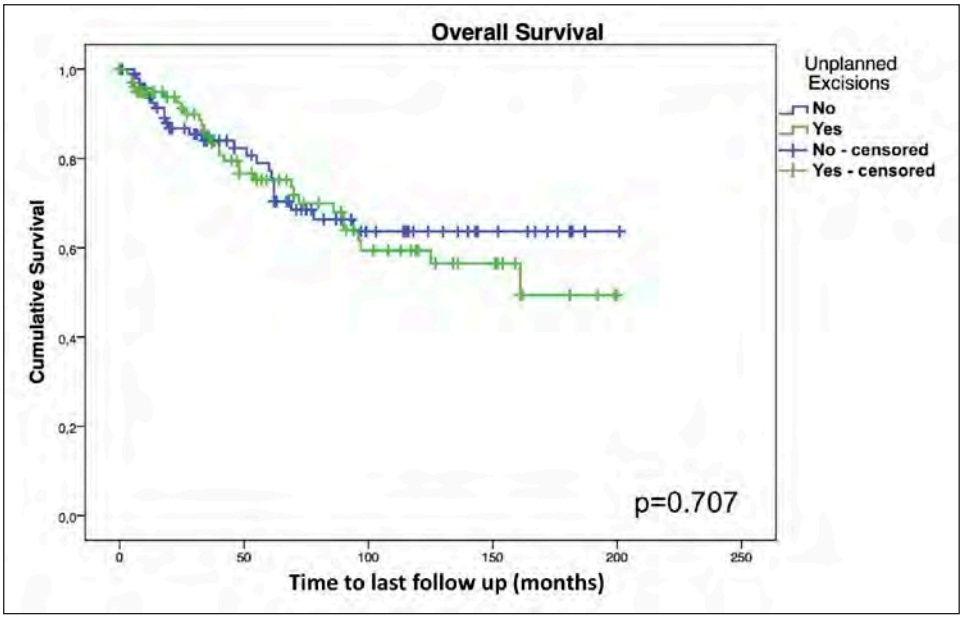
Objective: The heterogeneous clinical presentation of soft tissue sarcomas (STS) often impedes early diagnosis and adequate treatment. As a result, unplanned excisions (UE) of STS are not uncommon. Despite this inappropriate primary treatment, patients with UE tend to have a better prognosis following re-resection in comparison to initially adequately treated patients.

Therefore, this study was carried out in order to 1) define factors associated with an increased risk for UE, 2) identify the influence of UE on subsequent therapy and 3) evaluate its impact on overall-survival (OS).

Methods: Altogether, 525 STS patients treated between 1998 and 2015 were included (centre A: n=427, centre B: n=98). The mean patient's age was 59 years (range: 12–96 years). After a mean follow-up of 4.6 years, 308 patients were alive without (58.7%) and 59 with disease (11.2%), 91 patients had died due to disease (17.3%) and 67 due to other causes (12.8%).

Survival analyses were calculated excluding patients with primary metastasis at time of diagnosis (n=35). A matched propensity score analysis was performed to adjust imbalances in prognostic variables (e.g. tumour size) between UE-patients and directly referred ones.

Results: 198 patients had undergone an UE prior to referral (37.3%), with a similar incidence in both centres (p=0.36). All patients underwent definite surgery at the respective sarcoma centre. Superficial location (p<0.005), small tumour size (p<0.005) and a long history of symptoms (p=0.028) increased the risk for UE. UE-patients required more often plastic reconstruction (p<0.005) at re-resection as well as adjuvant radiotherapy (p=0.033).
The 5- and 10-year OS rates were 73.9% and 59.7% for all patients without distant metastasis at time of diagnosis, respectively. In naïve univariate analysis, patients with prior UE had a significantly better OS (Log-rank-test; p=0.032). After matched propensity score analysis, however, OS rates were similar for both groups (Log-rank-test; p=0.707; Fig 1).



Kaplan-Meier survivorship curve calculated after matched propensity score analysis showing similar overall-survival rates for patients with unplanned excisions and those without.

Conclusion: Factors increasing the risk for unplanned excisions are a long history of symptoms, small tumour size and superficial location. A better survival of patients with UE as found in naïve univariate analysis is obviously due to more favourable prognostic factors in this group, since after adjustment for these factors by propensity score matching, survival was similar. Thus, one can conclude that unplanned excision has neither a positive nor a negative effect on survival in patients with STS.

P2–Poster 186 2565082

FEASIBILITY OF BIOPSIES IN METASTATIC SOFT TISSUE SARCOMAS - RELEVANCE FOR TRANSLATIONAL TRIALS

Philipp Ammon; Sebastian Bauer
West German Cancer Center, Essen, Germany

Objective: Proof-of-concept studies for personalized treatments in sarcomas ideally include sequential biopsies in patients with metastatic disease. Location of metastases determines accessability as well as the type of biopsy procedure and could thereby impact recruitment. We have therefore sought to analyse the feasibility of biopsies by retrospectively reviewing imaging studies of patients with common soft tissue sarcoma subtypes.

Methods: Patients with leiomyosarcomas, liposarcomas or undifferentiated metastatic sarcomas for whom imaging was available in the hospitals PACS system were identified from an institutional database. Demographic and clinical data (covariates: location of primary, histological subtype, localization of metastases, number and date of chemotherapeutic treatment lines) were collected and CT or MRI scans were reviewed for location of metastases and for preferred biopsy procedure. Averaged cost estimates for biopsies were calculated for treatment lines and subtypes.

Results: 139 patients were identified of whom 12% were untreated while 23, 14, 16 and 34% of patients had received either 1, 2 3 or more than 3 treatment lines. Histologies were equally distributed. Majority of primaries were located in the abdomen (50%) and extremities (38%). Pattern of metastatic spread varied substantially between sarcoma subtypes. High rate of hepatic metastases in late line LMS were found as well as a predominance of pulmonary metastases in undifferentiated sarcomas. CT-guided biopsies seemed feasible in 78% of untreated patients and 90% of heavily pretreated patients. Notably, ultrasound-guided biopsies were considered possible in 37% in untreated and 55% of heavily pretreated patients.

Conclusion: CT-guided biopsies are feasible in the vast majority of patients regardless of treatment line. Cost-effective biopsies without ionizing radiation (ultrasound-guided biopsy or needle biopsy by sight) can be used in more than 50% of heavily pretreated patients but accessability may greatly vary based on the histological subtype.

P2–Poster 187 2565081

PREOPERATIVE ASSESSMENT OF INFILTRATIVE HISTOLOGIC GROWTH PATTERN IN EXTREMITY SOFT TISSUE SARCOMA

Jong Woong Park[1]; Han-Soo Kim[1]; Cheol Lee[2]; Ji Yeon Yun[1]; Ilkyu Han[1]
[1]Seoul National University Hospital, Seoul, Korea (the Republic of); [2]Seoul National University College of Medicine, Seoul, Korea (the Republic of)

Objective: Soft tissue sarcoma (STS) with an infiltrative histologic growth pattern, when compared to STS with an expansile pattern, may pose difficulties in local control and subsequent risk for local recurrence. Preoperative assessment of the presence of infiltrative histologic growth pattern, using preoperatively available clinicopathologic parameters, would be helpful in deciding treatment strategies.

Methods: A review of 170 patients who underwent surgery for extremity STS, with histologic documentation of growth pattern, was performed. Possible clinicopathologic factors

that might be associated with infiltrative histologic growth pattern were investigated with regard to patient demographics, tumor characteristics and MRI findings. Clinical or radiological factors which were found to have a statistically significant association with the histologic growth pattern ($p < 0.05$) were included in a multivariate logistic regression analysis to evaluate associations linking the histologic growth pattern. To test the accuracy of predicting the presence of infiltrative histologic growth pattern, receiver operating characteristic (ROC) curves were constructed.

Results: Of the 170 tumors, 76 (45%) showed infiltrative histologic growth pattern. STS with infiltrative growth pattern were more likely to be superficial ($p = 0.02$), higher histological grade ($p = 0.03$) and to present with infiltrative border on MRI ($p < 0.001$). On univariate logistic regression analysis, superficial location ($p = 0.03$), higher histological grade ($p=0.04$), histological subtype other than liposarcoma ($p < 0.001$) and infiltrative border on MRI ($p<0.001$) were significant. On multivariate analysis, histological subtype other than liposarcoma (OR = 4.75, $p = 0.002$) and infiltrative border on MRI (OR = 2.39, $p = 0.015$) remained as independent factors associated with infiltrative histologic growth pattern. Predictive index based on these 2 factors showed a fair predictive accuracy (ROC-AUC = 0.704) for predicting infiltrative histologic growth pattern.

Conclusion: Our data suggest that patients with histological diagnosis other than liposarcoma and infiltrative border on MRI can predict infiltrative histologic growth pattern in extremity STS. If an extremity STS of non-liposarcoma histology shows infiltrative tumor border on MRI, infiltrative histologic growth pattern can be expected.

P2–Poster 188 2561423

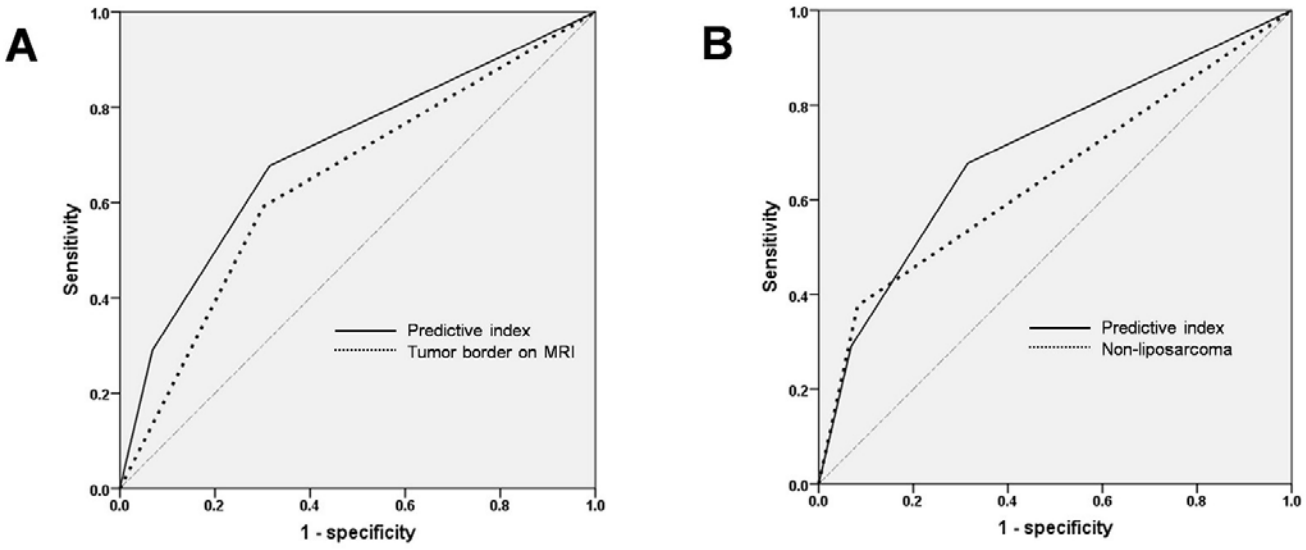
NEUTROPHIL-LYMPHOCYTE RATIO AS PROGNOSTIC PREDICTORS IN PATIENTS WITH SOFT TISSUE SARCOMA

Tomohito Hagi; Tomoki Nakamura; Yuki Yada; Takuya Kakimoto; Takao Matsubara; Kunihiro Asanuma; Akihiko Matsumine; Akihiro Sudo
Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Tsu, Mie, Japan

Objective: Several relevant prognostic factors for soft tissue sarcoma (STS) have been identified. The histological tumor grade, tumor size, and age are predictive factors for survival. Recently, the preoperative neutrophil-lymphocyte ratio (NLR) has been shown to be a prognostic factor for poor survival in patients with STS. The aim of this study was to determine whether the NLR predicts disease-specific survival in adult patient with STS.

Methods: We retrospectively reviewed 209 patients who were treated at our institution between 1995 and 2014. The patients comprised of 113 males and 96 females, with a mean age of 60.5 years (range, 16-92) at first presentation. The mean follow-up period was 58.5 months (range, 3-233). Blood samples were obtained prior to treatment in all patients.

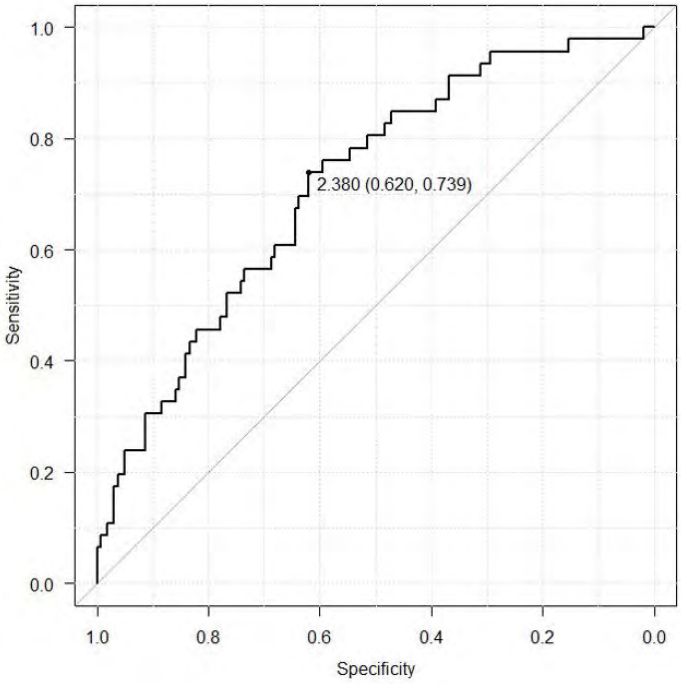
Results: The NLR varied from 0.54 to 7.59 (median 2.19, mean 2.62). NLR was related to tumor grade ($P<0.0001$). NLR had weak association with age (Spearman $\rho=0.281$, $p<0.0001$). In the receiver operating characteristic (ROC) analysis, a value of 2.38 was found to be an appropriate threshold for identifying patients at risk for death at 3 years



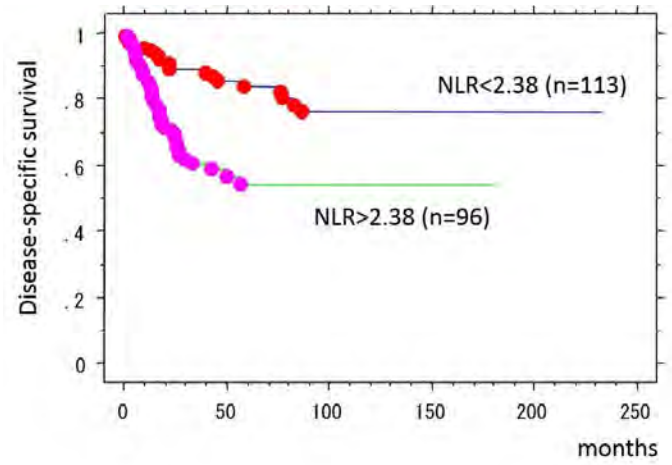
Pairwise AUC comparison of the predictive index with the tumor border on MRI alone and histological subtype other than liposarcoma in predicting infiltrative histologic growth pattern. (A) Pairwise area under the receiver-operating curve (AUC) comparison of the predictive index and the tumor border on MRI alone in predicting infiltrative histologic growth pattern. (B) Pairwise area under the receiver-operating curve (AUC) comparison of the predictive index and histological subtype other than liposarcoma alone in predicting infiltrative histologic growth pattern.

(Fig. 1). The area under the curve was 0.716. The patients with a higher NLR (>2.38) prior to initial treatment had a poorer disease-specific survival rate (54.1% at 5 years) than the patients with a lower NLR (<2.38) (83.7% at 5 years, p<0.0001)(Fig. 2). There were significant differences regarding the histological tumor grade (P<0.0001), tumor size (P=0.006), and patient age (P=0.04). On multivariate analysis, NLR remained significantly prognostic factor.

Conclusion: NLR is easy to measure and may be a helpful prognostic predictor in patients with STS.



ROC for the appropriate NLR for predicting survival.



Disease-specific survival (A : patients with a low NLR (<2.38), B : patients with a high NLR (>2.38)).

P2–Poster 189 2557539

RISK FACTORS INCREASING IN-HOSPITAL MORTALITY AFTER CHEMOTHERAPY FOR PATIENTS WITH MALIGNANT MUSCULOSKELETAL TUMORS

Toru Akiyama, MD, PhD; Kazuo Saita
Departments of Orthopaedic Surgery, Saitama Medical Center, Jichi Medical University, Saitama, Japan

Objective: Reducing the in-hospital post-chemotherapy mortality rate in patients with malignant musculoskeletal tumors is important for improving treatment outcome. Previous studies on chemotherapy-related early death in patients with lymphoma, carcinoma, and sarcoma have investigated malignant tumor groups overall but did not focus on specific malignant tumor types. This study aimed to investigate the risk factors associated with in-hospital post-chemotherapy mortality in patients with primary malignant musculoskeletal tumors, using data from a national inpatient database in Japan.

Methods: Using a Japanese national inpatient database, we retrospectively identified 5039 patients (2920 men and 2131 women; mean age, 39 years) who underwent curative chemotherapy for malignant musculoskeletal tumors between 2007 and 2010. We extracted data on the patients' characteristics, complications, chemotherapeutic agent use, comorbidities, and in-hospital death. Logistic regression analyses were performed to analyze factors affecting in-hospital post-chemotherapy death in these patients.

Results: The overall in-hospital mortality rate was 1.1%. Higher in-hospital mortality rates were significantly associated with a greater volume of blood transfusion (>2500 mL) (odds ratio [OR], 49.71; 95% confidence interval [CI], 22.24 - 111.12; p < 0.001), diabetes mellitus (OR, 3.05; 95% CI: 1.21 -7.70; p = 0.019), and older age (OR, 3.05; 95% CI, 1.11 - 8.37; p = 0.031). Different drug combinations did not have any significant effect on in-hospital mortality rates.

Conclusion: Higher in-hospital post-chemotherapy mortality rates were associated with massive blood transfusion, which was associated with a 16-fold higher risk of in-hospital mortality compared with other risk factors. Blood transfusion volume should be considered an important indicator for deciding whether the next cycle of chemotherapy is administered continuously or not.

P2–Poster 190 2545084

REAL-WORLD TREATMENT PATTERNS OF PATIENTS WITH METASTATIC SOFT TISSUE SARCOMA IN THE UNITED STATES

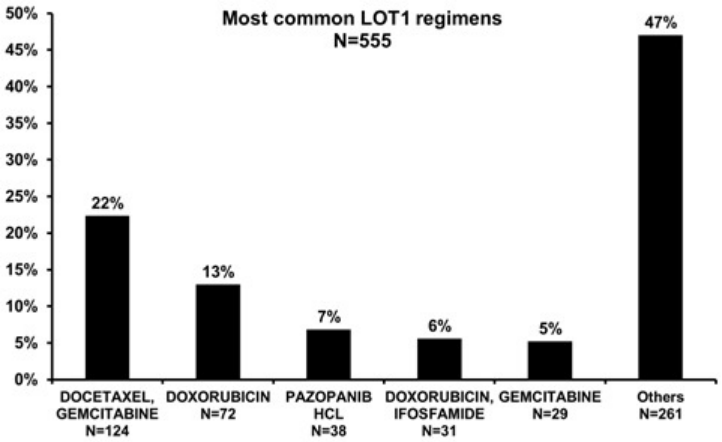
Victor M. Villalobos, MD, PhD[1]; Stacey DaCosta Byfield[2]; Sameer Ghate[3]; Oluwakayode Adejoro[2]; Jose Perez[3]
[1]University of Colorado Anschutz Medical Campus, Denver, CO, USA; [2]Optum, Eden Prairie, MN, USA; [3]Novartis, East Hanover, NJ, USA

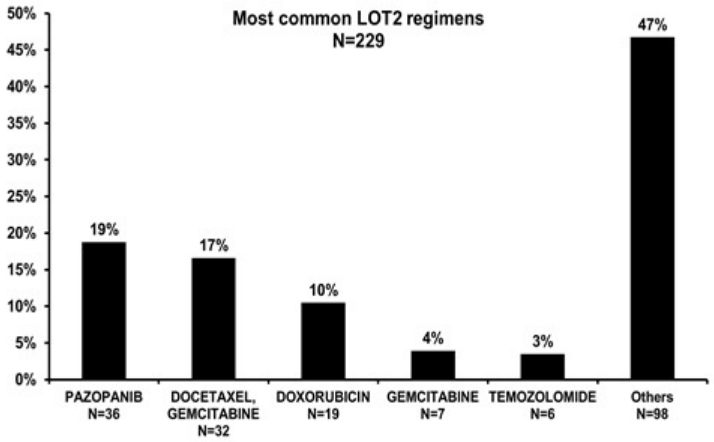
Objective: Few studies have examined real-world treatment patterns of patients with metastatic soft tissue sarcoma (mSTS) since the approval of pazopanib in 5/2012 as a treatment option in the US; pazopanib efficacy in adipocytic STS or gastrointestinal stromal tumors has not been demonstrated. The goal of this study was to describe characterisitcs of patients who initiate treatment for mSTS and examine treatment patterns by line of therapy.

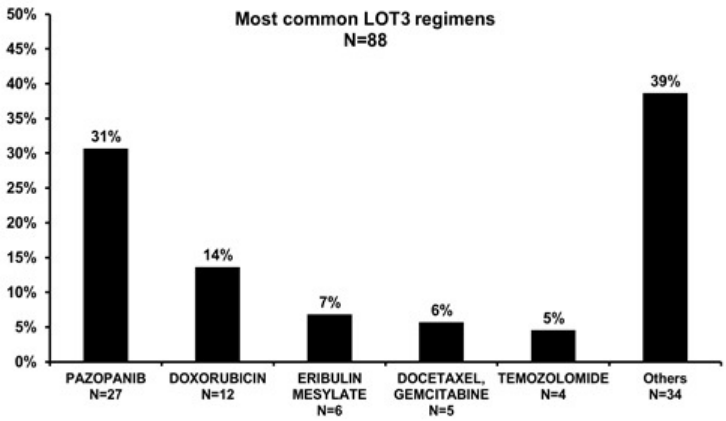
Methods: A retrospective study was conducted using a large, national US claims database from 1/2006-9/2015. Adult STS patients (≥2 claims with ICD-9-CM 171.xx) with metastatic disease (≥1 claim with ICD-9-CM 196.xx-199.0x) were required to have ≥1 claim for a NCCN-recommended therapy and be continuously enrolled in the health plan for ≥ 6 months prior (baseline period) and ≥1 month after (follow-up period) the first treatment for mSTS. Line of therapy (LOT) periods were created based on receipt and timing of NCCN-recommended therapy for mSTS. Patients were followed until the earliest of end of health plan enrollment, death or end of the study period. The number of LOTs initiated during the study period was examined and the most common regimens by LOT were assessed, as well as duration of therapy by LOT regimen.

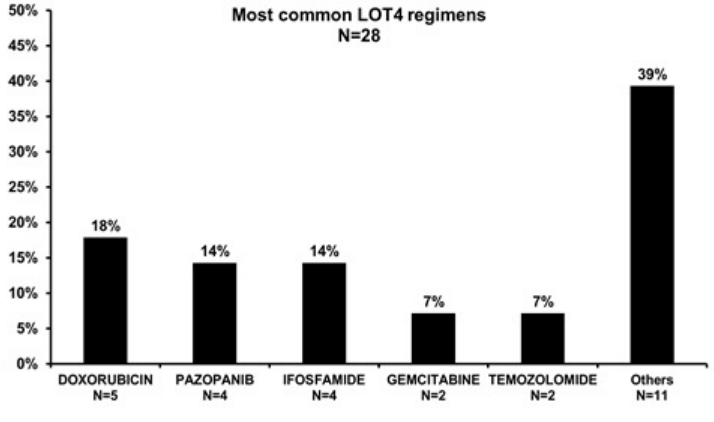
Results: A total of 555 mSTS patients met all study criteria; 65% commercially insured and 35% Medicare Advantage enrollees. Mean age was 59 years (standard deviation, SD 16 years) and 54% were male. The mean length of follow-up was 326 days (SD 265 days). During the study period, 41% (n=229) of patients initiated ≥2 LOTs; 16% (n=88) had ≥3 LOTs and 5% (n=28) had ≥4 LOTs. The mean durations of LOT1 to LOT4 were 111 days (SD 89 days), 85 days (SD 69 days), 90 days (SD 62 days) and 94 days (SD 76 days), respectively. The most common regimens by LOT are shown in the Figure. Docetaxel+gemcitabine was most common in LOT1, pazopanib in LOT2 and LOT3, and doxorubicin in LOT4. Among patients with pazopanib in LOT2 and LOT3, the most common prior regimen was docetaxel+gemcitabine (47% and 30% respectively).

Conclusion: Choice of regimen by LOT among patients with mSTS is varied; < 65% of patients in any LOT received the 5 most common regimens. Pazopanib, the only approved targeted therapy, is being adopted in second and later lines of therapy and is mostly given post









docetaxel+gemcitabine. Future studies should examine optimal sequencing of treatment and compliance with therapy for best outcomes by STS subtype.

P2–Poster 191 2529964

TREATMENT OF BONE AND SOFT-TISSUE SARCOMA PATIENTS IN JAPAN – THE DISTRIBUTION OF PATIENTS AND MEDICAL SPECIALTIES BY CANCER TOPOGRAPHY AND TREATMENT MODALITY

Makoto Endo, MD, PhD; Momoko Iwamoto; Shunichi Toki; Takeshi Hirose; Takenori Uehara; Masato Sugawara; Tomoaki Mori; Koki Shimizu; Eisuke Kobayashi; Yoshikazu Tanzawa; Fumihiko Nakatani; Hirokazu Chuman; Takahiro Higashi; Akira Kawai
National Cancer Center, Tokyo, Japan

Objective: Sarcoma clinical guidelines often emphasize the evaluation of patients by an expert multidisciplinary team, and thus in many countries, care is centralized to treatment centers. However, there are no standard guidelines for referrals of sarcoma patients in Japan, and the overall picture of where and by whom they are treated has never been systematically investigated.

Methods: We used hospital-based cancer registry and health claims data of sarcoma patients diagnosed in Japan in 2012 and 2013. We analyzed the distribution of patients across hospitals and the extent of centralization of care across treatment modality (surgery, radiation, neoadjuvant, and adjuvant chemotherapies) and cancer topography.

Results: We identified 1032 bone and 7257 soft-tissue sarcoma (STS) patients who were newly diagnosed in 2012 and 2013. Bone sarcomas occurred in the limbs in 55% of the patients, with 73% treated by orthopedic surgeons and 12% by pediatricians. Care was weakly centralized to 9 high-volume hospitals (> 10 new cases per year) and 120 hospitals with 1-9 new cases. Care was greatly decentralized for STS (particularly surgical care). STS patients were treated in 382 hospitals in total, including 272 hospitals with 1-9 new cases. The distribution of medical specialties depended heavily on cancer topography: 50% of STS occurred in connective tissues (among them, 70% were treated by orthopedic surgeons), 12% in the peritoneum and retroperitoneum (33% urologists, 38% general surgeons, 9% gynecologists), 11% in the uterus (95% gynecologists), and 8% in the skin (64% dermatologists and 23% plastic surgeons). Analysis of medical specialties administering chemotherapies to 318 connective tissue STS patients revealed that orthopedic surgeons provided neoadjuvant/adjuvant chemotherapies to much (> 60%) of the patients.

Conclusion: We found that sarcoma treatment is not only decentralized, but also uncoordinated across medical specialties in Japan due to its diverse cancer topography and lack of standard guidelines for referrals of sarcoma patients. One possible problem in this situation is that a patient with STS is more likely to be treated in a hospital where sarcoma patients are rarely treated. Results of this study suggest the need to establish strategies to centralize patients, especially for STS, to treatment centers where they can be managed by a multidisciplinary team.

P2–Poster 192 2541168

IMPACT OF SUPERVISED PHYSICAL EXERCISE ON FATIGUE AND QUALITY OF LIFE IN ADULT SARCOMA PATIENTS

Leopold Hentschel[1]; Wadim Kisel[3]; Michael Kramer[2]; Frank Kroschinsky[2]; Martin Bornhäuser[2]; Hornemann Beate[1]; Markus K. Schuler[2]
[1]University Cancer Center, University Hospital Carl Gustav Carus, Dresden, Germany; [2]Department of Internal Medicine I, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [3]Department of Orthopaedics and Trauma Surgery, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

Objective: Physical exercise can alleviate cancer related fatigue. To our knowledge, there is no randomized controlled trial (RCT) examining the effect of a non-pharmacological intervention on fatigue in patients with advanced sarcoma. This study aims to test the effect of a 12 week exercise program on fatigue and quality of life (QoL) during chemotherapy.

Methods: 23 adult sarcoma patients were included as part of a subset analysis of a larger RCT, exploring the effect on fatigue of two different exercise programs versus standard of care. Patients in the control group (CG) did either not undergo any specific program or were taught an individualized strength and endurance exercises to be performed five times per week. In the intervention group (IG) patients received additional supervised exercise sessions. Primary outcome was *general fatigue* at 12 weeks (T2), secondary outcomes included QoL (assessed with the EORTC QLQ-C30), walking distance as well as remaining fatigue-dimensions of the Multidimensional Fatigue Inventory (MFI). Minimal clinically important differences (MCID) describe the smallest difference, which patients feel as an improvement without disturbing side effects or excessive costs. It was used to analyze patients' perceived benefits.

Results: The mean age of patients in CG was 48 ± 17.46 and in IG 55.27 ± 16.24 years. More patients were under palliative treatment in IG (8/11) than in CG (6/12). Sarcoma entities are shown in table 1. At baseline (T1), CG reported higher initial pain (p= 0.02), loss of appetite (p= 0.05) and financial difficulties (p= 0.04). At T2, physical fatigue (p=

0.01) and reduced activity (p= 0.05) significantly worsened in the CG while there was no significant change in IG. Between groups, we found no significant difference at T2 in any of the fatigue dimensions. Details are reported in table 2.

Moreover, there was a clinically important decrease of fatigue burden in all dimensions (with exception of physical fatigue) in the IG, while all fatigue-dimensions increased in CG. Details are reported in figure 1. Neither global QoL nor symptoms significantly changed between IG and CG at T2. Details on quality of life and symptoms can be obtained from table 2.

Conclusion: A supervised physical exercise can clinically meaningful alleviate fatigue in patients with advanced sarcoma undergoing active treatment. The analysis of this subsample could be a prerequisite for larger RCTs to test the effect of physical exercise on fatigue, physical capability and quality of life.

Table 1: sarcoma entities

	Tumor entity	Intervention	Treatment stage
Control Group	Rhabdomyosarcoma (n= 3) Ewing Sarcoma (n= 2) Liposarcoma (n= 2) Soft Tissue Sarcoma other (n= 5)	chemotherapy (n= 9) radiation (n= 1) after surgery (n= 9)	curative (n= 6) palliative (n= 6)
Interventional Group	Osteosarcoma (n= 1) Pleomporphic Sarcoma (n= 2) Leiomyosarcoma (n= 2) Synovial Sarcoma (n= 2) Soft Tissue Sarcoma other (n= 4)	chemotherapy (n= 11) radiation (n= 0) after surgery (n= 2)	curative (n= 3) palliative (n= 8)

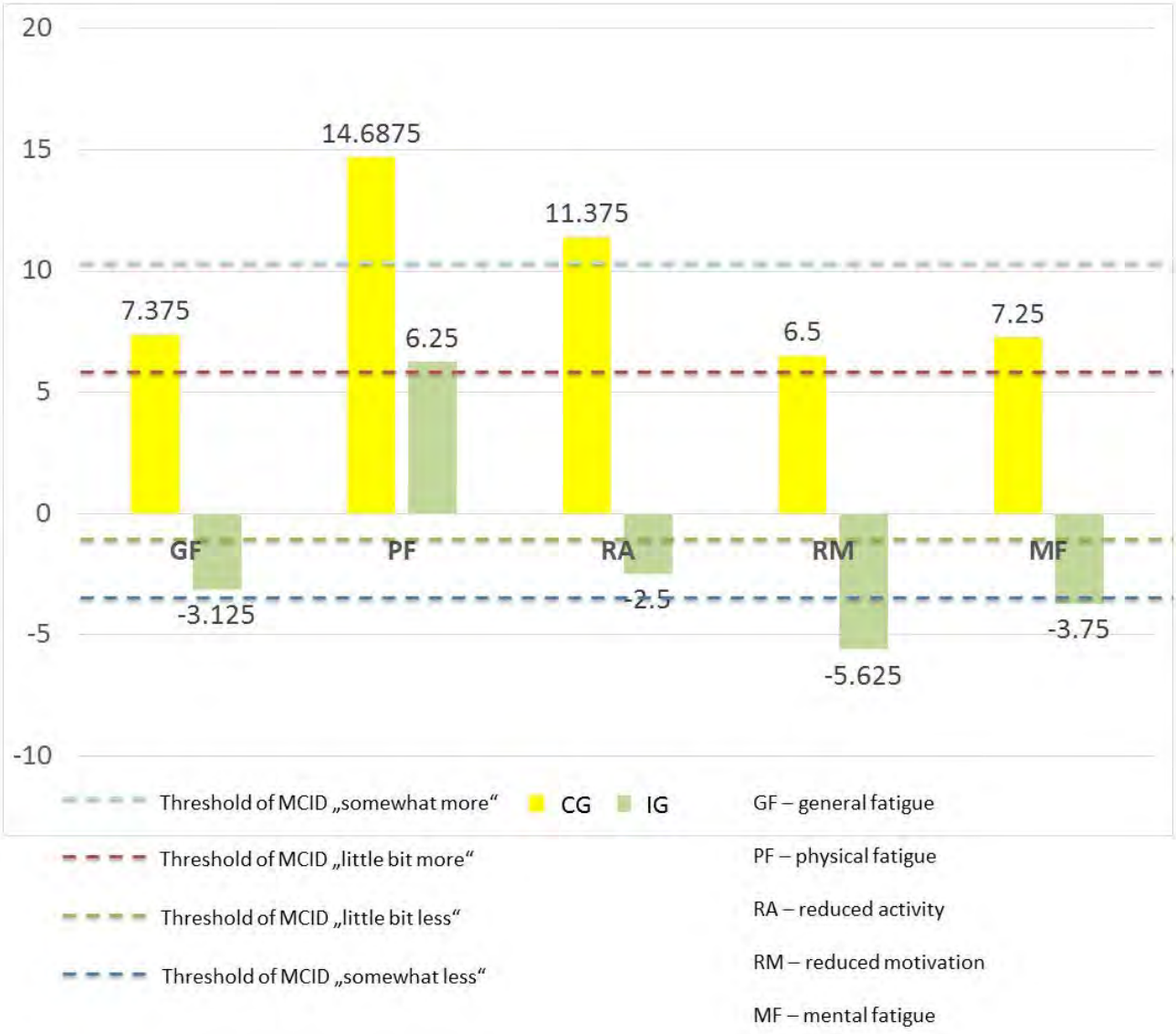


Table 2: means and significances of fatigue and quality of life

		Mean ± SD at T1	p(T1)	Mean ± SD at T2	P (T1 - T2)	p(T2)
MFI - General fatigue	CG IG	11,00 ± 3,64 10,50 ± 4,12	0,77	12,18 ± 4,00 10,00 ± 4,81	0,26 0,28	0.27
MFI - Physical fatigue	CG IG	10,3 ± 4,00 10,30 ± 3,71	0,75	13,18 ± 3,79 11,30 ± 4,42	0,01 0,29	0.31
MFI - Reduced activity	CG IG	10,00 ± 3,07 10,90 ± 4,68	0,59	11,82 ± 3,54 10,50 ± 5,34	0,05 0,10	0,51
MFI - Reduced motivation	CG IG	7,42 ± 2,94 9,70 ± 3,92	0,13	8,46 ± 3,45 8,80 ± 2,62	0,20 0,12	0,80
MFI - Mental fatigue	CG IG	7,75 ± 2,99 9,20 ± 4,69	0,39	8,91 ± 2,91 8,60 ± 3,24	0,13 0,14	0.82
QLQ-C30 - Global health	CG IG	56,25 ± 13,35 64,17 ± 13,64	0,19	55,30 ± 18,36 59,17 ± 21,68	0,75 0,72	0.66
QLQ-C30 Physical functioning	CG IG	72,22 ± 14,45 82,67 ± 17,83	0,14	67,27 ± 15,90 78,00 ± 22,01	0,44 0,94	0.21
QLQ-C30 Role functioning	CG IG	50,00 ± 38,27 65,00 ± 40,41	0,38	45,45 ± 22,47 58,33 ± 33,56	0,61 0,92	0.31
QLQ-C30 Emotional functioning	CG IG	70,14 ± 17,93 80,00 ± 22,64	0,27	72,73 ± 17,91 68,33 ± 21,08	0,71 0,13	0.61
QLQ-C30 Cognitive functioning	CG IG	83,33 ± 21,32 83,33 ± 19,24	1,00	74,24 ± 20,23 78,33 ± 22,29	0,10 0,54	0.66
QLQ-C30 Social Functioning	CG IG	45,83 ± 28,54 66,67 ± 19,25	0,06	50,00 ± 37,27 68,33 ± 19,95	0,59 0,75	0.18
QLQ-C30 Fatigue	CG IG	48,15 ± 23,85 38,89 ± 14,10	0,29	44,44 ± 28,97 36,67 ± 31,88	0,80 0,99	0.56
QLQ-C30 Nausea and vomiting	CG IG	18,06 ± 35,15 1,67 ± 5,27	0,16	10,61 ± 13,48 5,00 ± 8,05	0,39 0,32	0.27
QLQ-C30 Pain	CG IG	38,89 ± 22,84 16,67 ± 15,71	0,02	25,76 ± 31,94 16,67 ± 23,57	0,16 0,10	0,47
QLQ-C30 Dyspnoea	CG IG	25,00 ± 28,87 30,00 ± 29,19	0.69	24,24 ± 26,21 33,33 ± 31,43	0,86 0,22	0.48
QLQ-C30 Insomnia	CG IG	27,78 ± 23,92 16,67 ± 28,33	0,33	27,27 ± 29,13 16,67 ± 28,33	0,83 0,89	0.41
QLQ-C30 Appetite loss	CG IG	25,00 ± 25,13 6,67 ± 14,05	0,05	24,24 ± 39,70 3,33 ± 10,54	0,89 0,89	0.12
QLQ-C30 Constipation	CG IG	11,11 ± 21,71 23,33 ± 27,44	0,26	27,27 ± 38,92 16,67 ± 23,57	0,09 0,10	0.47
QLQ-C30 Diarrhea	CG IG	2,78 ± 9,62 3,33 ± 10,54	0,90	9,09 ± 15,57 3,33 ± 10,54	0,39 0,56	0.34
QLQ-C30 Financial difficulties	CG IG	38,89 ± 39,78 10,00 ± 16,10	0,04	42,42 ± 42,40 20,00 ± 23,31	0,44 0,67	0.16

MFI - Multidimensional Fatigue Inventory; QLQ-C30 - European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30; CG - control group; IG - interventional group; SD - standard deviation

P2–Poster 193 2540447

PATIENT-DIRECTED INTERVENTION TO IMPROVE QUALITY OF LIFE (QOL) FOR PATIENTS WITH SOFT TISSUE SARCOMA (STS) UNDERGOING PALLIATIVE TREATMENT: A MULTICENTER, CLUSTER-RANDOMIZED, CONTROLLED TRIAL OF THE GERMAN INTERDISCIPLINARY SARCOMA GROUP

Leopold Hentschel[1]; Ulrich Schuler[2]; Hornemann Beate[1]; Andrea Schilling[3]; Janet Freitag[4]; Stephan Richter[4]; Markus K. Schuler[4]

[1]University Cancer Center, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [2]University Palliative Center, University Hospital Carl Gustav Carus, Dresden, Germany; [3]Department of Social Work, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [4]Department of Internal Medicine I, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

Objective: In spite of evolving therapeutic options for the treatment of advanced STS, the balance between efficacy and toxicity still remains a major concern. Therefore, it is crucial to assess treatment effectiveness both as disease-related and Patient Reported Outcomes (PRO). Growing experience demonstrates the feasibility of electronic data capturing of PRO. Furthermore, the role of a structured multi-professional intervention for supportive care remains undefined in STS. The YonLife trial (NCT02204111) aims to test the feasibility and assess the effect of a tailored palliative intervention in adult STS patients under palliative treatment with trabectedin.

Methods: The YonLife trial is the first prospective, multi-center, cluster-randomized, controlled, proof of concept study of patients with advanced STS to explore the effect of multi-professional expert-consensus derived treatment proposals on QoL. Adult patients undergoing treatment with trabectedin are being recruited in seven German hospitals. The seventh hospital serves as a reference center in order to pretest the planned study design. A 1:1 cluster randomization of the hospitals for multi-professional intervention or standard of care is applied. Patients are requested to answer standardized PRO-measures on a tablet-PC four times during nine weeks of treatment, which enables immediate scoring, adaptive testing and full Web access to the obtained data. The primary objective is the explorative analysis of the change of QoL-score after nine weeks. Secondary objectives include feasibility aspects and changes of further PRO.

Results: Enrollment began in October 2014 and so far 62 out of 77 planned patients have been included.

Conclusion: In due course, the YonLife trial will provide more knowledge about QoL in patients with advanced STS. For the first time, PRO are electronically assessed and included in a prospective trial in this disease. Additionally, the benefit of tailored palliative intervention also will be investigated.

