Histology-driven and non histology-driven therapy of adult STS

Paolo G. Casali
paolo.casali@istitutotumori.mi.it

Disclosures

	Employment	Consultant / Advisory	Stock	Honoraria	Research funds	Testimony	Other
Amgen Dompé	no	no	no	no	yes*	no	no
Bayer	no	yes	no	no	yes*	no	no
Glaxo SK	no	yes	no	no	yes*	no	no
ImClone	no	no	no	no	yes*	no	no
Infinity	no	no	no	no	yes*	no	no
Janssen Cilag	no	no	no	yes	Yes*	no	no
Lilly	no	no	no	no	yes*	no	no
Merck SD	no	yes	no	no	yes*	no	no
Molmed	no	no	no	no	yes*	no	no
Novartis	no	yes	no	yes	yes*	no	yes**
Pfizer	no	yes	no	yes	yes*	no	no
PharmaMar	no	yes	no	yes	yes*	no	yes**
Sanofi-Aventis	no	yes	no	no	yes*	no	no
Schering Plough	no	no	no	no	yes*	no	no

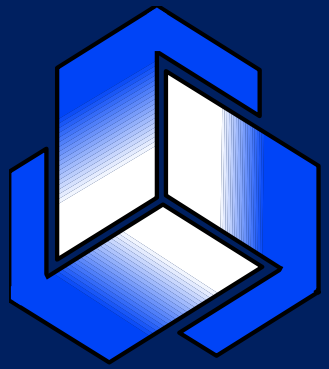
yes = myself, compensated
* = funds received by my institution for clinical studies and research activities in which I am involved
** = travel coverages for medical meetings

STS: advanced disease

R <

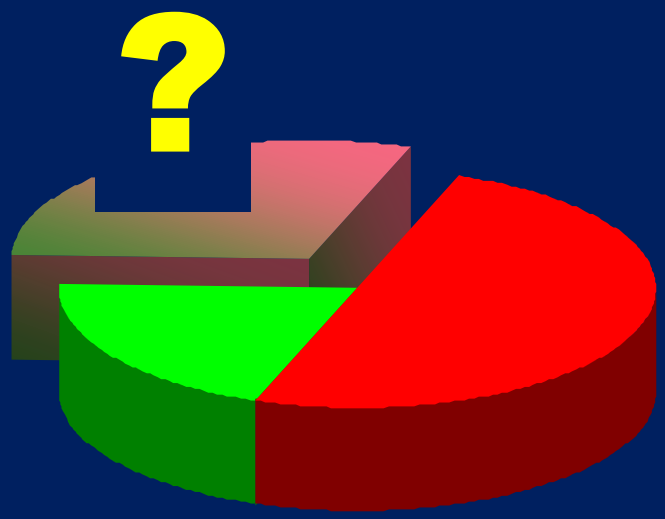
ADM 75 mg/sqm

ADM 75 mg/sqm + IFX 7.5 g/sqm



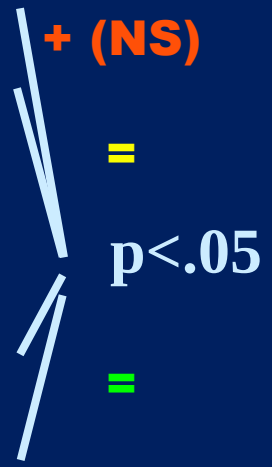
EORTC
Soft Tissue & Bone Sarcoma Group

Multiagent chemotherapy > single agent chemotherapy?!



ADM vs ADM+IFX in advanced STS

	no. pts.		Regimen	OR	OS
ECOG, 1993	90	ADM	80 mg/mq	20%	=
	88	ADM	60 mg/mq	34%	+ (NS)
		IFX	7500 mg/mq		
	84	ADM	40 mg/mq	32%	=
		CDDP	60 mg/mq		
		MMC	8 mg/mq		
SWOG/CALGB, 1993	170	ADM	80 mg/mq	17%	=
		DTIC	1000 mg/mq		
	170	ADM	60 mg/mq	32%	=
		IFX	60-7500 mg/mq		
		DTIC	1000 mg/mq		



ADM vs ADM+IFX in advanced STS

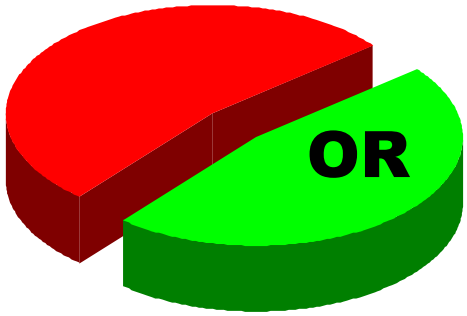
	no. pts.		Regimen	OR	OS
EORTC, 1991	244	ADM	75 mg/mq	24%	=
	233	ADM	50 mg/mq	27%	=
		IFX	5000 mg/mq		
	135	ADM	50 mg/mq	27%	=
		DTIC	750 mg/mq		
		CTX	500 mg/mq		
		VCR	1.5 mg/mq		

