

STS clinical recommendations: discussion



Alessandro Gronchi MD
alessandro.gronchi@istitutotumori.mi.it

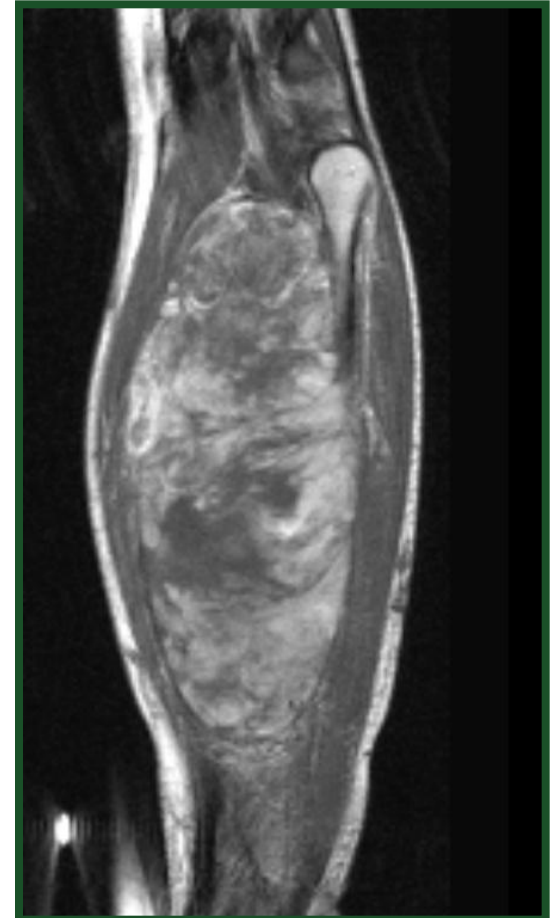
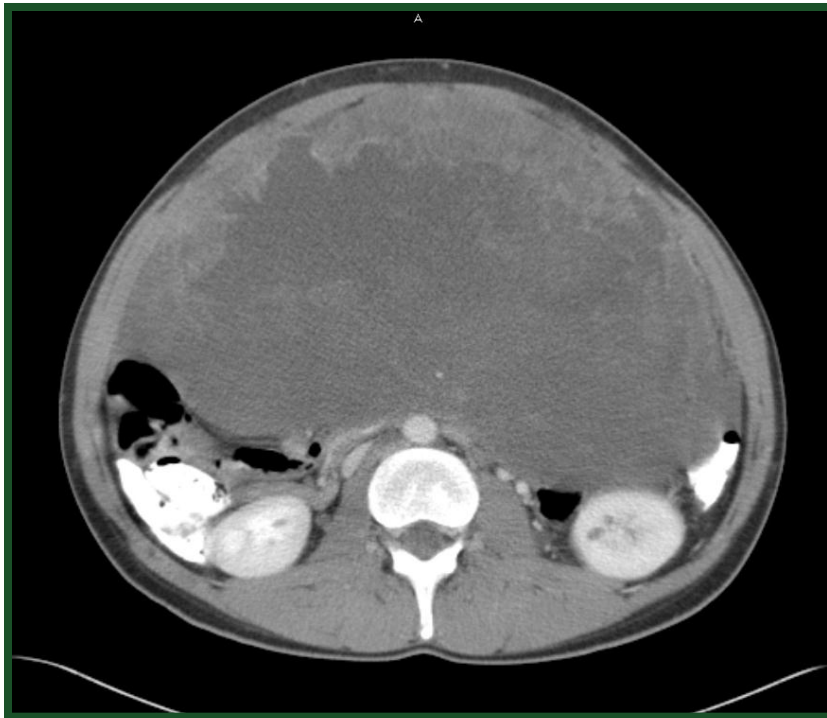
Disclosure slide

- I have no conflicts of interest to declare

Discussion Outlines

- Synchronous metastases at presentation
(Stage IV disease)
- Standard approach to isolated pulmonary metastases
- Locally advanced primary tumor
- 2nd line CT in advanced STS

31 yr old male with Stage IV disease



The standard approach would be:

- Palliative CT with Adriamicine alone or in combination with Ifosfamide

See plenary tomorrow afternoon

...but we do already know

- The combination of adriamidine and ifosfamide is able to achieve a higher response rate.

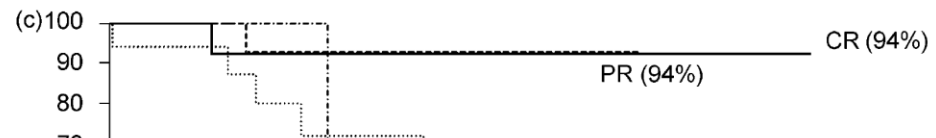
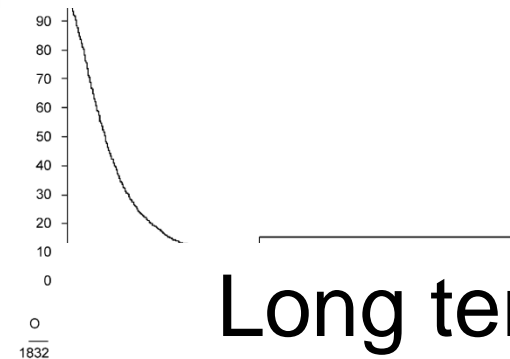
Advanced soft-tissue sarcoma: a disease that is potentially curable for a subset of patients treated with chemotherapy[☆]

J-Y. Blay^{a,*}, M. van Glabbeke^b, J. Verweij^c, A.T. van Oosterom^d, A. Le Cesne^e,
J.W. Oosterhuis^c, I. Judson^f, O.S. Nielsen^g