P2–Poster 194 2529827

USING A MODIFIED DELPHI PROCESS TO IDENTIFY QUALITY INDICATORS FOR SARCOMA SERVICES

Michelle Ghert, MD, FRCSC[1]; Cassandra McKay[2]; Amanda Wong[2]; Sherrie Hertz[2]; Charles Catton[4]; Jonathan Irish[4]; Rita Kandel[3]

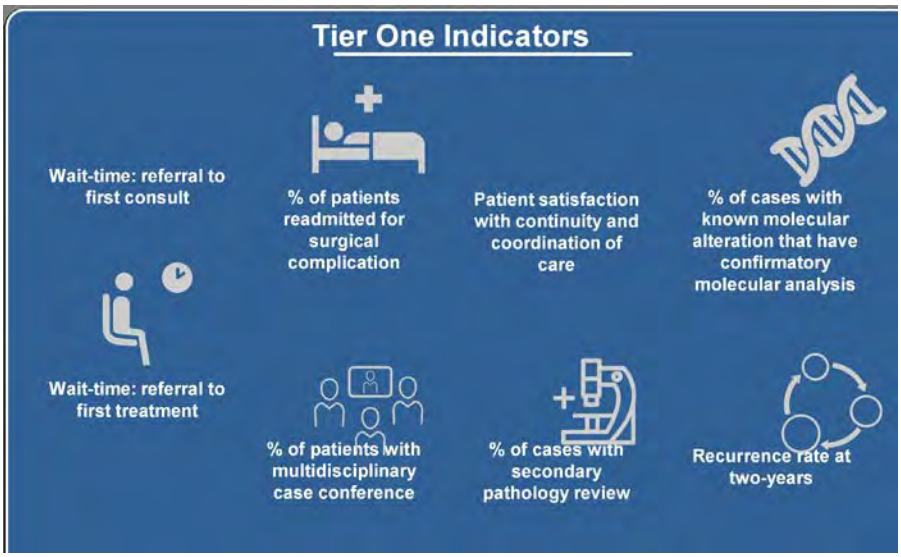
[1]Surgery, McMaster University, Hamilton, ON, Canada; [2]Cancer Care Ontario, Toronto, ON, Canada; [3]Mount Sinai Hospital, Toronto, ON, Canada; [4]University Health Network Princess Margaret Hospital, Toronto, ON, Canada

Objective: The appropriate investigation, management and rehabilitation of patients with sarcoma require a high degree of coordination among healthcare disciplines. The Provincial Sarcoma Services Plan provides an overview of how adult sarcoma services are organized in Ontario. In order to measure the implementation of the Plan and the quality of sarcoma services across the care continuum, there was a need to identify key quality indicators (QI).

Methods: A modified Delphi process was used to identify QIs relevant to sarcoma care in Ontario. Potential QIs were identified through a systematic literature review and were suggested by Working Group members. Clinicians, administrators and allied health professionals involved in sarcoma care across the province participated in two electronic questionnaires to assess identified indicators on five criteria: usefulness, validity, action-ability, discrimination and feasibility. An Expert Panel meeting was held to deliberate the results and identify and prioritize the key QIs based on criticality for the Program.

Results: Twenty possible QIs were identified through a literature review and 89 potential QIs were suggested by working group participants. Through the modified Delphi process, eight top ranked indicators, classified as Tier One Indicators, were identified as the most critical for evaluating the quality of the sarcoma services in Ontario. These eight indicators, shown in **Figure 1**, covered multiple domains of the disease spectrum (number of QIs in parentheses): overall treatment related wait-time measures (n=2), overall process measure (n=1), pathology (n=2), surgery (n=1), and overall patient outcomes (n=2).

Conclusion: A systematic, consensus-based approach was used to determine relevant QIs for the Sarcoma Program. The eight Tier One QIs will provide a means of evaluating the quality of sarcoma care as outlined in the Provincial Sarcoma Services Plan in an effort to provide coordinated access to expert, multidisciplinary sarcoma care.



P2–Poster 195 2565122

SURVIVAL IN SOFT TISSUE SARCOMA (STS) FOLLOWING PRESENTATION OF FIRST METASTASIS OR OLIGOMETASTASES

Gerard Walls; Shane Zaidi; Omar Al-Muderis; Komel Khabra; Charlotte Benson; Robin Jones; Ian Judson; Aisha Miah
The Royal Marsden NHS Foundation Trust, London, Surrey, United Kingdom

Objective: Metastastic STS is associated with poor outcomes. Oligometastases, defined as those metastases affecting one or a limited number of organs, is increasingly recognised as an opportunity to control disease burden in the longer term. 25% STS cases develop pulmonary oligometastases (PM). Surgery, radiofrequency ablation (RFA) and radiotherapy (RT) are recommended in selective cases, but supportive data are lacking. Currently at our institution, treatment is decided following multidisciplinary discussion of individual cases. The investigators evaluated the selection of local therapy and current prognosis of patients with their first (oligo)metastasis.

Methods: Retrospective analysis of a prospectively collected database of all new STS cases discussed at a tertiary centre MDM 2009-2012, which developed metastatic disease. Overall survival (OS) and progression-free survival (PFS) following local therapies, palliative systemic therapy and best supportive care (BSC) were calculated.

Results: 223 patients (111 male) discussed at the tertiary MDM developed new metastases. Overall survival at median follow-up of 2 years was 37%. Median age at diagnosis was 59 years. Median disease-free interval was 1.2 years. Median OS from treatment of metastasis 1.3 years. The 2-year survival data for patients managed by palliative and targeted therapies are presented in Tables 1 and 2 respectively. Median PFS for treated PM 1.6 years, non-PM 0.5 years. Further survival data is available in Figure 1. Limitations of the study: low patient numbers and diversity of histology, pre-treatment and relapse site.

Conclusion: The survival of patients with metastatic STS varies by treatment, amongst other factors. Patients receiving surgery for metastatic disease or targeted therapies for oligometastases have better outcomes compared with palliative strategies. The selection of patients for local therapies remains unclear however it may be that those with naturally indolent disease have been chosen. Histological diversity and clinician bias may also have a role. The results presented equip oncologists for conversations with patients, and assist with case selection for local therapies. This study provides useful preliminary data for the NCRI Sarcoma CSG's research strategy in this field. Factors including quality of life measures that appropriately stratify patients to treatments should be investigated in a controlled randomised trial.

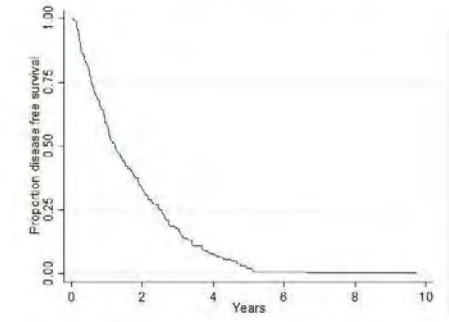
Table 1: 2-year OS following palliative treatment of first recurrence

Palliative Treatment	2 year OS
Chemotherapy (n=125)	27%
Surgery (n=50)	60%
Best Supportive Care (n=40)	3%

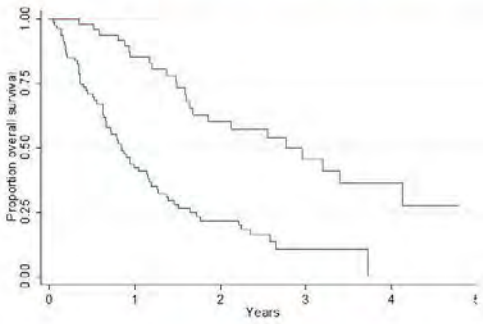
Table 2: 2-year OS and PFS for patients presenting with oligorecurrence

Targeted Treatment	2 year PFS	2 year OS
Metastectomy	20%	62%
Radiofrequency Ablation	14%	54%
Radiotherapy	0%	40%

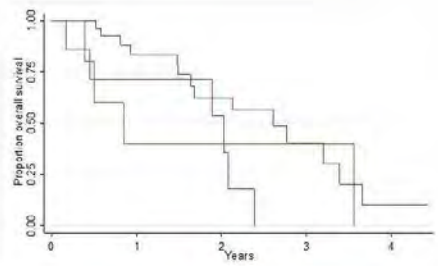
Figure 1: Kaplan-Meier analyses of DFS (all patients), OS (chemotherapy V surgery), OS and PFS (targeted therapies)



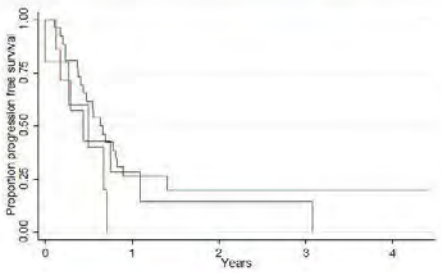
Disease-free survival (all patients)



OS for palliative **chemo** (excl GIST) versus **surgery**



OS for **metastastectomy** versus **RFA** versus **RT**



PFS for **metastastectomy** versus **RFA** versus **RT**

P2–Poster 196 2570715

ADULT RHABDOMYOSARCOMA: A RETROSPECTIVE ANALYSIS OF 40 PATIENTS TREATED AT A SINGLE INSTITUTION

Ann Raldow[1]; Alex Jacobson[2]; Saveli Goldberg[2]; Haotong Wang[2]; Edwin Choy[3]; Gregory M. Cote[3]; Francis Hornicek[4]; Thomas F. DeLaney[2]; Yen-Lin Chen[2]
[1]Department of Radiation Oncology, UCLA, Los Angeles, CA, USA; [2]Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA; [3]Department of Medical Oncology, Massachusetts General Hospital, Boston, MA, USA; [4]Department of Surgical Oncology, Massachusetts General Hospital, Boston, MA, USA

Objective: Rhabdomyosarcoma (RMS) is a soft tissue malignancy thought to originate from immature striated skeletal muscle cells. Nonetheless, RMS can arise in sites where skeletal muscle is not normally found. RMS is rare in adults, accounting for 2-5% of adult soft tissue sarcomas, and most often arises in the head and neck region. Experience with treatment of adults with RMS is limited, but data suggest that adults have inferior outcomes compared with children. The purpose of this retrospective study is to review the clinical outcomes of adult patients diagnosed with RMS.

Methods: The clinicopathologic features, treatment methods, and disease outcomes were reviewed retrospectively for 40 adults (patients ages 18 years or older) with RMS treated between 2003 and 2015 at a single institution. Overall survival (OS) and recurrence-free survival (RFS) were estimated using the Kaplan-Meier method.

Results: Mean age was 45 (range: 19-81), median follow-up time was 16.2 months, (range 0.8 – 140 months) and 23 (57.5%) of patients were female. Patients presented with localized (24, 60.0%), regional (4, 10.0%), distant (11, 27.5%), and undetermined (1, 2.5%) extents of disease. Tumor sites included head & neck (15, 37.5%), upper extremity/shoulder (2, 5.0%), lower extremity (6, 15.0%), thorax (1, 2.5%), trunk (2, 5.0%), spine/sacrum/bony pelvis (1, 2.5%), abdomen/pelvis/peritoneum/gastrointestinal tract (7, 17.5%), retroperitoneum (2, 5.0%), gynecologic (3, 7.5%), and ill-defined/not specified (1, 2.5%). RMS histology groups were alveolar (13, 32.5%), pleomorphic (9, 22.5%), embryonal (7, 17.5%), and not otherwise specified (11, 27.5%). Patients were treated according to the following categories: No Surgery & No radiation (RT) (3, 7.5%), Surgical Treatment, No RT (7, 17.5%), No Surgery, RT alone (17, 42.5%), Preoperative RT -> Surgery (6, 15.0%), Preoperative RT -> Surgery -> Postoperative RT (1, 2.5%), Surgery -> Postoperative RT (6, 15.0%) The majority of patients received chemotherapy on presentation (33, 82.5%); vincristine, adriamycin, cyclophasphamide alternating with ifosfamide and etoposide (VAC/IE) was the most common regimen. 5-year OS and RFS were 34.4% (95% CI: 18.1-51.3) and 31.8% (95% CI: 14.8-50.4), respectively.

Conclusion: Adult RMS is an aggressive tumor with a significant incidence of metastatic recurrence; however, there are long-term survivors. Further study is necessary to determine whether adult patients who adhere to guidelines for treatment of pediatric RMS have superior outcomes.

	Overall Survival (95% CI)	Recurrence Free Survival (95% CI)
6 months	89.7% (74.8-96.0)	81.7% (65.3-90.8)
1 year	72.3% (54.6-84.1)	58.6% (40.8-72.7)
2 years	38.7% (21.9-55.2)	47.7% (29.9-63.5)
5 years	34.4% (18.1-51.3)	31.8% (14.8-50.4)

P2–Poster 197 2569029

A MODEL FOR INTERNATIONAL MULTIDISCIPLINARY TEAMS TO ADDRESS THE SARCOMA DISEASE BURDEN IN LOW- AND MIDDLE-INCOME SETTINGS

Theoneste Nkurunziza[1]; Dayo Fadelu[3]; Cyprien Shyirambere[6]; Djamilla Uwimanzi[1]; Raphael Kalengayi[5]; Belson Rugwizangoga[2]; Thierry Zawadi [4]; Faustin Ntirenganya[2]; Jennifer Kreshak[7]

[1]Inshuti Mu Buzima/Partners in Health, Kigali, Rwanda; [2]Centre Hospitalier Universitaire de Kigali, Kigali, Rwanda; [3]Dana Farber Cancer Institute, Boston, MA, USA; [4]Kanombe Military Hospital, Kigali, Rwanda; [5]King Faisal Hospital, Kigali, Rwanda; [6]Inshuti Mu Buzima/Partners in Health, Butaro, Rwanda; [7]Harvard Medical School, Boston, MA, USA

Objective: Cancers represent 27% of all global NCD deaths under the age of 70. More than two-thirds of these occur in low- and middle-income countries (LMIC). The economic cost of this disease burden is estimated to be greater than 1 trillion USD. Although over 80% of new cancer cases require surgery, less than 25% of these patients have access to safe, timely surgical care. Despite this high global burden, cancer treatment is often considered too costly and complex to undertake safely and successfully in LMICs.

Methods: A multidisciplinary team was built to address care needs of sarcoma patients in an LMIC. Local care providers saw patients at the largest national referral hospital, the national cancer center, and several district hospitals. Sarcoma specialists visited for a few weeks to months to teach and advise. Using e-medicine, local care providers partnered full-time with sarcoma experts at a major United States cancer center and hospitals to discuss cases and care plans.

Results: National treatment protocols modeled on international standards were written/implemented for osteosarcoma and Ewing sarcoma, including detailed chemotherapy regimens. Surgeries were perfomed by local general surgeons and a trained musculoskeletal oncologic surgeon, who advised surgical treatment plans. Chemotherapy was administered at the local cancer center by internists, general practitioners, pediatricians, and nurses; treatment plans were guided by medical and pediatric oncology, radiation oncology, pathology, radiology, and surgical oncology experts at the U.S. center. Care was closely integrated between local hospitals via dedicated nurses. Treatment plans were discussed during weekly phone meetings which served as tumor boards; communication flowed freely at all times by email and individual phone calls. Pathology specimens were reviewed at the local cancer center, by telepathology, and/or at one of the U.S. hospitals.

Conclusion: This novel multidisciplinary, international team demonstrates that partnership between local LMIC providers and foreign specialists brings knowledge and skills to patients in the absence of robust “on the ground” expertise. Doing so has the additional benefit of helping to train local providers. This effort increases the amount and quality of sarcoma care until the country is able to build their own teams of local specialty care providers. Moreover, it serves to build strong international, bidirectional partnerships.

P2–Poster 198 2544196

THE OUTCOME OF LIMB SALVAGE SURGERY IN DEVELOPING COUNTRY, KHCC EXPERIENCE

Ahmad Shehadeh
KHCC, Amman, Jordan

Objective: Limb salvage surgery (LSS) became the standard surgical treatment for bone sarcomas since the late 1970s; however, LSS has high cost and numerous complications that make it less applicable in developing countries.

To Show that LSS in developing countries, can be compared to developed countries, when; team work, expert surgeon and enough resources are available.

Methods: Since July 2006, a multidisciplinary team of sarcoma was established. This team consisted of pediatric and medical oncologists, radiation oncologists, radiologist, nurse coordinator and a full-time orthopedic oncology surgeon. The team was supported by a service for physical therapy. Clinical practice guidelines were established and a special protocol for rehabilitation following surgery was applied. One hundred and thirty three patients with malignant or benign aggressive bone tumors presented at the study period, 18 patients received primary amputation, 115 patients received LSS (87 % of all patients) included in our analysis, with mean follow up of 34 months (range, 6-70 months). Tumors were located in the extremities (n=104), in the scapula (n=4) and the pelvis (n=7).

Results: At 4 yr. median follow up, local control was achieved in 89% of patients , 84% of patients has no complications,8% developed infection,97% of limbs survived, MSTS functional score=87%.

Conclusion: Our early results are encouraging. Patients with sarcoma are managed better within a multidisciplinary team that is familiar with highly specialized procedures including LSS. The early outcomes of our cases are comparable to that in developed countries in term of local control and prosthesis related complications.

P2–Poster 199 2565841

THE NOSARC PROJECT, A NATIONAL, PROSPECTIVE AND POPULATION-BASED STUDY OF MUTATIONS AND MECHANISMS IN SARCOMAS, AND PRECLINICAL VALIDATION OF NOVEL TARGETED THERAPIES, WITH THE INTENTION TO LEAD TO CLINICAL TRIALS

Ola Myklebost, Dr Philos[2]; Bodil Bjerkehagen[3]; Kjetil Boye[4]; Heidi Glosli[5]; Kirsten S. Hall[4]; Nina Jebsen[6]; Heidi A. Korsmo[1]; Heidi Knobel[7]; Susanne Lorenz[1]; Leonardo A. Meza-Zepeda[1]; Else Munthe[1]; Stine Næss[4]; Eivind Smeland[8]; Eva W. Stratford[1]; Olga Zaikova[4]

[1]Inst. for Cancer Research, Oslo Univertsity Hospital, Oslo, Norway; [2]Clinical Science, University of Bergen, Bergen, Norway; [3]Pathology, Oslo University Hospital, Oslo, Norway; [4]Oncology, Oslo University Hospital, Oslo, Norway; [5]Pediatrics, Olso University Hospital, Oslo, Norway; [6]Oncology, Haukeland University Hospital, Bergen, Norway; [7]Oncology, St Olav University Hospital, Bergen, Norway; [8]Oncology, University Hospital for Northern Norway, Tromsø, Norway

Objective: The Norwegian Sarcoma Consortium, NoSarC, is a subproject of the Norwegian Cancer Genomics Consortium (see cancergenomics.no and nosarc.no), and is a clinical scale model for the introduction of personalized strategies for orphan cancers. One objective is to understand better sarcoma biology. However, we also hope to identify biomarkers indicating sensitivity to therapies already developed and approved for treatment of more common cancers. A subproject is to validate candidate therapies in preclinical sarcoma models, to support their clinical use. This unique project is based on the collaboration with the clinical sarcoma centres in all health regions of Norway, and is intended to feed new candidate approaches to trial designs adapted for small patient groups, hopefully as part of international networks like SSG and WSN.

Methods: We have initiated collection of a prospective, population-based biobank of samples from all patients treated at the Norwegian university hospitals with sarcoma centres. Current funding allows collection of 2-3 annual cohorts, but the intention is 5, i.e. up to 1000 patients, although we do not get fresh tumour tissue from all. We are also developing new *in vivo* and *in vitro* models representing the most aggressive sarcomas, to obtain improved models with known germline and somatic variants.As a complementary strategy, we are doing medium-scale drug screens to discover new therapies not predictable from genome data.

Results: Currently we have samples from almost 400 patients, and frozen tumour tissue from the majority. NGS exome analysis is on-going, and the first batch of germ line data has been used as a validation cohor for the International Sarcoma Kindred Study (Ballinger et al, Lancet Oncology, in press). Several targets, including FGFR and PARP inhibitors, are being investigated in sarcoma models, and with in vivo pdx results, clinical investigations may be initiated.

Conclusion: A population-based sarcoma cohort is an important resource for investigation on mechanisms and new therapeutic targets, new biomarkers, and genetic predisposition. A panel of preclinical models complements these discoveries by allowing mechanistic studies and preclinical validation of drug activity in mesenchymal cells and tissues. We hope this will lead to new treatment options that may be evaluated in clinical trials.

P2–Poster 200 2558371

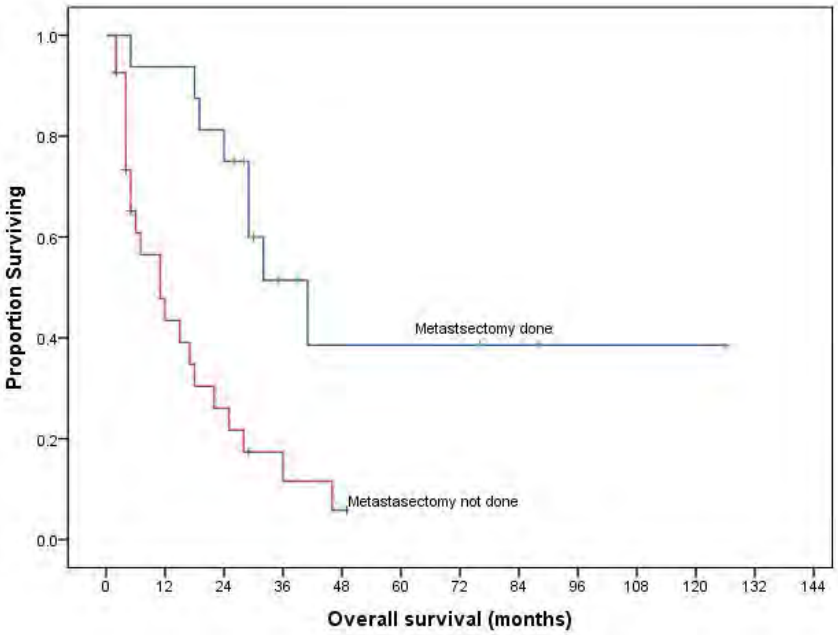
OUTCOME AFTER SURGERY FOR EXTREMITY SOFT TISSUE SARCOMA IN PATIENTS PRESENTING WITH METASTASIS AT DIAGNOSIS

Chandra Kumar Krishnan[2]; Han-Soo Kim[1]; Ilkyu Han, MD, PhD[1]

[1]Orthopedic Surgery, Seoul National University Hospital, Seoul, Korea (the Republic of); [2]Cancer Institute (WIA), Chennai, India

Objective: Around 12-23% of extremity STS patients present with synchronous metastatic disease at diagnosis. Although the prognoses of these patients are generally poor, some patients live a prolonged life and even are cured of the disease. Identifying the prognostic factors of this subgroup of patients would be helpful in deciding treatment strategies. Prognostic factors of STS patients with metastasis, such as time from initial surgery to metastasis, the performance of metastasectomy and histological grade have been mostly derived from studies targeting STS with metachronous metastases. However, there are only a few studies devoted to extremity STS patients with synchronous metastasis at diagnosis and details on clinicopathological characteristics of these patients remain limited. This study sought to analyze the survival and to identify clinicopathologic factors associated with survival in extremity STS patients presenting with upfront metastasis.

Methods: Among these 476 patients who had undergone surgical removal of extremity STS at our institute, we iden-



Metastasectomy as a prognostic factor for survival. Patients who underwent metastasectomy had a prolonged survival than patients who did not undergo metastasectomy (p=0.001).

tified and included 55 patients (12%) who presented with synchronous metastasis at diagnosis and were reviewed. Patient, tumor and treatment related factors were analyzed for possible prognostic effect on survival.

Results: The median survival of all patients was 22±4.1 months. The 2-year and 5-year survival rates were 45.6% and 18.0% respectively. In univariate analysis, tumor location in lower extremity (p=0.041) and the performance of metastasectomy (p=0.001) were significantly associated with better survival. In multivariate analysis, only the performance of metastasectomy remained significant (HR=3.8, p=0.012). The median survival of patients who underwent metastasectomy was significantly longer than that of patients who did not undergo metastasectomy (41±8.4 months vs. 11±3.8 months, p= 0.001).

Conclusion: Extremity STS patients with upfront metastasis have a poor prognosis. Patients who undergo metastasectomy may have a better chance for prolonged survival.

P2–Poster 201 2565590

CLINICAL FEATURES OF HIGH-GRADE EXTREMITY AND TRUNK SARCOMAS IN PATIENTS AGED 80 YEARS OR OLDER: THE REASONS FOR INFERIOR OUTCOMES

Jungo Imanishi, MD[1]; Lester W. Chan[2]; Matthew Broadhead[2]; Samuel Y. Ngan[4]; John Slavin[3]; Grant Pang[2]; Peter F. Choong[2]

[1]Orthopaedic Oncology and Surgery, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [2]Orthopaeics, St. Vincent's Hospital Melbourne, Fitzory, Victoria, Australia; [3]Pathology, St. Vincent's Hospital Melbourne, Fitzory, Victoria, Australia; [4]Radiation Oncology, Peter MacCallum Cancer Center, East Melbourne, Victoria, Australia

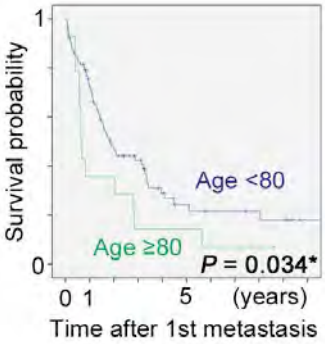
Objective: The aim of this study was to investigate the clinical features and oncological outcomes of high-grade soft tissue sarcomas in the elderly patients in comparison with the younger population, and to assess possible factors that may account for differences in outcomes between age groups.

Methods: This is a single-institutional retrospective study of consecutive non-metastatic, high-grade extremity and trunk sarcomas surgically treated between 1996–2012, with ≥2 years of follow-up for survivors. Patient characteristics and oncological outcomes were compared between age groups, using Chi-square or Fisher-Exact test and Log-Rank or Wilcoxon test, respectively. Patient survivals were calculated in the forms of overall survival (OS), disease-specific survival (DSS), metastasis-free survival (MFS) and local-recurrence-free survival (LRFS). Deaths of other causes were censored for DSS, but deaths of treatment-related complications were regarded as disease-specific mortality.

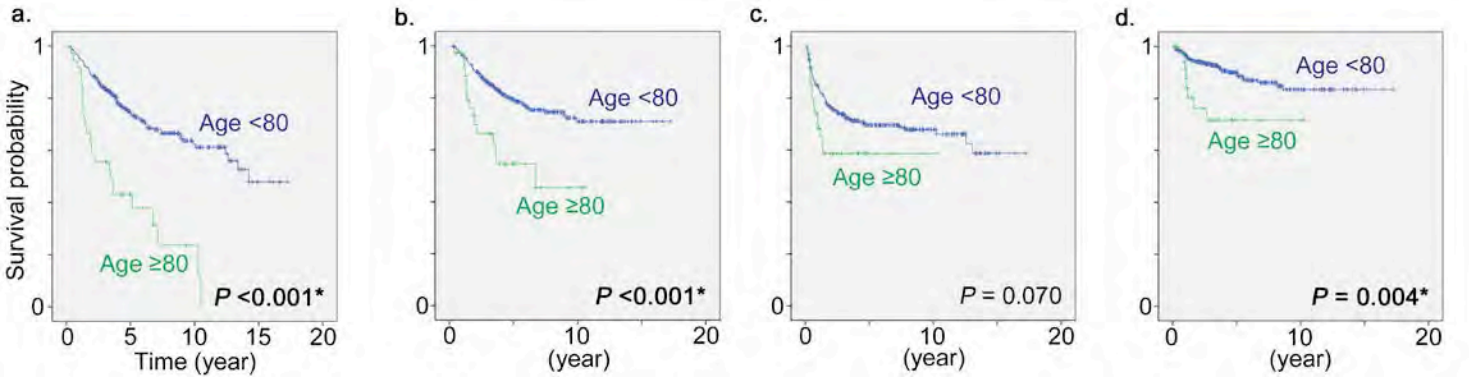
Results: A total of 333 cases were eligible for this study. Thirty-six patients (11%) were aged ≥80 years. The median follow-up for survivors was 82.5 (range: 24–206) months. The older group was more often higher FNCLCC grade (*P* = 0.008), with different histotype distribution, but there were no significant difference in surgical margin status (*P* = 0.21). Among the 333 cases, 111 deaths (20/36 deaths those aged ≥80 and 91/297 for those aged <80) were obsereved, of which 31 (6/20 for those aged ≥80 and 25/91 for those aged <80) were regarded as death of other causes. Five-year OS, DSS, MFS and LRFS estimated by the Kaplan-Meier method were 45% (≥80 years) vs. 75% (<80 years) (*P* <0.001), 55% vs. 80% (*P* <0.001), 59% vs. 70% (*P* = 0.07), 72% vs. 90% (*P* = 0.004), respectively. A significant difference was also observed in DSS after first metastasis (*P* = 0.03). Cox analysis with backward elimination method

revealed 'age ≥80 years' as an independent risk factor for local failure and disease-specific mortality, with hazard ratios of 2.60 (95% confidence interval: 1.18–5.71) and 2.52 (1.44–4.44), respectively.

Conclusion: Local control and disease-specific survival for high-grade soft tissue sarcomas were significantly worse in patients aged ≥80 years. Our data suggests that multi-morbidity is not the only cause of inferior clinical outcomes of the geriatric patients. Aggressive tumor biology, higher local recurrence rate and less aggressive treatment for advanced conditions may alternatively explain the inferiority.



Disease-specific survival after first metastasis of FNCLCC grade 2 and 3 sarcomas in patients aged <80 and ≥80 years.



Overall survival (a), disease-specific survival (b), metastasis-free survival (c) and local-recurrence-free survival (d) of FNCLCC grade 2 and 3 sarcomas in patients aged <80 and ≥80 years.

Table 1. Comparison in tumor characteristics between age groups

Characteristics		Age ≥80 years	Age <80 years	P value
Patient gender	Male	23 (64%)	166 (56%)	0.36
Tumor location	Trunk	5 (14%)	30 (10%)	0.48
Histotype	UPS	23 (64%)	110 (37%)	<0.001
	MLS	1 (3%)	15 (44%)	
	Synovial sarcoma	1 (3%)	38 (13%)	
	Leiomyosarcoma	3 (8%)	27 (9%)	
	Myxofibrosarcoma	6 (17%)	23 (8%)	
	Others	2 (6%)	55 (19%)	
FNCLCC grade	Intermediate (G2)	5 (14%)	107 (36%)	0.008
	High (G3)	31 (86%)	190 (64%)	
Adjuvant chemotherapy	(+)	0 (0%)	20 (7%)	0.14
Adjuvant radiotherapy	(+)	32 (89%)	262 (88%)	0.63
Surgical margin	Intralesional or Marginal	4 (11%)	17 (6%)	0.21

UPS undifferentiated pleomorphic sarcoma; MLS myxoid liposarcoma P value for Adjuvant chemotherapy was calculated by 2-tailed Fisher-Exact test.

P2–Poster 202 2525004

DISTANT METASTASIS IN PATIENTS WITH MYXOFIBROSARCOMA

Hiroyuki Tsuchie[1]; Mitsunori Kaya[2]; Hiroyuki Nagasawa[1]; Makoto Emori[2]; Naohisa Miyakoshi[1]; Toshihiko Yamashita[2]; Yoichi Shimada[1]

[1]Orthopedic Surgery, Akita University Graduate School of Medecine, Akita, Akita, Japan; [2]Orthopedic Surgery, Sapporo Medical University School of Medicine, Sapporo, Japan

Objective: An unfortunate clinical feature of myxofibrosarcoma is frequent local recurrence. Although almost all reports on myxofibrosarcoma have been focused on local recurrence, they have not discussed distant metastasis. We evaluated the tendencies regarding clinical and histological features of metastasis of myxofibrosarcoma.

Methods: Fifty-eight patients with myxofibrosarcoma were treated in our hospitals (28 males and 30 females, with a mean age of 70 years), and a total of 16 consecutive patients (27.6%) with distant metastases were included in this retrospective study (9 males and 7 females, with a mean age of 77 years). Because there was no patient complicated by both lung and lymph node metastasis, we compared the age, sex, tumor size and location, FNCLCC grade, AJCC stage, and times of the first metastasis from the initial examination between the lung and lymph node groups. In addition, we examined factors affecting the prognosis.

Results: The median follow-up period was 42.9 months (range: 8-142). Eleven of the 16 (68.8%) patients developed pulmonary metastases. The sites of extra-pulmonary metastases were the lymph nodes in 5 (31.3%) of the 16 patients, bone in one patient, subcutaneous in one patient, intramuscular in one patient, and the peritoneum in one patient. The median time in patients who developed distant metastases was 17.4 months (range: 0-59). The onset of the first metastasis in the lung metastasis group (10.3 ± 5.0 months) was significantly shorter than in the lymph node group (32.8 ± 17.7 months) ($P<0.05$). Treatments for metastases were surgery for 4 patients, chemotherapy for 4 patients, and radiotherapy for 5 patients, and outcomes of the 16 patients were NED in 6 patients, AWD in 3 patients, and DOD in 7 patients. The 5-year survival rate of the lung metastasis group was 25% and that of the lymph node group was 100%, and the survival rate in the lymph node metastasis group was better than in the lung metastasis group ($p<0.05$).

Conclusion: Not only lung metastasis but also lymph node metastasis occurs frequently in patients with myxofibrosarcoma.

P2–Poster 203 2569809

A WHOLE BODY MRI STUDY IN TP53 MUTATION CARRIERS AT RISK OF MULTI-ORGAN CANCER

Mandy L. Ballinger, PhD[1]; Sue Shanley[2]; Nicholas Ferris[7]; Kate Moodie[3]; Marion Harris[4]; Alison Trainer[2]; Eveline Niedermayr[5]; Mary-Anne Young[2]; Kate McBride[6]; Bimal Parameswaran[3]; Paul James[2]; David Thomas[1]

[1]Cancer Division, Garvan Institute of Medical Research, Darlinghurst, New South Wales, Australia; [2]Familial Cancer Centre, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [3]Cancer Imaging, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [4]Familial Cancer Centre, Monash Health, Melbourne, Victoria, Australia; [5]Research Division, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [6]University of Sydney, Sydney, New South Wales, Australia; [7]Monash Imaging, Monash Health, Melbourne, Victoria, Australia

Objective: *TP53* is the strongest known genetic risk factor for development of sarcoma. *TP53* mutation carriers have an extremely high lifetime risk of cancer, but comprehensive risk management guidelines are lacking. Internationally, several emerging unpublished reports suggest benefit from surveillance from whole body magnetic resonance imaging (WBMRI). Here we report the prevalence and incidence of investigable lesions of an Australian WBMRI screening program.

Methods: The schedule includes annual whole body MRI, physical examination, full blood evaluation, breast MRI (females), fecal occult blood test (FOBT) and 2-5 yearly colonoscopy/endoscopy. Participants complete psychological measures and cost diaries.

Results: Of 27 participating *TP53* mutation carriers (17F, 10M; age 18-63yrs), 13 individuals report 20 prior cancers. Twelve of 27 baseline scans identified suspicious lesions warranting further investigation (thallium scan, PSA, 9 targeted US/MRI and 5 targeted MRI/US and biopsy). Three clinically asymptomatic malignancies were detected (well-differentiated liposarcoma in the lumbar region; 2 Gleason score 7 & 8 prostate cancers). Twelve second year and 6 third year WBMRI scans have resulted in only one further investigation (chest CT), identifying a benign lung nodule. Baseline physical examinations triggered follow up in 14/27 participants including 7 dermatology reviews, 3 US, biopsy and excision of lip lesion and one gynaecology referral. All blood evaluations (51) and other surveillance tests (8 breast MRI, 16 FOBT, 9 colonoscopies and 6 endoscopies) completed in the course of the study have been normal. Psychological assessments indicate no lasting adverse effects due to participation in the surveillance program.

Conclusion: The detection of 3 localised asymptomatic cancers in 27 screened subjects is higher than the expect-

ed yield from MRI mammography in *BRCA1/2* mutation carriers (2/100). Together with the absence of a negative psychological impact, these data support further evaluation to determine the optimal surveillance schedule.

P2–Poster 204 2570538

PLEOMORPHIC RHABDOMYOSARCOMA: A SINGLE INSTITUTION EXPERIENCE

Anna Maria Frezza[1]; Paola Collini[2]; Chiara Colombo[3]; Carlo Morosi[4]; Silvia Stacchiotti[1]; Salvatore Renne[2]; Claudia Sangalli[5]; Marco Fiore[3]; Stefano Radaelli[3]; Paolo Casali[1]; Alessandro Gronchi[3]

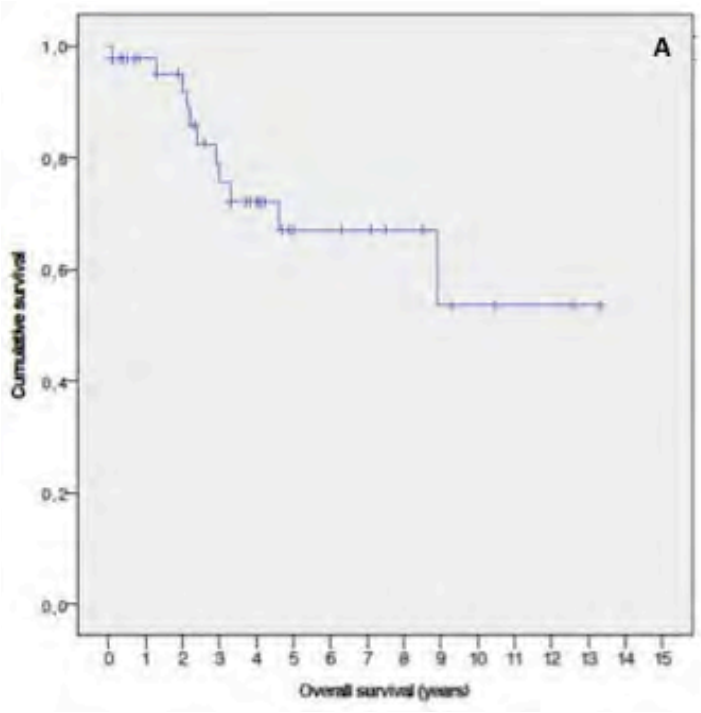
[1]Medical Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [2]Pathology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [3]Surgery, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [4]Radiology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [5]Radiation Oncology, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

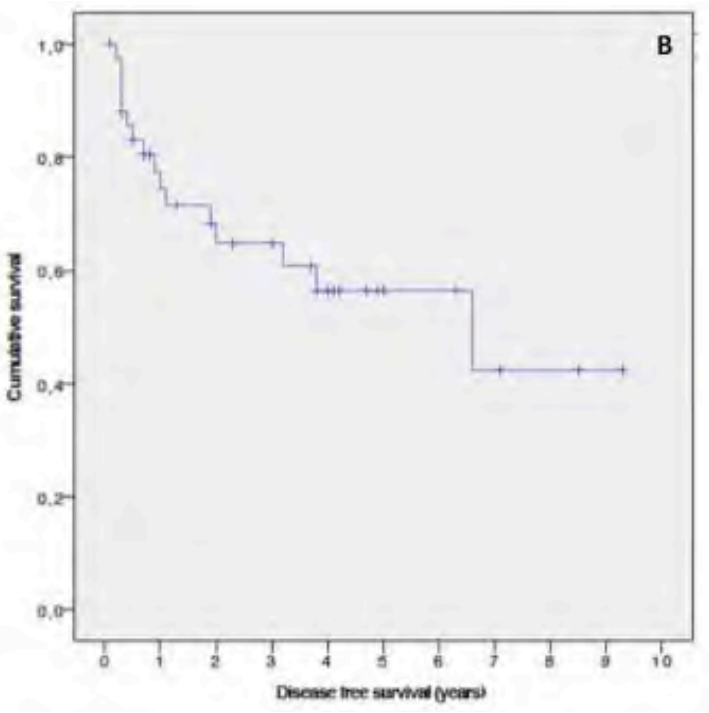
Objective: Pleomorphic rhabdomyosarcoma is a rare type of soft tissue sarcoma whose natural history is still poorly understood and the best management is to be defined.

Methods: Between 2002 and 2015, 44 patients with localised disease underwent surgery at Istituto Nazionale Tumori, Milan, Italy. Diagnosis was reviewed by an expert pathologist and confirmed on the basis of consistent morphology and immunohistochemical positivity for rhabdomyoblastic markers (myogenin). Patient characteristics, treatment and outcome were analysed.

Results: Among 44 consecutive patients included, 34 were males, 10 females. Median age at diagnosis was 56 years (range: 25-85). Lower limbs were the most common primary site (22 patients; 1 head and neck, 6 upper limbs, 11 trunk, 2 urogenital, 2 retroperitoneal). Median size of the lesion at diagnosis was 6 cm (range: 2-20). All patients received surgery at our institution, 41 for primary disease and 3 for local recurrence (LR). Resection margins at the time of the first surgery were negative in 39 patients, positive in 5. Overall, 21 patients received radiotherapy (RT; 11 preoperative, 10 postoperative), 20 chemotherapy (CT) with anthracycline and ifosfamide (AI; 15 preoperative, 4 postoperative, 1 both); 9 received preoperative chemo-radiotherapy. Of the 7 patients who received preoperative CT only, 5 achieved SD and 2 were not evaluable for response; of the 9 patients who received preoperative CT/RT, 6 achieved PR and 3 SD. With a median follow up of 3 years, 27 patients are currently alive with no evidence of disease. Six patients were lost at follow up. Disease recurrence rate was 36% (LR in 3 patients, metastatic progression in 9, both in 4). The most common site of metastatic progression was the lung. Median overall survival (OS) is unreached (fig. 1a). Median disease free survival (DFS; fig. 1b) was 6.6 years (95% CI: 1.2-12.0). Size > 5 cm was shown to be a significant predictor of OS (P=0.023). In patients developing metastatic progression, signs of activity were seen with trabectedin and gemcitabine plus vinorelbine.