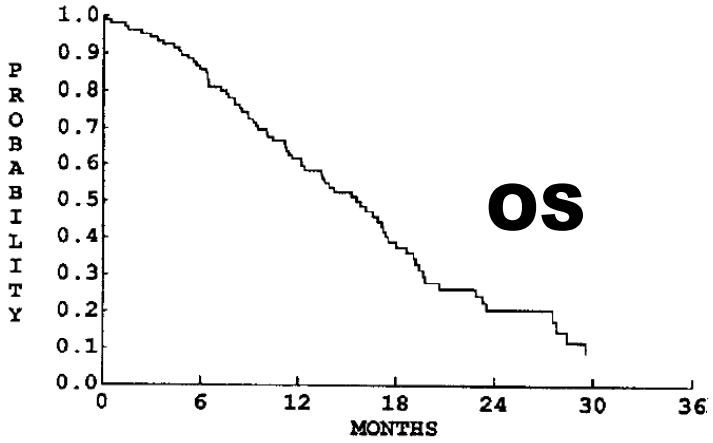
Response to Mesna, Doxorubicin, Ifosfamide, and Dacarbazine in 108 Patients With Metastatic or Unresectable Sarcoma and No Prior Chemotherapy

By Anthony Elias, Louise Ryan, Aaron Sulkes, Jerry Collins, Joseph Aisner, and Karen H. Antman

In this phase II trial, 105 eligible patients with no prior chemotherapy and advanced sarcoma received doxorubicin, ifosfamide, and dacarbazine (DTIC) with mesna uroprotection (MAID). Starting doses of these drugs were 60, 7,500, and 900 mg/m^2 divided over 72 hours by continuous infusion, respectively. Mesna was given for 84 to 96 hours at 2,500 mg/m^2/d. Myelosuppression was dose limiting, causing the only toxic death (sepsis). Nonhematologic toxicity consisted predominantly of anorexia and vomiting. Severe mucositis, macroscopic hematuria, renal tubular acidosis, renal failure, and CNS toxicity occurred in less than 5% of cycles. No cardiotoxicity was detected. The overall response rate (10% complete response [CR]) was 47% (95% confidence intervals, 5% to 18% and 37% to 57%, respectively). Most responses (~70%) were observed within two cycles. Median times to progression were 10 and 9 months, respectively. Histologic high tumor grade, lesions less than 5 cm, and less than 1 year from diagnosis to study entry correlated with the probability of response. The median survival was 16 months. Time from diagnosis to study entry, peformance status, and extent of disease, but not histologic grade, correlated with survival. Following CR, two patients remain disease-free at 32 and 16 months. Of the 15 additional patients rendered disease-free with surgery, two remain disease-free at 30 and 18 months with no further therapy. While most relapses occurred in sites of prior involvement, death from CNS metastases occurred in 11 of the 80 patients with high-grade sarcomas, of whom seven were still responding systemically (three complete responders). Because of its substantial response in this phase II trial, the MAID regimen is being compared with doxorubicin and DTIC alone in advanced sarcomas and to observation in the adjuvant treatment of high-grade sarcomas in randomized trials.

J Clin Oncol 7:1208-1216. © 1989 by American Society of Clinical Oncology.





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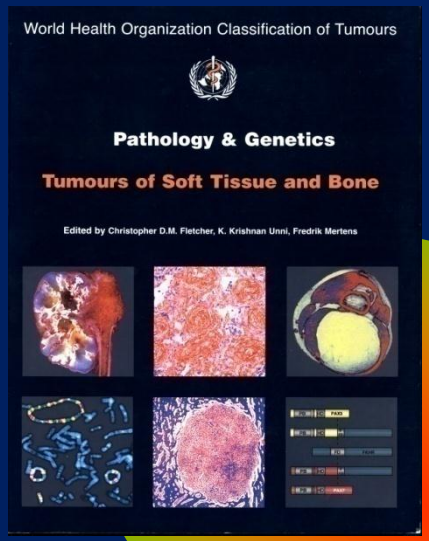


Adipocytic tumours
- Well deifferentiated / dedifferentiated liposarcoma
- Myxoid / round cell liposarcoma
- Pleomorphic liposarcoma
- .....

Fibroblastic / myofibroblastic tumours
- Fibromatosis (desmoid)
- Solitary fibrous tumour / haemangiopericytoma
- Low grade myofibroblastic tumour
- Infantile fibrosarcoma
- Adult fibrosarcoma
- Mixofibrosarcoma
- .....