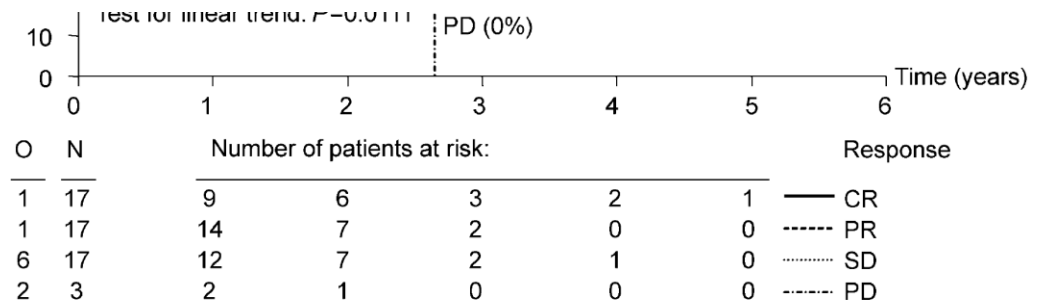
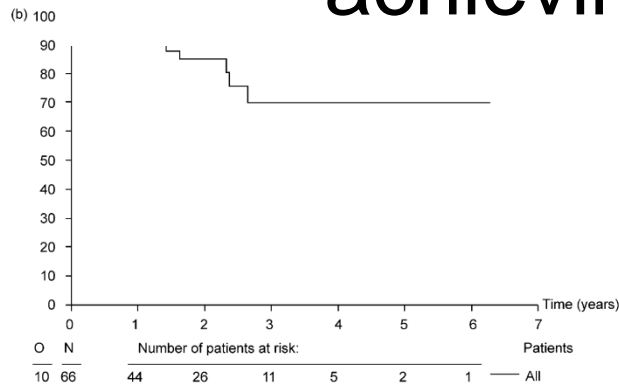
- 2187 pts
- 8% surviving > 5 yrs
- CT induced CR:
 - 5 times better than PR
 - 10 times better than SD
 - 5 times better than PD
- OS after the 5th yr of CR and PR was even (were residual disease operated ?)

Advanced soft-tissue sarcoma: a disease that is potentially curable for a subset of patients treated with chemotherapy[☆]

J-Y. Blay^{a,*}, M. van Glabbeke^b, J. Verweij^c, A.T. van Oosterom^d, A. Le Cesne^e, J.W. Oosterhuis^c, I. Judson^f, O.S. Nielsen^g



Long term survivors are only patients achieving a complete remission



So response is important

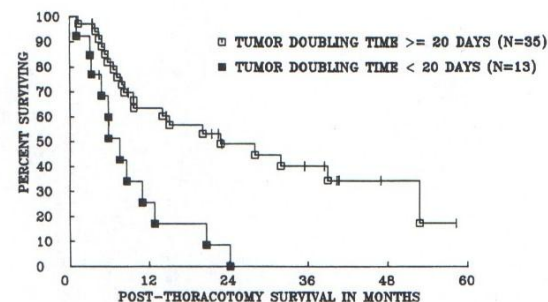
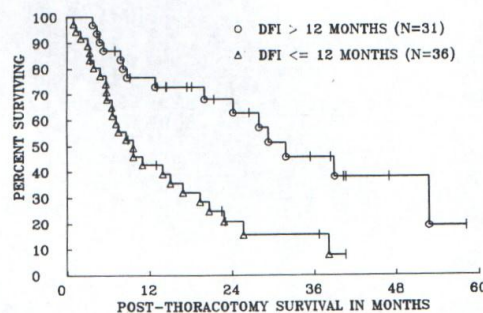
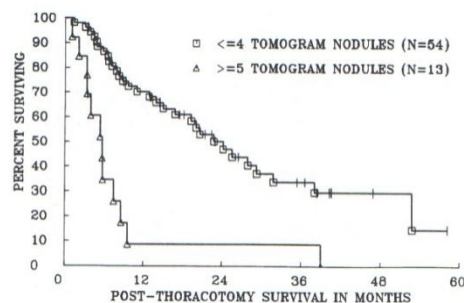
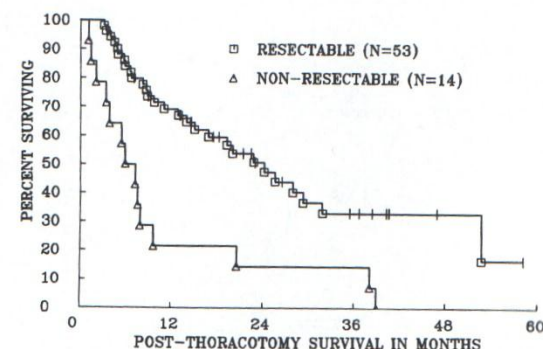
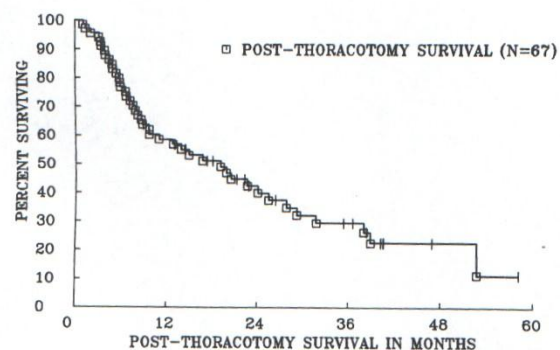
- For quality of life
- For survival

Standard approach to isolated lung metastases is surgery

The fastest way to achieve complete remission



Analysis of prognostic factors in patients undergoing resection of pulmonary metastases from soft tissue sarcomas