Conclusion: Pleomorphic rhabdomyosarcoma is an aggressive disease mainly arising in extremities and affecting older patients. Recurrence rate and survival in this series, the largest currently available, is favourable compared to previously reported series, suggesting the hypothesis that a multimodal treatment approach could improve outcome in this subgroup.





P2–Poster 205 2570674

PEDIATRIC-TYPE RHABDOMYOSARCOMA IN ADULTS: A RETROSPECTIVE ANALYSIS FROM THE SPANISH GROUP FOR RESEARCH ON SARCOMA (GEIS)

Nadia Hindi, MD[1]; Pablo Luna[2]; Antonio Lopez-Pousa[3]; Jordi Rubio[4]; Claudia Valverde[5]; Javier Martinez-Trufero[6]; Jeronimo Martinez[7]; Maria Angeles Sala[8]; Juan Luis Arranz[9]; Fatima Toscano[10]; Rosa Alvarez[11]; Juana Maria Cano[12]; Nuria Lainez[13]; Ana de Juan[14]; Javier Martin-Broto[1]

[1]University Hospital Virgen del Rocio, Seville, Spain; [2]University Hospital Son Espases, Palma de Mallorca, Spain; [3]San Pau University Hospital, Barcelona, Spain; [4]Instituto Catalan de Oncologia (ICO), Girona, Spain; [5]University Hospital Vall d'Hebron, Barcelona, Spain; [6]University Hospital Miguel Servet, Zaragoza, Spain; [7]University Hospital La Arrixaca, Murcia, Spain; [8]University Hospital Basurto, Bilbao, Spain; [9]Fundacion Jimenez Diaz, Madrid, Spain; [10]Hospital Juan Ramon Jimenez, Huelva, Spain; [11]University Hospital Gregorio Marañon, Madrid, Spain; [12]University Hospital Ciudad Real, Ciudad Real, Spain; [13]Navarra Hospital, Pamplona, Spain; [14]University Hospital Marques de Valdecilla, Santander, Spain

Objective: Rhabdomyosarcoma (RMS) in adults is a rare and aggressive disease. Standard chemotherapy regimens developed in pediatric population fail to obtain similar results in adults. The aim of this retrospective study is to describe the experience of the Spanish Group for Research on Sarcoma (GEIS)

Methods: Pts diagnosed with RMS (excluding pleomorphic histology) from august 1994 to march 2016 and included in the on-line GEIS registry were reviewed. Data regarding clinical and histopathological characteristics, therapy and survival were collected. Radiological responses were evaluated by RECIST. Kaplan-Meier method was used for overall survival (OS) and event-free survival (EFS).

Results: We identified fifty-six pts with RMS: Median age at diagnosis 28.5y (17-72), M/F=27/29. Twenty-five pts had alveolar RMS, 26 pts embryonal RMS, five pts RMS non-other specified (NOS). Site of primary tumor was head and neck in 23 pts, pelvis in 15 pts, limbs in 13 pts, and other in 5 pts. Stage at diagnosis was localized/metastatic in 43/13. Those pts with localized disease underwent surgery 31/43, radiotherapy 30/43 and chemotherapy 39/43 (median number of cycles 6.5) and achieved complete clinical remission (CR) in 25/43. With a median follow-up from diagnosis of 20 mos (1-152), 28/43 pts have relapsed, with a median EFS of 16.3 mos (95% CI 5.3-27.3) and 18/43 pts have died, with a median OS of 78.8 mos (95% CI 1-157), and 2 and 5-year OS rates of 88% and 65% respectively. OS according to IRS risk group (Standard/High/Very high risk) was: not achieved/81.5mos/19.6mos respectively (p=0.005). Those pts achieving a CR after upfront therapy had a median OS of 70.8mos and those pts with residual disease had a median OS of 40.8mos (p<0.0001).

Those pts with advanced disease at diagnosis underwent surgery 9/13, radiotherapy 4/13 and chemotherapy 12/13, and achieved complete clinical remission (CR) in 2/13. With a median follow-up from diagnosis of 11.5 mos (1-258), 6/13 pts have died, with a median OS of 31.3 mos (95% CI 10-52), and 2 and 5-year OS rates of 76% and 46% respectively.

Conclusion: IRS risk group and complete remission after upfront therapy were prognostic in adult pts with pediatric-type RMS. Outcome from our series is superior for what expected for this population.

P2–Poster 206 2570340

PRIMARY PSEUDOMYOGENIC HEMANGIOENDOTHELIOMA OF BONE: AN ANALYSIS OF 21 CASES TREATED AT ISTITUTO ORTOPEDICO RIZZOLI

Alberto Righi[1]; Marco Gambarotti[1]; Marta Sbaraglia[2]; Daniel Vanel[1]; Angelo Paolo Dei Tos[2]; Piero Picci[1]

[1]Department of Pathology, Rizzoli Institute, Bologna, Italy, Bologna, Italy; [2]Department of Pathology, Treviso Regional Hospital, Treviso, Italy

Objective: Pseudomyogenic haemangioendothelioma (PMHE) is a rarely metastasizing vascular tumor exhibiting peculiar clinical and pathological features, Mainly described in soft tissue, PMHE is often multicentric with distinctive involvement of different tissue planes. Few cases of primary PMHE of bone have been described in the literature so far.

Methods: To better define the clinical behavior of PMEH occurring primarily in bone, we reviewed all 541 cases of primary bone vascular tumors from 1956 through 2016 present in our records.

Results: After morphological and radiological revision associated with immunoistochemical analysis, we reclassified 21 cases as primary PMEH of bone. These patients included 18 male and 4 female individuals ranging in age between 12 and 66 year (median 25 years).

Fifteen patients had multiple tumors with a distinct regional distribution: 12 cases were restricted to the lower extremity, 2 cases to the upper extremity and one case to the spine and pelvis. Six patients presented with a single lesion localized in the proximal tibia (2 cases), in a finger (1), in lumbar vertebra (1), in proximal femur (1) and in metatarsal bone (1). Twelve cases (57.1%) showed a soft tissue involvement. On imaging all cases were well circumscribed and all but two were lytic and homogeneous. Patients received various treatments (curettage, resection, and amputation) according to the dimension, stage, and

multifocality of the lesions. Surgical margins were wide or marginal in resections and amputations. Three patients underwent adjuvant radiotherapy and two patients received adjuvant chemotherapy (taxane or gemcitabine) following curettage of the largest tumor nodule. Follow-up data were available for all but one patient with a mean of 138 months. Four patients, treated with curettage, recurred with a mean of 13 months after the first diagnosis. All but three patients were alive without disease at the time of the last follow-up (range: 3-288 months, median: 148 months). Three patients were alive with local disease without metastases at the time of last follow-up (3, 17 and 19 months respectively).

Conclusion: Pseudomyogenic haemangioendothelioma is also found as a primary bone tumor wherein it seems to pursue the same clinical behavior as in the soft tissue. Among the most important characteristics are the multifocality (most often in the lower extremities), and the tendency to recur locally in absence of systemic spread. The role of radiotherapy or chemotherapy needs to be further elucidated.

P2–Poster 207 2554120

SARCOMA CLINICAL RESEARCH IN THE LAST DECADE: A CLINICALTRIAL.GOV REGISTRY REVIEW

Emanuela Marchesi, PhD[2]; Irene Quattrini[2]; Piero Picci[1]
[1]Laboratry of Experimental Oncology, Isituto Ortopedico Rizzoli, Bologna, BO, Italy; [2]Italian Sarcoma Group, Bologna, Italy

Objective: Despite the programs of the regulatory agencies to promote the development of new drugs in rare disease, the number of Clinical Trial (CT) in sarcomas by pharmaceutical companies is very limited. Aimed to explore the panorama of sarcomas research in the last decade and retrieve information useful to play strategies to obtain more effective treatments for patients, a ClinicalTrial.gov repository review was done.

Methods: Data from 2006 to May2016 were extracted from Clinicaltrial.gov, selecting all the sarcoma studies: phase, funding source, enrollment, status, interventions, results reporting and updates were analyzed.

Results: Among all the oncology CT, 2.2% were on sarcomas and the 1.8% funded by industry is with new drugs. Of the 738 CT on sarcomas 61.7% are disease-specific and 38.2% include them as solid tumors, in broad trials. Independent research cover 77.3% of all and 74.2% of CT with drugs. Trials funded by nonprofit are more likely to be phase II (43.9%) but the number of phase III + phaseII/III is higher in absolute, for nonprofit (46 *vs* 19). Enrollment for sarcoma specific CT, range from 711-0 for profit and from 1167-0 for nonprofit; 23.6% ≥100 patients (9.0% profit vs 14.5% no profit; p<0.001). CT with the most recently approved drugs are about 10% (mostly nonprofit) while those with the new immune checkpoint inhibitors are 2.7% (6.2% in all the oncology CT). Sarcoma cooperative groups cover in EU 37.9% of the independent research and globally 16.1% (p<0.0013). Of the completed CT, 74.3% do not have results reported in the registry and their periodical update is met for <35%.

Conclusion: Given the limit that ClincalTrial.gov is not a database but a register created to promote the transparency of the research, its information could provide an idea of the CT scenario. Our review confirms that sarcoma research is very limited and mostly relies on independent research that is able to achieve large enrollments and a valuable number of phase III CT, with a great support from disease-cooperative groups. Nonprofit institutions are those involved in frontline research for new treatment strategies with innovative drugs. The publication of the CT results in the registry is extremely important for rare diseases and the lack of this information fails to achieve the deontology commitment to sarcoma patients who can benefit of the transparency of research. For this reason is essential to promote the awareness of the importance of a complete and correct use and update of the CT repository.

P2–Poster 208 2570720

SYSTEMATIC MULTIDISCIPLINARY APPROACH TO RADIATION ASSOCIATED ANGIOSARCOMAS (RAAS) OF THE BREAST

Ivy A. Petersen, MD[1]; Amy Degnim[3]; Steven I. Robinson[2]; Robert Mutter[1]; Scott Okuno[2]
[1]Radiation Oncology, Mayo Clinic, Rochester, MN, USA; [2]Medical Oncology, Mayo Clinic, Rochester, MN, USA; [3]Surgery, Mayo Clinic, Rochester, MN, USA

Objective: Angiosarcomas that arise in irradiated breast can be difficult to identify early and a challenge to control due to their ability to spread rapidly and diffusely in the lymphatics of the skin.Surgery is a mainstay of treatment, but there is no uniform approach used to treat RAAS.To assess our institutional experience a review was performed of the treatment of RAAS.The outcome of these patients prompted development of a prospective treatment approach.

Methods: Using the outcome of our prior experience, a multidisciplinary group assembled to design a uniform prospective plan to manage RAAS.Representatives from surgery, radiation oncology and medical oncology disciplines were involved.The group determined criteria to be used in this population, established specific routines for initial evaluation, criteria for inclusion in the treatment regimen, and a schedule that would allow for treatment of these patients two possible regimens.Finally a follow-up schedule was agreed upon to ensure uniformity of continued long term evaluation of this population.

Results: A complete algorithm was detailed. Primary patients and those with recurrence after surgery alone were candidates.Surgery with wide margins and primary or flap closure were included.Photographs were done at the time of presentation, after neoadjuvant chemotherapy, radiation and at the time of surgery to ensure document width of margin.MRI was used to stage and document response.CT scan of the chest was selected to evaluate for metastatic disease.Because of the unknown benefit of radiation and chemotherapy in small early RAAS, it was elected to use of wide local excision alone without flap reconstruction in this select population, but patients were evaluated by the group to confirm this approach.For more advanced disease or where flap closure was felt to be required, aggressive neoadjuvant therapy with Taxane-based chemotherapy followed by chemoradiation to 50 Gy and then surgical resection was planned.Initial use of the algorithm has been successful in enhancing consistency in the management of a rare malignancy.

Conclusion: Coordinated effort is needed to determine the optimal therapy for rare tumors such as RAAS.Early use of this algorithm has been successful across the institution and enhanced the communication of treatment plans across disciplines.Case examples and adherence to the algorithm with responses of patient will be compared to the initial retrospective review case.

P2–Poster 209 2570216

THYROXINE DEPLETION MODULATED BY EXOGENOUS L-TRIIODOTHYRONINE MAY EXTEND SURVIVAL IN ADVANCED SARCOMA PATIENTS

Rony Weitzen[1]; Aleck Hercbergs[2]
[1]Oncology, Sheba Medical Center, Ramat Gan, Israel; [2]Radiation Oncology, Cleveland Clinic, Beachwood, OH, USA

Objective: Prior pre-clinical and clinical studies indicate that lowering serum free thyroxine was associated with extended survival in patients with terminal cancers. The objective of this study was to substitute the less pro-oncogenic L-triiodothyronine [T3] for L-thyroxine [T4] as replacement therapy and monitor outcomes in hypothyroid metastatic sarcoma patients.

Methods: All 13 patients had Stage 4 soft tissue sarcoma [STS] malignant disease deemed incurable by conventional means. The patients received various chemo/Bio-therapy (kinds and lines) for sarcoma as well as had additional surgery or radiotherapy. (i.e.tumorectomy for synovial sarcoma and also cryotherapy for very small pulmonary mets). Serum FT4 and TSH were serially monitored to enable adjustments to drug therapy. Patients were converted abruptly from L-T4 (50-100 mcg daily). After a week 'washout' period, exogenous L-T3, 15-37.5 mcg/day was begun in two daily divided doses. In all patients FT4 levels had declined below the reference range to a nadir by 4 weeks. Survival is calculated from date of of L-T4 cessation.

Results: M:F ratio 8:5, Median age 65 ([range 31-70)]. TUMOR TYPES: Liposarcoma -1, Endometrial Stromal Sarcoma -1, Leiomyosarcoma Uterus - 5, Synovial sarcoma - 2, Undifferentiated sarcoma - 3, Fibrosarcoma -1. RESPONSE: 3 Patients CR, 7 had SD, 3 had PR. Median follow up is 10 months [4-60 months], Median Survival is not yet reached. One patient [Synovial sarcoma] is disease-free at 60 months.

Conclusion: In metastatic sarcoma survival may be prolonged in L-T3 supplemented patients.

FT4 depletion is enabled by L-T3 substitution for L-T4 to maintain euthyroid hypothyroxinemia .Since thyroxine is a potent cancer growth factor -its withdrawal removes a key driver of tumor growth and proliferation and enhances response to treatment longevity

P2–Poster 210 2521934

MARRIAGE AND FERTILITY IN LONG-TERM SURVIVORS OF CHILDHOOD, ADOLESCENT AND YOUNG ADULT (AYA) HIGH- GRADE SARCOMA: A JAPANESE SINGLE-CENTER EXPERIENCE

Tsukasa Yonemoto[1]; Miyako Takahashi[2]; Mitsue Maru[3]; Akiko Tomioka[4]; Masahiro Saito[5]; Yuko Araki[6]; Makiko Tazaki[2]; Miyako Tsuchiya[2]; Shintaro Iwata[1]; Hiroto Kamoda[1]; Takeshi Ishii[1]
[1]Chiba Cancer Center, Chiba, Japan; [2]National Cancer Center, Tokyo, Japan; [3]Konan Women's University, Kobe, Japan; [4]Tokyo Healthcare University, Tokyo, Japan; [5]Oizumi Gakuen Child & Adolescence Clinic, Tokyo, Japan; [6]NEC Corporation, Kawasaki, Japan

Objective: Marriage and fertility are very important aspects of human life that may markedly influence each person's life history. We investigated the marital status and the presence or absence of children in survivors of childhood, adolescent and young adult (AYA) high-grade sarcoma, and examined the influence of these factors on the quality of life (QOL) of these survivors.

Methods: Thirty-eight survivors of childhood and AYA high-grade sarcoma (18 males, 20 females) participated in a questionnaire survey on marital status and presence or absence of children, as well as on the health-related QOL (HR-QOL), using Short Form 36 Survey. Diagnoses among these survivors were osteosarcoma (28 participants), Ewing's sarcoma (4 participants), synovial sarcoma (4 participants) and others (2 participants). Age at the initial consultation ranged from 4 to 24 years (mean: 15.9 years). Age at the time of this survey ranged from 25 to 52 years (mean: 35.9 years). The interval from the completion of treatment until this survey ranged from 5 to 37 years (mean:

18.6 years). Survivors' siblings aged 25 years or older (n=45: 28 males, 17 females) were enrolled as controls.

Results: Eight (44.4%) of the 18 male survivors were married, of whom five (62.5%) had children. Nineteen (67.9%) of the 28 male siblings were married, of whom 14 (73.7%) had children. Fifteen (75.0%) of the 20 female survivors were married, of whom 14 (93.3%) had children. Twelve (70.6%) of the 17 female siblings were married, of whom 9 (75.0%) had children. The proportions of male survivors who were married and who had children, respectively, were lower than those of male siblings. Forty-three children were born to 23 survivors. However, there was no congenital anomaly in any child. The proportion of ifosfamide-treated male survivors with children was significantly lower than that non-ifosfamide-treated male survivors (p=0.018). With respect to the influence of marital status on HR-QOL, married survivors had significantly higher scores than unmarried survivors for the SF-36 domains vitality (p=0.045) and mental health (p=0.038).

Conclusion: The results of our questionnaire survey reveal that among the male survivors of high-grade sarcoma, the proportions of those who were married and of those having children were lower than those of male siblings, suggesting that strategies providing support for marriage and child-rearing may be necessary for the male survivor group. In the married group, mental QOL was high.

P2–Poster 211 2527022

SARCOMA AND TYPE 1 DIABETES

William Breen, BA[1]; Yogish Kudva[3]; Scott Okuno[2]
[1]Mayo Medical School, Mayo Clinic, Rochester, MN, USA;
[2]Medical Oncology, Mayo Clinic, Rochester, MN, USA;
[3]Endocrinology, Mayo Clinic, Rochester, MN, USA

Objective: The relationship between cancer and Type 1 Diabetes (T1D) is controversial. Several studies suggest that T1D confers a modest increase in risk for gastric, cervical, and endometrial cancers. The specific prognostic effect that T1D has on sarcoma has not been described. We retrospectively reviewed patients with both T1D and sarcoma to examine a hypothesis that patients with T1D have sarcomas that do not behave as aggressively as would be expected.

Methods: After IRB approval, a retrospective review from 2000 - 2014 was performed of pts diagnosed with both T1D (any age) and sarcoma (age ≥18). Local Control, Median Time to Metastasis, and Overall Survival were calculated using Kaplan-Meier methods, and defined from sarcoma diagnosis date. Overall Survival was compared to a predicted 12-yr survival date calculated from the nomogram by Kattan et al JCO 2002.

Results: Seventeen pts were identified. Median age of sarcoma diagnosis was 42 (17-77) yr. 12/17 patients were male. The most common anatomical region affected was the lower limb (7/17). Histologies included osteosarcoma (n=4), leiomyosarcoma (n=2), liposarcoma (n=2), and one of each: angiosarcoma, chondrosarcoma, fibrosarcoma, GIST, Kaposi's sarcoma, MPNST, neurofibrosarcoma, small round cell, and spindle cell sarcoma. Median size of tumor was 7 (1.3-16.8) cm. 11/13 tumors with available tumor grade were high grade. One patient had metastatic disease at presentation. 10/17 patients received chemotherapy (CMT), 16/17 underwent resection, and 9/17 received radiation. CMT was neoadjuvant, adjuvant, or palliative in (n=5), (n=3), and (n=2), respectively. 6/17 had local recurrence, including 4/15 who had r0 resection, at a median of 68.2 (1.9-162) months. Median time to metastasis was 26.9 (6.9-74.8) months. Median survival after metastasis was 11.3 (0.8-66.9) months. The most common sites of metastasis were lung (3/4) and liver (2/4). 88.2% were still alive at last median follow-up of 72.7 months. 5-year survival was 94.1%. Actual 12-yr survival was 88.2%, compared with an expected 12-yr survival of 46.4%.

Conclusion: Our data, albeit with small data set, clinically suggests that patients with T1D who develop sarcoma have a better overall survival than would be expected. Confirmation with a larger cooperative data set is needed and is planned.

P2–Poster 212 2565859

BMI AS A RISK FACTOR FOR TOXICITIES IN ADVANCED STS PATIENTS TREATED WITH TRABECTEDIN

B. Vincenzi[1]; G. Armento[1]; M. Silletta[1];
M. Spalato Ceruso[1]; G. Catania[1]; D. Santini[1]; G. Tonini[1];
G. Badalamenti[2]; L. Incorvaia[2]; G. Maltese[3]
[1]Oncology, Campus Bio-Medico, Rome, Lazio, Italy;
[2]Section of Medical Oncology , University of Palermo, Palermo, Italy; [3]Gynecology Oncology Unit, Fondazione IRCCS National Cancer Institute, Milan, Italy

Objective: There are some previous studies exploring the role of BMI (Body Mass Index, defined as the weight in kilograms divided by the square of the height in metres) as a risk factor for toxicity related to chemotherapies in many different cancer patients populations. At the best of our knowledge no data are actually available about the role of BMI as a risk factor of development of toxicities related to Trabectedin in STS(Soft Tissue Sarcoma) patients. The aim of this study is to evaluate the role of BMI as a risk factor for STS patients treated with Trabectedin.

Methods: 51 STS patients treated with Trabectedin (at standard dose) after progression to at least one chemotherapy regimen with anthracycile+ifosfamide were considered evaluable. The patients were retrospectively enrolled from two reference centres of the treatment of

STS in Italy. Prior to receiving Trabectdin each patient's BMI was recorded. The BMI groups were divided according to the World Health Organization classification (underweight with BMI<18,5, normal range with BMI between 18.50 and 24.99, overweight with BMI≥25.00). All patients in this study were treated with doses based on actual weight. Both side effects and haematological toxicities were recorded according to clinical practice.

Results: Of the 51 STS patients in this study, 18(35,3%) were underweight, 23(45,1%) were normal weight, 10(19,6%) were overweight. No statistically significant differences were identified neither in terms of number of Trabectedin cycles administered nor in terms of dose reductions comparing underweight patients with normal and overweight ones. In terms of toxicities only G3/4 neutropenia was identified more frequently in the group of underweight patients (9/18) in comparison with normal and overweight patients (6/33) with a P value of 0.025. Also febrile neutropenia was recorded more frequently in the group of underweight patients (6/18 vs 3/33, P=0.05). All the other haematological toxicities and non-haematological toxicities were equally distributed in the underweight and normal/overweight patients' group.

Conclusion: The results of this study show that there is no difference in toxicity amongst the different BMI groups, with exception of neutropenia. If confirmed in larger patients' series our data could suggest for the first time that BMI should be considered as a risk factor for neutropenia in STS underweight patients treated with Trabectedin.

PO 001 2565549

MDM2 RNA EXPRESSION IS ASSOCIATED WITH TUMOR PROGRESSION IN DEDIFFERENTIATED LIPOSARCOMA

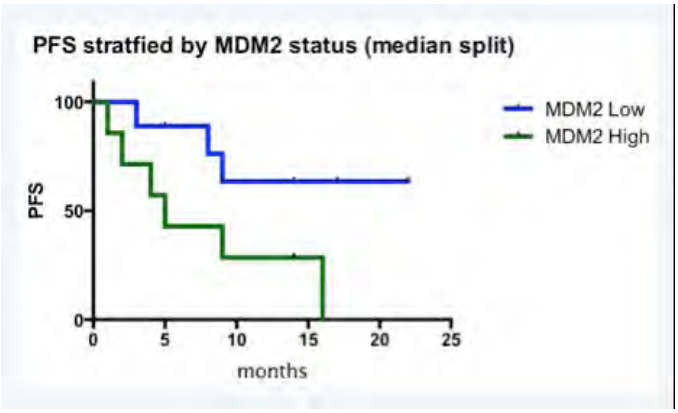
Kate Lynn Bill[2]; Manojkumar Bupathi[3]; Raphael Pollock[2]; James Chen[1]
[1]Department of Biomedical Informatics and Division of Medical Oncology, The Ohio State University, Columbus, OH, USA; [2]Department of Surgical Oncology, The Ohio State University, Columbus, OH, USA; [3]Department of Medical Oncology, The Ohio State University, Columbus, OH, USA

Objective: Soft tissue sarcomas (STS) are a rare and heterogeneous group of diseases where the prognosis is affected by histological grading, size and location. In adults, Dedifferentiated liposarcomas (DDLPS) are a common type of STS. DDLPS are characterized by the amplification of the 12q13-15 chromosomal loci and within this genomic amplification resides the mouse double minute 2 homolog (*MDM2*) oncogene that is expressed in 100% of patients. *MDM2* inhibits the tumor suppressor TP53 – critical in cell cycle regulation. Our previous data demonstrates MDM2s role in chemoresistance. Given MDM2's role in growth and proliferation we hypothesized that patients with lower expression in *MDM2* may have different rates of tumor proliferation.

Methods: We evaluated *MDM2* levels from 16 pathology-confirmed DDLPS specimens at The Ohio State University. Progression free survival was evaluated using RECIST time of last treatment. MDM2 levels were evaluated by PCR and compared to b-actin. Graphpad Prism was used to perform survival analysis.

Results: A total of 16 DDLPS patients were evaluated in this study. The mean age at diagnosis was 56 years (10 M: 6 F). *MDM2* levels were all amplified by FISH. Of the 16 patients, 9 patients had progression by RECIST criteria. 7 patients remain on surveillance at the time of data evaluation. Patients with elevated *MDM2* expression normalized to b-actin correlated with earlier relapse of liposarcoma as compared to those with lower expression by Kaplan-Meier analysis (Figure 1, log-rank, p = 0.04). The progression free survival (PFS) for patients with elevated *MDM2* expression was 5 months and was not reached in patients with low expression of *MDM2*.

Conclusion: This preliminary analysis demonstrates that MDM2 among DDLPS patients is heterogeneous. In addition, RNA expression of *MDM2* correlates with time to recurrence in patients with DDLPS. Future prospective trials are needed to validate these findings.



PO 002 2568095

SARCOIDOSIS MIMICKING PULMONARY METASTATIC LIPOSARCOMA

Takeshi Ishii; Tsukasa Yonemoto; Shintaro Iwata; Hiroto Kamoda
Chiba Cancer Center, Chiba, Japan

Objective: Sarcoma associated sarcoid reactions are rare, we present a case developed multiple pulmonary nodules mimicking metastatic liposarcoma and review the literature.

Methods: case report

Results: A 46-year-old man with 5cm size tumor of the left thigh was consulted to our hospital. Needle biopsy revealed the tumor was myxoid liposarcoma in left vastus lateralis muscle. He was treated with wide local excision of his primary tumor. The resected tumor was 4.5 x 4.0cm in size, grade 2 in FNCLCC grading. The surgical margin was negative. Patient didn't receive any adjuvant therapy. Fourteen months after the surgery, follow-up chest CT scan showed multiple pulmonary nodules without hilar lymphadenopathy. We diagnosed multiple pulmonary metastases from the liposarcoma. The metastasectomy by thoracotomy was not indicated because of over 10 pulmonary metastatic nodules in both lungs. FDGPET showed no abnormal uptake including pulmonary nodules. The patient received the combination chemotherapy of doxorubicin and ifosfamide. After 2 courses of the chemotherapy pulmonary nodules were decreasing in size and number. After further two courses of the chemotherapy there were only 3 nodules in left lower lobe detected by the chest CT. The metastasectomy by thoracotomy was performed. The histopathologic examination of the resected specimens showed epithelioid granulomas with lymphoid cell infiltration. Fifty months after the thoracotomy, the patient is alive with no evidence of the recurrence of liposarcoma and sarcoidosis. To date, sarcoid reactions have been reported in only 8 individuals with sarcoma. Among them only 1 case was recognized

sarcoid reactions in pulmonary nodules. Therefore in sarcoma patient sarcoidosis that shows multiple pulmonary nodules as our case are extremely rare. Huang reported that 7 of 45 cases with pulmonary nodules in sarcoma patients resulted in non-metastatic nodules and all the 7 cases showed solitary nodule. So our case with multiple pulmonary nodules easily can be misdiagnosed as sarcoma metastases. If we had not do the metastasectomy, we would continue further chemotherapy that could be avoid. And we would have considered this liposarcoma patient with pulmonary metastases had been cured by chemotherapy only.

Conclusion: We reported a very rare case of sarcoidosis mimicking pulmonary metastatic liposarcoma. Pulmonary metastasectomy always should be considered to avoid misdiagnosis and overtreatment if sarcoma patients showed pulmonary metastasis in chest CT.

PO 003 2540770

SOFT-TISSUE SARCOMAS: IMAGING CHARACTERIZATION AND RADIOLOGISTS ROLE

Rui T. Gil, Resident
Radiologia, Instituto Português de Oncologia de Lisboa, Lisboa, Lisboa, Portugal

Objective: To review the recommended imaging approach and principal imaging features of different soft-tissue sarcomas.

Methods: We retrospectively reviewed the cases of soft-tissue sarcomas treated in a tertiary institution during the last decade and selected the cases with most representative imaging features on Ultrasound, Computed Tomography and Magnetic Resonance Imaging.

Results: Ultrasound remains the appropriate technique in the initial imaging evaluation of suspected soft tissue tumor because it is readily available, radiation free, cost effective and excellent for the detection of even small lesions. However, Ultrasound has low specificity in characterization of soft tissue tumors and it may miss lesions in deep locations. Magnetic Resonance Imaging is the recommended method for further characterization of soft tissue tumors according to its better soft tissue contrast and because it allows precise and reproducible local staging for therapy planning. Larger and heterogeneous masses with early, peripheral and rapidly progressive enhancement after administration of intravenous contrast agent, favors the diagnosis of soft tissue malignancy. Although combinations of signal intensities reveal the different tumor components (fat, melanin, water and blood), providing information about the pathologic nature of soft tissue lesions, differentiation of different histologic types of soft-tissue sarcomas based on appearance alone is very difficult. Computed Tomography should be considered when the lesion is intrathoracic or intra-abdominal, when there is suspicion of bone involvement, or there are contraindications to Magnetic Resonance Imaging. Computed Tomography is also the preferred modality for the identification of pulmonary metastasis. Furthermore, if the lesion remains indeterminate or possible malignant after imaging investigation, a biopsy is indicated, and in most patients the method of choice is closed image guided biopsy performed by ultrasound or computed tomography.

Conclusion: Although most of the histologic types of soft-tissue sarcomas remain indeterminate after imaging investigation, radiologists play an important role in detection, diagnosis as well as pre and post operative management of patients with soft tissue sarcomas.

PO 004 2565808

MAGNETIC RESONANCE (MR) IMAGING INVESTIGATION OF SOFT TISSUE SARCOMA MISDIAGNOSED AS CHRONIC HEMATOMA

Naomasa Fukase, MD, PhD[1]; Ikuo Fujita[2]; Teruya Kawamoto[1]; Hitomi Hara[1]; Takuya Fujimoto[2]; Masayuki Morishita[1]; Etsuko Kamata[1]; Toshiyuki Takemori[1]; Ryosuke Kuroda[1]; Toshihiro Akisue[1]
[1]Orthopaedic Surgery, Kobe University, Kobe, Hyogo, Japan; [2]Orthopaedic Surgery, Hyogo Cancer Center, Akashi, Japan

Objective: MRI is essential to diagnose soft tissue tumors, but the misreading of images of soft tissue sarcoma as chronic hematoma may result in an unfortunate outcome. Moreover, some cases of hematoma enlarge over a one-month or longer course, termed chronic expanding hematoma, making differentiation between these tumors more difficult. In this study, we compared MR images between these tumors and clarified points of differentiation.

Methods: Of 283 soft tissue sarcoma patients treated at our hospital and related institutions between 2006 and 2013, 11 patients referred to our department after being initially diagnosed with hematoma and treated by a primary care physician (sarcoma group) and 12 patients histologically diagnosed with chronic hematoma in the same period (hematoma group) were investigated. In the sarcoma group, the development site was the thigh in 9, crus in 1, and pelvis in 1. The histologic type was MFH/UPS in 2, angiosarcoma in 2, clear cell sarcoma, leiomyosarcoma, myxoid liposarcoma, Ewing sarcoma, myxofibrosarcoma, synovial sarcoma, and pleomorphic rhabdomyosarcoma in one each. The outcome at the time of the final follow-up was CDF in 4, AWD in 3, and DOD in 4. The MRI findings were compared between the 2 groups.

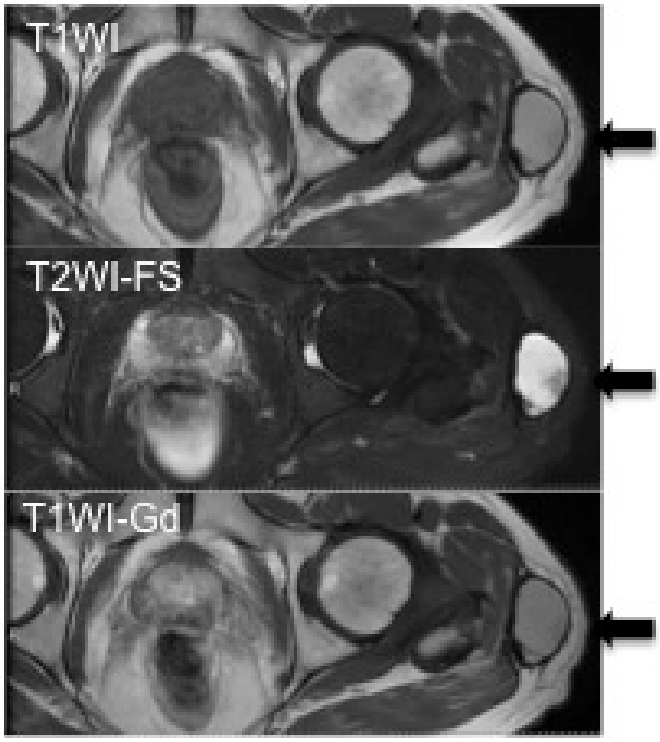
Results: 'A high intensity on T1WI' characteristic of chronic hematoma was noted in 10 (91%) and all patients in the sarcoma and hematoma groups, respectively. 'A capsule with a thickness of 2 mm or more and showing a low inten-

sity on both T1WI and T2WI' was noted in all patients in the hematoma group, but it was not noted in any patient in the sarcoma group. Nine patients were examined by contrast imaging in the sarcoma group, and a contrast-enhanced nodular lesion was observed in the tumor in 8 (89%) patients. In contrast, all patients were examined by contrast imaging in the hematoma group, a nodule enhanced lesion was not observed in any patient.

Conclusion: The points of differentiation of the MRI findings are the presence or absence of 'a capsule with a thickness of 2 mm or more showing a low intensity on both T1WI and T2WI' characteristic of chronic hematoma and a nodule enhanced on contrast imaging in the mass characteristic of soft tissue sarcoma. On the other hand, 'a high intensity on T1WI' was observed in both groups, suggesting that this finding is likely to lead to the misdiagnosis of soft tissue sarcoma as chronic hematoma. When hematoma is suspected, differentiation from soft tissue sarcoma is essential based on these imaging pitfalls.

MRI findings of the 2 groups

	Sarcoma group	Hematoma group
high intensity on T1WI	91%	100%
capsule with a thickness of 2 mm or more	0%	100%
contrast-enhanced nodular lesion in the mass	89%	0%



An axial view MRI of chronic hematoma in the lateral aspect of the left thigh.

PO 005 2565935

INTRAOSSEOUS SYNOVIAL OF THE BODY OF SCAPULA

Pedro M. Serrano[1]; João Esteves[1]; Vânia Oliveira[1]; André Coelho[2]; Pedro F. Cardoso[1]
[1]Orthopaedics, Centro Hospitalar do Porto, Porto, Portugal; [2]Pathology, Centro Hospitalar do Porto, Porto, Portugal

Objective: Synovial Sarcoma (SS) represents 5-10% of all soft tissue sarcomas.It affects adolescents and young adults. The majority are patients between 15 and 35 years. Being contiguous to a bone it can induce periosteal reaction, erode and/or invade the cortical but these situations are rare, occurring in 15-20% of the cases. As a bone tumour, SS is extremely rare. To our knowledge only 10 cases were reported to date.
Here is reported the case of a patient with a huge SS of the body of the scapula that underwent resection and is disease-free with a 8 year follow up.

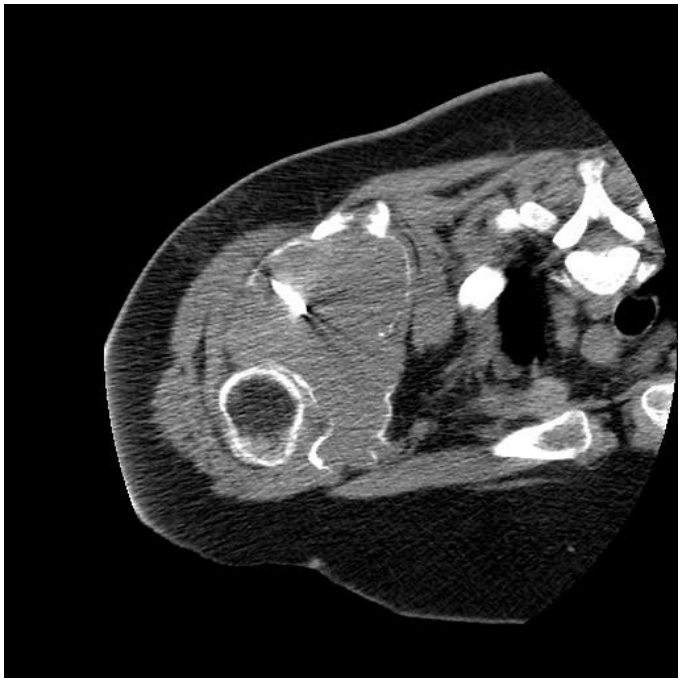
Methods: Female, 56, with a huge osteolitic tumour of the entire body of the scapula, with joint and soft tissue invasion. MRI showed no involvement of neurovascular structures in axillary planes. A CT-guided trucut biopsy was made: ovoid or spindle cells forming irregular and short fascicles, with a small cytoplasm and oval, slightly irregular nuclei with scarce mitotic activity (4/10 high power fields). There was a prominent hemangiopericytoma-like vascular architecture. The immunohistochemestry showed positivity for vimentin, and focal positivity for cytokeratins AE1/AE3 and CAM 5.2 (figure 2). It was negative for muscular markers, CD34 and Epithelial Membrane Antigen (EMA). The diagnosis of monophasic, grade II synovial sarcoma was then settled. No distant metastases or lymph nodes were detected (T2b,N0,M0,G2) and neodjuvant chemotherapy including ifosfamide, adriamicine and mesna has been initiated. Three months later a Thickoff-Linberg procedure was done without reconstruction.

Results: The exam of the specimen, through extensive sampling, didn't reveal any epithelial component that could had been absent from the microbiopsy in a biphasic tumour, confirming the diagnosis: monofasic synovial sarcoma. Margins were wide. Tumour necrosis was 40%. It was decided not to do adjuvant chemotherapy. Function was 63.8 points in Dash score, after physical therapy.

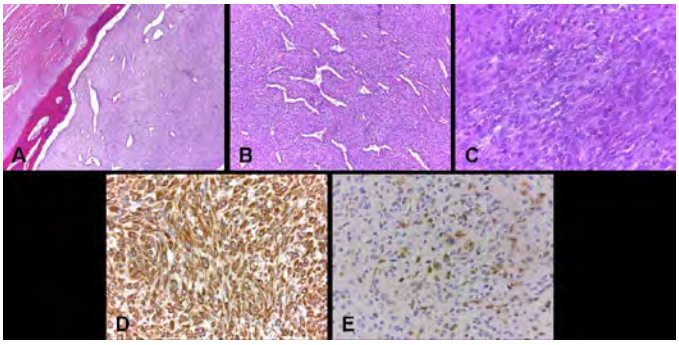
4 years later there was a recurrence treated with wide excision and radiotherapy. Function stayed the same and, with 8 years follow up, she is disease free.

Conclusion: This SS of the body of the scapula is doubtless intraosseous as proven by the CT-scan. From the microscopic point of view it integrates the characteristics of the monophasic form with its ovoid/spindle cells and the hemangiopericytoid-like vascular component. The specific t(x;18) (p11.2;q11.2) chromosomal abnormality present

in more than 90% of SS was not studied by the time of diagnosis but was recently confirmed.



CT-guided core needle biopsy



Monophasic Synovial Sarcoma**. A -** (HE 40x); A solid tumor with elongated vessels. In this picture, a rim of cortical bone is seen, in accordance with its intraosseous nature. **B -** (HE 100x); Prominent hemangiopericytic-like vessels are seen within the tumor. **C -** (HE 400x); Spindled cells with plump, slightly irregular nuclei and scant cytoplasm, arranged in small fascicles. **D -** (Vimentin 400x); Very positive expression in neoplastic cells, highlighting the spindled morphology. **E** - (CAM5.2 400x); Focal expression of low molecular weight citokeratins in neoplstic cells.

PO 006 2537662

SOFT TISSUE SARCOMA: PREDICTING CLINICAL BEHAVIOR BASED ON TRADITIONAL HISTOLOGIC GRADE

Whitney M. Guerrero, MD[2]; Richard A. Erali[1]; Martin D. Fleming[3]

[1]College of Medicine, UTHSC Memphis, Memphis, TN, USA; [2]Surgery, UTHSC-Memphis, Memphis, TN, USA; [3]Surgical Oncology, UTHSC-Memphis, Memphis, TN, USA

Objective: Soft tissue sarcoma (STS) is a rare malignancy, accounting for less than 1% of yearly cancer diagnoses. Liposarcomas (LS) are the most common, representing 20% of STS. Prognosis is traditionally based on histologic grade, however the clinical course is variable and often discordant with predicted behavior. We sought to identify patterns within tumor subtypes, in this case LS, that might shed light on the limits of traditional grading systems and help predict those patients with a poor prognosis who might benefit from the addition of radiation or chemotherapy.