So-called fibrohistiocytic tumours
- Pleomorphic MFH / Undifferentiated pleomorphic sarcoma
- .....

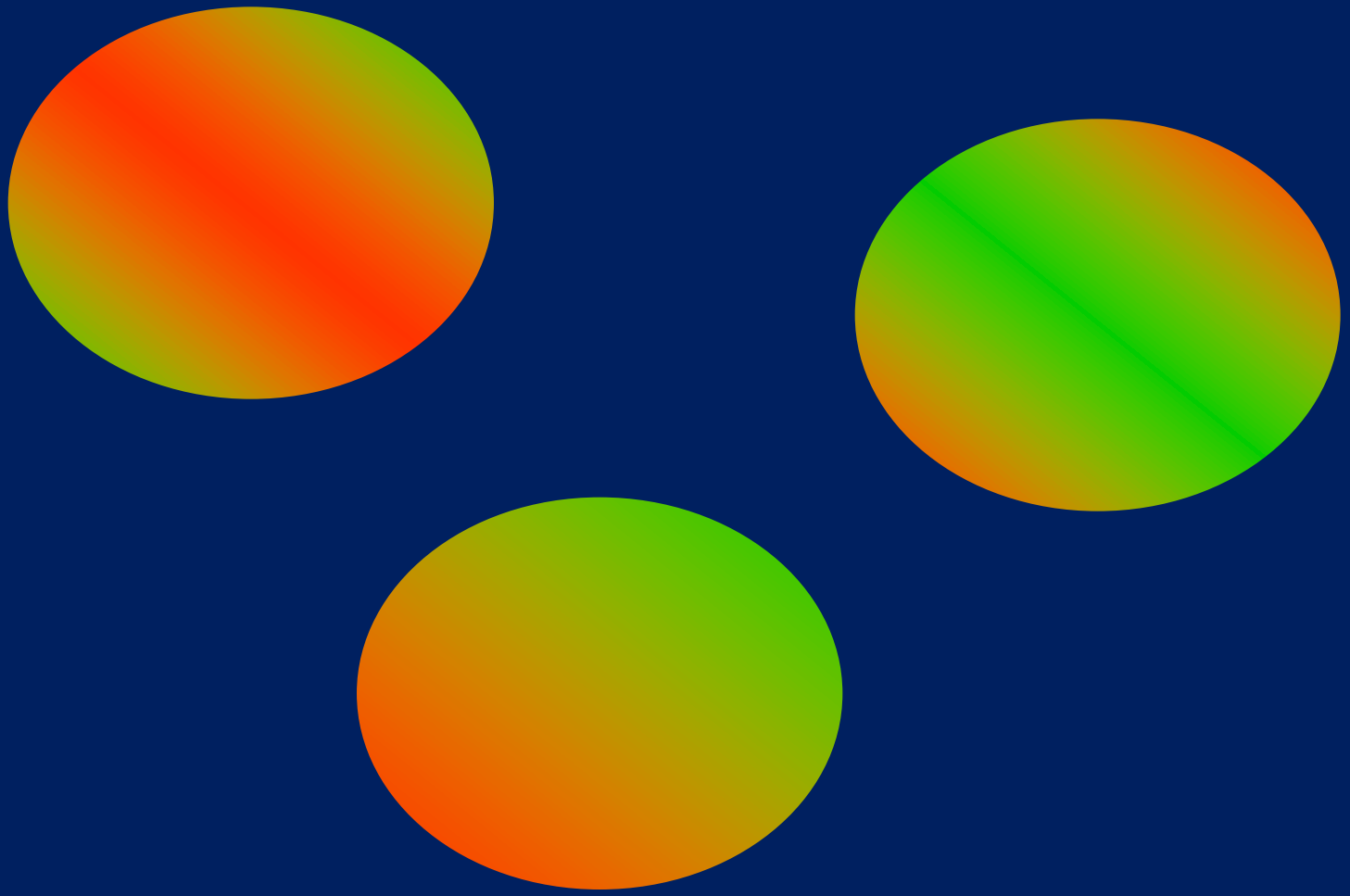
Smooth muscle tumours
- Leiomyosarcoma
- .....