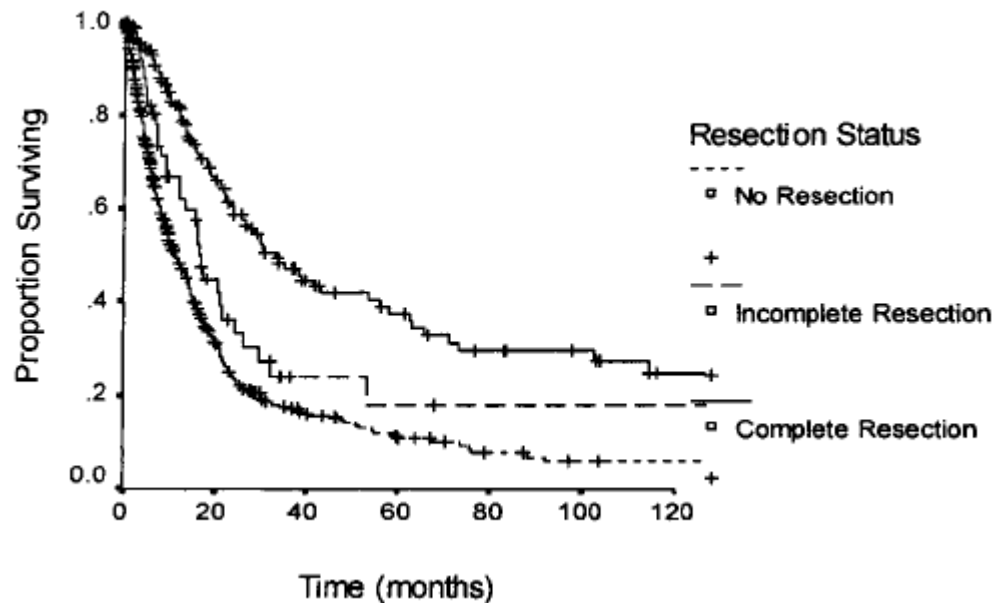


Pulmonary Metastases From Soft Tissue Sarcoma

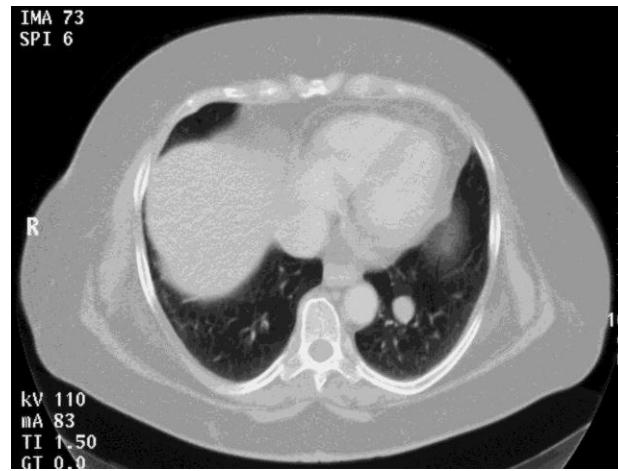
Analysis of Patterns of Disease and Postmetastasis Survival

Kevin G. Billingsley, MD,* Michael E. Burt, MD, PhD,* Ellen Jara, BS,* Robert J. Ginsberg, MD,* James M. Woodruff, MD,†
Denis H.Y. Leung, PhD,‡ and Murray F. Brennan, MD*

*From the Departments of *Surgery, †Pathology, and ‡Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York*



Ann Surg 1999;5:602



- Number of lesions
- Free interval

Infact in general CT would be an
option

Perioperative Chemotherapy in Patients Undergoing Pulmonary Resection for Metastatic Soft-Tissue Sarcoma of the Extremity

A Retrospective Analysis

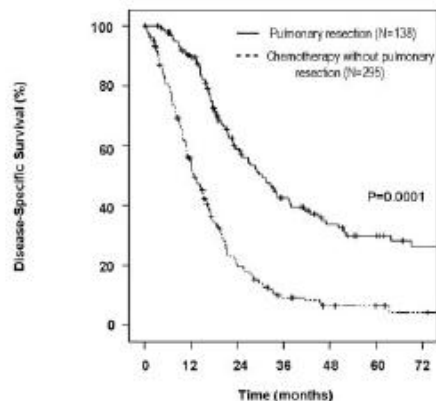
Robert J. Canter, MD¹
 Li-Xuan Qin, PhD²
 Robert J. Downey, MD³
 Murray F. Brennan, MD¹
 Samuel Singer, MD¹
 Robert G. Maki, MD, PhD⁴

¹ Division of Surgical Oncology, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York.

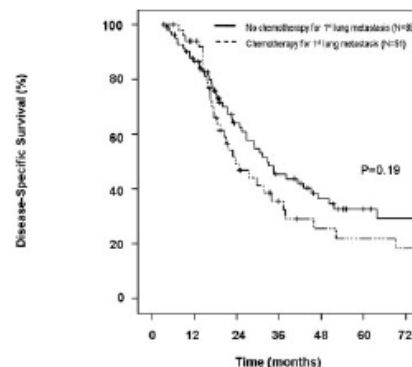
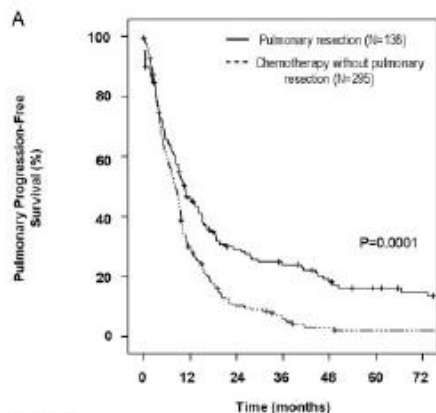
² Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York.

³ Division of Thoracic Surgery, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York.