Methods: After IRB approval, a retrospective review was performed for patients treated by academic and community surgeons at our institution for STS from 2004-2015. Demographic and clinicopathologic variables were recorded and long-term outcomes described. Pathology grading systems were examined and compared for uniformity and alignment with long-term clinical outcomes.

Results: A total of 133 patients were treated for STS in the study period, 37 with LS. This large subset cohort was compared to STS as a whole and used to evaluate the consistency and predictive accuracy of traditional grading systems. The cohorts were evenly matched with respect to age, sex, race, BMI, and mean follow up (Table 1a). There were significant differences in the percentage of patients with high grade disease: 41% of LS patients vs. 77% of STS patients (p=0.0001). Both were similarly likely to receive chemotherapy or radiation therapy (Table 1b). All LS patients were treated surgically compared to 87% of STS patients (p=0.022). Average tumor volume was larger for LS than for STS (4818 mL vs. 2251 mL, p=0.034). The complication rates were similar for both cohorts (Table 1c). The incidence of lung metastasis for STS was higher than that for LS (14.2% vs. 2.7%, p=0.053). LS and STS were equally likely to recur (14% for LS, 11% for STS, p=0.61).

Conclusion: In our patient population, LS are uniformly resected. Compared to STS, LS are less likely to have metastases at diagnosis, but are larger at. Despite low grade classification, observed recurrence rates of LS and STS are not significantly different, and in our study there are cases of low grade tumors with pulmonary metastases. This mismatch in traditional pathologic grade and clinical course suggests that a new, less subjective grading system based on each tumor's individual genome may be warranted.

TABLE 1: LIPOSARCOMA V. SOFT TISSUE SARCOMA

	LS (N=37)	STS (N=133)	
[a] DEMOGRAPHICS	N (%)	N (%)	p
Age (years)	57.2	59.3	0.55
Sex			
Male	17 (47)	58 (44)	0.40
Female	20 (53)	75 (56)	0.80
Race			
African American	16 (43)	62 (42)	0.72
Caucasian	21 (57)	83 (57)	0.54
Other	0	2 (2)	0.45
BMI	30.8	28.2	0.18
Mean Follow Up (months)	35.2	30.5	0.45
[b] TREATMENT			
Surgery	37 (100)	116 (87)	0.02
Neoadjuvant Chemotherapy	2 (5)	13 (10)	0.41
Adjuvant Chemotherapy	3 (8)	20 (15)	0.28
Radiation	10 (27)	56 (42)	0.10
[c] DISEASE PROFILE			
Recurrence	5 (14)	14 (11)	0.61
Metastasis	1 (3)	24 (18)	0.02
Lung Metastasis*	1 (100)	19 (79)	0.61
Any Complications	10 (27)	37 (28)	0.92
Clavien-Dindo Grade 1**	1 (10)	12 (32)	0.61
Grade 2**	7 (70)	18 (49)	0.23
Grade 3a**	0	0	-
Grade 3b**	2 (20)	7 (19)	0.94
Grade 4a**	0	0	-
Grade 4b**	0	0	-
Grade 5**	0	0	-

LS: liposarcoma, STS: soft tissue sarcoma. *Percentage shown is for patients with metastases **Percentage shown is for patients with complications

PO 007 2568396

CLEAR CELL SARCOMA-LIKE TUMOR OF THE GASTROINTESTINAL TRACT

Idoia B. Peris, Resident; Vicenç Artigas; Silvia Bagué; Manuel Rodríguez; Gemma Cerdán; Ana Sevio; Ana Virgili; Antonio Lopez

General Surgery, Hospital Santa Creu i Sant Pau, Barcelona, Spain, Spain

Objective: Clear cell sarcoma–like tumor of gastrointestinal tract (SCCGI) is a rare tumor characterized by multinucleated cells with giant pale cytoplasm. Since the first publication in 1993 by Ekford only 39 cases had been reported. They are positive for S-100 protein and implies gens fusion of EWSR1 and ATF1. The only curative treatment is a radical surgery. We evaluated our recent experience with a SCCGI.

Methods: We review the SCCGIT in our Sarcomas Unit. Clinical and radiological sintoms, surgical treatment, pathological and inmunohistochemical and genetic diagnosis, grade of surgical resection and clinical results were evaluated.

Results: Two patients. a women 33 years and male 45 years old with a acute intestinal occlusion. Abdominal CT detected a ileo-cecal neoplasm obstruction with multiple mesenteric lymph node dissemination. A PET-CT confirms the peritumoral nodal spread. A right hemicolectomy and a ileocolic-mesenteric linfadenectomy was done in both patients.

The pathological result defines an infiltrating tumor of the cecum with mucosal ulceration and extensive vascular and perineural invasion. Multiple metastasic pericolic lymph nodes were affected. Tumor cells are predominantly epithelial with eosinophilic cytoplasm with prominent nucleoli compatible with clear cell *(fig 3).* Immunohistochemistry was positive for S -100 protein, CD68, and vimentin. The gene rearrangements study by FISH technique were positive for EWSR1 gene in both cases and confirming the SCCGI diagnosis.

Chemotherapy with 5 cycles of Adriamycin (75 mg/m2) was administrated in the male and obtained a partial response with lymph nodes persistence. A more extensive lymphadenectomy confirmed an important residual nodal involvement.

In the second patient, six month after primary surgery, a surgical liver metastases resection was done. The pathological study confirm the SCCGIT and FISH technique detected a positive gene rearrangement EWSR1.

Conclusion: SCCGI is a rare mesenquimal intestinal sarcoma manifested with an intestinal occlusion. There is highly cellular infiltration which frequently obliterate the bowel or gastric wall. The detection of a positive S-100 protein and the rearrangement for EWSR1 gene are the most important for the definitive diagnosis.

The only challenge for this patients is a radical intestinal resection and extended linfadenectomy. Hepatic metastasis surgery should be evaluated in multidisciplinary consensus. Radiotherapy or chemotherapy treatments could be considered in a palliative setting .

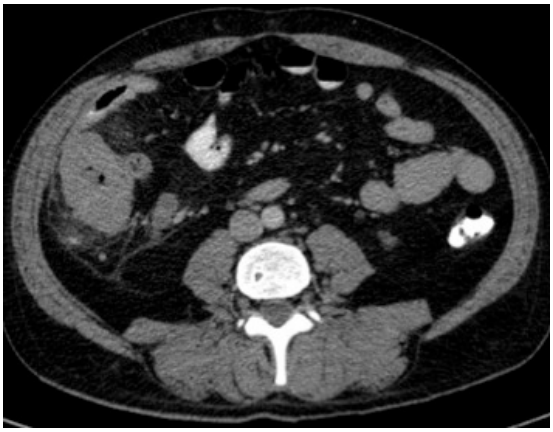


Fig 1. CT Ileo-cecal tumour with pathological ileocolic and middle colic territory nodes

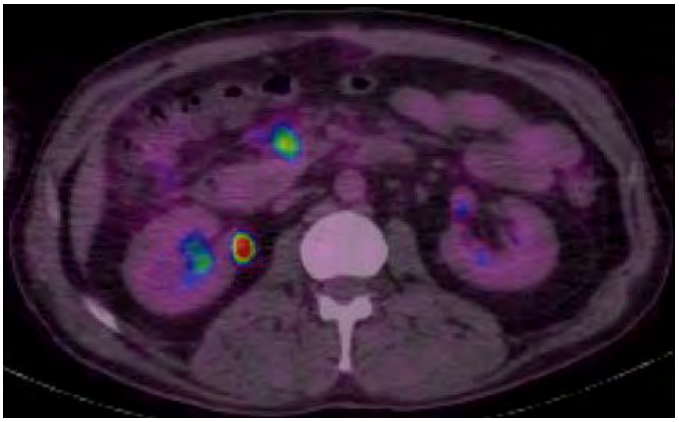


Fig 2. PET-CT with extensive residual lymph node involvement

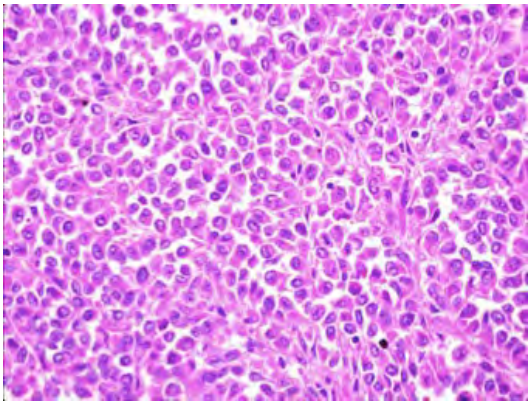


Fig 3. Epithelial image with eosinophilic cytoplasm with prominent nucleoli.

PO 008 2544200

CORE NEEDLE BIOPSY IS A SAFE AND ACCURATE METHOD TO DIAGNOSE BONE AND SOFT TISSUE SARCOMA

Ahmad Shehadeh
KHCC, Amman, Jordan

Objective: Classic teaching has advocated the use of open biopsy to diagnose and grade extremity sarcoma. Reported advantages of core needle (Tru-cut) biopsy include the minimal morbidity, cost, and time. The perceived disadvantage has been diagnostic inaccuracy, and sample insufficiencyTo present an institutional experience in core needle biopsy without image guidance; for diagnosis and grading of bone sarcoma with palpable soft tissue component and soft tissue sarcoma.

Methods: From July 2006 till April 2011, 42 patients received core needle biopsy on outpatient bases at orthopedic oncology clinic at King Hussein Cancer Center (KHCC). Fifteen patients with Bone sarcoma with palpable soft tissue component (Osteosarcoma n=6, Ewing's sarcoma n=6, Chondrosarcoma, Giant Cell Tumor and metastatic leiomyosarcoma to bone one each), and 27 patients with Soft tissue sarcoma (STS). Twenty located in the thigh and femur, 5 in the buttock and iliac bone, 6 in the upper limb and 4 in other places ,all biopsies were performed by the lead author using a 12 gauge Tru-cut needle, under local anaesthesia, 6 to 8 cores were obtained by redirection of the needle through the same entry with correlation to the MRI extent and location of the lesion. Radiological size of the tumors ranged from 5-30 cm. All samples were sent to KHCC pathology lab for study.

Results: All specimens obtained were adequate to make the diagnosis. All histological diagnoses were concordant with the resection diagnosis; two biopsies graded low were found to be intermediate to high on the resection specimen. Two patients developed hematoma, and treated with local compressive dressing.

Conclusion: When performed by expert sarcoma surgeon and read by expert pathology lab, the result of core needle biopsy for Soft tissue sarcoma and bone sarcoma with extra osseous component, provide accurate diagnostic information for malignancy and grade, adequate core needle biopsy enables to avoid open biopsy which decreases tissue planes contamination and facilitate subsequent resection of the biopsy tract.

PO 009 2561466

THE VALUE OF CORE NEEDLE BIOPSY IN THE APPROACH TO MUSCULOSKELETAL TUMOURS

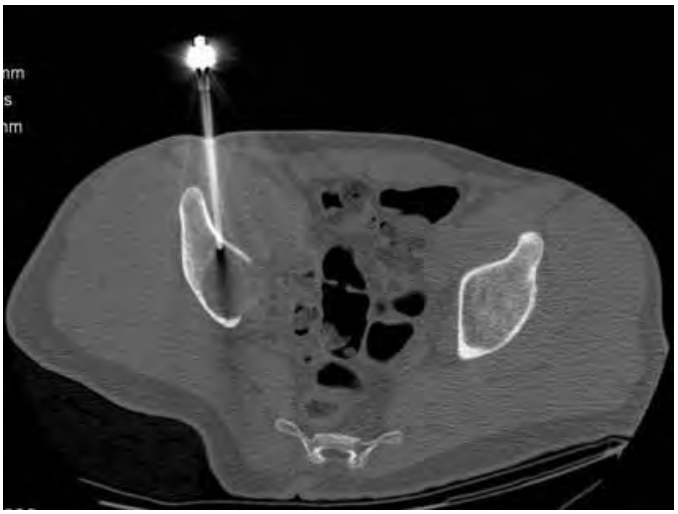
Pedro F. Cardoso[1]; João Esteves[1]; Vânia Oliveira[1]; André Coelho[2]; Tiago Couto[3]
[1]Orthopaedics, Centro Hospitalar do Porto, Porto, Portugal; [2]Pathology, Centro Hospitalar do Porto, Porto, Portugal;
[3]Radiology, Centro Hospitalar do Porto, Porto, Portugal

Objective: In specialized centres, where pathologists integrate all the clinical and image information, core needle biopsy (CNB) is considered the best procedure to reach an accurate diagnosis. It is a minimally invasive technique, performed in an outpatient basis without general anaesthesia or hospitalization, as well as having a much lower cost. The purpose of this study was to evaluate the diagnostic accuracy of CNB, and to analyse to which extent this method enables the initiation of treatment, clarifying its role in addressing musculoskeletal tumours.

Methods: Between January of 2003 and December of 2013 (11 years) 456 patients underwent CNB. All procedures were performed by the same team: an orthopaedic surgeon for bone lesions and a radiologist for the soft tissue. Samples were analysed by 2 pathologists. There were 222 males and 234 females with an average age of 51,6 years (2-90). All CNB were performed under image guidance. All soft tissue lesions (n=92) were done under ultrasonography image control. Fluoroscopy or CT scan were used to guide bone biopsies (n=364). A diagnosis was considered to be accurate when it was confirmed by incisional biopsy, surgical specimen or ulterior clinical and imaging evaluation as in some benign tumours, metastases and hematopoietic lesions no histological confirmation is needed. The minimum follow up was 2 years. Exclusion of disease was included in the group of diagnosis.

Results: With CNB 431 diagnosis were possible (94,5%). Diagnoses were: 86 metastases, 95 primitive malignant tumours, 127 benign tumours, 43 hematologic diseases, 32 infections, and in 48 cases there was no disease. Accuracy rate was 99,3%. Regarding determining malignancy CNB had 99,6% sensitivity, 100% specificity, 100% positive predictive value and 99,5% negative predictive value. Among the 25 inconclusive samples 19 (76%) were benign lesions and 6 (24%) were malignant. There were 3 wrong diagnoses. In one of them a malignant tumour was wrongly diagnosed as a benign one. In the other 2 lesions, CNB pointed a correct benign diagnosis but it was not accurate.

Conclusion: The high diagnostic yield and accuracy of CNB show the reliability of this technique in the diagnosis of all type of musculoskeletal lesion. In 94,5% of the cases, the treatment was initiated based on the biopsy diagnosis. Only in one case the malignancy of the lesion was misdiagnosed.



The percutaneous biopsy is presently the best and most appropriated approach when facing an unknown bone or soft tissue lesion.

Clinical characteristics of bone and soft tissue lesions diagnosed by CNB

Total	Type	Gender	Mean age (range)	Anatomical location	Image guidance
456 biopsies	Bone 364 Soft tissue 92	Male 222 Female 234	51,6(12-90)	L. Limb 158 U. Limb 77 Spine 95 Pelvis 84 Trunk 42	Ultrasonography 92 CT-scan and Radioscopy 364

PO 010 2565661

LONGITUDINAL CHANGE IN QUADRICEPS CROSS-SECTIONAL AREA AFTER WIDE RESECTION OF QUADRICEPS MUSCLE FOR SOFT TISSUE SARCOMA: CT SCAN BASED STUDY

Munenori Watanuki; Masami Hosaka; Kou Hayashi; Shinichirou Yoshida; Eiji Itoi
Orthopaedic, Tohoku University Hospital, Sendai, Japan

Objective: The quadriceps muscle group is one of the most common site for extremity soft tissue sarcomas. Several studies reported that the degree of quadriceps resection has a strong impact on the isometric strength of the muscle and functional outcome. There is no report about the longitudinal changes in strength of the residual muscle after extensive quadriceps muscle resections. The quadriceps cross-sectional area (CSA) has been shown to correlate with quadriceps muscle strength and knee function. The aim of this study was to investigate the longitudinal changes in CT-based quadriceps cross-sectional area after quadriceps resection.

Methods: From 2008 to 2013, 10 patients had quadriceps resection. The average age of patients was 62. CT scan was taken preoperatively and postoperatively at 6, 12, and 24 months. Midthigh quadriceps muscle CSA was assessed from a 1-mm CT slice. Analysis of variance (ANOVA) was used to examine correlations between gender, number of resected muscles, and the affected quadriceps CSA changes from 6 to 24months. Simple linear regression analysis was used to examine correlations between age, the unaffected quadriceps CSA changes from preoperative to 6 months, the unaffected quadriceps CSA changes from 6 to 24 months, and the affected quadriceps CSA changes from 6 to 24 months.

Results: The CSA of the affected quadriceps were significantly smaller (average 20%) than those of the unaffected side at 6 months. Eighteen months (6 - 24mo) longitudinal changes in CSA of the affected limb slightly increased (average 3.6%) (Fig 1A). The CSA of the unaffected limb increased significantly from preoperative to 6 months (average 10%). The CSA of the unaffected quadriceps significantly decreased from 6 to 24 months (average 6%) (Fig 1B). Univariate analysis showed that the affected quadriceps CSA changes from 6 to 24 months correlate with gender (P<0.05) and the unaffected quadriceps CSA changes from 6 to 24 months (P<0.01). A multiple regression analysis showed that, only changes in the CSA of the unaffected limb from 6 to 24months exhibited a significant positive correlation with change in the CSA of the affected limb during the same period (R2=0.60, p<0.05) (Fig 2).

Conclusion: This study suggests that the CSA of residual quadriceps muscle might recover to a certain degree over time, even after extensive quadriceps muscle resections, and the maintenance of physical activity after discharge might improve affected limb function.

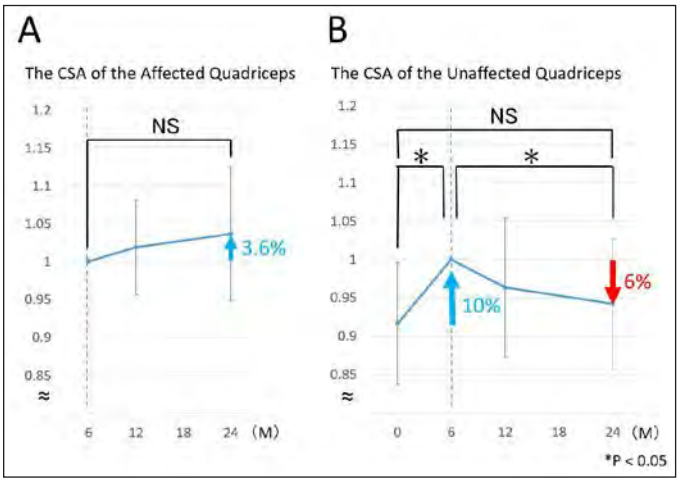


Fig 1. Longitudinal changes in quadriceps CSA

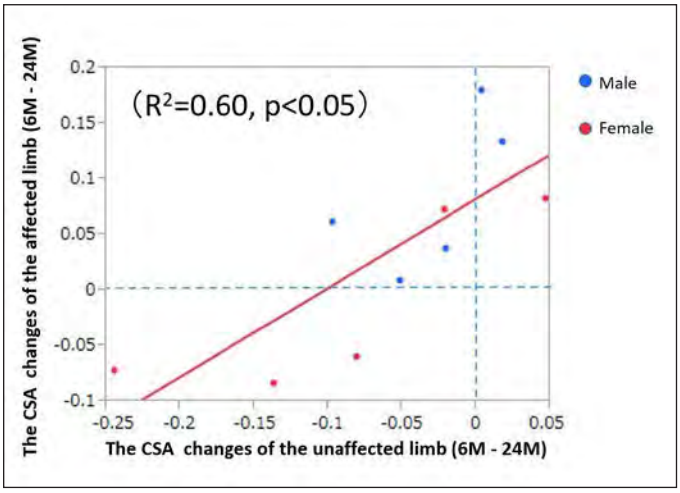


Fig 2. Correlation of changes of the unaffected and the affected quadriceps CSA.

PO 011 2544197

SOFT TISSUE SARCOMAS ABUTTING THE BONE, WHERE SHALL THE KNIFE STOPS? A PROPOSED GUIDELINE FOR SURGICAL TREATMENT

Ahmad Shehadeh
KHCC, Amman, Jordan

Objective: The incidence, surgical treatment and effect on overall survival and recurrence of bone invading/abutting soft tissue sarcoma, still poorly described in the literature. To present an institutional experience regarding; surgical treatment and outcome of soft tissue sarcoma abuts the bone.

Methods: From July 2006 -Dec. 2013, 125 patients with wide local/compartment resection, at KHCC. Twenty five patients (20%) the tumor were abutting the bone and 6 of them (5% of the total) there was MRI evidence of cortical invasion , 22 patients as first presentation and 3 as recurrent disease, age 15-65 year, Median age 49 years.

Tumor location includes: extremity 21, one case pelvic and one case chest wall, once case sacrum.

Three Surgical options were used: **first**, soft tissue resection along with segmental bone resection , was afforded to all patients with soft tissue sarcoma whom MRI scan show Medullary canal invasion or total/subtotal encasement of the bone by the soft tissue tumor, 2 patients in our group received this kind of treatment. **Second**, soft tissue subperiosteal resection with no bony excision, was afforded to all patients whom MRI scan show bone abutment with no invasion, 18 patients received this modality, and **third**, soft tissue resection along with the involved adjacent piece of bone cortex , and 5 patients received this modality.

Results: At mean follow up of 38 months, (16-58), 4 patients died due to metastatic disease, 2 of them who had bone invasion and 2 who did not have bone invasion, and 2 patients developed local recurrence (8%).One patient developed radiation related femur fracture. 5 years event free survival was 53% and overall survival 76%, 3/6 patients with bone invasion proved to have true invasion on pathology study.

Conclusion: This is a small group retrospective pilot study; the results show that STS abutting bone probably do not lead to worse outcome. Our proposed guideline for surgical management of different scenarios of soft tissue tumor with adjacent bone abutment/invasion can be the basis for objective mean to plan the management of this subtype of soft tissue sarcoma. Larger size study is needed to expand this guideline.

PO 012 2570690

THE ROLE OF ISOLATED LIMB PERFUSION IN THE TREATMENT OF SOFT TISSUE SARCOMAS OF THE EXTERMITIES

Hugo Vasques; Vitor Farricha; Joana Bartolo; Nuno Abecassis
Surgery, Instituto Português Oncologia (IPO), Lisbon, Portugal

Objective: To demonstraste that Isolated Limb Perfusion is a good treatment option when amputation is the only surgical solution to soft tissue sarcomas of the extermities.

Methods: Retrospective analisys of a single center experience over 30 years (between 1993 and 2013), with 73 isolated limb perfusions performed.

Results: In patatients with soft tissue sarcomas of the extermities that amputation was the only surgical solution, isolated limb perfusion allowed a surgical ressection in 73,1% of those patients. We preserved the limb in 71,4% of patients that otherwise would need an amputation.

Conclusion: Isolated limb perfusion allows a high rate of limb sparing surgery in patients with unresectable soft tissue sarcomas of the extermities that otherwise would need an amputation

PO 013 2570154

LYMPHATICOVENULAR ANASTOMOSES FOR LYMPHOEDEMA COMPLICATED WITH SEVERE LYMPHORRHEA FOLLOWING RESECTION OF SOFT-TISSUE SARCOMAS OF THE ADDUCTOR COMPARTMENT

Hiroshi Kobayashi[1]; Takuya Iida[1]; Masachika Ikegami[1]; Ryoko Sawada[1]; Yusuke Shinoda[1]; Sakae Tanaka[1]; Hirotaka Kawano[2]
[1]The University of Tokyo Hospital, Tokyo, Japan; [2]University of Teikyo, Tokyo, Japan

Objective: The adductor compartment of the thigh is the second most common site for soft-tissue sarcomas in the lower limbs. Resection of soft tissue sarcoma in this site resulted in frequent wound complications. The main cause of wound complication is lymphedema and lymphocele, and conservative treatment is not always successful.

Lymphaticovenous anastomosis (LVA) is a surgical treatment that improves lymphatic drainage by anastomosing lymphatic vessels to a cutaneous vein under surgical microscopy using 11/0 or 12/0 nylon sutures. LVA is reported to reduce limb diameter and lymphocele, especially after treatment of breast cancer and gynecologic cancer.

In the current study, we describe the successful treatment using LVA on 2 cases of lymphedema and lymphorrhea after the surgery of sarcoma occurring at the adductor compartment.

Methods: Between 2000 and 2015, 2 cases had wound complication among surgically treated patients with soft tissue sarcoma at the adductor compartment. Two patients treated with LVA included pleomorphic liposarcoma and undifferentiated pleomorphic sarcoma. Clinical and radiographic results are presented.

Results: LVA was performed successfully in 2 patients. In both cases, lymphorrea was observed the following day of wide resection of the tumor. In case 1, simultaneous multisite LVA was performed using an operating microscope under local anaesthesia. Six LVAs and ligation of lymphatic vessels causing lympharrea was performed 1 month after the operation. Lymphatic vessels causing lymphorrea were confirmed by intraoperative indocyanine green (ICG) lymphography. Lymphorrhea was immediately disappeared after LVA. In case 2, four LVAs were performed under local anaesthesia, 1 week after the operation because lymphorrea resulted in the inhibition of wound healing.

Lymphorrhea was also disappeared soon after LVA, and wound attachment was completed after LVA.

Conclusion: LVA could be a useful and not invasive method to treat and to prevent the lymphorrhea and wound complication after the surgery for soft-tissue sarcomas in adductor compartment.

PO 014 2565868

OUTCOMES OF AMPUTATION FOR TREATING SARCOMAS OF THE LIMBS

Marta S. Silva; Pedro M. Serrano; Luis Barros; João Esteves; Pedro Leite; Vânia Oliveira; Pedro F. Cardoso
Centro Hospitalar do Porto, Porto, Portugal

Objective: At the present time, limb-salvage surgery is the most common surgical approach for treating sarcomas. However, when it isn't possible, amputation is needed. The aim of our study is to evaluate outcomes of sarcomas that underwent amputation.

Methods: Retrospective and observational study, where patients with sarcomas of the extremities that underwent amputation between 2003 and 2015 were included. A total of 22 patients were identified, with a medium age of 61.7 years.

Results: Tumours were mostly located on the lower limb (68.2%) and 40,9% in the hands and feet. Condrosarcomas constituted the most frequent histologic type (22.7%) and 68,4% were high grade tumours. Amputation was mainly performed with curative intent (95.0%) and transtibial amputation was the most frequent type performed (23.8%). Among the reasons for amputation, tumour extension was the most common (68.1%), followed by neurovascular invasion (19.1%) and palliation for ulcerated tumour (9.5%). Local recurrence was the motive in 38.0% of the patients. The medium survival time in this group was of 41.4 months. Only one patient had local recurrence (4.7%), but 57.1% of cases had distant metastases. Average functional outcome was 54.1%, and higher values of functionality were registered for upper limb amputees (64.1%) than lower limb amputees (48.2%).

Conclusion: Factors which may indicate the need for amputation are tumour extension, neurovascular bundle invasion, ulceration to skin and local recurrence. Despite being a potentially disabling surgery, patients that cannot undergo limb-salvage surgery may benefit from amputation, controlling the disease and maintaining acceptable function.

PO 015 2570687

SURGICAL OUTCOME OF SOFT TISSUE SARCOMA OF THE ADDUTOR COMPARTMENT

Yoshikazu Tanzawa, PhD; Eisuke Kobayashi; Makoto Endo; Fumihiko Nakatani; Hirokazu Chuman; Akira Kawai
Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan

Objective: Tumours in anatomic regions near major neurovascular structures are difficult to resect. Complications following resection of a soft tissue sarcoma in the adductor compartment of the thigh are frequent and increase morbidity. To review the outcomes and complications of 34 consecutive patients with soft tissue sarcomas of the adductor compartment treated in our hospital from July 2000 to March 2014.

Methods: We retrospectively reviewed 34 patients (16 men and 18 women) with a mean age of 53 years. These patients were followed for a mean of 57 months (range, 7 to 133 months). Preoperatively, the pathological diagnosis was well differentiated liposarcoma (n=11), myxoid liposarcoma (n=4), synovial sarcoma (n=3), myxofibrosarcoma (n=3), malignant fibrous histiocytoma (n=3), leiomyosarcoma (n=2), rhabdomyosarcoma (n=2) and the others (n=6). Eight patients were given chemotherapy and six received adjuvant radiotherapy. The average size of the resected tumor was 12 cm. Oncological outcome, local control rate and wound complications were documented at the time of the latest follow-up.

Results: In 23 patients with high grade sarcoma the overall survival rate was 88% at 5 years. Clinical outcome status was continuous disease free in 25 patients, no evidence of disease in 1, alive with disease in 7, and died of disease in 1. During the follow-up period, three patients had local recurrence, and 7 had distant metastasis. Twenty-four patients had negative microscopic margins at definitive primary resection (71%), and 10 specimens (29%) had positive microscopic margins. Nine patients (26%) developed wound complications. Three of 4 patients who developed surgical site infection required further surgery. Two of 3 patients who had skin necrosis received pedicle skin flap. Two patients developed permanent lymphoedema. In our study, lesions involving the proximal adductor compartment at the level of the pubic ramii were associated with high rate of wound complications.

Conclusion: Good overall survival rate and local control rate can be achieved in patients with soft tissue sarcomas of the adductor compartment. The rate of major complications in our study (26%) was lower than in others (36% and 43%), but adductor muscle group resection carries a relatively high rate of wound complications requiring proper management. Further studies are needed to delineate the indications for microsurgical soft tissue coverage.

PO 016 2540073

CLINICAL MANAGEMENT OF SKIN INVOLVEMENT OF SOFT TISSUE SARCOMA

Manabu Hoshi; Naoto Oebisu; Yoshitaka Ban; Hiroaki Nakamura
Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Osaka, Japan

Objective: Malignant soft tissue tumors can invade skin and occasionally present malignant wounds characterized by bleeding, exudate, odor, and infection. Bleeding from the tumor impairs patients' quality of life and can be life threatening. This study aimed to highlight the clinical problems associated with skin involvement of malignant soft tissue tumors.

Methods: The patient group comprised 14 males and two females, with ages ranging from 23 to 87 years (mean 63.1). The average follow-up was 25.6 months. Clinical information concerning the problems and treatment courses associated with skin involvement of soft tissue sarcoma was investigated.

Results: Skin involvements were observed in 10 of 16 cases in male patients over 65 years. Tumors were located in the chest wall in seven cases. The mean diameter of tumors was 8.6 cm, and in 13 cases the histological diagnosis was high grade sarcoma. Skin involvement resulted in malignant wounds in 10 individuals. Six cases had undergone previous surgery. Surgical removal was done in 11, and amputation in two. Two patients received palliative treatment. After tumor removal, eight cases needed skin reconstruction, five by major musculocutaneous flap and three by skin graft. The 1-year survival rate was 69.5%, and the 5-year survival rate was 55.6%.

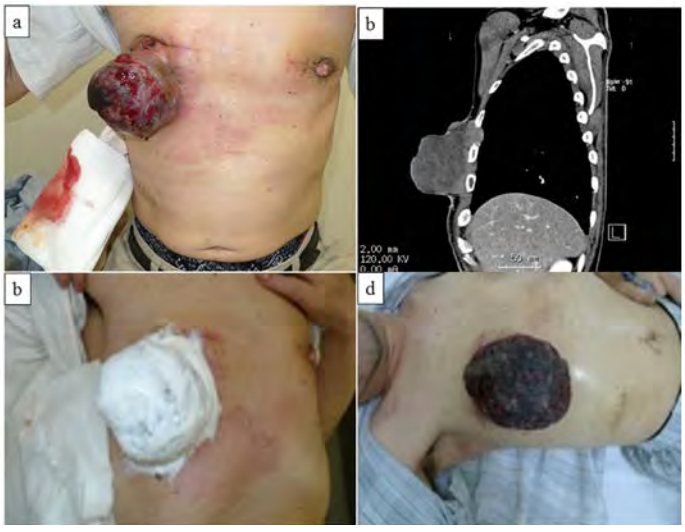


Fig. 1a. 44-year-old man. A malignant wound was associated with the tumor of the right breast: skin ulceration, bleeding, exudate, a strong odor, and infection were observed. B.Sagittal computed tomography shows the tumor protruding from the chest wall. The tumor also invades the intercostal area. c. The surface of the tumor has been painted with Mohs' paste. d The surface of the malignant wound has been chemically fixed; it became dry, black in color, and hard.

Conclusion: Wide resection and skin reconstruction was generally necessary to achieve local control, because of the large skin and soft tissue defects. To avoid exacerbating the systemic condition, topical Mohs' paste and zinc oxide starch powder was used as palliative treatment or for pre-operative local control.

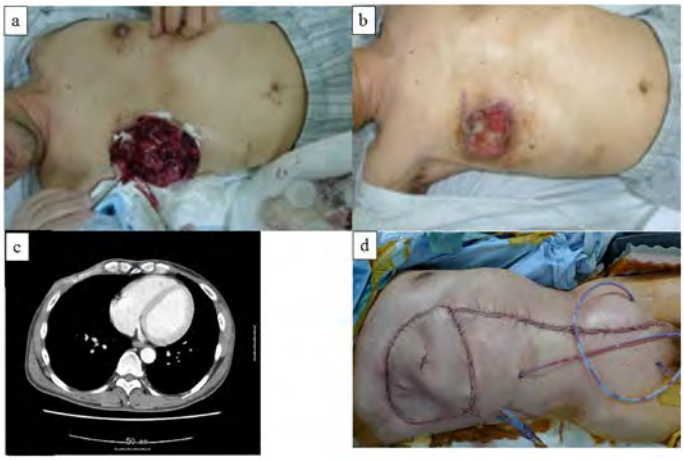


Fig2.a Appearance after cutting the surface of the tumor. b Pre-operative physical appearance of the chest wall. The tumor has shrunk remarkably. .Axial computed tomography demonstrates disappearance of the tumor. d.Wide resection and reconstruction with a rectus abdominis musculocutaneous flap were performed.

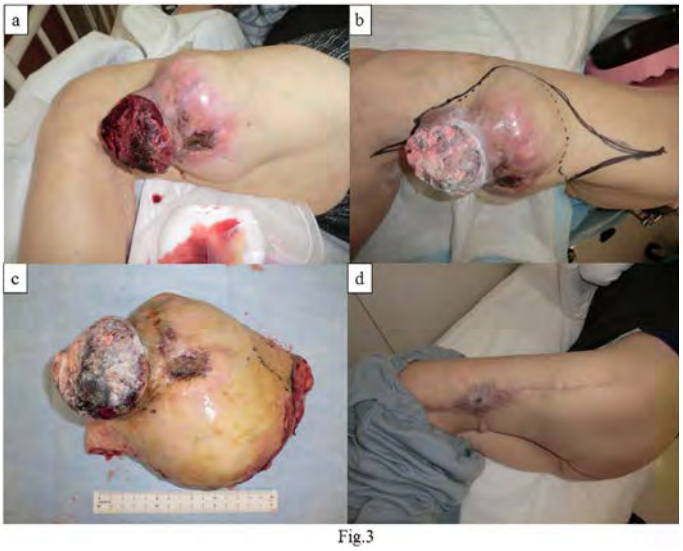


Fig.3

87-year-old patient
a. A malignant wound was associated with a tumor in the right thigh: skin ulceration, bleeding, exudate, and a strong odor were observed in this patient.
b. The surface of the tumor after topical application of zinc oxide starch powder.
c. Gross findings of the surgically resected specimens.
d. No local recurrence was observed at the last follow-up.

Clinical information of the patients with skin involvement of sarcoma

case	Age/Sex	Pathology	Size (cm)	Location	Previous surgery	Malignant wound	TNM	Stage	FNCLCC	Local Treatment	Adjuvant treatments	Chemoterapy	Follow-up (months)	Outcome
1	56M	MPNST	16.8	Chest wall	+	+	T2bN0M0	III	2	Palliation	Mohs paste	+	11	DOD
2	83M	Pleomorphic liposarcoma	14.1	Chest wall	-	+	T2bN1M1	IV	3	Wide resection + LDMF		-	3	DOD
3	23F	ASPS	8.6	Lower leg	-	+	T2bN0M1	IV	1	BK amputation		+	34	DOD
4	67M	Myxofibrosarcoma	8.6	Chest wall	-	-	T2bN0M0	IIB	2	Wide resection + PMMF		-	69	CDF
5	66M	Pleomorphic liposarcoma	8.5	Upper arm	-	+	T2bN0M0	III	3	Wide resection + LDMF		-	36	CDF
6	70M	Dedifferentiated liposarcoma	6.1	Chest wall	+	-	T2bN0M0	III	3	Wide resection		-	29	AWD
7	87M	UPS	13.1	Thigh	-	+	T2bN0M0	IIB	2	Wide resection + skin graft	Zinc oxide starch powder	-	9	CDF
8	67M	UPS	10.0	Forearm	-	+	T2bN0M0	III	3	BE amutation	Mohs paste	+	8	DOD
9	82M	Myxofibrosarcoma	3.7	Chest wall	-	+	T1aN0M0	IIA	2	Wide resection		-	21	CDF
10	58M	SFT	7.7	Thigh	+	-	T2bN0M0	IIB	2	Wide resection + skin graft		-	7	CDF
11	67F	Myxofibrosarcoma	9.5	Inguinal region	-	-	T2bN0M1	IV	3	Wide resection + LFMF		+	9	CDF
12	48M	Dedifferentiated liposarcoma	8.2	Buttock	+	-	T2bN0M0	IIB	2	Wide resection + skin graft		+	106	CDF
13	42M	UPS	5.1	Inguinal region	+	+	T2bN0M0	III	3	palliation	Zinc oxide starch powder	-	9	AWD
14	74M	Pleomorphic liposarcoma	7.2	Chest wall	+	+	T2bN0M0	IIB	2	Wide resection + LDMF		-	7	DOD
15	75M	Well differentiated liposarcoma	23.1	Thigh	-	+	T2bN0M0	IB	1	Marginal resection		-	35	CDF
16	44M	Pleomorphic liposarcoma	10.2	Chest wall	+	+	T2bN0M0	III	3	Wide resection + RAMF	Mohs paste	+	18	DOD

FNCLCC: National Federation of Centers for the Fight Against Cancer. MPNST: Malignant peripheral nerve sheath tumor. ASPS: Alveolar soft part sarcoma. UPS: Undifferentiated pleomorphic sarcoma. SFT: Solitary fibrous tumor. LDMF: Latissimus dorsi myocutaneous flap. PM: Pectoralis major musculocutaneous flap. RAMF: Rectus abdominis musculocutaneous flap. LFMF: Lateral femoral musculocutaneous flap. BK: Below knee. BE: Below elbow. DOD: Die of disease. CDF: Continuous disease free. AWD: Alive with disease

PO 017 2570552

TIMING OF RADIOTHERAPY INFLUENCES OUTCOME OF LIPOSARCOMA

Daniela Greto, MD[1]; Mauro Loi[1]; Domenico Campanacci[2]; Giovanni Beltrami[2]; Guido Scoccianti[2]; Icro Meattini[1]; Isacco Desideri[1]; Pierluigi Bonomo[1]; Lorenzo Livi[1]
[1]Sperimental Biomedical and Clinical Sciences, University of Florence, Florence, Italy; [2]Ortopedical Oncological Surgery, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence, Italy

Objective: The aim of the study is to analyze and compare the toxicity and clinical outcome of preoperative and postoperative radiotherapy (RT) in a specific histological soft tissue sarcoma (STS) subtype: Liposarcoma.

Methods: Data of 134 STS patients with locally advanced liposarcoma treated by surgery and RT were collected. Statistical analysis was performed to detect correlation between tumor- and treatment-related variables and outcome.

Results: Mean follow up was 3,4 years (range:1.6-9.5 years). Mean age was 51.5 years (range: 19-86 years). Fifty-four (40.3%) patients had FNCLCC Grade 3 disease. Thirty-two patients (23.9%) received neoadjuvant radiotherapy,45(33.6%) patients underwent brachytherapy(BRT) followed by RT; postoperative RT was delivered in 57(42.5%) patients. All patients underwent surgery:114(85.1%) wide, 18(13.4%) marginal and 2(1.5%) intralesional excisions. Chemotherapy was administered in 44 cases(32.8%).Acute

skin toxicity occurred in 58(43.3%) patients.Two patients developed wound complication. Grade II-III late fibrosis were 11.2%. Incidence of fibrosis was higher in the post-operative group than the preoperative one (p=0.034).Nine (6.7%) patients experienced local recurrence.Metastasis were detected in 28 (20.9%) patients; at univariate analysis grade III and preoperative radiotherapy correlate to higher risk of distant recurrence (p= 0.0019 and p=0.006, respectively).Impact of G3 [HR 2.17 (IC 95%: 1.03-4.56)] and postoperative radiotherapy [HR 0.4 (IC95%: 0.19-0.88)] were confirmed at multivariate analysis.At the last follow-up 105 (78.4%) patients were alive. At univariate analysis for OS the safety of surgery and grade were predictors of survival (p=0.000013 and p=0.0018, respectively); at multivariate analysis Grade III [HR 2.28 (IC 95%: 1.08-4.82)] and marginal excision [HR 2.22 (IC 95%: 1.29-18.7)] were confirmed independent predictors of OS. Disease specific survival (DSS) was also influenced by Grade III [HR 2.46 (IC95%: 1.00-6.06)] and marginal excision [HR 2.21 (IC95%: 1.03-4.76)].

Conclusion: Postoperative radiotherapy resulted in higher risk of late fibrosis.Timing of radiotherapy did not influence incidence of wound complications. High grade disease and safe surgery were confirmed as predictive factors of overall and specific disease survival.Distant metastasis were correlated with grade and preoperative radiotherapy. Improvement of chemotherapy might be explored in the neoadjuvant setting to prevent metastatic dissemination.