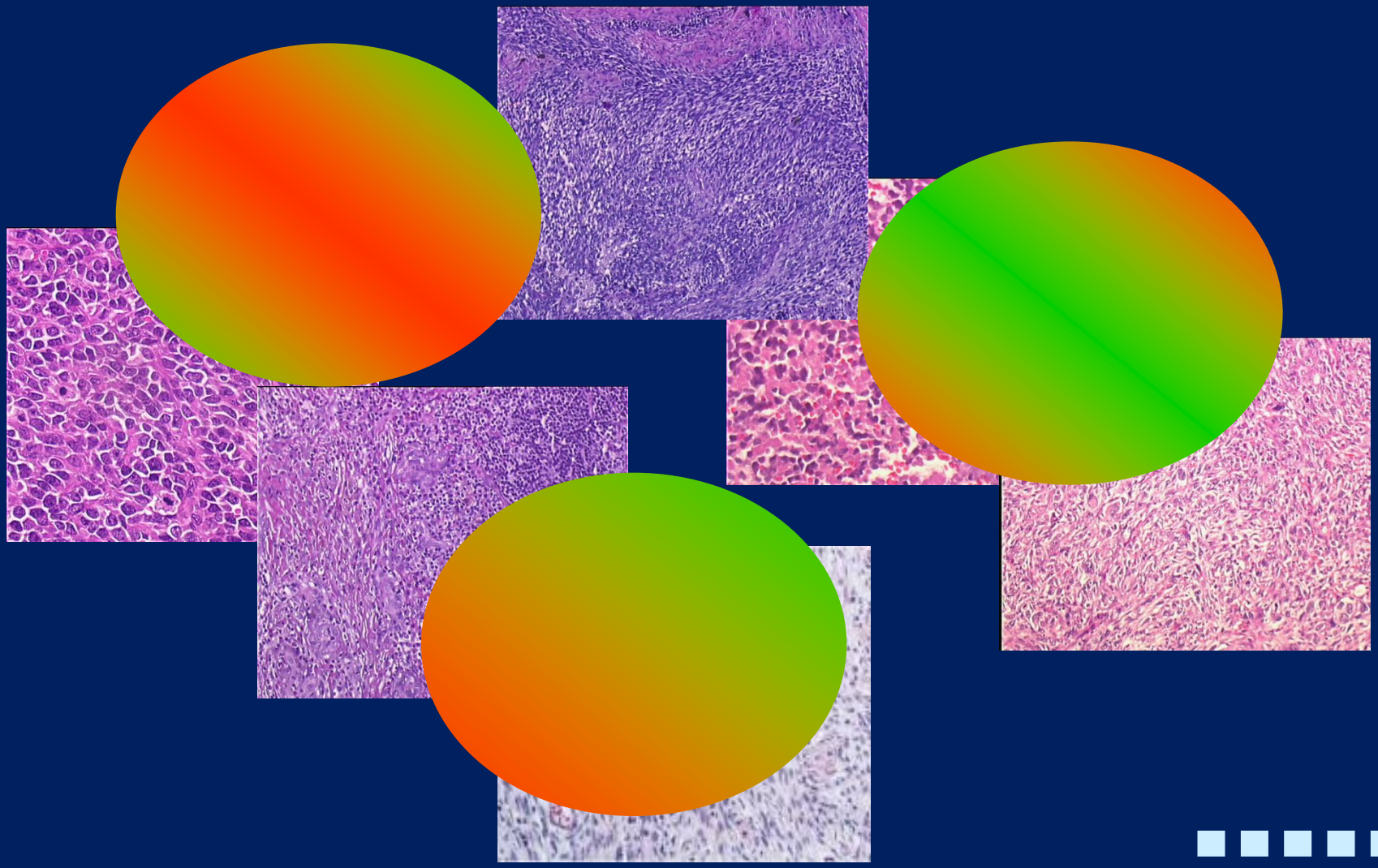
Skeletal muscle tumours
- Embryonal rhabdomyosarcoma
- Alveolar rhabdomyosarcoma
- Pleomorphic rhabdomyosarcoma

Vascular tumours
- Epithelioid haemangioendothelioma
- Angiosarcoma of soft tissue
- .....

Chondro-osseous tumours
- Mesenchymal chondrosarcoma
- Extraskeletal osteosarcoma

Tumours of uncertain differentiation
- Synovial sarcoma
- Epithelioid sarcoma
- Alveolar soft part sarcoma
- Clear cell sarcoma of soft tissue
- Extraskeletal myxoid chondrosarcoma
- Extraskeletal Ewing tumour
- Desmoplastic small round cell tumour
- Extra-renal rhabdoid tumour
- Malignant mesenchymoma
- Neoplasms with perivascular epithelioid cell differentiation (PEComa)
- Intimal sarcoma