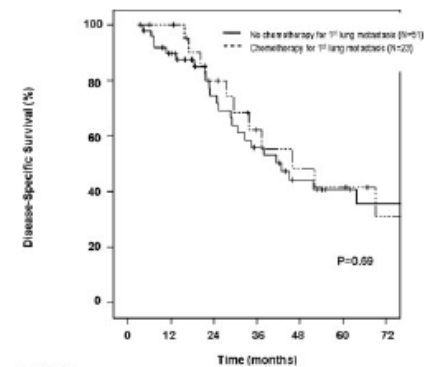
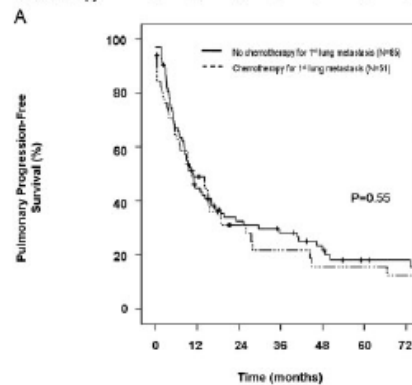
⁴ Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York.



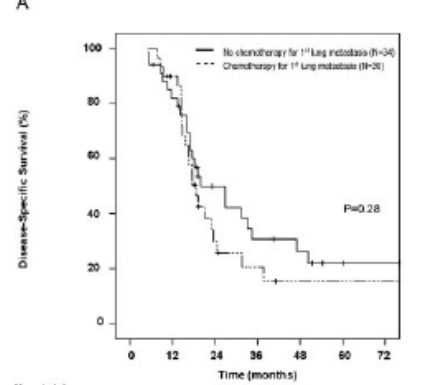
No. at risk	138	116	63	41	26	19	14
Resection							
No Resection	295	149	49	20	9	6	3



No. at risk	85	69	41	28	19	11	9
No Chemotherapy							
Chemotherapy	51	45	20	11	7	6	5



No. at risk	51	42	28	20	13	9	7
No Chemotherapy							
Chemotherapy	23	22	15	9	7	6	3



Cancer 2007;110:2050

In our case

- Free interval was zero → primary CT
- Pt young and symptomatic → the combo chosen for higher chance to obtain a response:
 - symptomatic relief
 - subsequent surgery
- Surgery of isolated metastases outside the lung typically indicated in MRC liposarcoma

Myxoid/Round Cell and Pleomorphic Liposarcomas

Prognostic Factors and Survival in a Series of Patients Treated at a Single Institution

Marco Fiore, MD¹
Federica Grosso, MD²
Salvatore Lo Vullo, BSc³
Elisabetta Pennacchioli, MD¹
Silvia Stacchiotti, MD²
Andrea Ferrari, MD²
Paola Colli
Laura Lozz
Luigi Maria
Paolo G. C.
Alessandro

¹ Department
tute, Milan, Italy.

² Department of Cancer Medicine, National Cancer Institute, Milan, Italy.

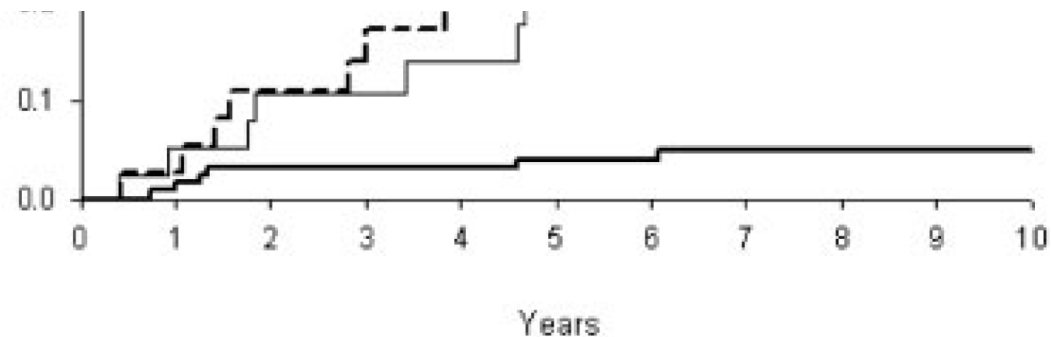
³ Department of Biostatistics, National Cancer Institute, Milan, Italy.

⁴ Department of Pathology, National Cancer Institute, Milan, Italy.

⁵ Department of Diagnostic Imaging and Radiotherapy, National Cancer Institute, Milan, Italy.



40% of the patients who metastasize develop only extrapulmonary mets



Standard 2nd line CT is Trabectedine



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Yondelis

Procedural steps taken and scientific information after the authorisation

No	Scope	Opinion/ Notification ¹ issued on	Commission Decision Issued ² / amended on	Product Information affected ³	Summary
R/0025	Renewal of the marketing authorisation	24/05/2012	03/08/2012	SPC, Annex II, Labelling, PL	Based on the review of the available information the CHMP is of the opinion that the quality, the safety and the efficacy of Yondelis continues to be adequately and sufficiently demonstrated and considers that the benefit/risk profile of this medicinal product continues to be favourable. The CHMP recommends the renewal of the Marketing Authorisation for Yondelis, subject to the conditions and obligations as laid down in Annex II to the Opinion. The CHMP recommends that the renewal be granted with unlimited validity. The MAH is requested to submit yearly PSURs unless otherwise specified by the CHMP. Additional data on the investigation to elucidate whether predictors of response to Yondelis in patients with soft tissue sarcoma can be identified (SOB 001) is awaited.