PO 018 2570528

POSTOPERATIVE RADIOTHERAPY FOR SARCOMA OF FOOT, HAND, ANKLE AND WRIST

Yeon Joo Kim[1]; Si Yeol Song[1]; Wonsik Choi[2]; Hyung Uk Je[3]; Jin-Hee Ahn[1]; Hye Won Chung[1]; Wanlim Kim[1]; Jong-Seok Lee[1]
[1]Asan Medical Center Univ. of Ulsan College of Medicine, SEOUL, Korea (the Republic of); [2]Gangneung Asan Hospital, Univ. of Ulsan College of Medicine, Gangneung, Korea (the Republic of); [3]Ulsan University Hospital, Univ. of Ulsan College of Medicine, Ulsan, Korea (the Republic of)

Objective: To know the local control, survivals, and complications of treating sarcomas in foot, hand, ankle and wrist with limb-sparing surgery (LSS) and postoperative radiotherapy (PORT).

Methods: Seventeen patients with soft tissue sarcomas (STS) in wrist, hand, ankle and foot who received PORT after LSS from August 2008 and November 2015 were retrospectively reviewed. Primary outcome was 5-year local recurrence free survival (LRFS). Secondary outcomes were 5-year disease free survival (DFS) and toxicities.

Results: The median age was 32 years (range, 12-78). The most frequent STS location was foot in 11 patients (64%) followed by 2 patients in wrist, hand, ankle, respectively. Fourteen patients (82%) received resection with flap grafts and the same number of patients achieved clear resection margins. The median postoperative radiation dose was 54 Gy (range, 46-60). Five patients also received chemotherapy. At the median follow-up of 39 months (range, 6-87), 5-year LRFS and DMFS were both 100%. Only one patient experienced grade 3 radiation dermatitis and there was no major wound complication. Radiation-induced bone fracture was occurred in 2 patients.

Conclusion: PORT after LSS showed excellent local control for STS in wrist, hand, ankle and foot. Considering the good local control and limb function saving without any significant toxicity, the combination of LSS followed by PORT could be an appropriate and safe modality for STS in distal extremities.

PO 019 2569722

NEOADJUVANT TRABECTEDIN PLUS RADIOTHERAPY IN HIGH GRADE SARCOMA OF THE LEG – CASE REPORT

Carolina Carvalho[1]; Antonio L. Silva[1]; João Freitas[2]; Ruben Fonseca[2]; Paulo F. Tavares[2]; Helena Garcia[3]; Jose M. Casanova[2]
[1]Department of Radiotherapy, Coimbra University Hospital, Coimbra, Portugal; [2]Bone and Soft Tissue Tumor Unit, Coimbra University Hospital, Coimbra, Portugal; [3]Department of Anatomical Pathology, Coimbra University Hospital, Coimbra, Portugal

Objective: Soft tissue sarcomas is a rare and very heterogeneous disease. Common presentation is a painless large lump or swelling in the extremities or retroperitoneum. Surgery and Radio/Chemotherapy are the standard therapy for sarcomas, but few data are available on neoadjuvant treatment. The use of neoadjuvant therapies potentially provides better control but it still remains an area of controversy. When preoperative radio-chemotherapy is used, tumor responses can result in clinically meaningful tumor shrinkage prior to surgery and, thus, may facilitate subsequent surgical resection. The pathological complete response or tumoral regression rate shows us the efficacy of this type of treatment.

Methods: This report describes a 76-year-old man with a soft tissue lesion in the proximal third of the right leg with 46x30x18 mm. He underwent a incision biopsy of the lesion and the pathology revealed a high grade spindle cell sarcoma. Thoraco-abdominopelvic CT didn't show metastasis. Tumor board decided for neoadjuvant chemoradiation. Because of the history of heart attack, the patient was unsuited to receive anthracycline-based chemotherapy. As an individual approach with the patient, trabectedin was chosen for the patient-tailored treatment. Trabectedin were

given on day 1 every 3 weeks at the dose of 1,5mg/m^2 body surface area, administered as an intravenous infusion over 24 hours, between September 2015 and March 2016, to a total of 9 cycles. Radiation was delivered with a total dose of 45Gy/25fr/5weeks to the right leg. There was no significant toxicity.

Results: Surgical resection with flap was performed and pathology confirmed a high grade spindle cell sarcoma, with skin ulceration, reaching striated muscle tissue; the tumor showed a very good pathological response with 80% of necrotic area. The patient is in surgery recovery with the aim of further adjuvant therapy (Trabectedin with or without radiotherapy).

Conclusion: This case support that Trabectedin plus Radiotherapy is a therapeutic option with significant efficacy and minimal toxicity in the neoadjuvant setting of patients with spindle cell sarcoma.

PO 020 2570583

TRABECTEDIN IN THE CLINICAL MANAGEMENT OF METASTATIC SARCOMA

Daniela Greto, MD[1]; Mauro Loi[1]; Domenico Campanacci[2]; Giovanni Beltrami[2]; Guido Scoccianti[2]; Icro Meattini[1]; Pierluigi Bonomo[1]; Isacco Desideri[1]; Lorenzo Livi[1]
[1]Sperimental Biomedical and Clinical Sciences, University of Florence, Florence, Italy; [2]Ortopedical Oncological Surgery, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence, Italy

Objective: Standard treatment of metastatic soft tissue sarcomas (STS) patients is an anthracycline-based chemotherapy, with a response rate of 10-25%. Trabectedin (T) showed a significant activity in the second line setting. Data of metastatic STS treated with T at the University of Florence were collected and analyzed.

Methods: A retrospective review was performed on 25 patients treated with T between September 2009 and April 2016 . Data regarding safety, progression-free and overall survival were analyzed and the impact of demographic (gender,age),tumor (histotype, synchronous/metachronous metastasis) and treatment (prior anthracycline chemotherapy, line and number of cycles of T) characteristics was assessed.

Results: Twenty five metastatic patients were treated with T. Median age was 60.0 years (20-76). Liposarcoma (8 cases) and Leyomyosarcoma (7 cases) were the most represented histotypes. Six (24%) patients had metastatic disease at diagnosis, while distant relapse occurred in 18 patients.Twenty-two patients received prior anthracyclines for a mean number of 4 cycles (range: 0-8). T was administered as second line treatment in 17(68%) patients , in third line in 7 (28%) cases and in fourth line in 1 (4%); mean number of T cycles was 3.6 (range:1-10). Hematologic toxicity G>2 occurred in 4 patients (1 severe pancytopenia, 1 anemia and 2 neutropenia) leading to discontinuation in 3 cases.Treatment was interrupted after 1 cycle in 4 patients (1 allergic reaction, 1 refusal, 2 referred to other sites) that were excluded from further analysis. At the time of the analysis, 9 patients died and 19 patients experienced disease progression.Median Time To Progression (TTP) was 11.9 weeks (5.4-127 weeks) while Median Overall Survival was 65.8 weeks (14.5-412.8 weeks).At the univariate analysis age older than 60 (p=0.032) and a previous number of anthracycline cycles superior to three (p=0.038)correlate with TTP. At multivariate analysis a prior course of more than three cycles of anthracyclines yielded a benefit on TTP, HR 0.26 (IC 0.09-0.76) p=0.014.No variables showed an impact on overall survival.

Conclusion: T is a well tolerated regimen in metastatic STS patients and is effective regardless of histotype and treatment line.Presumably due to its cytostatic effects, a prior course of cytotoxic chemotherapy might enhance its efficacy; future trials should address its role in combination or sequence with antiblastic agents or radiotherapy to exploit its efficacy in inducing long-lasting response.

PO 021 2547462

ADMINISTRATION OF TRABECTEDIN INFUSION IN AN AMBULATORY SETTING IN TREATING SOFT TISSUE SARCOMA - A SINGLE CENTRE EXPERIENCE

Sarah Welby
Christie NHS Foundation Trust, Manchester, United Kingdom

Objective: Soft tissue sarcomas (STS) are mesenchymal tumours that originate from the connective tissues of the body. Surgery is the standard treatment for patients with localised STS; for advanced STS (aSTS) and metastatic disease, chemotherapy and radiotherapy are also used. Trabectedin is a chemotherapy authorised for use in the treatment of adult patients with aSTS after the failure of anthracyclines and ifosfamide. Real-world studies have shown that trabectedin can be effectively administered through an ambulatory service. Reducing the time patients have to spend in hospital may improve their overall chemotherapy experience. Moreover, reducing inpatient admissions can lead to cost savings and could mean inpatient resources being freed up for patients on more complex chemotherapy regimens.

Methods: This is a review of the current evidence supporting the feasibility of treating patients with trabectedin in the ambulatory setting. In the spirit of Recommendation 33 from the 2015 ‘Achieving world class cancer outcomes: A strategy for England 2015–2020’ report, this review also includes a detailed case study of how the ambulatory

sarcoma service at The Christie NHS Foundation Trust, Manchester is currently run.

Results: Patients at The Christie hospital have received trabectedin as outpatients since 2008 leading to a reduction in patient hospitalisation for chemotherapy, and estimated savings of approximately £500 on the average cost of treatment per patient/per cycle (excluding drug costs).

Conclusion: Treating patients in the ambulatory setting allows them to spend more time out of hospital, with the potential to improve their overall experience of care. Personal experiences at The Christie hospital suggest that this reduction in time spent in hospital is particularly valued by patients with advanced metastatic disease.

PO 022 2559232

GEMCITABINE AND DOCETAXEL CHEMOTHRAPY FOR METASTASIS OF SARCOMA

Ryu Terauchi; Toshiharu Shirai; Shinji Tsuchida; Naoki Mizoshiri; Yuki Mori; Toshikazu Kubo
Department of Orthopaedics, Kyoto Prefectural University of Medicine, Kyoto, Kyoto, Japan

Objective: For chemotherapy to be regarded as effective against metastasis occuring after treatment for bone and soft tissue sarcoma, improvement of the overall and progression-free survival rates is essential. At our hospital, a protocol for using gemcitabine (GEM) and docetaxel (DOC) chemotherapy to treat metastasis is applied. The aim of our study was to evaluate the efficacy of this chemotherapy.

Methods: Subjects comprised 15 patients (mean age 53.9, range 27 to 76 years old) who developed bone and soft tissue sarcoma after surgery. Four patients had osteosarcoma, 4 had leiomyosarcoma, 4 had undifferentiated pleomorphic sarcoma, and the other 3 had other types. A GEM and DOC combination regimen was administered first, then GEM alone if patients developed CTCAE v4.0 grade 2. In cases where DOC was difficult to administer at outset, GEM alone was administered. Tumor shrinkage was observed during treatment, and if cases became operable surgical resection was performed and adjuvant chemotherapy continued. Treatment effectiveness was assessed periodically using thoracic CT with <20% increase in total area of imaged tumors defined as progression-free survival.

Results: The median overall survival time was 10.4 months (1.4 - 42.7) and the median progression-free survival time was 7.0 months (0.93 - 22.5). At 6.0 and 12 months, survival rates were 79% and 54.7% and the progression-free survival rates were 72.2% and 46.8%, respectively. The outcomes were 1 case of CDF, 1 of NED, 6 of AWD and 7 of DOD.. GEM/DOC was commenced in 12 cases, of which three were moved onto GEM alone. In no case did the GEM-alone regimen have to be stopped due to an adverse event.

Conclusion: The protocol at our hospital for both bone and soft tissue sarcoma gave good results. Compared with combined GEM and DOC regimen, GEM alone can be administered continuously for much longer because it tends not to cause adverse events. It is thought to be effective to continue chemotherapy for a long term with combination of surgery and raditation.

PO 023 2570507

TRABECTADIN ADN PROPHYLATIC REGIMENT: THE EXPERIENCE OF A CENTER

Ana M. Ferreira, MD[1]; Ana M. Simas[1]; Marta Soares[1]; Jose Dinis[1]; Mariana Afonso[2]; J. Flávio Videira[3]; Jorge Guimarães[3]
[1]Medical Oncology, Ipo-Porto, Porto, Portugal;
[2]Pathology, Ipo-Porto, Porto, Portugal;
[3]Surgery, Ipo-Porto, Porto, Portugal

Objective: Trabectedin, a marine-derived antineoplastic agent, has been registered by the EMA and recently by the FDA for the treatment of adult patients with advanced soft-tissue sarcoma (STS), after the failure of the treatment with anthracyclines and ifosfamide, or who are unsuited to receive these agents. Several clinical trials have shown that trabectedin has a favourable toxicity profile. The most frequently reported toxicity is haematological, as neutropenia. Hepatotoxicity, as elevated serum levels of AST/ALT, is also very frequent. At the IPO-Porto it is protocoled the treatment with a granulocyte colony-stimulating factor (G-CSF) for 10 to 12 days, and with oral dexamethasone, 4 mg/daily during 4 days, beginning 24 hours after each treatment with trabectedin. This analysis evaluates the toxicity profile of trabectedin for patients with advanced STS who were treated at IPO-Porto according to the local standard practice described above.

Methods: A retrospective chart review was performed on 17 patients diagnosed with different histologic subtypes of STS between 2010 and 2016 and treated with trabectedin (24 hours infusion q3w) between Sep/2012-May/2016; according to local standard practice. Data regarding safety was analysed.

Results: Median age at treatment onset was 60.46 years (n=13; SD=11.77 years). 41.2% (n=7) were females and 52.9% (n=9) were men. Tumours included leiomyosarcoma (41.2%), liposarcoma (41.2%), **myxofibrosarcoma** (5.9%), **mesenchymal** tissue neoplasm (5.9%) and synovial sarcoma (5.9%). Trabectedin was provided as third-line chemotherapy in 58.8% (n=10), as second-line chemotherapy in 29.4% (n=5) and as fourth-line in 5.9% (n=1). Median number of cycles was 4 (range: 1-9). 29.4% (n=5) patients continue to receive trabectedin and 64.7% (n=11) have concluded the treatment. Dose reduction did not occur. Treatment delays occurred in 35.5% (n=6). Toxicities occurred in 47.1% (n=8) for elevated liver enzymes, 29.4%

(n=5) grade 1, 11.8% (n=2) grade 2, 5.9% (n=1) grade 3; in 58.8% (n=10) for haematologic toxicity, 35.3% (n=6) grade 1 and 23.5% (n=4) grade 2; and in 5.9% (n=1) for renal toxicity. Treatment was discontinued in 52.9% (n=9) because of disease progression

Conclusion: Trabectedin has an acceptable safety profile as an anti-tumor agent. Our data further suggest that it may be beneficial to use the IPO-Porto protocoled treatment for reducing the haematological toxicity and hepatotoxicity of trabectedin

PO 024 2570524

PATTERN OF HEPATIC TOXICITY IN TRABECTEDIN TREATED PATIENTS – A SINGLE INSTITUTION STUDY

Paulo F. Tavares, Head of Medical Oncology; João Freitas; Ruben Fonseca; Sandra Santos; Jose M. Casanova
Bone and Soft Tissue Tumor Unit, CHUC, Coimbra, Portugal

Objective: Described in the literature, the most common form of hepatic toxicity induced by Trabectedin is elevation of seric transaminases (GPT/ALT and GOT/AST). We had a different experience in our unit and decided to study liver tests in Trabectedin treated patients.

Methods: From a total of 71 patients we excluded those that did less than 3 Trabectedin pulses, to get a total of 63 evaluable patients.

These patients did a total of 891 pulses. At least for the first 12 pulses the interval between pulses was 3 weeks. Some patients were changed for 4 weeks intervals afterwards. Liver toxicity prophylaxis was made with a 30mg bolus of IV Dexamethasone right before the Trabectedin 24 hours infusion, followed by 4 doses of 10mg bid. Emesis was controled with 1mg oral Granisetron bid for a total of 4 doses. For the rare patients with frank emesis, 3mg IV Granisetron was used instead. Anaphylaxis was further prevented with a mix of H1 and H2 inhibitors -- 2mg Clemastine and 100mg of Ranitidine in single bolus injections before Trabectedin. All patients were treated as in-patients with 48 hours admissions. All concurrent medications were reviewd and compared in all patients.

Blood tests were done before each pulse, so at least three weeks appart from the last pulse.

Results: Transaminases elevations were modest, rare, and quickly reversible. On the contrary, elevations in Alkaline Phosphatase and mainly in Gama Glutamyl Transpeptidase were sometimes quite high, more than 10 times the upper normal value, and maintained in time with no ovious tendency towards lowering nor aggravating in affected patients. Other liver function tests, namely Total Bilirrubin were not affected. No relation to renal function or concomitant medication was found.

Conclusion: This pattern of toxicity, although frightening for the less experienced, is quite well tolerated, not interfering in everyday life nor with other medications. No dose reduction was made and no pulse was ever postponed due to this. We didn't find any drug interaction that could be the cause of these alterations. We are convinced that it's safe to continue Trabectedin treatment indefinitely in these patients.

PO 025 2568888

THE MTOR PATHWAY IS AN EVOLUTIONARILY CONSERVED MECHANISM MEDIATING RESISTANCE TO TARGETED ANTI- CANCER THERAPY

Arcadi Cipponi[2]; David L. Goode[1]; David Thomas, FRACP, PhD[2]
[1]Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [2]Garvan Institute of Medical Research, Sydney, New South Wales, Australia

Objective: Drug resistance is the major challenge to improving survival for patients with metastatic sarcomas. Adaptive evolutionary mechanisms have been described in lower eukaryotes and prokaryotes that mediate resistance to pleiotropic environmental stresses. We hypothesize that such mechanisms mediate drug resistance in cancers, which may form the basis for novel therapeutic strategies.

Methods: We created model systems for studying drug selection, using a range of cancer cell lines, as well as non-genotoxic targeted therapies. We applied a high content functional genomic screen to identify both drug-specific and generic pathways mediating resistance, using a library of over 100,000 shRNAs to all known human coding genes.

Results: Differential responses are consistently observed to graduated (low and slow: LS) compared to severe (hard and high: HH) selection over a wide range of cell lines and drugs. LS yields efficient and rapid resistance, while HH creates tight bottlenecks with very few surviving clones over much longer timeframes. Distinct mechanism operate in each case. For LS, single nucleotide and indel variation targets known resistance genes, while HH is associated with gross chromosomal instability, without obvious targeting of known resistance pathways. HH (but not LS) is associated with impaired clonogenic capacity IN THE ABSENCE of selective pressure, implying a sustained, constitutive fitness penalty associated with the resistant, post-bottleneck state. This suggests 2-phase adapation--the first phase due to the primary selective stress, and the second phase to processes linked to adaptation itself. In addition to multiple new genes linked to the unfolded protein response, *TP53* and *CDK4* signaling, the genomic screen implicated

the MTOR pathway as critical to adaptation across all HH conditions, with enrichment of shRNAs targeting MTOR itself, as well as the PI3K pathway.

Conclusion: The MTOR pathway is a highly conserved mediator of adaptation to pleiotropic selective pressures from yeast to nematodes, including induction of the dauer survival state. MTOR is also a drug target. We show that impaired PI3K and MTOR signaling increases clonogenic survival under harsh selective stress across a broad range of human cancer types and selective pressures. These observations may shed light on the lack of clinical impact to date of drugs targeting both the MTOR and PI3K pathways, as well as strategies to prevent the emergence of resistance to targeted therapy.

PO 026 2565257

CHARACTERIZATION OF PAZOPANIB USE IN SARCOMA

Makala Pace[2]; Melissa Shepherd[2]; Jennifer Wright, MD[1]
[1]University of Utah, Salt Lake City, UT, USA;
[2]Huntsman Cancer Institute, Salt Lake City, UT, USA

Objective: Background: Pazopanib is an oral tyrosine kinase inhibitor approved by the FDA in April 2012 for second line use in advanced soft tissue sarcoma (STS). Since its approval, pazopanib has been widely used given its easy administration and relative tolerability. Due to its favorable features, it is sometimes also used as first line therapy or in bone sarcomas (ie, off-label use). The wholesale cost of pazopanib is $11255.63 per month, raising the question of when it is appropriate to use.

Objectives: The primary objective is to characterize the institution's general prescribing practice of pazopanib in sarcoma patients. The secondary objective is to describe the cost of pazopanib therapy to patients.

Methods: The records for all patients with a sarcoma diagnosis that were prescribed pazopanib between May 1, 2013 and May 1, 2016 were reviewed. Specific histologic subtype as well as patient age and duration of use were noted. Information on cost to patients was also collected when available. Descriptive statistics were calculated. Cost information remains under analysis.

Results: Pazopanib prescriptions were noted for n=31 sarcoma patients. The most common indications were leiomyosarcoma (n=11), liposarcoma (n=6), and chondrosarcoma (n=5). Prior number of treatment regimens ranged from 0-5 (median = 1). The duration of treatment ranged from one day to 3.04 years, with a mean of 0.37 years. Reasons for discontinuation of pazopanib were largely due to death and progression (n=15) as well as toxicity (n=6). Patients who discontinued for death or progression had a mean duration of treatment 2.9 months. Eight patients remain on treatment at time of analysis at a mean duration of 11.43 months. For histologic subtype, patients with chondrosarcoma had the longest (6.6months) and liposarcoma the shortest duration (2.1 months) of therapy. When pazopanib was given 1st through 3rd line, mean duration of therapy was 5.2 months; those receiving pazopanib as 4th line or greater therapy received therapy for only 2.3months. In comparison, progression free survival of the pazopanib arm ofn the PALETTE study was 4.6 months.

Conclusion: Pazopanib is frequently used in an off-label fashion for sarcoma patients. One quarter of patients in this review received pazopanib as a first line drug and twenty percent of indications were not for a soft-tissue primary site. However, patients with off label use by line of treatment or histologic subtype did not seem to fare worse than those treated by label indications.

PO 027 2567241

COMPLIANCE AND PERSISTENCE OF PAZOPANIB IN METASTATIC SOFT TISSUE SARCOMA PATIENTS IN THE UNITED STATES

Victor M. Villalobos, MD, PhD[1]; Stacey DaCosta Byfield[2]; Sameer Ghate[3]; Oluwakayode Adejoro[2]; Jose Perez[3]
[1]University of Colorado Auschutz Medical Campus, Denver, CO, USA; [2]Optum, Eden Prairie, MN, USA; [3]Novartis, East Hanover, NJ, USA

Objective: Pazopanib was approved in the US for second-line treatment of metastatic soft tissue sarcoma (mSTS) in 5/2012; pazopanib efficacy in adipocytic STS and gastrointestinal stromal tumors has not been demonstrated. Few real world studies describe pazopanib treatment. This study examines pazopanib compliance and persistence among mSTS patients.

Methods: A retrospective study was conducted using a large, national US claims database from 1/2006-9/2015. Adult STS patients (≥2 claims with ICD-9-CM 171.xx) with ≥1 claim for pazopanib were identified. Line of therapy (LOT) periods were created based on receipt and timing of NCCN-recommended therapy for mSTS. The index date was the start of the first LOT that included pazopanib after 5/2012. Continuous enrollment in the health plan for 6 months prior to (baseline period) and after (follow-up period) the index date was required. Persistence with therapy by LOT was defined as days to discontinuation (time on therapy before a 30-day gap). Compliance was estimated using proportion of days covered (PDC); the number of days covered by prescription divided by number of follow-up days (180 days); high compliance was PDC ≥80%. Differences by initial pazopanib LOT were examined using Fisher's exact test (categorical variables) and t-test (continuous variables).

Results: Ninety-six patients met study criteria; 82% com-

mercially insured and 18% Medicare Advantage. Mean age was 56 years (standard deviation (SD), 15 years), 42% were male and mean baseline Charlson score of 6.5 (SD 1.7; median 6). The median initial dose of pazopanib was 800mg (range 200mg to 857mg). Approximately 77% of patients discontinued pazopanib in the 6-month follow-up. Though not statistically significant, a lower percentage of patients with pazopanib in LOT1 discontinued compared to those receiving pazopanib in later LOTs. Mean persistence with therapy was 99 days (SD 57 days; median 90 days) and was generally higher among patients with pazopanib in earlier versus later LOTs; 116 days for LOT1 to 72 days for LOT5+. Estimates of high compliance were low overall (24%) but more patients who initiated pazopanib in LOT1 had high compliance (34%) compared to those who initiated pazopanib in later LOTs (<25%), though not statistically significant.

Conclusion: Most mSTS patients initiated pazopanib on recommended dose. Generally, persistence and compliance with pazopanib reduced with later LOTs. Further studies should investigate the reasons for low persistence, compliance and impact on outcomes.

PO 028 2570985

VERY PROLONGED RESPONSE TO TRABECTEDIN IN REFRACTORY UTERINE LEIOMYOSARCOMA: A CASE REPORT

Vanda Salutari, MD[1]; Ida Paris[1]; Anna Fagotti[1]; Maurizio D'Incalci[2]; Gian F. Zannoni[1]; Caterina Ricci[1]; Maria G. Distefano[1]; Gabriella Ferrandina[1]; Giovanni Scambia[1]

[1]Gynecology Oncology, Fondazione Policlinico Universitario A Gemelli, Rome, Italy; [2]Department of Oncology, IRCCS - Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy

Objective: Uterine leiomyosarcomas (U-LMS) are rare tumors that account for approximately 1% of all uterine malignancies, which have an extremely poor prognosis with survival rates among the lowest (~12 months) of all soft tissue sarcomas (STS). Whilst a total abdominal hysterectomy is the cornerstone of management of early disease, for recurrent or disseminated U-LMS, cytotoxic chemotherapy remains the mainstay of treatment but with no impact on survival. Trabectedin, a DNA-damaging agent with a mechanism of action that differs from that of traditional alkylating agents, is approved in Europe, USA and many other countries worldwide for the treatment of patients with advanced STS after failure of anthracyclines or for those patients who are unsuited to receive these agents.

Methods: We report the case of a 38-year-old woman with peritoneal metastatic uterine leiomyosarcoma refractory to adriamicine-ifosfamide and gemcitabine-docetaxel chemotherapy, who obtained a prolonged disease control following the treatment with trabectedin.

Results: The patient received 58 cycles of trabectedin 1.5 mg/m^2 given as a 24-hour i.v. infusion every three weeks over 50 months. Trabectedin treatment resulted in a partial response according to the Response Evaluation Criteria in Solid Tumors (RECIST) with good and predictable tolerability profile of the regimen. Marked tumor shrinkage allowed a surgical resection that histologically evidenced a complete necrotic response of the pelvic mass and peritoneal carcinosis. Molecular characterization pre- and post-trabectedin administration is still ongoing.

Conclusion: Our findings support that trabectedin represents a feasible option for prolonged treatment of metastatic U-LMS; however, further clinical studies are warranted to better understand the mechanism of long-lasting response to trabectedin.

PO 029 2557833

UNIDIRECTIONAL INTRAOPERATIVE RADITION THERAPY TO TREAT RETROPERITONEAL SARCOMA USING CIVATECH SHEET PLANAR BRACHYTHERAPY: A CASE REPORT

Dian Wang, MD, PhD[1]; Minh Luu[2]; Heming Zhen[1]; Neilayan Sen[1]; Julius Turian[1]; James Chu[1]; Ross Abrams[1]

[1]Radiation Oncology, Rush University Medical Center, Brookfield, WI, USA; [2]Surgery, Rush University Medical Center, Chicago, IL, USA

Objective: Dose escalation via EBRT or traditional IORT to treat retroperitoneal sarcoma is often limited by adjacent normal tissue tolerance. Recently an innovative unidirectional Pd-103 brachytherapy (CivaTech) is developed, however, there are no reports of this device being used to treat retroperitoneal sarcoma. The purpose of this case report is to describe the safety and feasibility of using this new IORT device to boost retroperitoneal sarcoma after preoperative RT and to evaluate the planning target volume (PTV) dosimetry pre and post the implant.

Methods: This 39-yo woman completed preoperative IMRT (49.91Gy in 23 fractions) to her recurrent liposarcoma involving left retroperitoneum. Prior to surgery she underwent a new CT simulation (the same position) for IORT boost planning (2 mm axial slices). The deep surface of the tumor along the left iliopsoas muscle was predicted for high risk recurrence after resection and PTV was delineated via a joint effort between a radiation oncologist and a surgeon. Eclipse Treatment Planning (Varian, Palo Alto CA) was used for dosimetry planning. A 5 x 15 cm (8 mm source spacing, total # of sources = 108, 0.8 U per seed) sheet was chosen to prescribe 25 Gy to at least 98% of the PTV (D_{98} ≥ 100%). She returned for the post-implant CT at 2.5 weeks (one half-life of Pd-103) and 3 months (five half-life of Pd-103).

Results: This sarcoma was resected. The CivaTech sheet was placed with Pd-103 seeds facing down over the high risk field. Absorbable stitches were used to secure the Civa sheet to the retroperitoneum below. Normal tissue structures including left kidney were then allowed to fill the space. The entire procedure lasted for approximately 10 min. Her postoperative course was not eventful. At the 2.5-week follow-up all 108 seeds were identified on the CT image and 90% of the PTV volume is shown to have received full prescription dose coverage (D90 ≥100%). At the 3-month followup the CT images showed congregation of the seeds, but all seeds were located in the tumor bed, and none of them migrated distantly. The seeds have shifted their position slightly due to the biological absorption of the plastic sheet holding the sources into the matrix

Conclusion: CivaTech planar brachytherapy source is an innovative unidirectional IORT option suitable and feasible for the treatment of retroperitoneal sarcoma. The comparison of pre- vs. post- implant dosimetry showed excellent dose coverage of PTV, and also there was no seed migration distantly at 3 mos.

PO 030 2565143

PROGNOSTIC RELEVANCE OF SUBTYPE IN LOCALLY ADVANCED SYNOVIAL SARCOMA WITH NEOADJUVANT CHEMOTHERAPY

Tatsunori Shimoi[1]; Kan Yonemori[1]; Emi Noguchi[1]; Mayu Yunokawa[1]; Ayumu Arakawa[2]; Chitose Ogawa[2]; Akira Kawai[3]; Hirokazu Chuman[3]; Akihiko Yoshida[4]; Kenji Tamura[1]

[1]Breast and Medical Oncology, National Cancer Center, Tokyo, Japan; [2]Pediatric Oncology, National Cancer Center, 5-1-1 Tsukiji, Tokyo, Japan; [3]Musculoskeletal Oncology and Rehabilitation Medicine, National Cancer Center, 5-1-1, Tsukiji Chu-o-ku Tokyo, Japan; [4]Pathology and Clinical Laboratories, National Cancer Center, 5-1-1, Tsukiji Chu-o-ku Tokyo, Japan

Objective: Synovial sarcomas comprise approximately 5-10 % of all soft tissue sarcomas, however, are relatively chemosensitive. The optimal local management of localized synovial sarcoma is complete tumor resection especially locally advanced synovial sarcoma. The main objective of this study is to assess prognostic factor in locally advanced synovial sarcoma who were resected after neoadjuvant chemotherapy despite initially unresectable.

Methods: Between July 2007 and May 2016, a total 17 consecutive patients with localized synovial sarcoma were treated at the National Cancer Center in Japan. Patients included in this study received definitive sarcoma therapy (neoadjuvant chemotherapy, surgery, and/or radiation therapy). Age at diagnosis, gender, tumor specific data (subtype, size (≤5cm, 5-10cm, ≥10cm), location, depth, surgical margins), therapy (chemotherapy, surgery and radiation), necrosis status (≥90%) after neoadjuvant chemotherapy, and clinical outcome were collected retrospectively. Survival rates were determined using the Kaplan-Meier (K-M) method. Event free survival (EFS) was defined as the time between diagnosis and relapse or death from synovial sarcoma. To study the association of the prognostic factors with patient survival, K-M survival curve analysis using Log-rank test was performed ($p \leq 0.05$ was considered statistically significant.).

Results: Clinicopathologic features of the 17 patients in the current study are shown in Table 1. The median age was 30 (range 5-59), male were 8 patients (47%), and all patients received ifosfamide based neoadjuvant chemotherapy. The median cycles of neoadjuvant chemotherapy was 3 (range 2-6) and total perioperative chemotherapy cycles were 6 (range 2-6). All patients underwent an R0 surgical resection. All tumors without one tumor (which was not tested) harbored SS18 gene rearrangement as detected by FISH or RT-PCR analysis. With a median follow up of 3 years, a total 7 patients relapsed. Moreover, all sites of relapse were the lung. The median EFS was 621 days (range 244-1702). In univariate analysis, EFS was statistically better for monophasic subtype compared with biphasic subtype ($p = 0.048$). There was only one patient who had had Necrosis over 90 % after neoadjuvant chemotherapy. The patient has no relapse for 1607 days after surgery.

Conclusion: With ifosfamide based neoadjuvant chemotherapy, monophasic subtype might relate to good prognosis factor of EFS.

Patients characteristics

Characteristics	N (%) N=17
Gender Male Female	8 (47) 9 (53)
Age at diagnosis, Median (range)	30 (5-59)
Primary Site Lower extremity Upper extremity Trunk Head and Neck Thoracic Retroperitoneal/intraabdominal	4 (24) 5 (29) 1 (6) 0 5 (29) 2 (12)
Depth Deep Superficial	8 (47) 9 (53)
Primary Tumor Size (cm) ≤5 5-10 ≧10	4 (24) 7 (41) 6 (35)
Subtype Monophagic Biphagic	12 (71) 5 (29)
Margin status R0	17 (100%)
Necrosis ＞90% Yes No	1 (6) 16 (94)
Adjuvant radiotherapy Yes No	2 (12) 15 (88)
Perioperative chemotherapy Ifosfamide based	17 (100)

Univariate analysis of prognostic factors in Event free survival

Characteristics	Univariate analysis P
Gender Male / Female	0.17
Age Over 30 years old / under 30 years old	0.71
Depth Deep / Superficial	0.58
Primary Tumor Size (cm) ≤5 / 5-10 / ≥10	0.13
Subtype Monophagic / Biphagic	0.048

PO 031 2570531

PRIMARY AND SECONDARY ANGIOSARCOMAS: A SINGLE-CENTER EXPERIENCE

Daniela Greto, MD[1]; Mauro Loi[1]; Calogero Saieva[2]; Domenico Campanacci[3]; Giovanni Beltrami[3]; Guido Scoccianti[3]; Laura Trombetta[1]; Isacco Desideri[1]; Pierluigi Bonomo[1]; Lorenzo Livi[1]

[1]Sperimental Biomedical and Clinical Sciences, University of Florence, Florence, Italy; [2]Molecular and Nutritional Epidemiology Unit, ISPO (Cancer Research and Prevention Institute), Florence, Italy; [3]Ortopedical Oncological Surgery, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence, Italy, Florence, Italy

Objective: Angiosarcomas are malignant tumors deriving from endothelial cells. Angiosarcoma of the breast can occur as a primary tumor or as a secondary tumor associated with radiotherapy (Radiation Associated Angiosarcomas: RAAS)

Methods: Fifteen patients with breast angiosarcoma were treated in a period of twenty years at University of Florence. Angiosarcomas were considered RAAS if the tumor occurred in a previous radiation field and after a delay of at least 3 years from the end of radiation treatment.

Results: Mean follow up was 5.6 years (range: 0.1-19.3). Mean age of primary angiosarcomas and RAAS was 40 years (range: 17-60 years) and 52.2 years (range: 49-86 years), respectively. All breast angiosarcomas were females (93.3%) while one male (6.7%) had a primary thoracic wall angiosarcoma. All 7 primary angiosarcomas were diagnosed as deep breast mass, whereas 8 secondary tumors had clinical skin manifestations in six cases: nodules and macules on the previous surgical site in 2 and 3 patients, respectively and 1 skin ulceration.

Mean latency between radiotherapy and the development of angiosarcoma was 12.5 years (range: 3-26 years).

All patients underwent surgery, in detail: mastectomy was performed in four (26.7%) primary angiosarcoma and in 6 (40%) RAAS; two (13.3%) RAAS patients and three (20%) primary angiosarcoma patients underwent lumpectomy. At the last follow up 12 patients were alive, one RAAS patient and one with primary tumor have had a cancer related death. Overall survival was 33.8%.

One local recurrence occurred in a secondary angiosarcoma patient, the mean time of local failure was 0.3 years; local recurrence free survival was 92.9%.Distant metastasis were diagnosed during the follow up in one (6.7 %) RAAS patients and one (6.7%) with primary tumor, the mean time of distant progression was 2.5 years (range: 0.4-4.6 years).At the Kaplan Meyer any parameters was statistically significant for overall survival, local and distant recurrence

Conclusion: The clinical outcome of primary and secondary angiosarcoma did not differ in this retrospective study. Even if the incidence of radiation induced angiosarcoma is low, since women with breast carcinomas have an improving prognosis, clinical and radiological evaluations are needed for a long follow up period because early detection is essential considering the poor prognosis

PO 032 2564890

AN UNUSUAL LOCAL INVASION OF MYXOID LIPOSARCOMA

Yusuke Minami, Dr, PhD[2]; Eisuke Kobayashi[1]; Akira Kawai[1]; Hirokazu Chuman[1]; Atsushi Okawa[2]

[1]Division of Musculoskeletal Oncology, National Cancer Center Hospital, Tokyo, Japan; [2]Orthopedic Surgery, Tokyo Medical and Dental University, Tokyo, Japan

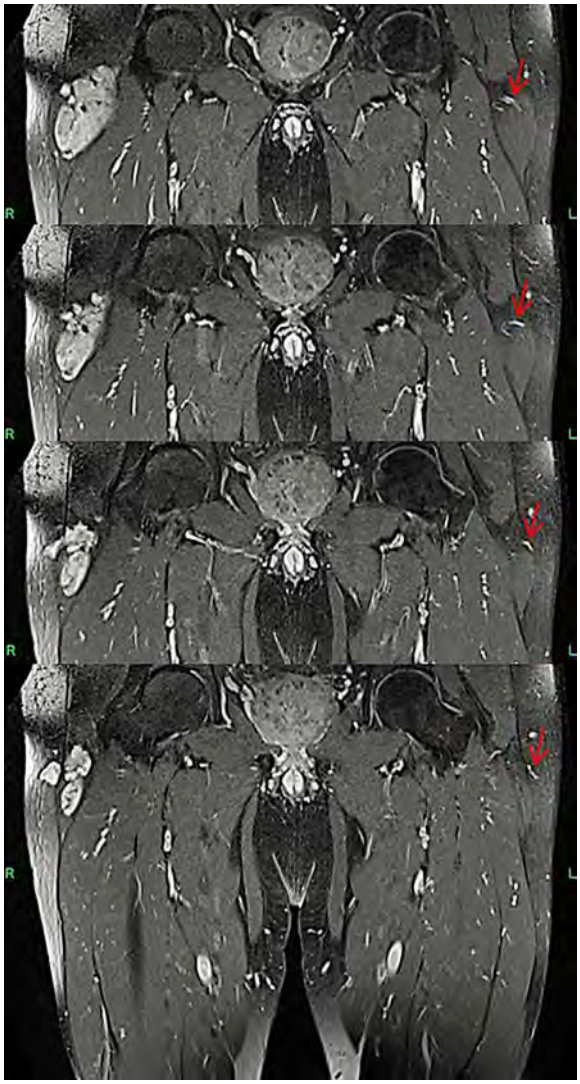
Objective: Iliotibial tract (ITT), another name iliotibial band, is a robust fibrous connective tissue which covers lateral aspect of the thigh. Based on the standard concept of safety margin in surgery for bone and soft tissue sarcomas, ITT is considered as one of the most dependable barriers to acquire a safety margin due to its physical strength as a thick membrane.

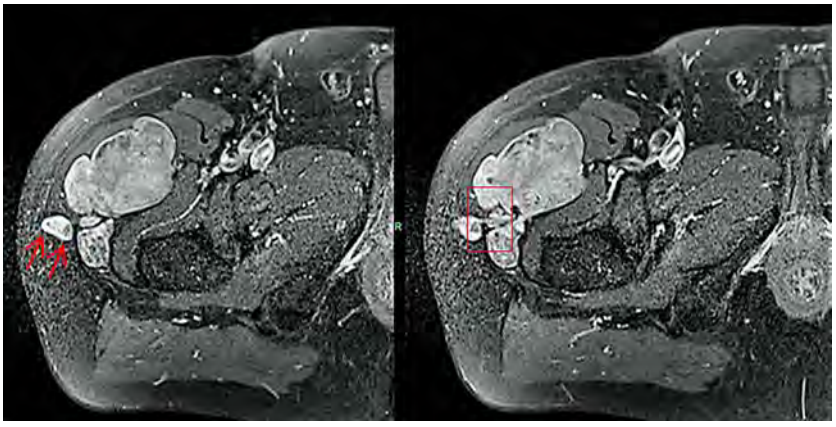
Methods: We reported a case of myxoid liposarcoma arising from the deep part of right thigh which extended into the subcutaneous lesion beyond the ITT.