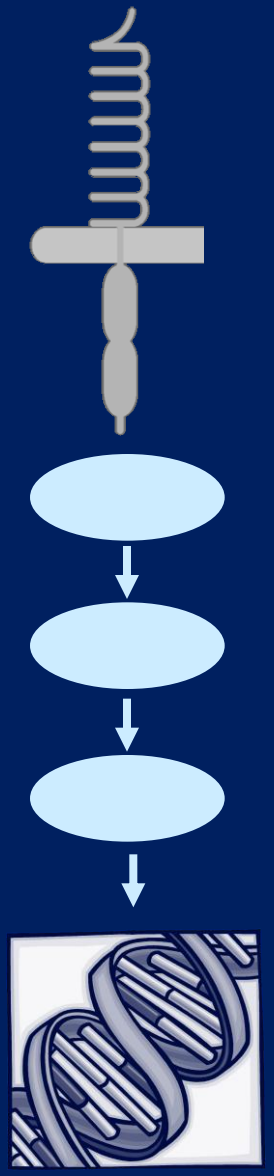


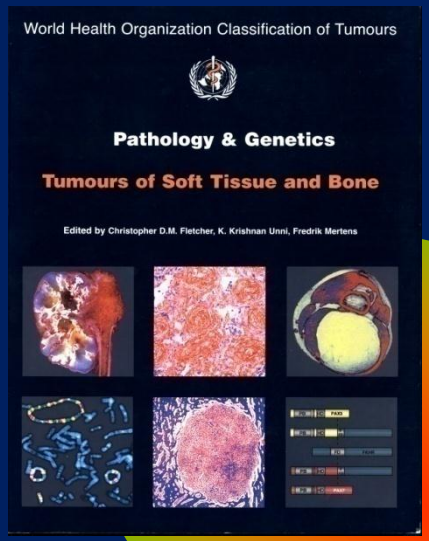
statistical precision

clinical precision

statistical precision

clinical precision





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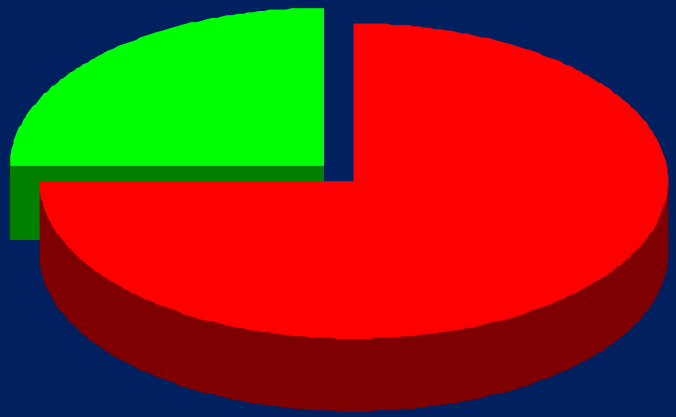
- Intimal sarcoma