This is all the more true for MRC
Liposarcoma

Efficacy of trabectedin (ecteinascidin-743) in advanced pretreated myxoid liposarcomas: a retrospective study

Federica Grosso, Robin L Jones, George D Demetri, Ian R Judson, Jean-Yves Blay, Axel Le Cesne, Roberta Sanfilippo, Paola Casieri, Paola Collini, Palma Dileo, Carlo Spreafico, Silvia Stacchiotti, Elena Tamborini, Juan Carlos Tercero, Josè Jimeno, Maurizio D'Incalci, Alessandro Gronchi, Jonathan A Fletcher, Silvana Pilotti, Paolo G Casali

Lancet Oncol 2007; 8: 595-602

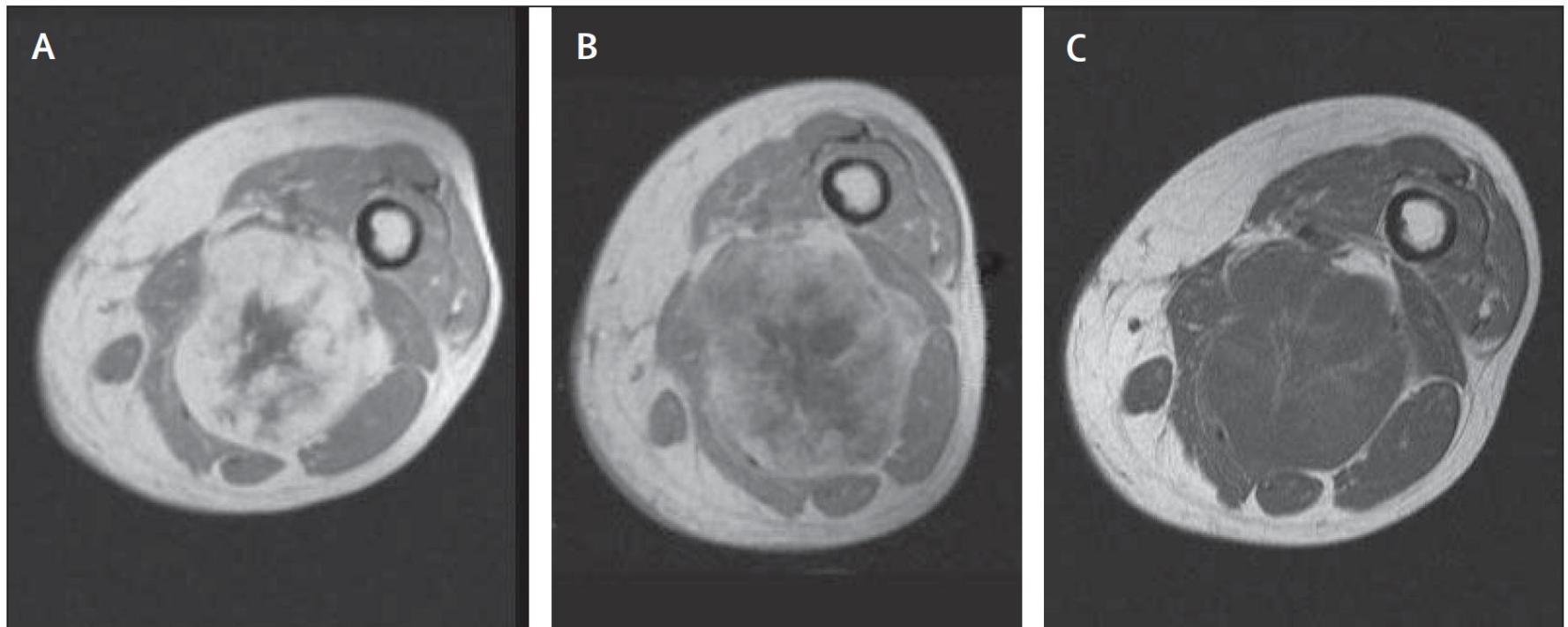


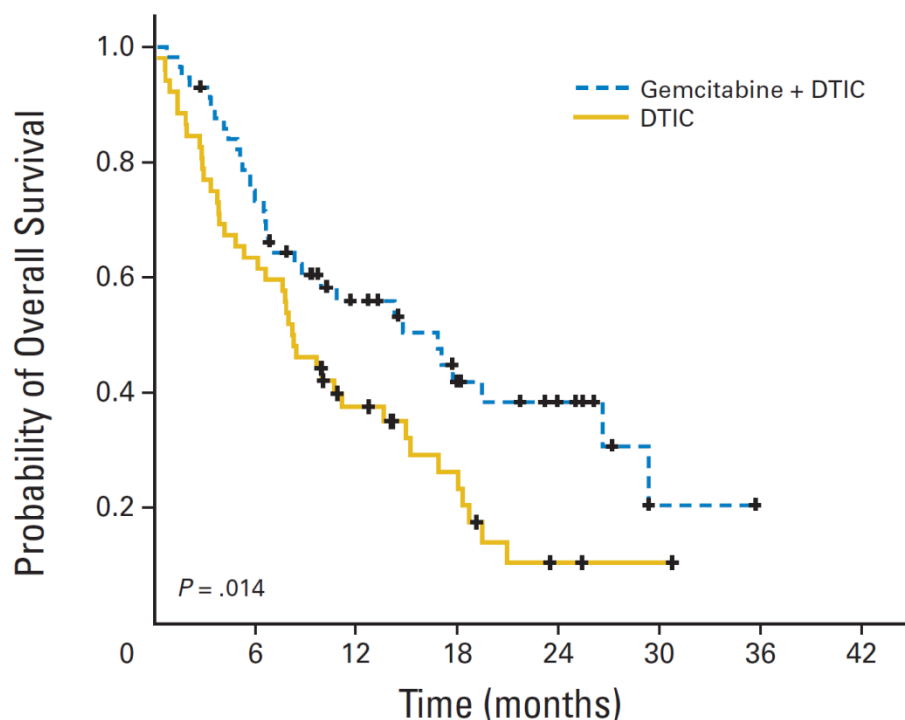
Figure 1: MRI of left thigh showing progressive decrease of contrast enhancement without tumour shrinkage in patient 26

Baseline MRI (A); after one course of trabectedin (B); and after four courses of trabectedin (C).