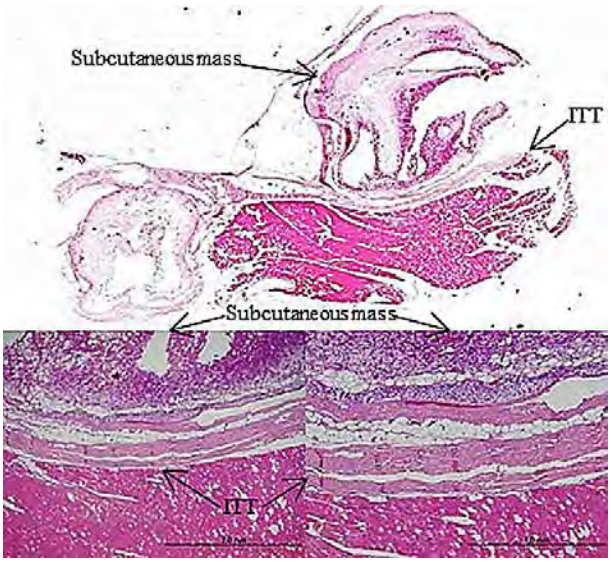
Results: A 60-year-old male with a large mass was admitted to our hospital. Magnetic resonance imaging (MRI) demonstrated a well-defined and gadolinium-enhanced mass (9 × 7 cm) in his right thigh. MRI also revealed a smaller mass extending into the subcutaneous tissue beyond the iliotibial tract (ITT) (Fig. 1, red triangle). Needle biopsy from the large mass confirmed the histological diagnosis of

myxoid liposarcoma with <5% round cell components. We performed wide excision of the tumor using ultrasonography to confirm the location of the impalpable subcutaneous smaller lesion. A histopathological examination (red square in figure 1) showed that the tumor had no direct invasion into the ITT (Fig. 2). One year and six months after the surgery, the patient has shown no sign of recurrence.
The ITT is a robust fibrous connective tissue which covers the lateral aspect of the thigh and it is considered to be the greatest barrier to ensuring a safety margin in musculoskeletal surgery. Preoperative sequential MRI in the present case showed a perforating vessel through the ITT originating from a branch of the lateral femoral circumflex artery (LFCA) on the opposite side (Fig. 3, arrows). A gap at the tumor site and relatively indolent tumor growth might allow for such unfamiliar development of a tumor, even against a robust barrier.

Conclusion: To our knowledge, no previous study has reported such unique extension of a soft tissue sarcoma beyond the ITT. Surgeons should thus be aware of the potential vulnerability of the ITT. A careful preoperative examination is warranted to obtain a safe margin in sarcoma surgery.







PO 033 2570457

PRIMARY CARDIAC SARCOMA: REPORT OF 3 CASES TREATED WITH COMBINED MODALITY

Eduardo C. Netto, MD[1]; Margarida Ferreira[2]; Maria Teresa Alexandre[2]; Antonio Mota[1]; Rute Pocinho[1]; João Freire[2]

[1]Radioterapia, IPO Lisboa, Lisbon, Lisbon, Portugal; [2]Oncologia Médica, IPO Lisboa, Lisbon, Portugal

Objective: Primary cardiac sarcoma (PCS) is a rare entity with poor prognosis. The median overall survival remains dismal, from 6 months to a few years. We present 3 consecutive cases from a reference Cancer Center.

Methods: We conducted a retrospective chart review of 3 patients diagnosed between March 2005 to March 2015.

Surgery report, radiotherapy (RT) planning and chemotherapy (ChT) data were recorded. Toxicities were classified via CTC 4.0.

Results: Three cases were diagnosed in 2 men and 1 woman with ages of 18, 49 and 61 year-old. Two had malignant undifferentiated sarcoma and one a synovial sarcoma. All patients underwent surgery as a primary treatment followed by sequential chemoradiation. Surgery was performed with declared R1 ressection at all cases. Adjuvant RT was delivered in 2 patients. Median 3D conformal dose image-guided radiotherapy was 60Gy in 30 fractions delivered through planned with (n= 2) or without (n = 1) 4DCT. Doxorrubicine and ifosfamide were used concomitantly as adjuvant treatment in all cases. Most frequent toxicity was grade 2 esophagitis (3/3). With a median follow up of 25 months, 2 patients developed distant metastases in lung and bone, at 25 and 32 months, respectively. The only patient that did not received RT developed an operable local recurrence 14 months after initial surgery. He underwent salvage resection followed by adjuvant RT. Median cardiac ejection fraction was 61% at metastases diagnosis. However, no patient had developed local recurrence after RT or major adverse cardiovascular event (MACE). One patient is still alive without evidence of disease at 15 months after treatment.

Conclusion: PCS is a treatment challenge for a multidisciplinary team. In this report, multimodality therapy (surgery, RT, and ChT) was feasible and RT sustained local control even after salvage surgery. No patient developed treatment-related MACE but further improvements are needed to enhance metastases control.

PO 034 2564927

THE POTENTIAL RISK OF THE SUPERFICIAL SOFT TISSUE SARCOMA

Takashi X. Shimoji, PhD; Jun X. Manabe; Hirotaka X. Koyanagi
Orthopaedic Surgery, Saitama Cancer Center, Ina Town, Saitama Pref., Japan

Objective: Soft tissue sarcoma located in the superficial layer has some clinical problems such as unplanned resection.

We'd like to reveal clinical problems of superficial soft tissue tumors and discuss about it.

Methods: We defined the superfical soft tissue sarcoma as it located in the subcutaneus tissue, skin and supeficial muscle membrane in this presentation.

We looked into the differences (age, sex, location, histological types, size, invasive growth and treatment) between 31 cases of the superficial soft tissue sarcoma and 88 cases of the deep located soft tissue sarcoma through January 2011 to December 2014 treated in our institute.

Results: We find following issues; there''re 42% of the superfial soft tissue sarcoma which showed invasive growing, and 26% of them got an unplanned resection. And 45% of them needed a reconstruction with various soft tissue reconstructions. On the other hand, the deep soft tissue sarcoma are showed less invasive growing (30%), taking another unplanned pre-operation (8%) and less necessity of a reconstruction (18%).

Among 8 unplanned resection cases, all cases were not performed ehough medical examinations such as needle biopsy and medical image examination.

Conclusion: The superficial soft tissue sarcomas tend to get unplanned resection and showed invasive growth more than deep soft tissue sarcoma.

This lead them to get more high invasive surgery and even more soft tissue reconstruction would be needed.
Enough medical examination and proper treatment would be critical for the superficial soft tissue tumors.

PO 035 2565235

A RETROSPECTIVE CHART REVIEW OF ADULTS DIAGNOSED WITH SOFT TISSUE AND BONE SARCOMA AS TREATED AT A NON-ACADEMIC COMMUNITY CANCER CENTER

Shawn L. Price, MD; Kelsey Holmes
Orthopaedic Surgery, Norton Cancer Institute, Louisville, KY, USA

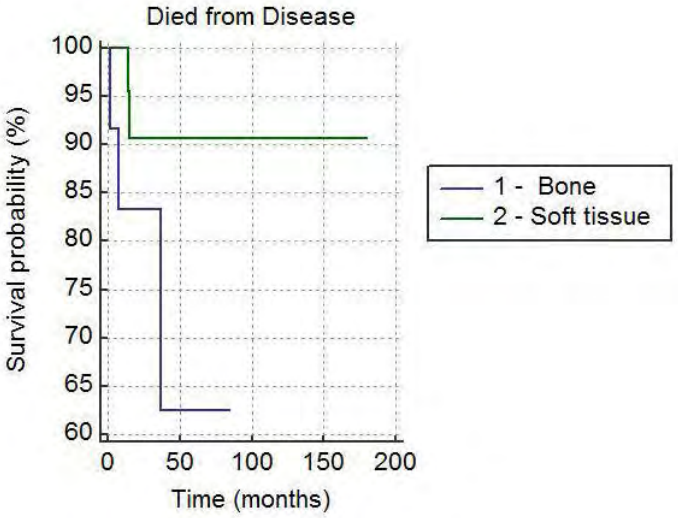
Objective: To determine the margin status, rates of local recurrence or metastatic disease, and survival of adult patients diagnosed with bone or soft tissue sarcoma (STS) and treated at a non-academic community cancer centers.

Methods: We performed a chart review of a total of 52 patients treated for bone or soft tissue sarcoma at a community cancer center. The chart was reviewed for demographics, histologic subtype, grade, stage at diagnosis, the use of adjuvant therapy, margin status for surgical patients, the development of local recurrence and or metastatic disease, patients lost to tertiary cancer centers and surviorship.

Results: There were a total of 52 patients, 15 bone sarcomas and 37 soft tissue sarcoma whose charts were reviewed. Two patients with both bone (n=13) and ST (n=35) sarcoma were lost to tertiary cancer centers. The majority of bone sarcoma patients were AJCC Stage IIb and AJCC Stage III for soft tissue sarcomas at diagnosis. One patient with bone sarcoma and 3 with STS presented with Stage IV disease. Radiation therapy was given to 61%(53 preop, 11% post-op) of patients with soft tissue

sarcoma. Chemotherapy was given to 7 patients with STS, 2 of which demonstrated metastatic disease after negative margin resection. Chemotherapy was given to 8 patients and radiation therapy was given to 2 patients with bone sarcoma, one for palliation and another for positive resection margin. A positive margin occurred in one patient of 13 patients with bone sarcoma who had undergone resection. This patient had an unplanned procedure at another facility prior to presentation. A positive margin was encountered in one STS patient who had undergone unplanned resection prior to presentation and one planned positive margin in another patient who rejected an oncologic procedure. Negative margins were obtained in 94% patients with STS who underwent oncologic resection and 10 patients with bone sarcoma. Local recurrence occured in 1 STS and bone sarcoma patient, and metastasis developed in 7 patients treated for STS and 2 patients treated for primary bone sarcoma. Twenty seven percent of bone sarcoma and 8.5% of STS patients died of disease.

Conclusion: Herein we present a small cohort of bone and soft tissue sarcoma patients treated at a non-academic community cancer center. Our percentage of negative margins, local recurrence rate, rate of metastasis, and survivorship support the treatment of sarcoma patients at non-academic, non-tertiary referral centers by sarcoma trained providers.



PO 036 2570669

GASTRIC METASTASE OF LUNG SYNOVIAL SARCOMA - A RARE ENTITY

Daniela V. Macedo; Isabel Fernandes; Andre Mansinho; Luis Costa
Oncologia Médica, Hospital Santa Maria - Centro Hospitalar Lisboa Norte, Lisbon, Portugal

Objective: Synovial sarcoma accounts for about 10% of adult soft tissue sarcomas, with 80–90% located in the limbs. It has a propensity for local recurrence and lung metastases. Gastrointestinal tract involvement is rare. Owing to the rarity of this tumor in the gastrointestinal tract, the appropriate treatment is uncertain.

Methods: The authors present one clinical case of gastric metastase of a lung primary synovial sarcoma.

Results: This case concerns a 63 years old male, smoker, who in 2013 due to symptoms of dry cough and dyspnea resorted to his physician, having been identified a large mass on right lung in imaging tests, suspected of primary tumor of lung. It underwent pneumonectomy and histology was compatible with primary lung synovial sarcoma, confirmed with detection of t (X; 18) translocation and expression of SYT-SSX fusion protein. Due to radical surgery and no recommendations for adjuvant treatment he was proposed to surveillance. Three years later he started to epigastric pain and haematemesis which conditioned an endoscopic examination where was identified a gastric lesion suspected of neoplasia, being placed hypothesis of primary gastric tumor (second tumor). Histological result of gastric biopsy revealed it to be a synovial sarcoma metastasis, and was confirmed again the presence of the t (X; 18) translocation. After multidisciplinary discussion and absence other suspicious lesions in staging imaging he was proposed for total gastrectomy. Currently it remains in surveillance with no evidence of disease.

Conclusion: Due to the rarity of gastrointestinal metastasis of synovial sarcomas it is difficult to have recommendations regarding optimal treatment. Our case and the review of the literature support surgical resection as a curative treatment. However, late recurrence is well documented for synovial sarcoma, so these sarcomas should have a wider margin of excision and nodal dissection.

PO 037 2569544

TUMOR-VOLUME DOUBLING TIME OF SOFT TISSUE SARCOMAS

Masachika Ikegami, MD; Hiroshi Kobayashi; Yusuke Shinoda;
Ryoko Sawada Orthopedics, The University of Tokyo Hospital, Tokyo, Japan

Objective: The purpose of this study is to evaluate the growth rate of primary and metastatic sites of soft tissue sarcomas(STS) by calculating tumor-volume doubling time(TDT) on serial CT or MRI, and to determine whether TDT is associated with survival after the first metastasis in STS.

Methods: Imaging studies of 53 metastatic STS patients were used in this study. Thirty-seven patients had measurable primary sites, and 43 patients had measurable metastases in at least two sequential CT or MRI. All patients

did not receive any anti-tumor treatment on the primary or metastatic sites in the past 4 weeks and between the imaging studies. The mean age og the patients was 64 years (range 14-90). There were 39 male and 14 female patients. the mean maximum diameter of metastasis at first diagnosis was 21.2mm. fourteen patients had undifferentiated pleomorphic sarcoma, 5 had myxofibrosarcoma, 4 had leiomyosarcoma, 3 had malignant peripheral nerve sheath tumor, 3 had extraskeletal Ewing sarcoma, 3 had dedifferentiated liposarcoma, 3 had undifferentiated round cell sarcoma, and 18 had other types of STS.

Results: The median TDT of primary(pTDT) and metastatic sites(mTDT) were 45 days (14-1100) and 29 (5-1637), respectively. Ten patients (27%) had pTDT of less than 30 days, 25 (68%) had less than 90 days, and 33 (89%) had less than 180 days. Twenty patients (48%) had mTDT of less than 30 days, 40 (93%) had less than 90 days. Twenty-eight patients had measurable primary and metastatic sites. pTDT was shorter than mTDT in 21 patients (75%). The ratio of mTDT to pTDT was 0.05-4.52 (median 0.51). The univariate analysis revealed significantly poorer predictive values for mTDT. A multivariate analysis showed that mTDT to be an independent predictor of survival. pTDT was not a significant prognostic factor.

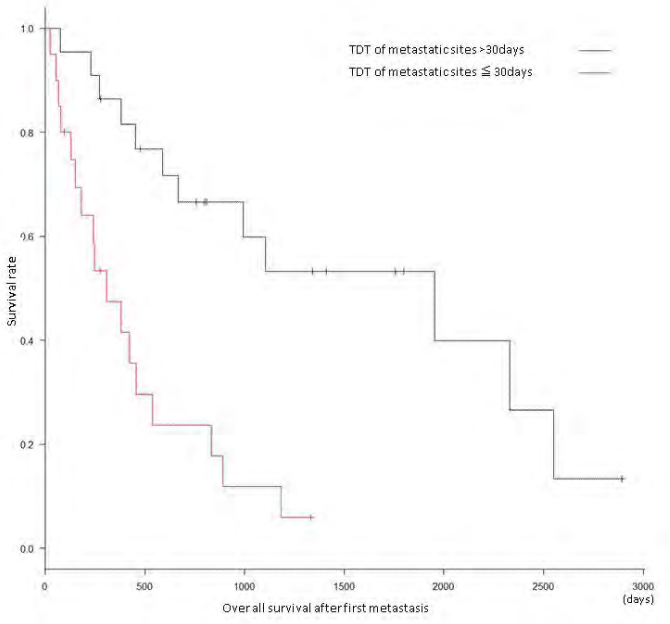
Univariate survival analysis in soft tissue sarcoma patients with metastasis

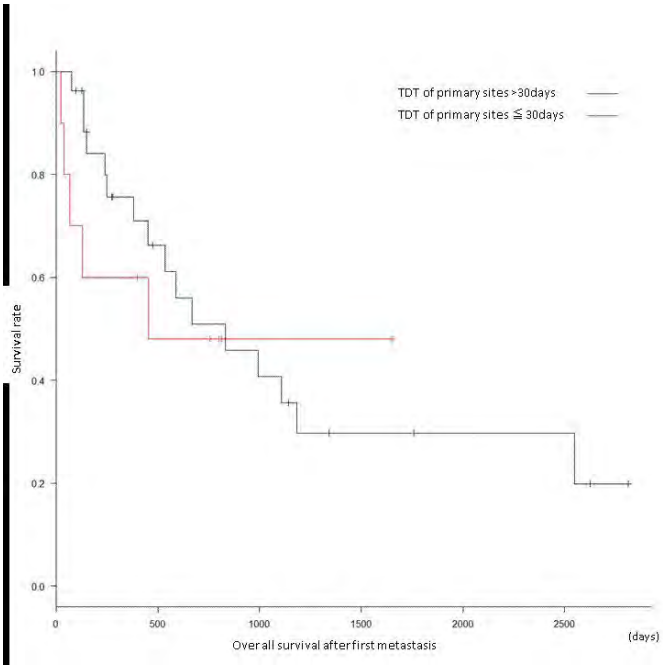
Characteristics	n	3-year survival (%)	P value
Age			0.46
≧65	24	44.1	
<65	29	39.1	
Gender			0.22
Male	40	35.9	
Female	13	57.1	
Maximum tumor size of metastatic sites			0.12
≧10mm	31	32.0	
＜10mm	22	55.0	
Metastasis at presentation			0.87
Yes	24	40.0	
No	29	39.8	
Tumor-volume doubling time of primary sites			0.69
≧30 days	27	40.7	
＜30 days	10	48.0	
Tumor-volume doubling time of metastatic sites			0.0003
≧30 days	22	59.9	
＜30 days	20	11.9	

Multivariate survival analysis in soft tissue sarcoma patients with metastasis

Variables		HR(95% CI)	P value
Gender	Female	0.85(0.30-2.41)	0.77
Maximum tumor size of metastatic sites	≧10mm	1.87(0.81-4.34)	0.14
Tumor-volume doubling time of metastatic sites	＜30 days	4.78(2.00-11.39)	0.0004

Conclusion: It is reported that TDT of metastatic sites is shoter than primary sites in colon cancer(24 vs 8 weeks), hepatic cancer(13 vs 6 weeks), and breast cancer(30 vs 14 weeks). We revealed that the TDT of STS is shorter than other types of malignant tumors. The growth rate of metastatic lesions are about twice of primary lesions in STS, that is similar to other tumors. As treatment delay might result in poor prognosis, we should follow-up STS patient in the view of TDT.





PO 038 2544097

FERTILITY PRESERVATION OF MALE PATIENTS WITH HIGH-GRADE MALIGNANT BONE AND SOFT TISSUE TUMOR BEFORE CHEMOTHERAPY IN JAPANESE SINGLE INSTITUTION

Manabu Hoshi; Naoto Oebisu; Yoshitaka Ban; Hiroaki Nakamura
Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine, Osaka, Osaka, Japan

Objective: Fertility preservation including sperm cryopreservation before chemotherapy is not prevalent among orthopedic oncologists in Japan. The purpose of this study was to report the result of our trial for fertility preservation in male patients with high-grade malignant bone and soft tissue tumor.

Methods: A total of 15 male patients under age of 45 years old, with high-grade bone and soft tissue tumor, were examined. The median age at the diagnosis was 27.0±11.1 years, with a range from 8 to 42 years. Soon after rapid pathology confirmed that tumor histology was high-grade malignant tumor, we informed all the patients about the issues related to male infertility due to chemotherapy. If they hope, we offered to visit clinic of reproductive specialists for fertility preservation. Clinical features of the patients and the method of fertility preservation were investigated.

Results: Most unmarried and childless patients showed their interest of fertility preservation. Five patients (33.3%) used sperm cryopreservation and one (6.7%) patient preserved his hemi-testis due to elective dysfunction after surgery for colon cancer. Married and childed patients did not preserve fertility.

Conclusion: For young male patients with high-grade bone and soft tissue tumor, infertility after chemotherapy would raise a serious concern in the future. Informed consent including counseling regarding the potential risk of chemotherapy before treatment should be done, without delay of start of cancer treatment. Orthopedic oncologists are encouraged to offer sperm banking to young male at risk of infertility before cancer chemotherapy.

Table.1 Relevant clinical and sociological patient characteristics and techniques of fertility preservation.

Case	Age/Gender	Histopathology	Type	Anatomical site	AJCC	Stage	Marriage status	Child	Fertility preservation	Method
1	16M	Rhabdomyosarcoma	Soft	Buttock	T2bN0M0	IV	Unmarried	-	-	None
2	34M	Synovial sarcoma	Soft	Forearm	T1bN0M0	II	married	+	-	None
3	39M	Synovial sarcoma	Soft	Foot	T1aN0M0	II	married	+	-	None
4	34M	Extraskeletal mesenchymal chondrosarcoma	Soft	Lower leg	T2bN0M0	III	married	+	-	None
5	37M	Extraskeletal myxoid chondrosarcoma	Soft	Thigh	T2bN0M0	III	Unmarried	-	+	Testis preservation
6	42M	Epithelioid sarcoma	Soft	Index finger	T1aN0M0	II	Unmarried	-	+	Sperm preservation
7	28M	Extraskeletal mesenchymal chondrosarcoma	Soft	Neck	T2bN0M0	III	Unmarried	-	+	Sperm preservation
8	27M	Epithelioid sarcoma	Soft	Forearm	T2bN1M0	IV	Unmarried	-	+	Sperm preservation
9	11M	Ewing sarcoma	Bone	Femur	T2N0M0	IIB	Unmarried	-	-	None
10	15M	Osteosarcoma	Bone	Tibia	T2N0M0	IIB	Unmarried	-	-	None
11	8M	Osteosarcoma	Bone	Femur	T2N0M0	IIB	Unmarried	-	-	None
12	27M	Osteosarcoma	Bone	Humerus	T2N0M0	IIB	Unmarried	-	+	Sperm preservation
13	9M	Osteosarcoma	Bone	Femur	T2N0M1	IV	Unmarried	-	-	None
14	19M	Osteosarcoma	Bone	Humerus	T1N0M0	IIA	Unmarried	-	+	Sperm preservation
15	13M	Osteosarcoma	Bone	Femur	T2N0M0	IIB	Unmarried	-	-	None

PO 039 2565901

REAL-WORLD TREATMENT PATTERNS AND SURVIVAL FOR PATIENTS WITH ADVANCED SOFT TISSUE SARCOMA RECEIVING SYSTEMIC THERAPY IN SPAIN

Daniel S Mytelka[1]; Maria Lorenzo[2]; Dana Stafkey-Mailey[3]; Yulia D'yachkova[4]; Saurabh P. Nagar[5]; Sean D. Candrilli[5]; James A. Kaye[6]; Jose A. López-Martín[7]
[1]Eli Lilly and Company, Indianapolis, IN, USA; [2]Lilly Research Center, Windlesham, United Kingdom; [3]Formerly RTI-HS, Durham, NC, USA; [4]Eli Lilly GmbH, Vienna, Austria; [5]RTI Health Solutions, Durham, NC, USA; [6]RTI Health Solutions, Waltham, MA, USA; [7]12 de Octubre University Hospital, Madrid, Spain

Objective: Characterize real-world treatment patterns and survival in Spain for patients with advanced soft tissue sarcoma (STS) not amenable to surgery or radiotherapy.

Methods: Physicians in Spain completed a web-based retrospective medical record review for patients ≥18 years old who received ≥1 line of systemic therapy for advanced STS (other than Kaposi's sarcoma or gastrointestinal stromal tumors) from 1/1/2005 to 21/2/2014. Demographic and clinical characteristics (performance status [PS]; WHO histological classification; stage at diagnosis), treatments, and survival were recorded. Data were reported overall, by line of therapy, and by histological subtypes.

Results: Thirty-four physicians provided data for 203 patients. Patients' mean (SD) age at advanced STS diagnosis was 56.6 (13.1) years, with 61% male. The most frequent histological subtypes were leiomyosarcomas (22%), liposarcomas (22%), and vascular sarcomas (12%). Sixty-eight percent of study patients had stage IV cancer at initial diagnosis, and 46% had an ECOG PS of 2 or higher. Forty-two percent of patients had >1 and 10% had >2 lines of therapy. The five most common first-line chemotherapy regimens were doxorubicin (35%), doxorubicin/ifosfamide (15%), docetaxel/gemcitabine (10%), paclitaxel (6%), and ifosfamide (5%); the most common in second-line were ifosfamide (22%), trabectedin (17%), docetaxel/gemcitabine (13%), pazopanib (10%), and doxorubicin (10%). The most frequently used supportive medications were analgesics (65%), antiemetics (60%), and corticosteroids (31%). In first-line treatment, the average response rate was 42%; the average response rate in second-line treatment was 24%. Median survival estimates from start of first- and second-line therapy were 16.3 (Q1:Q3=8.2:30.8) and 12.0 (Q1:Q3=7.3:21.6) months, respectively.

Conclusion: This retrospective medical record review provides data on real-world advanced STS-related treatment and survival in Spain. Results point to critical unmet needs for more effective treatment options improving survival among patients with advanced STS.

PO 040 2553241

EXTRASKELETAL MYXOID CHONDROSARCOMA: AN EVALUATION OF 20 CASES

Jared L. Harwood; Paul E. Wakely; Tom Scharschmidt
Ohio State University, Delaware, OH, USA

Objective: Extraskeletal myxoid chondrosarcoma (EMC) was first described in 1972 and is a rare soft tissue sarcoma of unknown differentiation, characterized in most cases by a translocation involving NR4A3 and EWSR1 that results in the fusion protein EWSR1-CHN. Despite its indolent behavior (58% overall survival at 15 years), there is a 40% incidence of metastases.

Purposes of this poster include:
1. As this represents the largest series of patients we are aware of in the literature, we wanted to evaluate the cytomorphology and patient characteristics.
2. We review the literature and demonstrate the utility of fine needle aspiration in the diagnosis of EMC.

Methods: A retrospective list was generated of 20 chronological specimens (18 patients) with an actual and/or tissue diagnosis of EMC. Patient characteristics and ancillary test results were obtained and pathologic slides maintained.

Results: No IRB was deemed necessary in the collection of this data. The average age of our patients was 63.1 years old. 5 of 18 patients were female (27.8%). 1 patient died of disease. Otherwise, all actual FNA diagnoses corresponded with the specimen tissue diagnosis. 2 patients had a local recurrence, 3 with metastatic disease, while the other patients presented with primary disease. 16 specimens underwent ancillary testing and of those 11 were + for EWSR1, 1 was + for NR4A3.

Conclusion: We present a retrospective analysis of 20 cases of EMC, the largest we are aware of in the literature in order to further elucidate characteristics of this very rare sarcoma. Given the high correlation between our tissue and FNA diagnoses, we feel that FNA is a reasonable alternative for diagnosis at centers where pathologists have both the exposure and expertise required.

PO 041 2566323

ADVANCED SOFT TISSUE SARCOMA: SYSTEMIC TREATMENT PATTERNS AND SURVIVAL IN FRANCE

Daniel S Mytelka[1]; Maria Lorenzo[2]; Dana Stafkey-Mailey[3]; Yulia D'yachkova[4]; Saurabh P. Nagar[5]; Sean D. Candrilli[5]; James A. Kaye[6]
[1]Eli Lilly and Company, Indianapolis, IN, USA; [2]Lilly Research Centre, Windlesham, United Kingdom; [3]Formerly RTI-HS, RTP, NC, USA; [4]Eli Lilly GmbH, Vienna, Austria; [5]RTI Health Solutions, Durham, NC, USA; [6]RTI Health Solutions, Waltham, MA, USA

Objective: To characterize real-world treatment patterns and survival in France for patients with advanced soft tissue sarcoma (STS) not amenable to surgery or radiotherapy.

Methods: Physicians based in France completed a retrospective web-based medical record review for patients ≥18 years old who received ≥1 line of systemic therapy for advanced STS (other than Kaposi's sarcoma or gastrointestinal stromal tumors) between 1/1/2005 and 15/8/2015. Patient demographic and clinical characteristics (age; histological subtype), treatments (regimen[s]; dates), and clinical outcomes (progression; death) were recorded. Results were summarized overall, by line of therapy, and by histological subtype.

Results: Thirty-five physicians in France provided data for 201 patients. Physicians reported on average that 9% of patients with advanced STS in their practices did not receive systemic cancer-directed therapy. Patients' mean age at advanced STS diagnosis was 57.9 (SD=12.6) years, with 52% female. The most frequent histologic subtypes were leiomyosarcoma (28%), liposarcoma (12%), and vascular sarcoma (10%). Fifty-two percent of patients had stage IV STS at initial diagnosis. Fifty-four percent of patients received >1 and 23% had >2 lines of therapy. The four most common 1st-line chemotherapy regimens were doxorubicin and doxorubicin/ifosfamide (both 28%), epirubicin/ifosfamide (8%) and trabectedin (5%); in 2nd-line they were trabectedin (19%), pazopanib (15%), docetaxel/gemcitabine and ifosfamide (both 14%). During 1st-line treatment, response rate was an average of 45%, with the highest rate for patients receiving trabectedin (64%; N=11) and the lowest rate for patients receiving doxorubicin (37%; N=57). Most patients received an additional line of therapy following 1st-line treatment with doxorubicin (60%) and doxorubicin/ifosfamide (79%), whereas "alive but no further therapy" was the most common status following 1st-line treatment with epirubicin/ifosfamide (65%), trabectedin (82%), and paclitaxel (90%). Median (95% CI) survival estimates from start of 1st- and 2nd-line therapy were 23 (17:26) and 19 (14:28) months, respectively.

Conclusion: Results from this retrospective medical record review illustrate substantial heterogeneity in treatment of patients with advanced STS in France. Continued advances in treatment options for advanced STS in France remain important.

PO 042 2565639

SOFT TISSUE SARCOMAS: PROGNOSTIC FACTORS AND OUTCOME IN A SERIES OF 278 PATIENTS TREATED AT THE PORTUGUESE INSTITUTE OF ONCOLOGY IN LISBON

Maria Teresa Alexandre, Medical Doctor[1]; Susana Esteves[2]; Ana Luís[1]; João Freire[1]; António Moreira[1]; Filipa Santos[3]; Maria Lemos[3]; Vitor Farricha[4]; Hugo Vasques[4]; Nuno Abecassis[4]; Eduardo Netto[5]; Margarida Ferreira[1]

[1]Medical Oncology, Instituto Portugues de Oncologia de Lisboa, Lisbon, Portugal; [2]Biostatistics, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [3]Pathology, Instituto Português de Oncologia de Lisboa, Lisbon, Portugal; [4]General Surgery, Instituto Português de Oncologia de Lisboa, Lisbon, Portugal; [5]Radiation Oncology, Instituto Português de Oncologia de Lisboa, Lisbon, Portugal

Objective: Sarcomas are a rare group of tumors with many differing behaviors and histologies. A multidisciplinary approach and treatment in referral centers are needed to achieve an optimal care for these patients (pts).

Methods: Retrospective analysis of all consecutive soft tissue sarcoma (STS) pts age ≥18 years treated at our Institution between January 2006 and December 2010. Ewing sarcoma, chondrosarcoma, Kaposi, dermatofibrosarcoma protuberans and visceral sarcomas were excluded. Tumor characteristics were evaluated for treatment outcome and prognostic factors.

Results: Of 278 pts with STS, 141 (51%) were female and 137(49%) male, with a median age of 61(range 18-99) years. Leiomyosarcoma (28%), liposarcoma (27%) and sarcoma NOS (15%) were the most common histologies. High grade in 71% of pts, tumor size ≥ 10cm in 46% and deep seated tumors in 67% were found. Extremities were the most common site (63%). Of the 278 pts admitted, 21(8%) presented with distant metastasis and 257 (92%) with localized disease. Of these, 77(28%) were referred immediately after unplanned surgery and 27(10%) after local relapse. Surgical margins were positive in 52(21%) pts. Relapses were observed in 114 pts (45%): local in 58(23%), systemic in 37(15%) and both in 19(8%). The median time to relapse after surgery was 2.3 years. Local relapse occurred more frequently in pts previously treated outside our Institution (32% vs 20%). Adjuvant radiotherapy and chemotherapy were given in 55% and 8% of pts, respectively. After a median follow-up of 4.6 years the 5-years overall survival (OS) was 47% (CI95%, 41-54%). Median OS for localized disease was 4.9 years and 1.1 years for metastatic disease. Liposarcoma was the histology associated with a better 5-years OS (67%). On univariate analysis, radiotherapy (HR 0.43, CI95% 0.25-0.74) and large margins of resection (HR 0.16, CI95%,0.08-0.32) were associated with reduced relapse risk. On multivariate analysis high grade (HR 4.25, p<0.001), deep tumors (HR 1.89, p=0.017), relapse (HR 3.39, p<0.001) and age (HR 1.02, p=0.005) were independent negative prognostic factors for survival.

Conclusion: As published in other series high grade, deep tumor location, relapse and age were found to be adverse prognostic factors. Unplanned surgery was not a significant factor for survival, probably due to the rescue treatments done soon after referral. A high number of deep, big and high grade tumors in our study, accounted for a worse survival.

PO 043 2569587

REGORAFENIB USE IN 3 PATIENTS WITH GIST IN THIRD LINE

Marta Soares, MD[1]; Ana M. Ferreira[1]; Jose Dinis[1]; Mariana Afonso[2]; Jorge Guimarães[3]

[1]Medical Oncology, IPOPORTOFG, Porto, Portugal; [2]Pathology, IPOPORTOFG, Oporto, Portugal; [3]Surgery, IPOPORTOFG, Oporto, Portugal

Objective: To present the experience with Regorafenib in third line treatment of GIST.

Methods: Review of data files of 3 patients treated with regorafenib in IPOPORTOFG.

Results: 59 y woman submitted to surgery in December 2005. She had a segmentectomy of the ileum (3 cm mass) with peritoneal implants. Exon 11 mutation GIST. She started imatinib 400 mg daily, in march 2006 with a good tolerance. In June 2013 (7 years and 3 months after) she progressed with growth of the peritoneal implants, imatinib dose was increased to 800 mg. In march 2014 she progressed and started 37,5 mg of sunitinib, with partial response and necessity to reduce to 25 mg due to hematologic toxicity. In December 2014 she progressed and she started regorafenib160 mg in march 2015 with disease stabilization and with G1 hand foot syndrome, G2 diarrhoea, hypothyroidism G2 controlled with medication. She is still on therapy 15 months after with SD. 61 years old woman submitted to a laparotomy and removal of a mass with 14 cm in the stomach in July 2004. High risk GIST in the stomach. She was proposed to follow-up at that time. In July 2008 a CAT scan showed peritoneal implants and she started 400 mg of imatinib, with good tolerance and partial response. In august 2011 (3 years later) she progressed and imatinib was raised to 800 mg. In July 2012, 1 year after 800 mg of imatinib she progressed and started 37.5 mg of sunitinib. She had a G2 hypertension, G1 stomatitis controlled with medication. June 2015, 3 years after sunitinib she progressed and started regorafenib 160 mg. She has SD and the dose of regorafenib was reduced to 80 mg due to G3 hand foot syndrome. She is still on therapy 12 months after. 66 years old woman submitted

to gastrectomy in April 2007. She had an intermediate risk GIST and she stayed in surveillance until July 2011 when hepatic lesions appeared. The biopsy showed GIST metastasis. She started 400 mg imatinb in august 2011, the dose of imatinib was reduced to 200 mg due to a liquenoid dermatitis. She stayed on 200 mg with SD until march 2015 (3 years and 8 months), when she progressed and started 37.5 mg of sunitinib. She had to reduce the dose to 25 mg due to skin toxicity. She progressed after 8 months of sunitinb and started regorafenib 160 mg in December 2015. She progressed in april 2016, 4 months after. She is going to start pazopanib.

Conclusion: Regorafenib is a therapy with good results in GIST even in third line treatment. In our patients dose with peritoneal implants showed better results.

PO 044 2545184

FOLLOW UP OF METASTATIC GIST PATIENTS ON TARGETED TREATMENTS WITH ABDOMINAL ULTRASOUND: REDUCING RISKS WITHOUT JEOPARDIZING SURVIVAL

Branko Zakotnik, MD, PhD[1]; Simona Jereb[2]; Mojca Unk[1]; Erika Matos[1]; Darja Erzen[3]
[1]Medical Oncology, Institute of Oncology Ljubljana, Ljubljana, Slovenia; [2]Department of Radiology, Institute of Oncology Ljubljana, Ljubljana, Slovenia; [3]Department of Surgery, Institute of Oncology Ljubljana, Ljubljana, Slovenia

Objective: The recommended diagnostic procedure for follow-up of metastatic GIST patients on targeted treatments is contrast enhanced CT of the abdomen (ceCTa). It poses several hazards, such as allergic/anaphylactic reactions, kidney damage and radiation exposure. Abdominal ultrasound (aUS), a much less hazardous diagnostic procedure could be probably used in the follow up of these patients without jeopardizing survival. We report the treatment outcome in metastatic GIST patients with a follow-up protocol incorporating aUS.

Methods: Patients with histologically confirmed, c-kit positive metastatic GIST had before starting imatinib a ceCTa and an aUS. They were followed up every 3-4 months with clinical/laboratory evaluation and an aUS, In case of suspected disease progression based on these follow-up procedures a ceCTa was performed.

Results: We treated 81 patients. The median time of follow up was 66 months (maximum 115 months). The median time to progression and overall survival was 52 months (95% CI 42-61) and 72 months (95% CI 64-81), respectively. In average 19,2 aUS and only 1.7 ceCTa per patient were performed in the follow-up period.

Conclusion: Incorporating an aUS for follow up of metastatic GIST patients treated with targeted therapy could reduce the risk of allergic/anaphylactic reactions, less kidney damage, lower their exposure to radiation and reduce health costs without jeopardizing survival.

PO 045 2566331

MARGINS DEFINITION AND FRENCH GUIDELINES (GFPO, GSF-GETO) FOR THE PATHOLOGICAL REPORTING OF THE SURGICAL RESECTION SPECIMEN OBTAINED AFTER CHEMOTHERAPY IN BONE SARCOMAS

Anne Gomez-Brouchet, Pathologist[1]; François Gouin[2]; Gonzague de Pinieux[3]; Perrine Marec-Berard[4]; Corinne Bouvier[5]; Frédérique Larousserie[6]; Jean-Marc Guinebretiere[7]; Nathalie Gaspar[8]; Fabrice Fiorenza[9]; Philippe Anract[6]; Jérôme Sales de Gauzy[1]; Laurence Brugieres[8]; Eric Mascard[10]
[1]France, University of Toulouse (IUCT Oncopole), Toulouse, France; [2]CHU Nantes, Nants, France; [3]CHU Tours, Tours, France; [4]Institut Leon Berard, Lyon, France; [5]CHU La Timone, Marseille, France; [6]CHU Cochin, Paris, France; [7]Institut Curie, Paris, France; [8]Institut Gustave Roussy, Paris, France; [9]CHU Limoges, Limoges, France; [10]Hôpital Necker, Paris, France

Objective: The UICC definition of residual disease (R0, R1, R2) is not sufficiently accurate and allows variable interpretation of margins, as well as the meaning of “scar tissue“. We elaborated a standardized pathologic report to evaluate margins and response to neoadjuvant therapy after surgical resection of a bone tumor and defined microscopic margins compared to “scar” and residual cells.

Methods: The Enneking and TNM (AJCC/UICC) staging were used as references for assessing the guidelines and the standardized report. A cut off of more than 2mm was collectively choosen as an acceptable limit to qualify a surgical resection as clear (R0). R0 and R1 status are both defined by the pathologist and the R2 status by the surgeon.

Results: Margins have collectively been defined as: R2 for macroscopic intra-lesional resection, R1 for possible microscopic residuals and R0 for resection more than 2 mm of the tumor or less than 2 mm with a normal anatomical space. The R1 goup was subdivided into 3 categories : R1a = Resection in scar tissue (fibrosis, oedema, foamy macrophages, inflammatory cells) ; R1b = Resection in normal tissue but in close contact with tumour, less than 2 mm, without any normal anatomical space ; R1c = Microscopically intralesional resection or resection in coagulative necrosis.

The pathology report should be made by an accredited bone tumor pathologist and specify the clinical and surgery's data, the diagnosis made on the biopsy before the chemotherapy.

Macroscopic examination should include the topography and the size of both resection and tumour, should describe the appearance of the tumour and the methodology of specimen's sections. If possible photography's will be enclosed in the definitive report. Microscopic examination should notify the average and highest percentage of residual tumor cells after neoadjuvant chemotherapy according to the Huvos and Rosen grading. The percentage should be present on a schema of the surgical resection that will be scanned in the definitive report. Margins should be quoted with the distance in mm of infiltrating tumor from the nearest margin and the nature of tissue at this margin. Bone and soft tissue margins should be identified.

Conclusion: Standardized reporting is intended to establish a unique language to improve the managment of bone sarcomas in the specialized centres or multidisciplinary meetings and to facilitate collaboration between cancer units and networks. It also will provide a common database with reliable data (NETSARC, RESOS).

PO 046 2566498

ADOLESCENTS AND YOUNG ADULTS (AYA) OSTEOSARCOMA (OST) OF THE JAW: THE CHALLENGE IN MANAGEMENT

Christopher Kuo; Paul Kent
Pediatrics, Rush University, Chicago, IL, USA

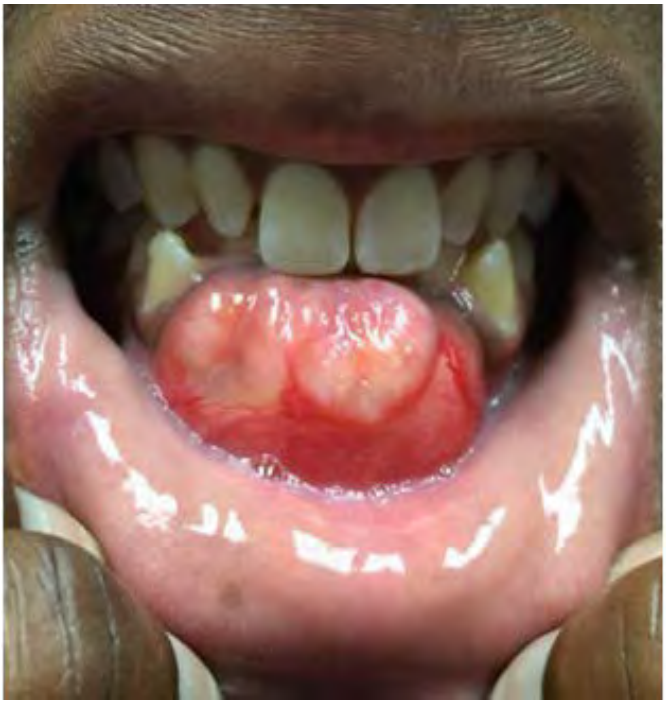
Objective: While OST most commonly affects the metaphyseal growth plates in the long bones, OST of the jaw is rare and comprises of only 6-7% of all OST. Although the treatment with osteosarcomas in the long bones is well established, it is currently still controversial in OST of the jaw. The aim of this abstract is to report and discuss a case of OST in the mandible of a 23 year-old man and the treatment and management dilemma of OST of the jaw.