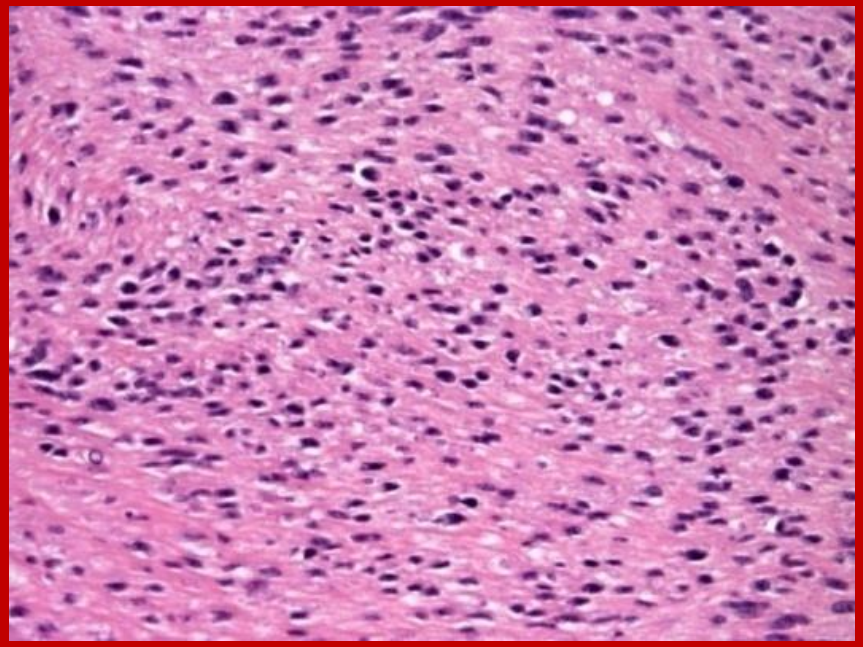
T-STS

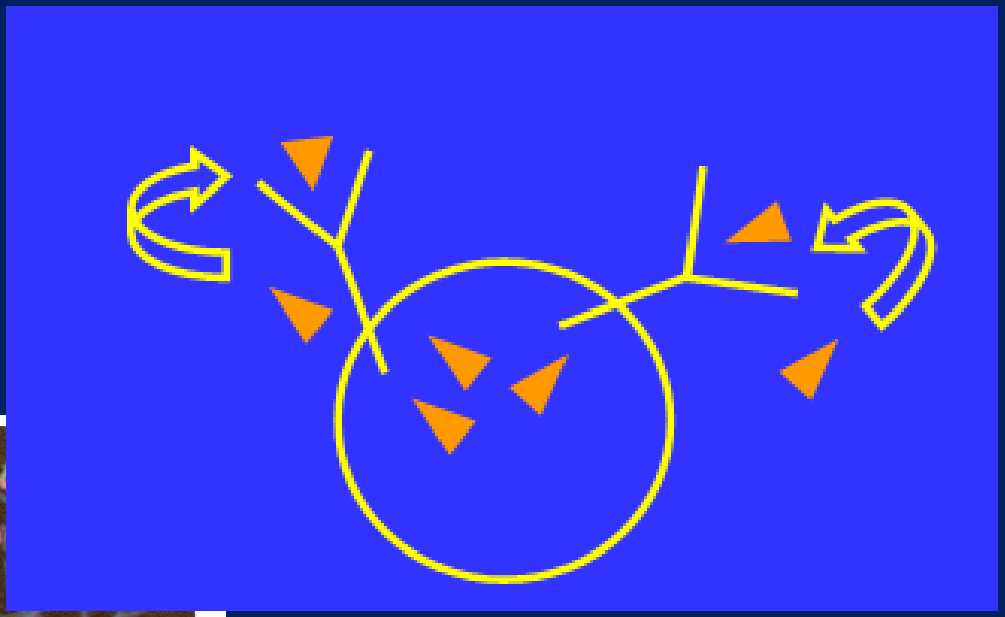
simple cariotype
with complex translocations