Would have that be the same in
other STS subtypes ?

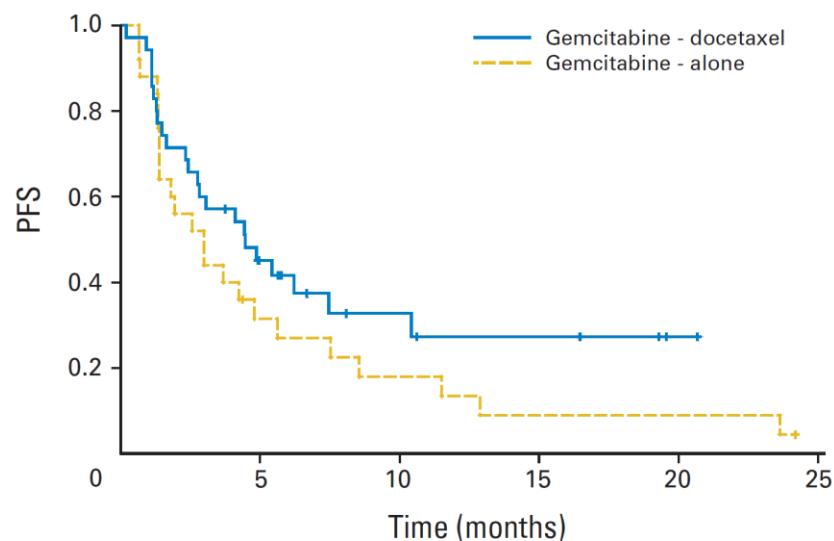
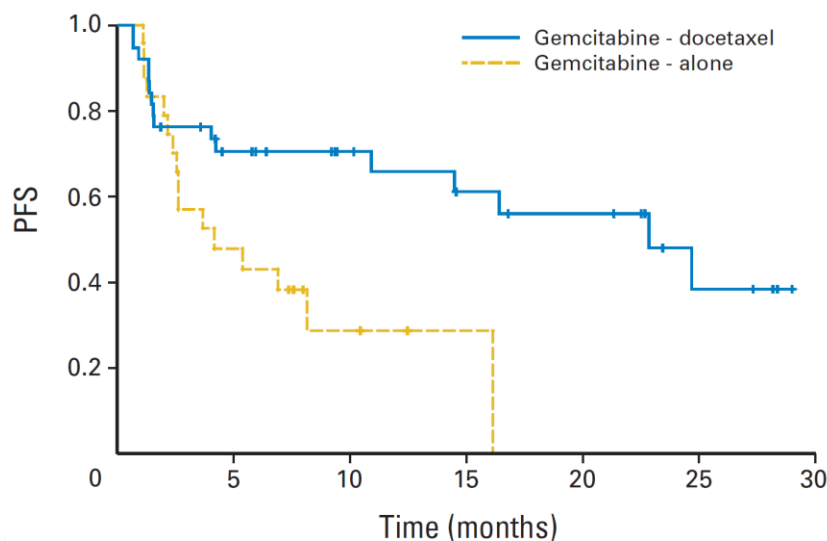
Randomized Phase II Study Comparing Gemcitabine Plus Dacarbazine Versus Dacarbazine Alone in Patients With Previously Treated Soft Tissue Sarcoma: A Spanish Group for Research on Sarcomas Study

Xavier García-del-Muro, Antonio López-Pousa, Joan Maurel, Javier Martín, Javier Martínez-Trufero, Antonio Casado, Auxiliadora Gómez-España, Joaquín Fra, Josefina Cruz, Andrés Poveda, Andrés Meana, Carlos Pericay, Ricardo Cubedo, Jordi Rubió, Ana De Juan, Nuria Láinez, Juan Antonio Carrasco, Raquel de Andrés, and José M. Buesa†