Methods: We conducted a retrospective chart review consisting of patient's diagnosis, pathology reports, radiology scans and medical records.

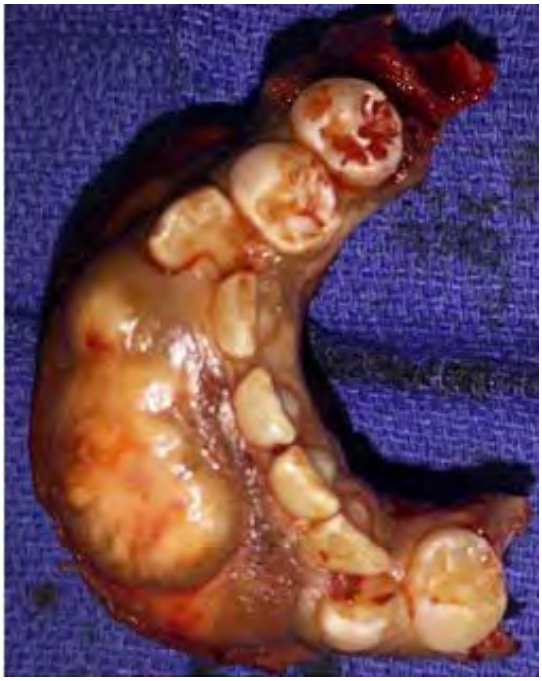
Results: A 23 year-old man presented with an asymptomatic enlarging mass originally suspected as a dental abscess treated with cefdinir, referred by a periodontist for evaluation and treatment of suspected tumor of the mandible at the floor of the mouth. Computed tomography (CT) examination showed a 1.0 x 3.2 x 2.9 cm exophytic lesion arising from the anterior alveolar cortex of the mandible in the symphyseal region with multifocal chondroid calcifications. Biopsy showed features of chondrosarcoma and highly cellular conventional osteosarcoma. The diagnosis of chondroblastic osteosarcoma was then made based on the presenting clinical features, histologic findings and CT images. Initial workup with bone scan, CT chest were negative for metastasis.

An extensive discussion was done in regards to risk and benefits of immediate surgery compared to neoadjuvant chemotherapy used in conventional OST. Ultimately, the patient decided to undergo neoadjuvant approach through the standard COG AOST0331, off protocol with standard arm of high-dose methotrexate (M), doxorubicin (A), and cisplatin (P). At week 12, AP was given preoperatively due to timing of multiple surgical teams (Ear/Nose/Throat, orthopedics and plastic surgeons). Tumor was excised with negative surgical margin. He subsequently completed 29 weeks of chemotherapy with only two minor delays in methotrexate infusion due to mucositis and emotional stress and is in complete remission pending mandibular reconstructive surgery.

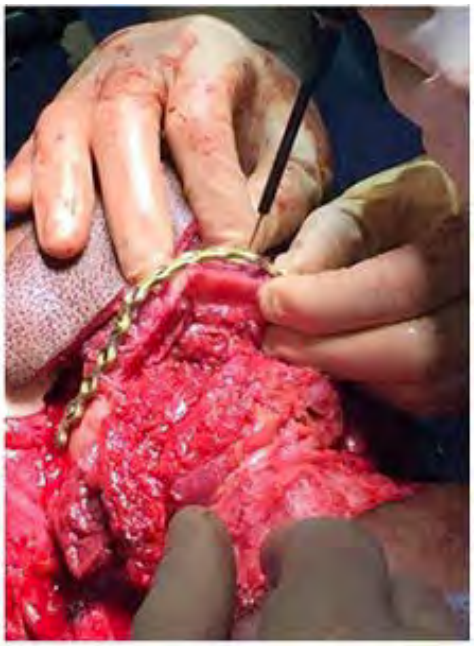
Conclusion: Since the introduction of neoadjuvant chemotherapy, cure rates of long bone OSTs has increased from 10% to 60-70%. However the role of neoadjuvant chemotherapy in OST of the jaw is currently unclear where controversies continue to exist. We hope to show neoadjuvant chemotherapy is tolerable, does not delay surgical management and have significant good prognostic values for AYA patients with localized OST of the jaw.



Initial presenting mass.



Wide excision of mandibular tumor. Left fibula osteocutaneous free flap, with mandibular reconstruction, segmental osteotomy of mandible, neo-mandible, vestibuloplasty, and adjacent issue transfer, lower lip, 5 x 2 cm. Largest diameter 4.0 cm in with focal areas of tumor necrosis (>90% viable). Surgical margins are free of involvement, the closest margin at less han 1 mm (deep anterior resection margin). Lymph node dissection was negative for tumor.



CONVENTIONAL OSTEOSARCOMA, CHONDROBLASTIC TYPE,

PO 047 2540371

COMPUTER ASSISTED PLANNING FOR SURGICAL RESECTION OF BONE TUMORS

Amir Sternheim, MD[1]; Prakash R. Nayak[1]; Michelle Arkhangorodsky[2]; Michael Daly[2]; Jimmy Qiu[2]; Harley Chan[2]; Robert Weersink[2]; Jonathan Irish[2]; David Jaffray[2]; Peter Ferguson[1]; Jay Wunder[1]
[1]Mount Sinai Hospital, Toronto, ON, Canada;
[2]UHN Network TECHNA Institute, Toronto, ON, Canada

Objective: To evaluate the benefit of computer assisted planning compared to traditional planning in complex bone tumor resections in a sawbones model.

Methods: Using a novel navigation system and 3-dimensional (3D) planning we compared a computer assisted to a non-assisted plan to resect a distal femur parosteal osteosarcoma in a saw-bone model. This was identical to an actual patient scenario. Eight surgeons participated.

Results: In the computer assisted cuts there were 4 positive margins cut in two tumor resections. In the unassisted group there were 12 positive margin cuts in all 8 tumor resections. This was significantly different with regard to possitive margin resections (P value<0.05), as well as for separate cuts (P value<0.05).

Conclusion: Computer assisted planning significantly decreased the risk of positive margin resection in this sawbones model. This proof of concept study sets the ground for developing intuitive planning systems.

PO 048 2544249

A QUALITATIVE STUDY TO DETERMINE BARRIERS AND FACILITATORS ENCOUNTERED IN COLLABORATIVE PROSPECTIVE RESEARCH IN ORTHOPAEDIC ONCOLOGY

Marilyn Swinton[1]; Juan Pablo Zumárraga[2]; Walter Parizzia[3]; Michele Boffano[4]; Werner Hettwer[5]; Nicholas Bernthal[6]; Kurt Weiss[7]; Timothy Damron[8]; Marcos Galli Sera[3]; Peter Ferguson[9]; Andre Spiguel[10]; Benjamin Miller[11]; Lukas Nystrom[12]; Roberto Velez[13]; Michelle Ghert, MD, FRCSC[1]

[1]Surgery, McMaster University, Hamilton, ON, Canada; [2]Universidade Sao Paulo, Sao Paulo, Brazil; [3]Austral University, Buenos Aires, Argentina; [4]CTO Hospital, Torino, Italy; [5]National University Hospital, Copenhagen, Denmark; [6]UCLA, Los Angeles, CA, USA; [7]University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [8]SUNY, Syracuse, NY, USA; [9]University of Toronto, Toronto, ON, Canada; [10]University of Florida, Gainesville, FL, USA; [11]University of Iowa, Iowa City, IA, USA; [12]Loyola University, Chicago, IL, USA; [13]Hospital Vall D'Hebron, Barcelona, Spain

Objective: The objective of this study was to identify barriers and facilitators encountered by surgeons in large-scale collaborative research in orthopaedic oncology, with the goal of streamlining future collaborative efforts in the field.

Methods: All surgeons who are involved in or have expressed interest in the ongoing Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) trial were invited via email to participate in an in-person focus group to discuss barriers and facilitators encountered in collaborative research in orthopaedic oncology. The resulting focus group discussion was digitally recorded, transcribed verbatim and anonymized. The focus group transcript was coded using conventional content analysis and a qualitative descriptive approach – an analytic approach which aims to organize the data with little theoretical interpretation in the language of the participants.

Results: The 13 orthopaedic surgeons who participated in the in-person focus group discussion represented orthopaedic oncology practices from 7 different countries (Argentina, Brazil, Italy, Spain, Denmark, United States and Canada). Four categories and associated themes emerged from the discussion: (1) The Need for Collaboration in the Field of Orthopaedic Oncology due to the rare incidence of disease and the need for higher level evidence to guide treatment; (2) Motivational Factors for Participating in Collaborative Research including establishing proof of principle, learning opportunity, sense of community and answering a relevant research question; (3) Facilitators for Participating in Collaborative Research including leadership, institutional facilitators, authorship, trial set-up, trial momentum and Methods Centre support; and (4) Barriers to Participating in Collaborative Research including institutional barriers, personal level barriers, protocol barriers, paperwork, translation and lack of funding.

Conclusion: Orthopaedic surgeons involved in an ongoing international RCT are motivated to collaborate by many factors. However, there is a collective sense of fatigue experienced in overcoming barriers to participating in collaborative research, which was mirrored by a strong collective sense of the importance of, and need for collaborative research in the field of orthopaedic oncology. Overall, the experiences were felt to be educational and were thought to be important in guiding future collaborative initiatives.

PO 049 2544202

DOES METHOTREXATE HAS AN IMPACT ON SURVIVAL OF PATIENTS WITH OSTEOSARCOMA?

Ahmad Shehadeh
KHCC, Amman, Jordan

Objective: Osteosarcoma is the most common non-hematologic primary malignant bone tumor. Altholugh Methotrexate is included in all pediatric osteosarcoma treatment protocols, but there is little evidence in literature about its benefit. The objective of this study is to show if it is beneficial to include Methotrexate these protocols, and tumor necrosis impact on outcome.

Methods: Retrospective Chart review of 79 patients diagnosed with non-metastatic osteosarcoma of the extremities, from Jan 2003 to Dec 2011.twelve patients didn't receive neoadjuvant chemotherapy were excluded from the analysis,63 patients received Multiagent chemotherapy, 28 patients(group I) received Cisplatinum and Doxorubicin alone, while 35 patients (group II) received Cisplatinum, Doxorubicin and Methotrexate. Tumor necrosis was estimated in all resection specimen by the same pathologists team, stage and surgical margins were matching in both groups, we compared both groups in terms of: tumor necrosis(TN),rate of limb salvage ,and 5 year overall survival(OS).

Results: 17 patients (25%) only had necrosis >90%, TN>90% was seen in 8 patients in group I and 9 patients in group II(*p*- value=0.915),rate of limb salvage was 72%,60%(*p*-value=0.28),5 year OS was 68%,71%(*p*-value=0.91) for group I and II respectively. 5 year OS for patients with TN>90% ,TN<90% was 92%,63%(*p*-value=0.018) respectively.

Conclusion: Tumor necrosis remains an independent factor in prediction of survival in Osteosarcoma. Adding Methotrexate to chemotherapy regimen did not result in improved tumor necrosis, and 5 year overall survival. Given the cost of this agent, its value in chemotherapy protocols for pediatric Osteosarcoma should be further evaluated by randomized control trials.

PO 050 2567863

RADIATION RECALL COMPLICATING TREATMENT OF METASTATIC OSTEOSARCOMA

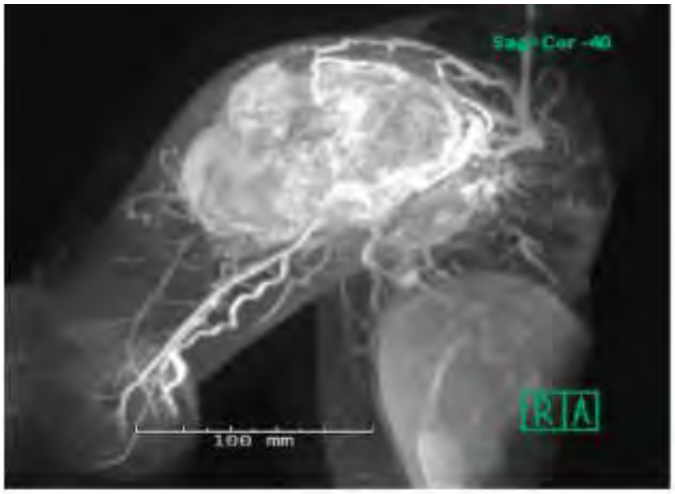
Caleb Oh; Antonio Logan; Caroline Kelmis; Graham A. Zolkowski; Paul Kent
Hematology/Oncology, Rush Hospital, Kildeer, IL, USA

Objective: Our goal is to increase awareness of radiation recall (RR) in children by describing this rare phenomenon in a case report. RR is an inflammatory reaction typically developing in a previously irradiated area after administration of chemotherapy. RR was first reported with dactinomycin in 1959 (Rad 1959; 73(2): 175), but has since been associated with a number of drugs, most commonly anthracyclines. The symptoms of RR ranges from mild erythema to severe tissue necrosis. The exact pathogenesis of RR has not been elucidated.

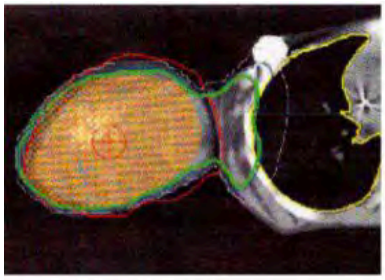
Methods: We conducted a literature search on Pubmed and Google scholar using keywords: “radiation recall”, “dermatitis”, “osteosarcoma” and “pneumonitis”.

Results: In published literature, only 2 existing cases of RR pneumonitis have been reported in children (Rad 1993 May; 187(2):465-7). Only 1 case of RR dermatitis has been reported in a child (JClinical Oncology 2013 June; 31:283-7).

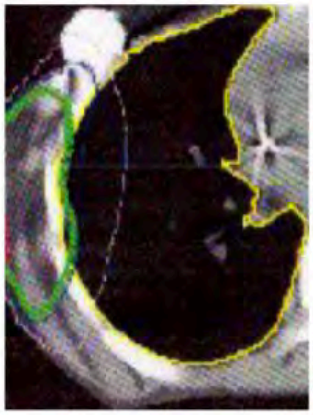
We describe a 7-year-old female who presented with unresectable osteosarcoma (OST) of the right proximal humerus (fig 1) and numerous metastatic lung lesions after receiving nonstandard treatment (IV Vitamin C, ozone, peroxide) and high-dose (5x800 rads) of stereotactic radiation to her primary tumor (fig 2) at outside institutions. Standard chemotherapy (methotrexate (MTX), doxorubicin (DOXO), cisplatin, ifosfamide, etoposide) was given, but consolidation and induction chemotherapy blocks were switched in order to delay the first exposures of DOXO. Despite delayed administration of DOXO, at week 10 the patient developed RR pneumonitis within the radiation field (fig 3), experienced high fevers, intense pain and developed a large open wound over the right arm (fig 4). Pain, fever and swelling from RR improved rapidly and was prevented in the future by giving prophylactic dexamethasone (DEX). The radiation pneumonitis resolved. Subsequently, the patient underwent bilateral thoracotomies with removal of all palpable lung nodules. The primary tumor remained unresectable and the patient ultimately required amputation. The patient remains in complete remission 4.5 years after diagnosis.



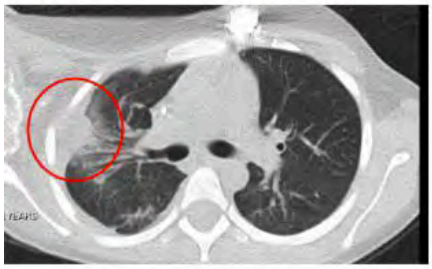
(Figure 1) MRI of unresectable osteosarcoma in right humerus at diagnosis



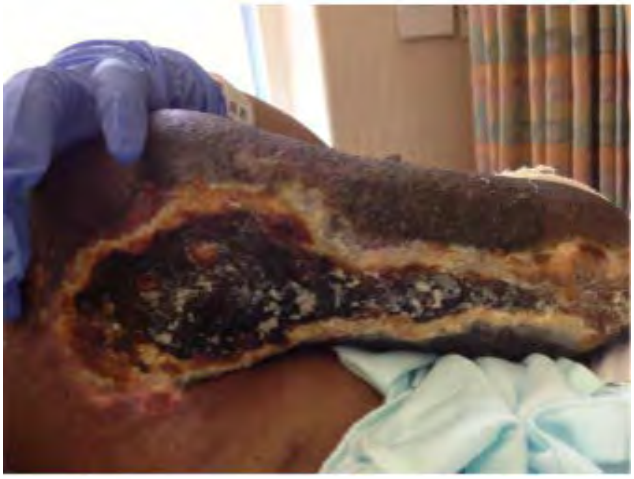
(Figure 2) Radiation dosimetry mapping



Close up of radiation dosimetry encroaching on right lung



(Figure 3) CT scan of RR pneumonitis



(Figure 4) RR of radiated humerus

Conclusion: Despite the inherent risk of RR with high dose radiation and DOXO, we were able to successfully give all prescribed chemotherapy by using DEX prophylactically and by delaying the first exposure of DOXO. We hope that this case can increase awareness of RR and offer a possible way to mitigate its dangerous effect.

PO 051 2541869

THE EWS-FLI1 FUSION TRANSCRIPT AND THE PROGNOSIS OF NORTHEASTERN MOROCCAN PATIENTS SUFFERING FROM EWING'S SARCOMA

Sara LOUATI[1]; Nadia Senhaji[1]; Meryem Azegrar[2]; Samia Arifi[2]; Khalid Amrani Joutei[1]; Laila Chbani[3]; Sanae Bennis[4]

[1]Laboratory of Bioactive Molecules, Structure and Functions, Faculty of Sciences and Techniques of Fez, Fez, Morocco; [2]Oncology Medical Department of Hassan II University Hospital, Fez, Morocco; [3]Pathology Department of Hassan II University Hospital, Fez, Morocco; [4]Biomedical and Translational Research Laboratory, Faculty of Medicine and Pharmacy, Fez, Morocco

Objective: Over 90% of the Ewing's sarcomas contain a fusion of the *EWS* and *FLI-1* genes and resulting from the translocation t (11; 22) (q24; q 12). At the molecular level, rearrangements *EWS-FLI-1* show great diversity. As the fundamental pathogenic lesion in Ewing's sarcoma, the molecular heterogeneity of these fusion transcripts may have functional and clinical significance.

The objective of this work is to look for fusion transcripts *EWS-FLI-1* of Northeastern Moroccan patients suffering from Ewing sarcoma and correlate results with the prognosis of these patients.

Methods: A clinical and pathological analysis was performed on 20 patients with Ewing's sarcoma. The chromosomal rearrangement *EWS* gene was sought by hybridization technique fluorescent in situ (FISH). Then the fusion transcripts *EWS-FLI-1* were identified by RT-PCR (reverse transcriptase polymerase chain reaction).

Results: The average age of patients is 17 years, ranging from 3 to 40 years with a male predominance. All cases are grading III according to the FNCLCC (Fédération Nationale des Centres de Lutte Contre le Cancer) with a common location in the lower limbs.

Ewing's sarcoma are composed of a proliferation of small round cells. 90% of them show an intense positivity, membrane and diffuse of the anti CD99 antibody. Rearrangement of *EWS* gene was noted in all cases, thus confirming the diagnosis.

A tuning of the RT-PCR was performed and the complement of the study is in progress to correlate the results with patient prognosis.

Conclusion: RT-PCR is now the basic definition of Ewing's sarcoma. The study of the effects of the chimeric protein in the cell opens up a lot of hopes for a targeted therapy. Similarly, the detection of the fusion transcript opens the door to a new molecular era in both diagnostic and prognostic in monitoring these cancers.

PO 052 2570217

OSTEOFIBROUS DYSPLASIA OF THE HUMERUS: A CASE REPORT

Shinichirou Yoshida[1]; Masami Hosaka[1]; Munenori Watanuki[1]; Kou Hayashi[1]; Kentaro Suzuki[3]; Eiji Itoi[1]; Masahito Hatori[2]; Mika Watanabe[1]; Shin Hitachi[4]

[1]Orthopaedic Surgery, Tohoku University Graduate School of Medicine, Sendai, Japan; [2]Orthopaedic Surgery, Tohoku kosai hospital, Sendai, Japan; [3]Orthopaedic Surgery, Miyagi Cancer Center, Sendai, Japan; [4]Diagnostic Radiology, Tohoku University Graduate School of Medicine, Sendai, Japan

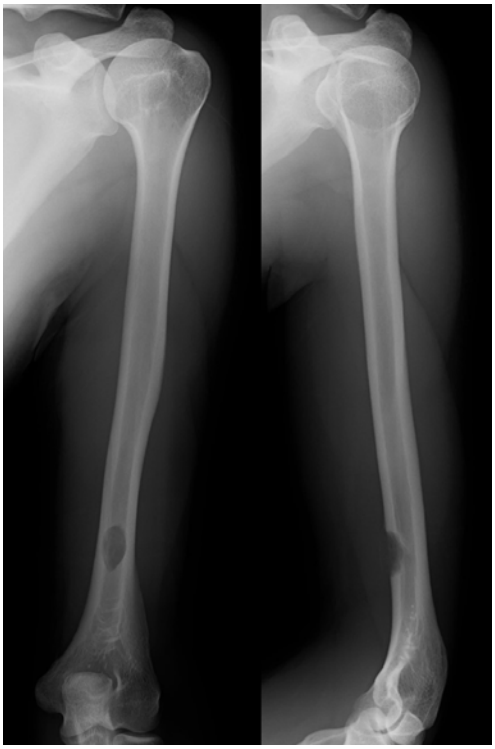
Objective: Osteofibrous dysplasia (OFD) is a benign fibro-osseous lesion commonly arising in the cortical bone of the anterior mid-shaft of the tibia during infancy and childhood. The purpose of this study is to report a distinct rare case of OFD arose in the humerus of an adult.

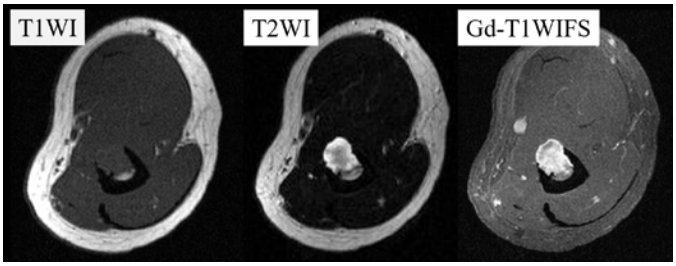
Methods: A 34-year-old male. He had felt left upper arm pain since 3 months ago without any traumatic episode. Plain radiographs showed osteolytic lesion in anterior cortical bone of the humeral shaft (Fig. 1). Computed tomography (CT) revealed calcifications inside the tumor. On Magnetic resonance imaging (MRI), the tumor showed low signal intensity on T1-weighted images and high signal intensity on T2-weighted images, and was enhanced by an injection of gadolinium (Fig. 2). The tumor extended surrounding soft tissue from cortical bone.

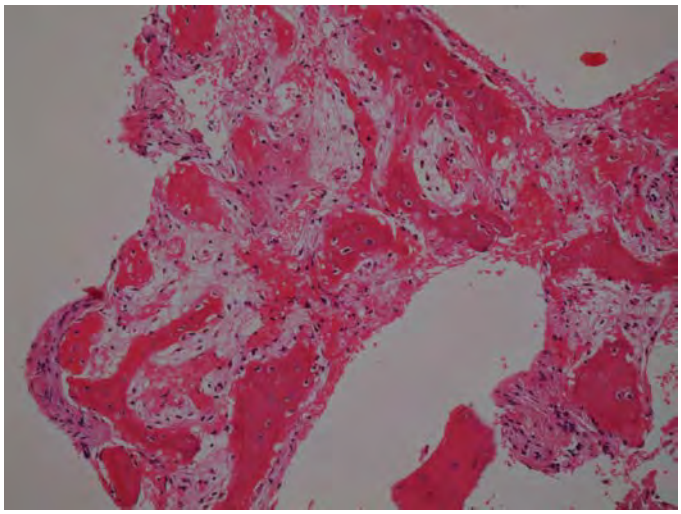
Core needle biopsy showed fibro-osseous lesion, and there are no evidences of malignancy. Curettage, ethanol treatment, and artificial bone graft were performed. Surgical specimen showed fibro-osseous lesion, irregular fragments of woven bone rimmed by osteoblasts. There are many spindle shaped osteoblasts in fibrous component (Fig.3). Finally, it was diagnosed as OFD. During the follow-up period of 4 years after the surgery, here is no recurrence.

Results: OFD is more commonly seen in boys during the first two decades of life, and the middle-third of the tibia is the most frequent site of involvement. Although there are some reports that OFD arose in the other sites include the ulna and radius, the case of arose in humerus is very rare. There are some differential diagnoses of this case include adamantinoma, fibrous dysplasia (FD), chronic osteomyelitis and osteoid osteoma. Adamantinoma, chronic osteomyelitis and FD were ruled out because there were osteoblasts without epithelial and inflammatory cells. Osteoid osteoma was excluded because of lack of nidus, calcifications and hyperplasia of surrounding cortical bone. For these reasons, the tumor was conclusively diagnosed as OFD. However, the possibility of OFD-like adamantinoma still remains because the histopathology is very similar between these tumors.

Conclusion: We reported an extremely rare case of OFD arose in the humerus of an adult.







PO 053 2565973

UNDIFFERENTIATED SARCOMA MASQUERADING AS A SACROCOCCYGEAL TERATOMA

Adam P. Kidwell, MD; Robert Hartemayer; Kacie Steinbrecher; Destiny Hause; Srikumar Pillai; Brett Mahon; Paul Kent
Rush Medical College, Chicago, IL, USA

Objective: Sacrococcygeal teratomas (SCT) arise in approximately 1 out of every 35,000 live births. Most SCTs are benign, and are diagnosed in patients under five months of age. Pelvic teratomas are associated with poor prognosis due to high risk of incomplete resection given the proximity of neurovascular structures. Also, residual SCTs often differentiate into malignant phenotypes. Here we present a newborn male with a pelvic mass that was clinically and radiologically consistent with SCT, but later proved to be a highly malignant undifferentiated sarcoma.

Methods: We conducted a literature search using the keywords “sacrococcygeal teratoma” and “pelvic undifferentiated sarcoma” on Pebmed and Google Scholar. There is one reported case of infantile fibrosarcoma misdiagnosed as SCT. There are also several cases of neuroblastoma being misdiagnosed as SCT. However, we found no such cases of an undifferentiated sarcoma being misdiagnosed as SCT.

Results: A male infant born at 31 2/7 weeks weighing 1745 grams was delivered via urgent C-section due to non-reassuring fetal status. After delivery, the child had reduced urine output, loss of vascular support and absent bowel sounds. Imaging studies demonstrated a large pelvic mass. Due to the patient’s age, tumor features, and location the infant was diagnosed with SCT (Figure 1). VMA, HVA and AFP were within normal limits. Peritoneal fluid showed no malignant cells. Tumor resection was scheduled on day 17 of life due to the compression of vital organs. The infant died intraoperatively.

Postmortem pathology of the tumor reveled a richly vascularized and hemorrhagic neoplasm without architectural differentiation. Thus, although the tumor was radiographically consistent with SCT, undifferentiated sarcoma was diagnosed on histology (Figure 2).

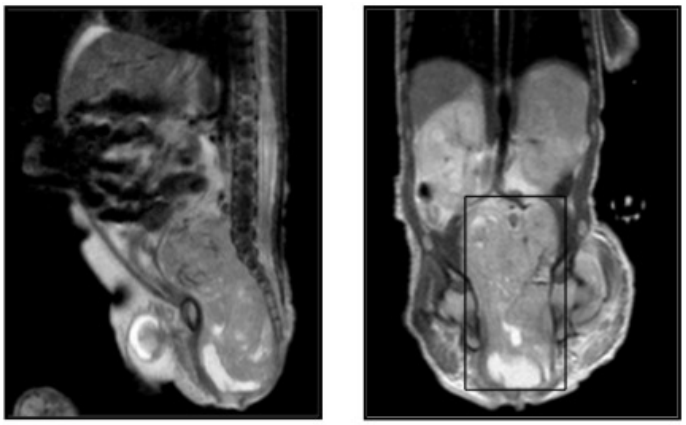
Conclusion: Here we describe the case of a neonate with a pelvic tumor with clinical and radiographic features of SCT that turned out to be an undifferentiated sarcoma on post-mortem histology. Thus, other clinicians should consider a highly malignant undifferentiated sarcoma in the differential diagnosis of SCT in the neonate. We recommend that all initially suspected SCT’s are confirmed by tissue biopsy. There are also clinical criteria that can help distinguish between SCT and rare malignant undifferentiated sarcoma, which could be used to help identify these aggressive lesions and most effectively tailor treatment (Table 1 and 2).

Defining Characteristics of Undifferentiated Sarcomas and Teratomas

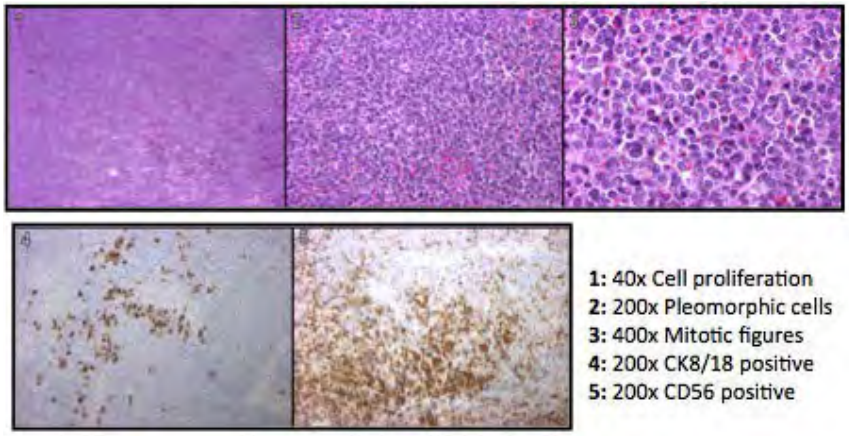
Characteristics	Undifferentiated Sarcoma	Sacrococcygeal Teratoma
Incidence:	Less than 0.7 per million live births (0.4% of all pediatric cancers)	33 per million live births (Accounts for 40% of all germ cell tumors)
Onset:	Diagnosed between 1 week to 17 years	Approximately 50 percent diagnosed prenatally (Almost all diagnosed before 5 months of age)
Severity:	Are malignant and severity can be dependent on size, location, and histological grade.	75 percent of SCT's are benign
Location:	46 percent of all sarcomas occur in the thigh and pubic area	Occurs predominantly at the midline
Gender Differences:	More common in males	More common in females (4:1)
Prognosis:	Overall a worse prognosis than SCTs	Worse with increasing degree of teratoma immaturity and location in the pelvic region

Imaging Differences Between Sacrococcygeal Teratoma and Undifferentiated Sarcomas

Imaging Findings	Sacrococcygeal Teratoma	Infantile Sarcomas
Feeding Vessel:	Middle sacral artery	No easily identifiable feeding vessel
Location:	Midline	Can have laterality
Composition:	1. Random arrangement of irregularly shaped cysts 2. Is not capsulated	1. Absent cystic regions 2. Can be capsulized by other tissues (skin)



Large mass in the presacral pelvis abutting, but not invading, the coccyx and sacrum containing fat, fluid, soft tissue, and calcifications.



The patient's tumor cells were weakly positive for FLI1, CD56, and focally positive for CD99 and cytokeratin 8/18. The tumor was negative for S100, desmin, myf4, CD79a, chromogranin, synpatophysin, CD3 and TdT.

PO 054 2565915

A SINGLE INSTITUTION EXPERIENCE OF 14-YEARS TREATING EWING SARCOMA - FOCUS ON LOCALIZED DISEASE

Ana Catarina Freitas, Resident[5]; Duarte Machado[5]; Cátia Pedro[4]; Marco Ramos[2]; Maria Teresa Alexandre[5]; Margarida Ferreira[5]; João Freire[5]; João Conceição e Silva[1]; Maria José Ribeiro[3]; Filomena Pereira[3]; António Moreira[5]

1Radiology, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [2]Biostatistics, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [3]Pediatrics, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [4]Radiotherapy, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal; [5]Oncology, Instituto Português de Oncologia de Lisboa, Lisbon, Lisbon, Portugal

Objective: Ewing sarcoma (ES) is a rare disease, curable by combined treatment with chemotherapy and / or either surgery, radiotherapy or both. The presence of metastasis is the most important prognostic factor and affects treatment approach.

Methods: Retrospective analysis of 109 consecutive ES patients (pts) treated at the Portuguese Institute of Oncology in Lisbon between January 2000 and December 2014. Aims: characterize clinical, demographic and treatment data, the related prognostic factors and evaluate the 5-years overall survival (OS) and the event-free survival (EFS) for non-metastatic pts, and the 5-years OS for the entire cohort.

Results: From a total of 109 pts, 67 had localized and 42 metastatic disease. The lung was the most common site of metastasis. With a median follow-up of 3.3 year, the 5-years OS of the global cohort was 56% (CI 95%, 5.6-20.4), 71% for localized ES, and 32% to metastatic ES. Of the 67 pts with localized disease, the most frequent location, 43% was axial (thoracic, spine and head and neck), followed by 33% in the extremities, and 24% abdominal and pelvic. The median age was 15 years (range 0.1-53). Fifty-five percent of pts had extra-osseous disease. High LDH and tumor volume ≥200ml was found in 69% and 39% of pts respectively. The EuroEwing-99 protocol treatment was used in 73% of pts. Previous unplanned surgery was done in 20 pts. Of the 47 pts submitted to neoadjuvant chemotherapy, 38 achieved partial or complete response. Local treatment was surgery in 22% pts, radiotherapy in 21% and both in 48%. The 5-years EFS for localized ES pts was 62%. Recurrence was observed in 21 pts (37%), 11 local, 11 systemic and 3 both. Only 2 pts achieved remission after a local treatment for the relapse. Median time to recurrence from diagnosis was 15 months, (range 3-115). Three-year survival after relapse was 20%. The most commonly used regimen at relapse was ICE (Ifosfamide, carboplatin and etoposide) and of the 3 pts submitted to high-dose therapy, none is alive. Multivariate analysis showed two significant independent predictors for relapse: age> 14 years (HR 1.03, p=0.008) and tumor volume≥ 200ml (p=0.023).

Conclusion: Our 5-years OS and EFS data were similar to the published literature. After relapse the prognosis was dismal. Only tumor volume and age were significant for relapse. Although some pts were submitted to unplanned surgery, this was not correlated with a poor outcome.

PO 055 2570260

GIANT CELL TUMOR OF BONE – CASE REPORT OF AN UNUSUAL TUMOR LOCATION WITH A MULTIDISCIPLINARY APPROACH

Maria Inês S. Sequeira[1]; Ana M. Simas[1]; Ana M. Ferreira[1]; Jose Dinis[1]; Mariana Afonso[2]; Sofia Conde[2]; Machado Carvalho[2]; Marta Soares[1]

[1]Medical Oncology, Instituto Português de Oncologia do Porto, Porto, Portugal; [2]Instituto Português de Oncologia do Porto, Porto, Portugal

Objective: Giant cell tumor of bone (GCTB) is a locally aggressive benign neoplasm with a predilection for local recurrence. Usually it appears in the epimetaphyseal region of femur or tibia; only 15% occurs in sacrum, pelvis and spine. The predominant symptom is pain. Surgery remains the primary treatment, however, radiotherapy (RT) and denosumab may have a role in recurrent disease.

Methods: Clinical data and literature review

Results: A 32 years-old man without relevant medical history, in Nov/2014 started with severe cervical pain with one month's evolution, with irradiation to the left arm and hypoesthesia of 3rd, 4th and 5th fingers, without another neurological deficits. In anamnesis the patient referred a work accident with a cervical traumatism 3 months before. A cervical MRI was executed and it showed a C7 lesion with soft tissue component. The biopsy revealed a giant cell bone tumor.

In Jan/2015 he was submitted to a tumor embolization and, after that, to a C7 corpectomy with arthrodesis of C6-D1, R2 surgery. Cervical pain decreased but fingers hypoesthesia kept. Histology of surgery confirmed giant cell bone cancer, well differentiated.

Multidisciplinary team proposed to adjuvant RT, which was performed to C5-D2 region, 50 Gy/25 fr in April/2015. After RT treatment, MRI showed a mass at RT level and the patient started denosumab 120 mg. There was a complete response to this drug.

GCTB is a rare entity first described in 1818. It comprises 5% of primary bone tumors and 21% of all benign bone tumors in adults. Typically occurs in 3rd and 4th decades. Although histologically benign, GCTB varies from indolent, static tumor to locally aggressive or metastatic tumor.

The mainstay of treatment is complete surgical excision, however incomplete resection is often associated with tumor recurrence rates up to 50%. In this setting, RT and denosumab are useful. RT is recommended in high risk patients, when complete excision is impossible or for recurrent GCTB. Denosumab is a monoclonal antibody RANKL inhibitor used in GCTB, once the malignant stromal cells secrete RANKL, which recruits osteoclast precursors and stimulates their differentiation to osteoclasts. The trials showed beneficial clinical effect, however, the optimal treatment duration and schedule remains unknown.

Conclusion: Surgery remains the primary treatment of localized GCTB. When complete surgery is not possible, RT and denosumab are a good treatment options. Multidisciplinary approach is crucial to offer the best treatment to the patient.

PO 056 2537845

IS SYMPTOM WORSENING (SW) ASSOCIATED WITH RECIST RESPONSE IN PATIENTS (PTS) WITH DESMOID TUMORS (DT)?

Nuria Kotecki; Armelle Renaud; Meriem Ben Haj Amor; Anne-Sophie Thomassin Defachelles; Thomas Ryckewaert; Vincent Gamblin; Yves-Marie Robin; Sophie Taieb; Nicolas Penel
Centre Oscar Lambret, Lille, France

Objective: DT is a rare, locally infiltrative tumor. Front-line 'watch-and-wait' policy with monitoring by MRI is recommended.

Methods: We retrospectively reviewed data from 27 consecutive pts with histologically-proven DT from 01/2007 to 12/2015. The study aims to investigate if SW is correlated with disease progression according to RECIST 1.1, volumetric changes or contrast enhancement (CE) over time. Clinical and MRI characteristics were assessed at diagnosis and at last follow up.

Results: The cohort consisted in 6 men (22%) and 21 women (77%) with a median age of 33 (10-77). The most common location was the abdominal wall (11, 40%). Median follow-up was 40 months (5-98). 15/27 (55%) pts received at least 1 systemic treatment including NSAID, tamoxifen, imatinib or methotrexate based chemotherapy**.** Increasing in pain, retraction, functional impairment were seen respectively in 11 (40%), 10 (37%) and 10 (37%) patients. Objective response, stable disease and disease progression according to RECIST 1.1 was found in 7 (26%), 13 (48%) and 7 (26%) pts, respectively. Objective response, stable disease and progressive disease according to volumetric changes was found in 8 (30%), 10 (37%), 9 (33%) pts, respectively. Size and volume changes were highly correlated ($p < .00001$.). We have described 2 "false" progressions characterized by increased of only 1 axis and decrease of other axis; this could be related to tumor retraction along the muscle fibers. We found that response assessment according RECIST was not associated with SW (Table). CE was assessable in 26 pts, with decrease CE in 10 pts (38%) and stable CE in 16 pts (62%). CE change and RECIST response were not correlated ($p = 0.697$). CE changes were not associated with worsening of pain ($p = 0.676$), retraction ($p = 0.126$) and functional impairment ($p = 0.126$).

Conclusion: SW was not associated with the response according to RECIST, volumetric or CE changes. Innovative methods for monitoring pts are needed.

	Objective responses (7)	Stable disease (13)	Progressive disease (7)	p
Increase in pain	3	5	3	0.974
Increase in retraction	2	4	4	0.438
Increase in functional impairment	2	3	4	0.438

PO 057 2571294

INTRALESIONAL CURETTAGE OF GRADE I CHONDROSARCOMA OF LONG BONES: 2 YEAR FOLLOW UP OF 8 CASES

Bhaskar S. Sugath, Fellowship Orthopaedic Oncology
Orthopaedics, Aster Medcity, Kochi, India, Trivandrum, Kerala, India

Objective: Diagnosis and treatment of grade 1 chondrosarcoma remain controversial. We performed a review of a single-center series with the aims of assessing the oncologic outcome of these patients, verifying if intralesional curettage can be adequate treatment, and defining clinical criteria to support the surgeon and the oncologist in decision-making for surgery and subsequent follow-up.

Methods: A retrospective study of 8 cases of grade 1 chondrosarcoma of long bones of lower limb which were treated with intralesional curettage was performed. Intralesional curettage with high speed burr was supplemented with fibular strut graft taken from opposite side. Standard clinical follow-up contained regular visits to the orthopaedic department, physical examination and radiological follow-up with plain X-rays and CT -Chest.

Results: Mean follow-up was 24 months. No patients developed local recurrence. No distant metastases were observed. Radiologically the fibular graft incorporation within the defect was successful. Functionally all doing well, no skin problems ,no joint stiffness were observed.All of them were started on touchdown weight bearing by six

weeks, partial weight bearing by 12 weeks and full weight bearing without support by 16 weeks

Conclusion: Grade 1 Chondrosarcoma of the appendicular skeleton with no aggressive imaging features can be treated with intralesional curettagewith high speed burr and fibular strut grafting. However, when aggressive biologic behavior is evident on imaging, segmental resection following surgical principles of malignant bone tumors seems more appropriate.