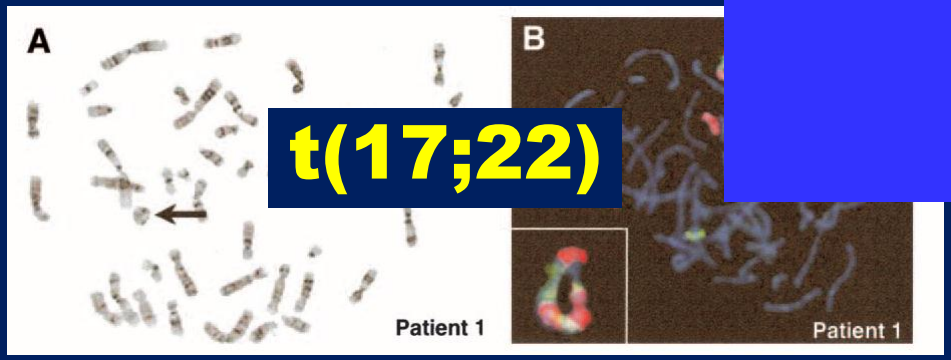


complex cariotype

Dermatofibrosarcoma







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COL1A1-PDGFB → PDGFB

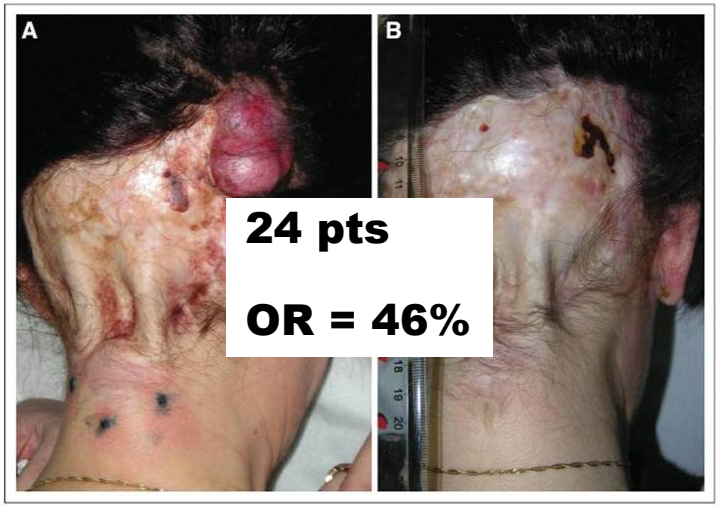
VOLUME 28 · NUMBER 10 · APRIL 1 2010

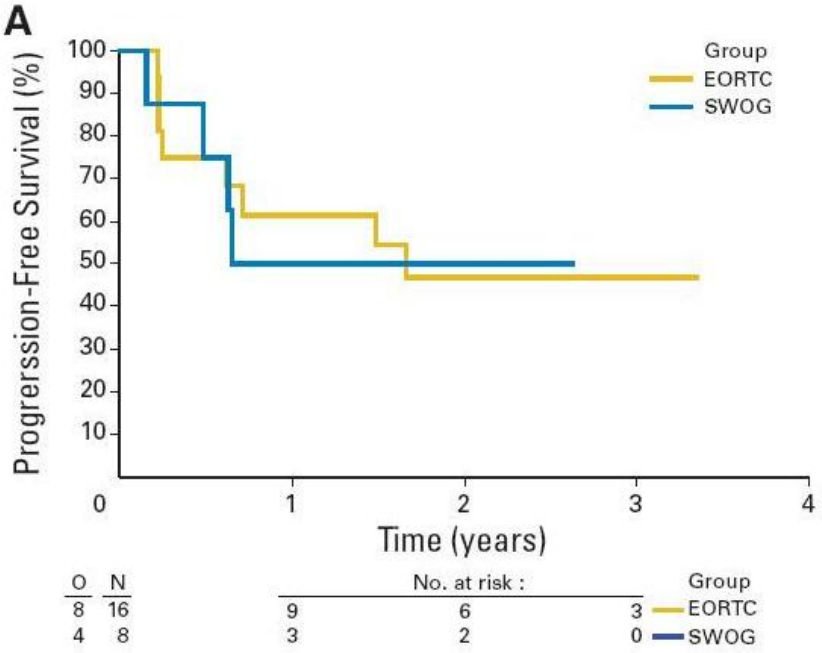
JOURNAL OF CLINICAL ONCOLOGY

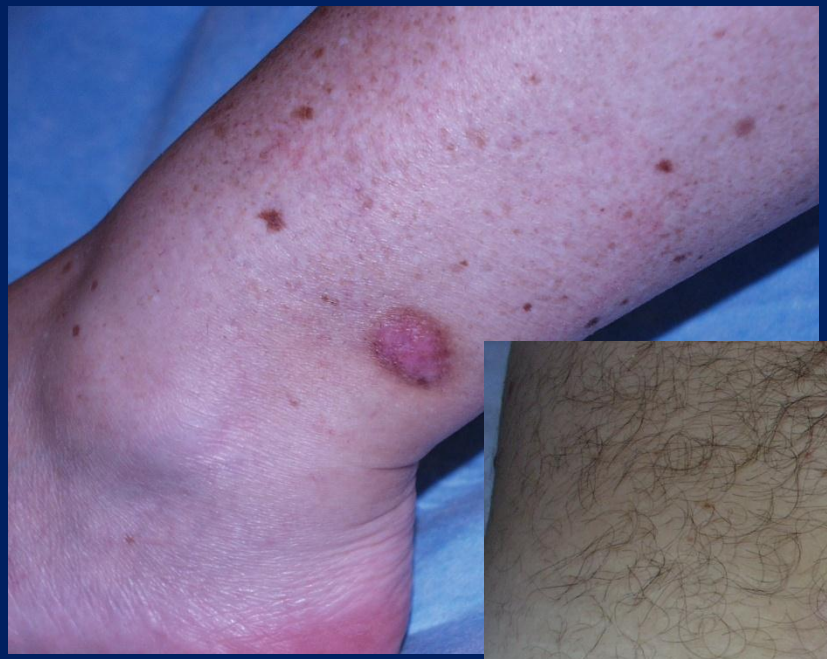
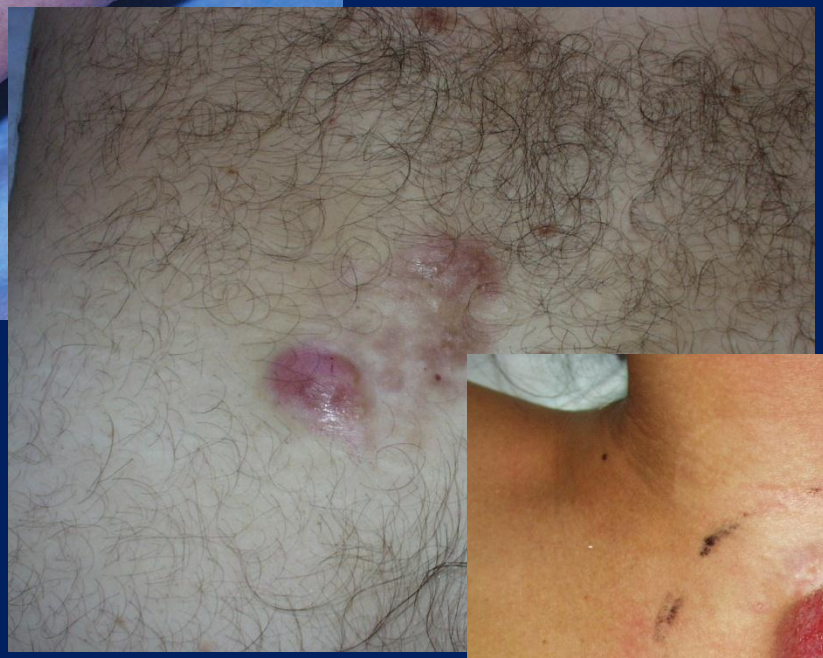
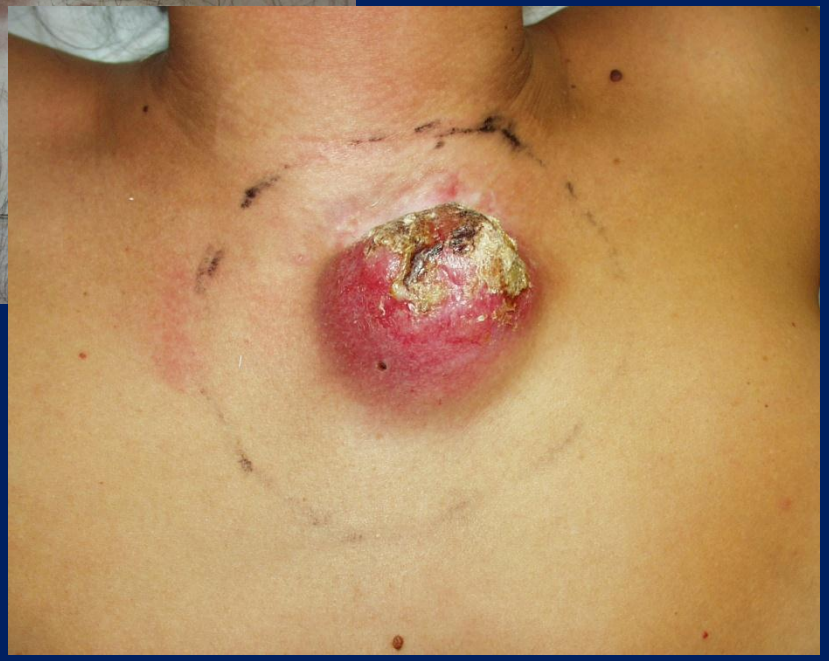
ORIGINAL REPORT