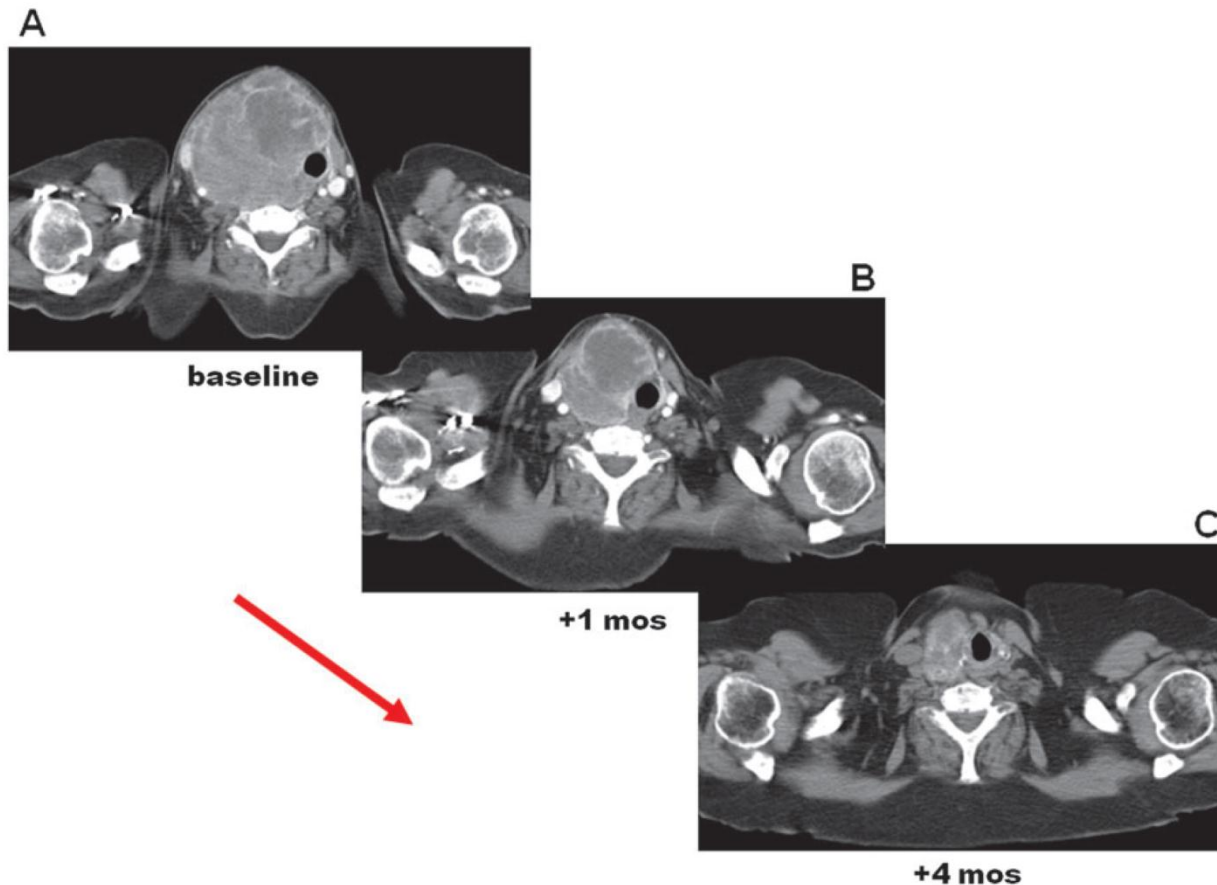
Randomized Phase II Study of Gemcitabine and Docetaxel Compared With Gemcitabine Alone in Patients With Metastatic Soft Tissue Sarcomas: Results of Sarcoma Alliance for Research Through Collaboration Study 002

Robert G. Maki, J. Kyle Wathen, Shreyaskumar R. Patel, Dennis A. Priebat, Scott H. Okuno, Brian Samuels, Michael Fanucchi, David C. Harmon, Scott M. Schuetze, Denise Reinke, Peter F. Thall, Robert S. Benjamin, Laurence H. Baker, and Martee L. Hensley



Gemcitabine in advanced angiosarcoma: a retrospective case series analysis from the Italian Rare Cancer Network

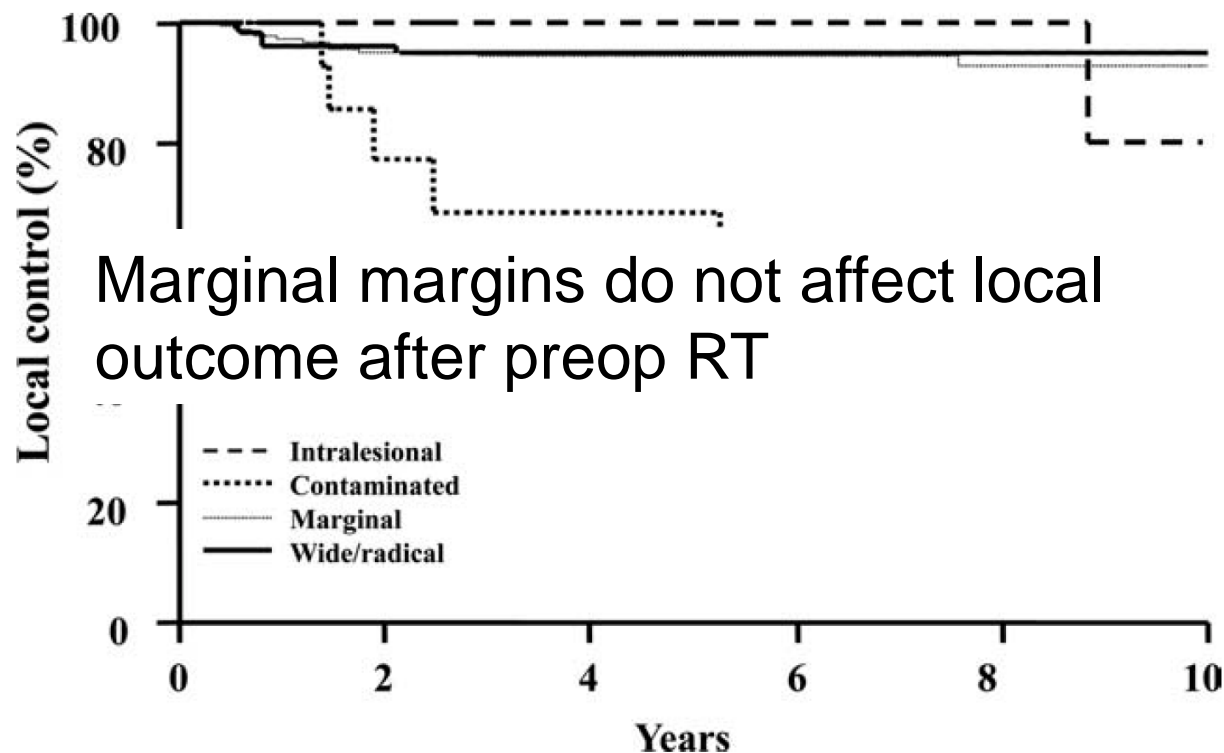
S. Stacchiotti^{1*}, E. Palassini¹, R. Sanfilippo¹, B. Vincenzi², M. G. Arena³, A. M. Bochicchio⁴, P. De Rosa⁵, A. Nuzzo⁶, S. Turano⁷, C. Morosi⁸, A. P. Dei Tos⁹, S. Pilotti⁹ & P. G. Casali¹⁰