This technique is a viable option in the reconstruction of cavitary bone defects following intralesional curettage of grade 1 chondrosarcoma.

PO 058 2535985

BIGH3 IS A UNIQUE AND NOVEL MECHANISM OF OSTEOLYSIS IN KIDNEY CANCER BONE METATASIS

Robert Satcher, MD, PhD[1]; Tianhong Pan[1]; Sue-Hwa Lin[2]
[1]Orthopaedic Oncology, MD Anderson Cancer Center, Houston, TX, USA; [2]Translational Molecular Pathology, MD Anderson Cancer Center, Houston, TX, USA

Objective: Bone metastasis from renal cell carcinoma (RCC) has a unique osteolytic phenotype that is resistant to pharmaceutical treatment. After forming, there is a high incidence of pathologic fractures and subsequent disease progression. Understanding the molecular mechanisms will identify strategies for treating bone metastases more efficaciously. An alternative and unexplored possibility for producing osteolysis in bone metastasis is osteoblast inhibition. Our central hypothesis is that factors secreted in the bone microenvironment by metastatic renal cell carcinoma cells inhibit bone formation, tilting homeostasis towards osteolysis. In this mechanism the osteoblast plays a central role. The objective of the proposed study is to characterize the effect of BIGH3, secreted by metastatic tumor cells, on the osteolytic phenotype of bone metastasis.

Methods: We used a SCID mouse RCC xenograft model and in vitro co-culture studies with osteoblast cell lines. We first isolated a clear cell RCC cell line, 786-O Bo that homes to bone and creates osteolytic metastasis. BIGH3 was then knocked down in 786-O Bo cell lines using shRNA, which were then evaluated for osteolytic metastasis formation via injection in SCID mice femora.

Results: A bone homing cell line (786-O Bo) was generated and used to create a mouse model for osteolytic metastasis. Conditioned medium from these cells inhibited primary mouse osteoblast (PMO) differentiation and mineralization, as demonstrated by decreased alkaline phosphatase activity and staining; decreased osteocalcin expression; and decreased mineralization in vitro. Proteomic analysis of secreted factors from concentrated conditioned medium of 786-O Bo cells showed that BIGH3, a 68 kDa protein involved in tumorigenesis, was secreted at high levels. Purified BIGH3 also was shown to inhibit PMO differentiation and mineralization. Next, BIGH3 knockdown 786-O Bo cell lines were created and tested in our mouse model for osteolytic metastasis. Compared with controls, osteolytic bone metastasis formation was decreased with knockdown cell lines.

Conclusion: BIGH3 is highly secreted by the bone metastastic kidney cancer cell line, 786-O Bo. BIGH3 appears to act on osteoblasts in the bone microenvironment, and specifically inhibits bone formation. Moreover, BIGH3 secretion promotes the formation of osteolytic bone metastasis. This mechanism has not been previously explored, but may play a significant role in metastatic disease by tilting bone homeostasis towards bone lysis.

PO 059 2570485

LYMPHOMA OF BONE AND SOFT TISSUES: DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS

Annika Müller[1]; Martin Dreyling[2]; Falk Roeder[3]; Andrea Baur-Melnyk[4]; Alexander Klein[1]; Thomas Knösel[5]; Volkmar Jansson[1]; Hans R. Dürr[1]
[1]Orthopaedic Oncology, Department of Orthopaedic Surgery, LMU Munich, Munich, Germany; [2]Medical Clinic III, LMU Munich, Munich, Germany; [3]Institute of Radiotherapy, LMU Munich, Munich, Germany; [4]Institute of Radiology, LMU Munich, Munich, Germany; [5]Institute of Pathology, LMU Munich, Munich, Germany

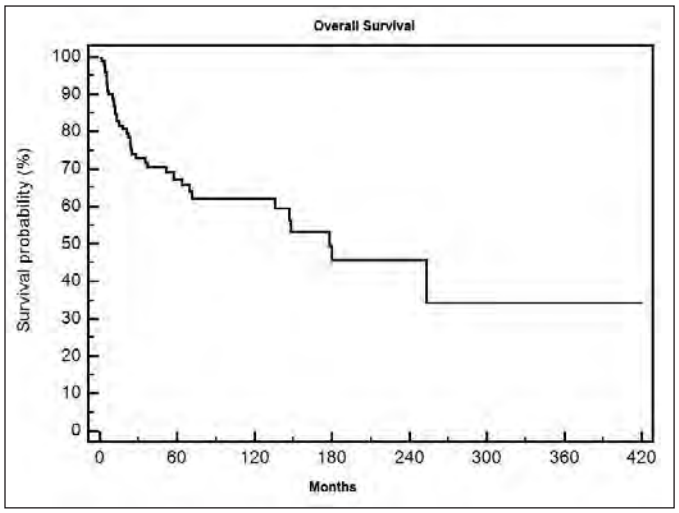
Objective: Malignant lymphoma of bone is rare, in advanced stage, it may be difficult to differentiate from osseous involvement in conventional lymphoma. The aim of this work was to show the typical clinical and radiological parameters of this lesion, local therapy and prognosis.

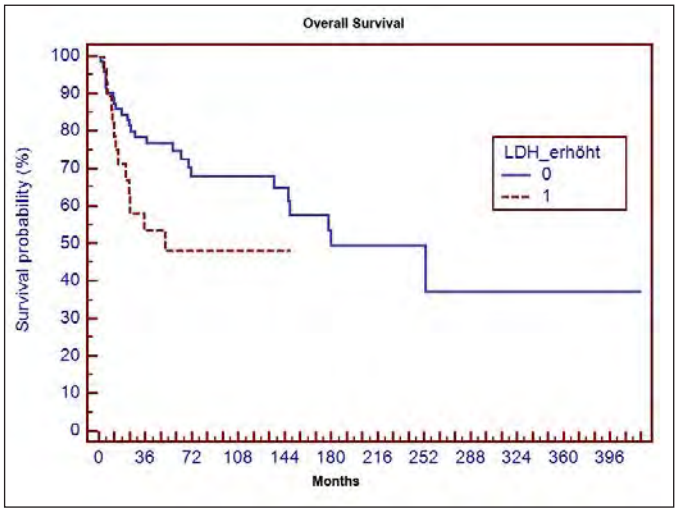
Methods: Between 1980-2015, 110 patients were treated with lymphoma of bone and/or soft tissue. The average age at diagnosis and surgery of 62 men was 59 years (21-98 years) that of the 48 women 61 years (21-101). Pelvic lesion were seen in 25 cases, spinal in 23, humeral in 15 (prox. 11), femoral in 9, scapular in 5, tibial in 6, fibular in 4, ulnar and radial in 2, at the trunk in 5, one in the foot, disseminated in 3 and soft-tissue lesions in 10 cases.

Regarding surgery an incisional biopsies was done in 41 cases, true-cut biopsies in 31, spinal surgery in 14, conservative therapy only in 12 cases, and otherwise a spectrum of osteosynthesis and endoprothetic reconstructions.
Main symptom was pain in 75% of the cases, followed by swelling (28%), neurology and fracture (16%), swelling of lymph nodes in 10%, restriction of movement in 5%, and B-symptoms in 9% of cases. Average time of symptoms was 9 months (0-198 months), median 3.6 months.

Results: 29% of the patients had multiple bone lesions, 67% an extraskeletal involvement. 40 patients died during the observation period. In the surviving patients, the follow-up was 8.5 to 421 months (means 102 months). Overall survival is demonstrated in Fig 1. After 10 years 60% of the patients were still alive. Of the surviving patients 93% were free of disease. Highly significant on survival was the age of the patients. Dissemination (skeletal and visceral) was prognostically not significant in the multivariate analysis. In addition to the age, the value of Lactatedehydrogenase (LDH) was the most important significant prognostic factor (Fig. 2, p <0.05).

Conclusion: Lymphoma of bone is a clinically and radiologically often difficult diagnoses. The prognosis is good with an overall survival of 60% after 10 years. Resection of the tumour is not necessary. The age (+/- 60 years) and the increase of LDH were the most important prognostic factors.





PO 060 2563993

THE IMPROVEMENT OF HYPOXIA BY TRANSCUTANEOUS CO2 APPLICATION BLOCKS THE PROGRESSIVE BONE DESTRUCTION IN A METASTATIC BONE TUMOR MODEL

Toshiyuki Takemori; Teruya Kawamoto; Takeshi Ueha; Mitsunori Toda; Etsuko Kamata; Masayuki Morishita; Naomasa Fukase; Hitomi Hara; Masahiro Kurosaka; Ryosuke Kuroda; Toshihiro Akisue
Kobe University Graduate School of Medicine, Kobe, Japan

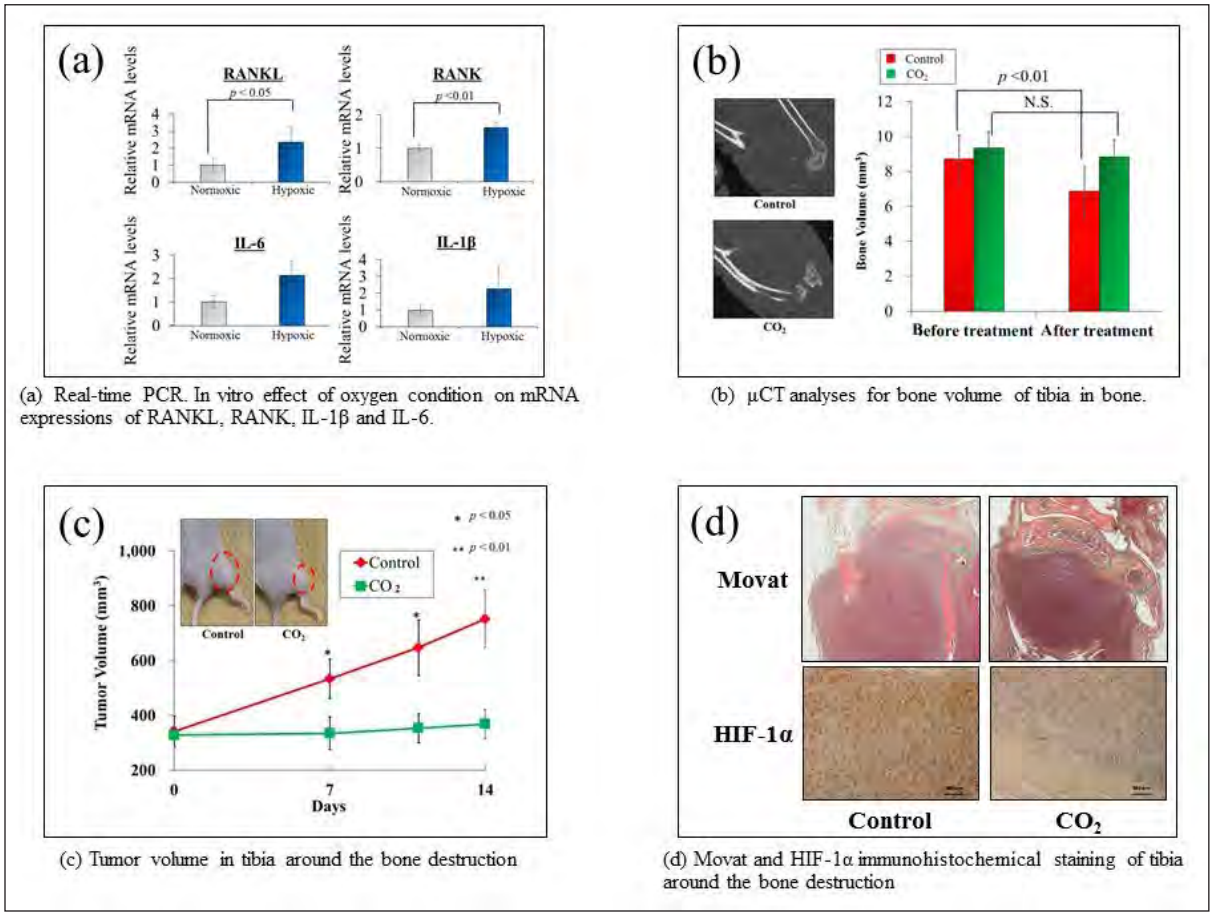
Objective: Hypoxia is a common feature of malignant tumors including metastatic bone tumors. In metastatic bone tumors, factors which associated with osteoclast differentiation and osteolysis, are known to play important roles for the bone destruction. We previously reported that transcutaneous CO_2 application system induced oxygenation in the treated tissue, and the system could improve hypoxia in malignant tumor tissues. Therefore, we hypothesize that hypoxia promotes the bone destruction via activating the factors, and that the improvement of hypoxia by transcutaneous CO_2 system could block the progressive bone destruction. In this study, we examined whether oxygen condition affects the expressions of osteoclast differentiation factors and the osteolytic factors *in vitro*, and the effects of improvement of hypoxia by the CO_2 system on bone destruction in bone metastatic model *in vivo*.

Methods: *In vitro* studies. A human breast cancer cell line, MDA-MB-231, was cultured in two different oxygen conditions; Normoxic (20% O_2) or Hypoxic (2% O_2) conditions. Expressions of factors for osteoclast differentiation (RANKL, RANK) and osteolysis (IL-1β, IL-6) in cells were assessed by real-time PCR.

In vivo studies. Eighteen nude mice were randomly divided into CO_2 (n=9) or control groups (n=9). MDA-MB-231 cells were injected into right tibia of mice for bone destruction. CO_2 or control treatment started after confirming bone destruction by μCT, and were performed twice weekly for 2 weeks. After the end of treatment, bone volume of the treated tibia was assessed by μCT. In tibia sections, expressions of HIF-1α and factors for osteoclast differentiation and osteolysis were immunohistochemically evaluated, and Movat Stain was also performed.

Results: In vitro, RANKL, RANK, IL-1β and IL-6 expressions were increased in hypoxic cells (a). *In vivo*, CO_2 treatment significantly blocked bone destruction and maintained bone volume in the treated tibia compared to the control (b, c, d). In the CO_2 group, positive staining of HIF-1α, RANKL, IL-1β and IL-6 was weak, and Movat stain revealed that CO_2 treatment maintained the bone structure.

Conclusion: In this study, we revealed that hypoxia enhanced the metastatic bone destruction, and that the improvement of hypoxia blocked the bone destruction.



(a) Real-time PCR. In vitro effect of oxygen condition on mRNA expressions of RANKL, RANK, IL-1β and IL-6.

(b) μCT analyses for bone volume of tibia in bone.

(c) Tumor volume in tibia around the bone destruction

(d) Movat and HIF-1α immunohistochemical staining of tibia around the bone destruction

The findings strongly suggest that transcutaneous CO_2 application could block the metastatic bone destruction via improving hypoxia with decreased expressions of the bone destruction factors.

PO 061 2552781

SURGICAL TREATMENT FOR METASTATIC BONE TUMOR OF EXTREMITY

Hitomi Hara[1]; Toshihiro Akisue[2]; Yoshitada Sakai[3]; Teruya Kawamoto[1]; Naomasa Fukase[1]; Masayuki Morishita[1]; Etsuko Kamata[1]; Toshiyuki Takemori[1]; Kenichiro Kakutani[1]; Yasuo Ejima[4]; Ryohei Sasaki[4]; Kotaro Nishida[1]; Ryosuke Kuroda[1]

[1]Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan; [2]Rehabilitation Science, Kobe University Graduate School of Health Sciences, Kobe, Hyogo, Japan; [3]Rehabilitation Medicine, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan; [4]Radiation Oncology, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan

Objective: Increase in number of cancer patients and improvement of the cancer treatment cause the increase in metastatic bone tumor. Skeletal-related events (SREs) with metastatic bone tumor greatly influence the quality of life (QOL) and the activities of daily living (ADL) of the cancer patients. We work on the multidisciplinary therapy for metastatic bone tumor since we established bone tumor board (BMB) in our hospital in 2013. The purpose of this study is to research and evaluate the surgical treatment for metastatic bone tumor of extremity in our hospital.

Methods: We performed a retrospective review of 57 sites who underwent surgical treatment for metastatic bone tumor of extremity between 2008 and 2015. Surgical procedures were divided into three groups: wide resection group (en bloc resection and reconstruction), intralesional resection group (curettage and cementation with or without internal fixation), and internal fixation group (only internal fixation). The Kaplan–Meier method was used to estimate postoperative survival, and univariate and multivariate analyses were performed to identify prognostic factors for overall survival. Regarding 23 patients followed up more than 6 months after surgery, we assessed and analyzed performance status (PS), Barthel Index (BI) for ADL, Euro-Qol 5 Dimensions (EQ-5D) for QOL, and numerical rating scale (NRS) for pain.

Results: The rates of preventive surgery for pathological fracture increased since 2013 (Fig. 1). The most common primary cancer was renal, followed by thyroid, lung, and breast cancer. 28 sites were located in the peritrochanteric, 15 sites in the other lower limb and 14 sites in the upper limb. The 3-year overall survival rate was 29.8% and the

median survival time after surgery was 17 months (Fig. 2). New Katagiri score, lung or liver metastases, surgical procedures were risk factors for the overall survival. PS, BI, EQ-5D and NRS were improved after surgery compared to preoperation (Fig. 3).

Conclusion: We believe that this direct communication between specialists in BMB is helpful to prevent pathological fracture with metastatic bone tumor. Surgical treatment for metastatic bone tumor was effective to reduce pain and improve PS, ADL and QOL after 3 months postoperatively. New Katagiri score, lung or liver metastases, surgical procedures were prognostic factors. In this study, we suggest that we can improve the prognosis by tumor resection (wide or curettage) with the aim of the local control of metastatic bone tumor.

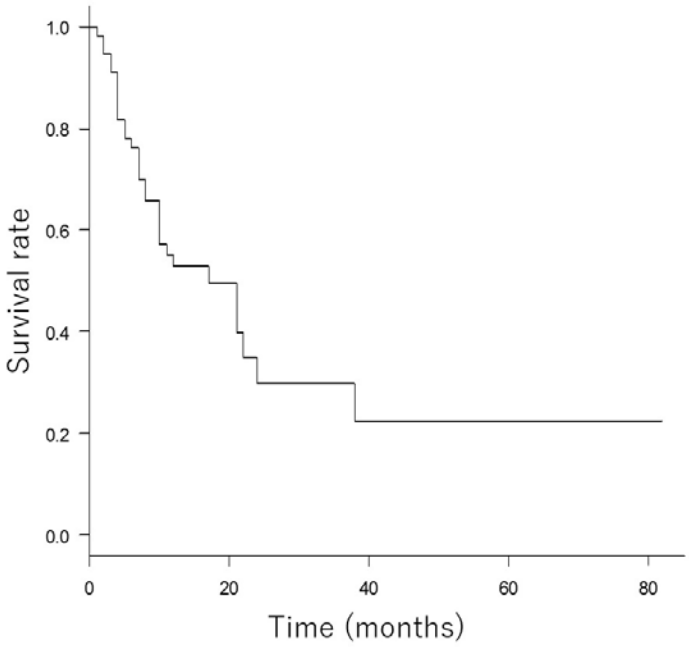


Figure 2.
Kaplan-Meier survival curve for all patients.

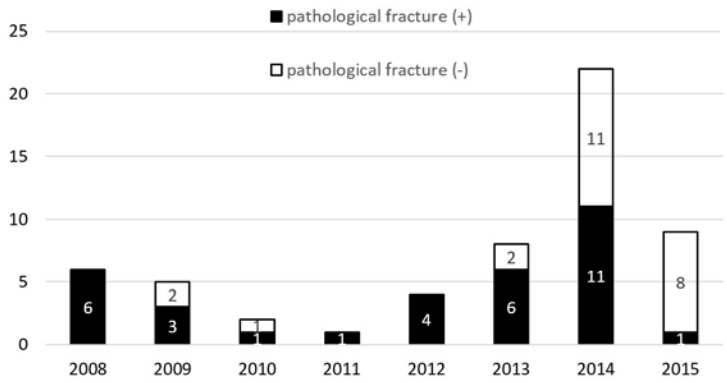
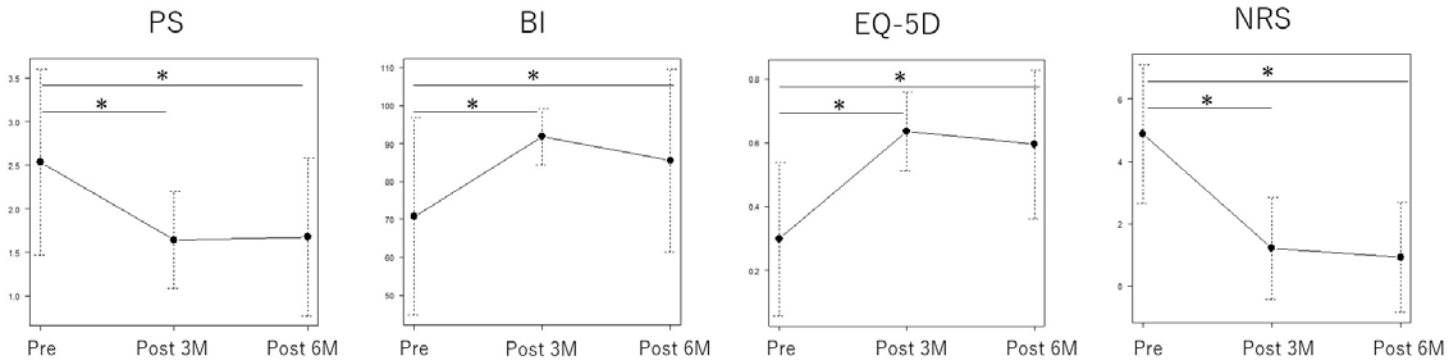


Figure 1.
Changes in the number of operations for pathological fractures at Kobe University Hospital.



Friedman test *P<0.05

Figure 3.
Line charts showing postoperative changes in PS, ADL, QOL and pain.

PO 062 2570495

INSUFFICIENCY FRACTURE AFTER RADIATION THERAPY

Michihito Miyagi, MD, PhD[1]; Hiroaki Ogihara[1]; Yoji Shido[2]
[1]Orthopedics Surgery, Hamamatsu Red Cross Hospital, Hamamatsu, Shizuoka, Japan;
[2]Orthopedics Surgery, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan

Objective: The Radiation therapy-induced insufficiency fracture caused sometime the severe pain, and it may be confused with the bone metastasis in cancer patients. Our purpose is to clarify the clinical and radiological features of the radiation therapy-induced insufficiency fracture in non metastatic bone.

Methods: Four patients of insufficiency fracture after the radiation therapy were included in this study. Thire diagnosed April 2015 and April 2016. There were one male and three females with a mean age of 63 years (range,44-80). We retrospectively analyzed the primary tumor, the part of fracture, total dose, the period from the end of radiation therapy to injury, the clinical data for each patient and the radiological findings.

Results: The primary tumors were a cervical cancer, a breast cancer, a lung cancer and a soft tissue sarcoma. A part of fracture was femoral head, rib bone, lumbar vertebra and proximal tibia, respectively. A mean of total dose was 56Gy (50.4-60)with conventional fraction. The period from the end of radiation therapy to injury was from 7 to 24 months (average 13 months). The diagnosis in first were a nerve pain, osteoarthritis and fracture. All chief complaint of them were sever pain. They had tenderness in local lesion. At first visit, only one patient of plain X-ray findings showed insufficiency fracture. This patient was referred our hospital 3 weeks after injury.

Conclusion: The more total radiation dose, the earlier bone fractures was occured. We find that insufficiency fracture was occurred in two years more than 50Gy, so we should save a radiation exposure to the bone as far as we are possible.

PO 063 2570603

AYTPICAL LOCATIONS OF AVASCULAR NECROSIS FROM ZOLEDRONIC ACID IMITATING METASTASIS

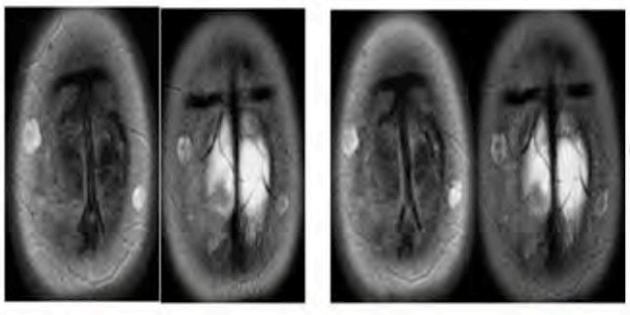
Graham A. Zolkowski; Antonio Logan; Caroline Kelmis; Caleb Oh; Paul Kent
Pediatric Hematology/Oncology, Rush University Medical Center, Chicago, IL, USA

Objective: Zoledronic acid (ZA), a 3rd generation bisphosphonate, is commonly used to treat osteoporosis and hypercalcemia, but more recently has shown activity in sarcoma patients *(Eur J Cancer. 2013 Jul;49(10):2384-91*). ZA works by inhibiting osteoclast-mediated bone resorption (Am J Cancer Res. 2016;6(3):677-689) but can cause bisphosphonate osteonecrosis with a prevalence between 3-12% in cancer patients and almost exclusively appears as osteonecrosis of the jaw (ONJ). (Supportive Care in Cancer 2010; 18:1099–1106) We describe 2 children who received ZA for bone sarcoma, which resulted in avascular necrosis (AVN) in atypical locations that clinically imitated metastasis.

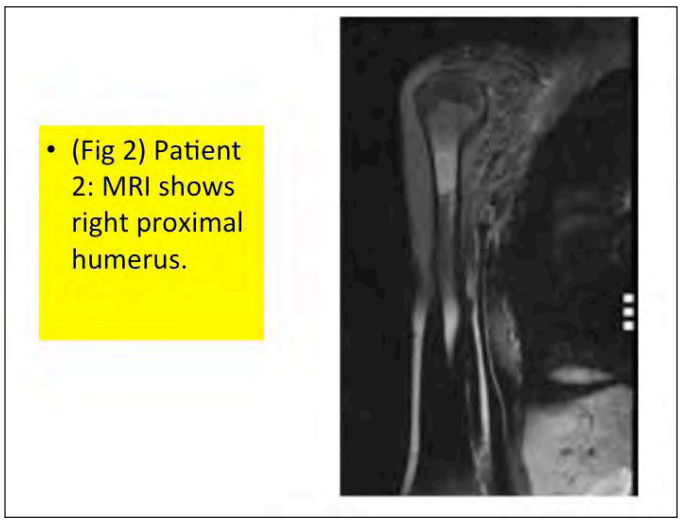
Methods: We searched Pubmed and Google Scholar, using the key words: “avascular necrosis,” “bisphosophonate osteonecrosis,” “zoledronic acid,” “sarcoma,” and “false negative metastasis.”

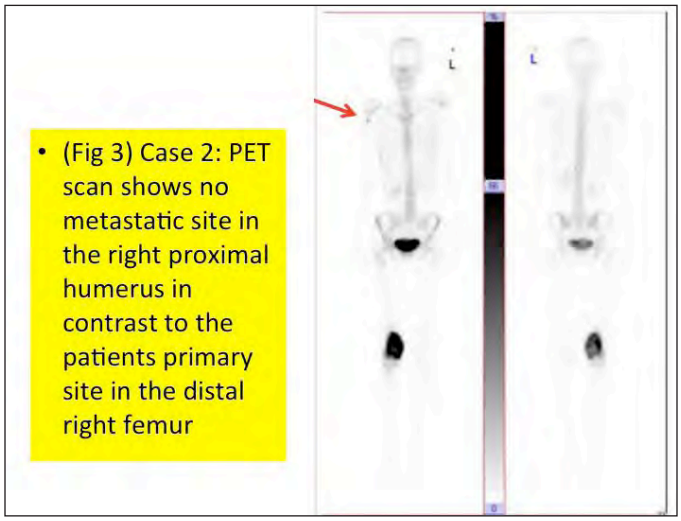
Results: Searches revealed 116 relevant case reports, but only 4 articles describing AVN outside ONJ, but yielded no similar cases to ours. Case 1: A 13-year-old female, was diagnosed with Ewing’s Sarcoma of the right proximal humerus with metastasis to the skull. She received standard chemotherapy with radiation to the primary and the skull metastasis. Following her treatment, she received monthly ZA as part of a research protocol. After 6 cycles of ZA, MRI screens showed apparent bony skull relapse (fig. 1). PET and bone scans were non-enhancing. Although the family refused a biopsy, lesions remained unchanged for 5 years and are now interpreted as consistent with AVN.

Case 2: A 17-year-old female was diagnosed with osteosarcoma of the distal right femur with lung metastases. She was treated on COG AOSTOP61, which includes monthly ZA with standard chemotherapy. After starting ZA, CT-PET and bone scan were equivocal (mild uptake) for bony metastases in multiple areas including the right proximal humerus while MRI, similar to case 1, was highly suggestive of metastatic disease (Fig 2 and 3). Initial biopsy and later resection of the humeral lesion showed complete necrosis without malignancy. This was also interpreted as ZA-induced AVN. The use of ZA continued per protocol without complication and the patient remains in clinical remission now 15 months after diagnosis.



(Fig 1) Case 1: MRI scans are 5 months and 4 days months apart, showing no change in bone lesions over time





Conclusion: ZA has an emerging role in the treatment of cancer. Physicians should be aware that AVN is a possible side effect of ZA that is not limited to commonly described regions of the body such as the mandible. These bone lesions may also be misinterpreted as metastasis.

PO 064 2552797

A CASE OF A PATIENT WITH AN ADENOCARCINOMA OF THE DISTAL FEMUR: IS IT TRULY A METASTASIS FROM UNKNOWN ORIGIN?

Hideto Obata
Orthopedic Surgery, Yukoukai General Hospital, Ibaraki, Osaka, Japan

Objective: There are often cases of patients who have a metastatic bone tumor from unknown origin and that is the first symptomatic lesion for them. In most of the cases, the primary cancer, and in some cases, other metastatic lesions are detected by detailed examinations. Even if the primary cancer is not found initially, it usually becomes apparent within at least one year. It is very rare that not only the primary cancer stays occult and undetected, but also no other metastatic lesion emerges for more than one year after a solitary metastatic bone tumor is surgically resected. Here we report a case of a patient with an adenocarcinoma of the distal femur who remains in a state with no evidence of disease for more than 29 months after surgical resection and endoprosthetic reconstruction.

Methods: Case: A 76-year-old male complaining of a pain on his right knee for one month was diagnosed with a bone tumor of his right distal femur by X-ray examination and MRI. After referral to us, he was examined generally by PET-CT and other tests, but no other tumor lesion was detected than the tumor of his right femur. The bone tumor was surgically resected by a wide margin and the distal femur and the knee joint were reconstructed with a megaprosthesis.

Results: Histopathological examination of the resected specimen revealed the tumor as a well-differentiated adenocarcinoma. Therefore, his disease was strongly suspected of a metastatic bone tumor from an unknown cancer. The primary lesion, however, has not been detected in spite of multimodal and repeated examinations post-operatively including PET-CT and fiberscopy of the upper and lower digestive organs. He is alive with no evidence of disease without any additional chemo- or radiotherapy after a follow-up period of 29 months. There was no local recurrence and no other distant metastasis. At a final follow-up, he is able to walk without any aid.

Conclusion: No case of a patient with an adenocarcinoma originated from the bone has been reported within our retrievals. Therefor, his tumor is considered as metastasis from unknown origin. It means that his primary cancer remains silent and occult for more than two years after a metastatic lesion became apparent. Further investigation and follow-up are required to elucidate the origin of his bone tumor.

PO 065 2570639

THE ILLUMINOSS INTRAMEDULLARY STABILIZATION DEVICE: POTENTIAL BENEFITS OVER STANDARD NAIL FIXATION FOR PATHOLOGIC HUMERUS FRACTURES

Jason Hoellwarth, MD; Kurt Weiss; Mark Goodman; Alma Heyl; Richard McGough
Orthopedics, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Objective: Pathologic humerus fractures are common, decreasing life quality for patients with a short life expectancy. Standard fixation with intramedullary nail (IMN) or cement-plate technique have drawbacks of mismatching intramedullary geometry and large incisions, respectively, and delaying radiation (XRT) until wounds heal. The IlluminOss (IO) intramedullary stabilization device, currently

under investigation, seeks to solve those issues. Via a 1cm proximal incision an intramedullary balloon is inserted past the fracture then filled with biocompatible liquid polymer that cures by through the application of visible light emitted from a fiber optic catheter; distal cross screws are optional. This can allow a wound-free radiation zone and a conforming rigid fixator to tamponade bleeding.

Methods: Retrospective analysis was performed of all pathologic humerus fractures occurring since 2010 stabilized by IMN or IO. IMN was exclusive until June 2015 when IO was introduced. Variables examined were patient age, gender, laterality, tobacco use, chemotherapy, tumor pathology, operative time, estimated blood loss, transfusion need, post-operative hospital stay, time to XRT, and post-operative complications.

Results: Seventeen patients (18 fractures) had IO and 55 patients (56 fractures) had IMN fixation. There was no statistical difference for age, gender, laterality, or transfusion need. No infections occurred. No IO patients required reoperation whereas 4 (7%) of IMN patients did. Significant differences of IO vs IMN were: tobacco use (78% vs 25%, p=0.0001); chemotherapy (83% vs 54%, p=0.0286); near-zero blood loss (67% vs 22%, p=0.0024); XRT within 24 hours (73% [44% within 8 hours] vs 3.4%, p=0.0001); operation minutes (59.6 vs 77.8, p=0.020) with 61% of IO taking under 1 hour vs 25% of IMN (p=0.088); and next-day discharge (56% [28% same day] vs 29%, p=0.049). One IO failed to polymerize intra-operatively, possibly due to balloon rupture; this was immediately converted to IMN.

Conclusion: The IlluminOss can change the approach to pathologic humerus fractures, proving safe, reliable, and fast. Intra- and post-operative complication rates are similar or better than IMN. Two benefits seem most promising. First, metastatic renal fractures were treated without embolization due to the IO's tamponade effect, and in general blood loss is less. Ergo secondly, IO can allow single-day outpatient fracture fixation, XRT, and discharge home, even in renal cell patients.

PROGRAM EVALUATION FORM

Please take the time to complete this evaluation at the end of this meeting. The information we collect will assist us in designing future courses. Return completed forms to the registration desk or mail to the CTOS office at PO Box 320574, Alexandria, VA 22320 or scan form to ctos@ctos.org.
Thank you for your assistance.

***Paolo G. Casali, MD**, 2016 Program Chair*

In general *(please circle)*

Did the program cover all the material you expected?	Yes	No	Unsure
Were your objectives in attending this meeting met?	Yes	No	Unsure
Did the faculty start each of their sessions with an overview?	Yes	No	Unsure
Were the audio/visuals appropriate for the content?	Yes	No	Unsure
Will this information have an impact on your practice?	Yes	No	Unsure

Please identify which session you enjoyed most: _____

_____

We are interested in identifying the elements of a successful meeting. Please rate the following in terms of their significance:

(please circle)	very important				not important
Opportunity for the audience to participate	1	2	3	4	5
Speaker's rapport with the audience	1	2	3	4	5
Conditions in the room (temperature, lights, etc.)	1	2	3	4	5
Use of summary statement at the beginning	1	2	3	4	5
Use of audio/visual equipment	1	2	3	4	5
A relaxed, discursive style	1	2	3	4	5

Please rate your preferences for the following presentation formats:

(please circle)	most favored				least favored
Lectures	1	2	3	4	5
Panel Discussions	1	2	3	4	5
Poster Sessions	1	2	3	4	5

Please list topics which you would like to see included on the program for the 2017 CTOS Annual Meeting:

_____

_____

Please identify those elements of the program which made it a unique learning experience: _____

_____

Which topics or sessions did you find to be <u>least</u> <u>beneficial</u> to you? _____

_____

How many days is the optimal length for a CTOS meeting? *(please circle)*

2 days 2.5 days 3 days 3.5 days

What is your preference for days of the week? *(please circle)*

Monday-Wednesday Thursday-Saturday Sunday-Tuesday Wednesday-Friday No Preference

Please evaluate the following meeting components: *(please circle)*

Appropriateness of Level:	Too Difficult		Appropriate Level		Too Easy
Overall Format & Organization:	Excellent	Very Good	Good	Fair	Poor
Audio/Visuals:	Excellent	Very Good	Good	Fair	Poor
Conference Meals:	Excellent	Very Good	Good	Fair	Poor
Accommodations:	Excellent	Very Good	Good	Fair	Poor
Were the meeting rooms easily accessible?	Yes	No			
Was the sound system adequate?	Yes	No			
Could you see the podium and screen?	Yes	No			

Compared with similar courses, overall this course was in the: *(please circle)*

Top 10% Top 30% Average Lower 30% Lower 10%

Indicate the best response: *(please circle)*

This program was related to my practice needs:	Strongly Agree	Agree	Disagree	Strongly Disagree
There was sufficient opportunity for discussion:	Strongly Agree	Agree	Disagree	Strongly Disagree
I had ample opportunity to meet the faculty:	Strongly Agree	Agree	Disagree	Strongly Disagree

How did you learn about this course? *(please circle)*

Brochure Society Mailing Personal Referral Internet

Would you be interested in serving on a committee? *(please circle)* Yes No

If 'yes', list your name and committee preference: _____

Please suggest locations (cities and countries) for future CTOS meetings: _____

_____

Please indicate your specialty or area of interest: *(please circle)*

Diagnostic Radiology Radiology Oncology Oncology Research Pathology Medical Oncology

Pediatrics Surgical Oncology Other *(please specify)* _____

Additional Comments: _____

_____

_____

_____

_____

_____

Thank you for your time in completing and returning this evaluation.

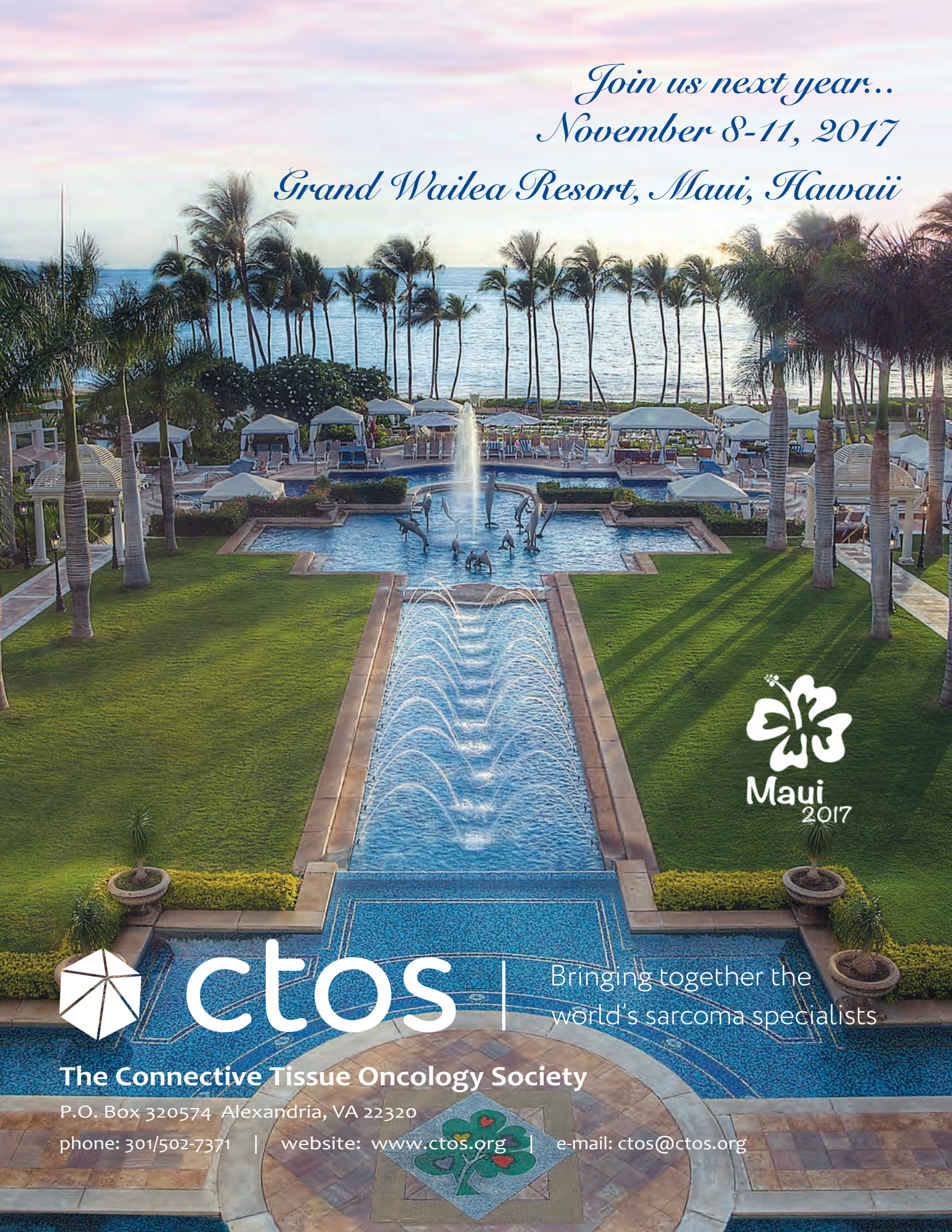
ctos | Bringing together the world's sarcoma specialists

The Connective Tissue Oncology Society

For more information,
Please visit the CTOS website:
www.ctos.org

P.O. Box 320574
Alexandria, VA 22320
Phone: 301/502-7371
e-mail: ctos@ctos.org

Barbara Rapp, Executive Director


Join us next year...
November 8-11, 2017
Grand Wailea Resort, Maui, Hawaii
Maui
2017
ctos
Bringing together the
world's sarcoma specialists
The Connective Tissue Oncology Society
P.O. Box 320574 Alexandria, VA 22320
phone: 301/502-7371 | website: www.ctos.org | e-mail: ctos@ctos.org