Preop CT-RT is an option in locally
advanced STS

The Significance of a Marginal Excision After Preoperative Radiation Therapy for Soft Tissue Sarcoma of the Extremity

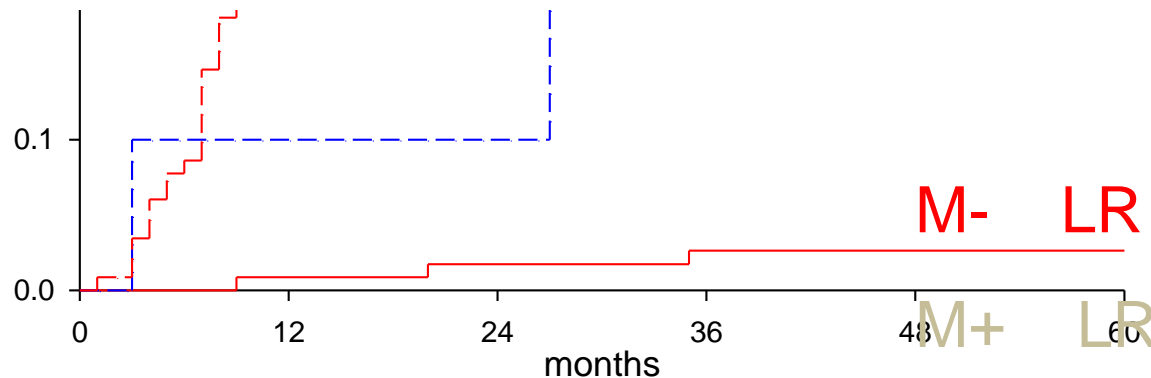
Roi Dagan, MD¹; Daniel J. Indelicato, MD^{1,4}; Lisa McGee, MD¹; Christopher G. Morris, MS¹; Jessica M. Kirwan, MA¹; Jacquelyn Knapik, MD²; John Reith, MD²; Mark T. Scarborough, MD³; C. Parker Gibbs, MD³; Robert B. Marcus, Jr, MD⁴; and Robert A. Zlotecki, MD, PhD¹



High-risk STS of limbs and trunk wall (164 pts)



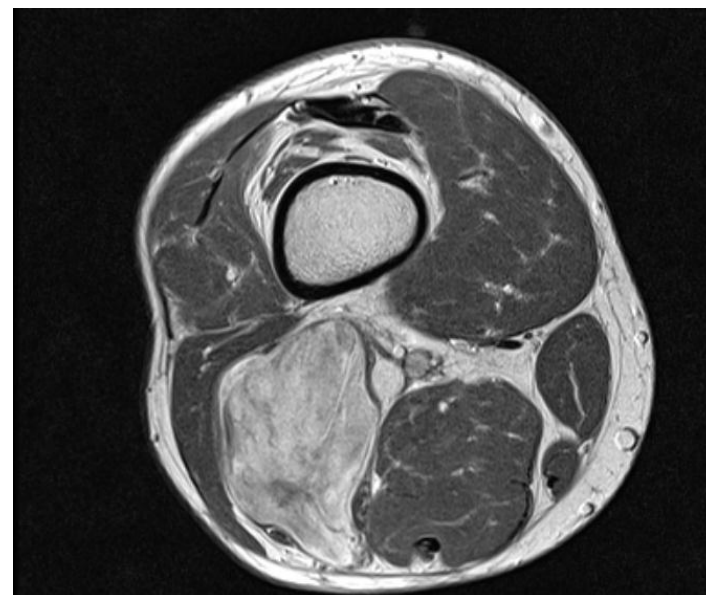
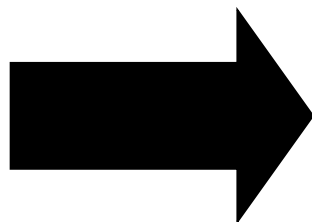
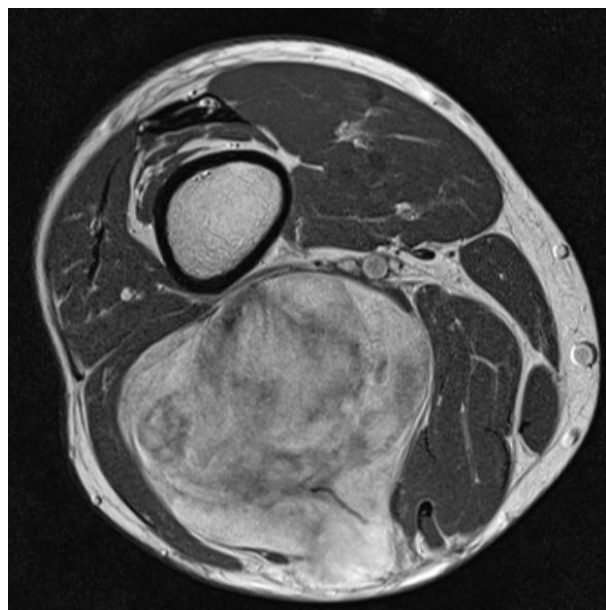
Positive margins do not affect
local outcome after preop RT



MRC liposarcoma are particularly
sensitive to RT

Myxoid liposarcoma

Preop RT alone may be very effective



In brief

- CT is the standard approach to stage IV disease
- The combination of Adriamidine and Ifosfamide to be chosen whenever response is an issue and can lead to CR
- Surgery of isolated metastases is often proposed
- 2nd line therapies should be tailored to histological subtype
- Preoperative CT, RT or both in locally “advanced” tumors can be of help