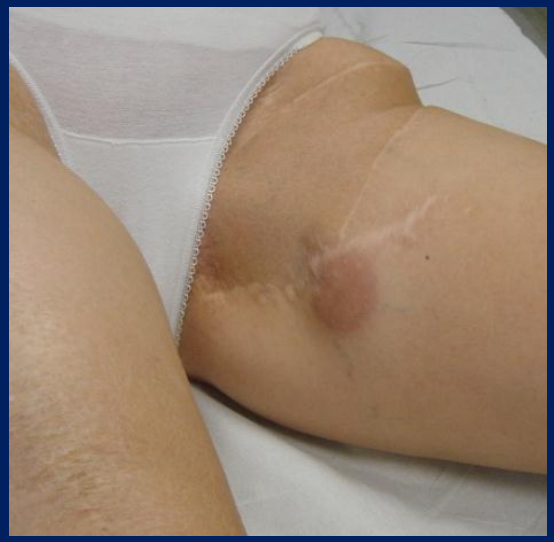
Imatinib Mesylate in Advanced Dermatofibrosarcoma Protuberans: Pooled Analysis of Two Phase II Clinical Trials

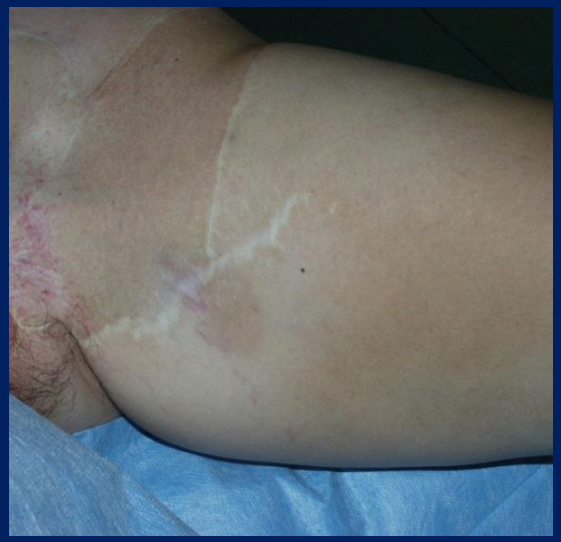
Piotr Rutkowski, Martine Van Glabbeke, Cathryn J. Rankin, Wlodzimierz Ruka, Brian P. Rubin, Maria Debiec-Rychter, Alexander Lazar, Hans Gelderblom, Raf Sciot, Dolores Lopez-Terrada, Peter Hohenberger, Allan T. van Oosterom, and Scott M. Schuetze



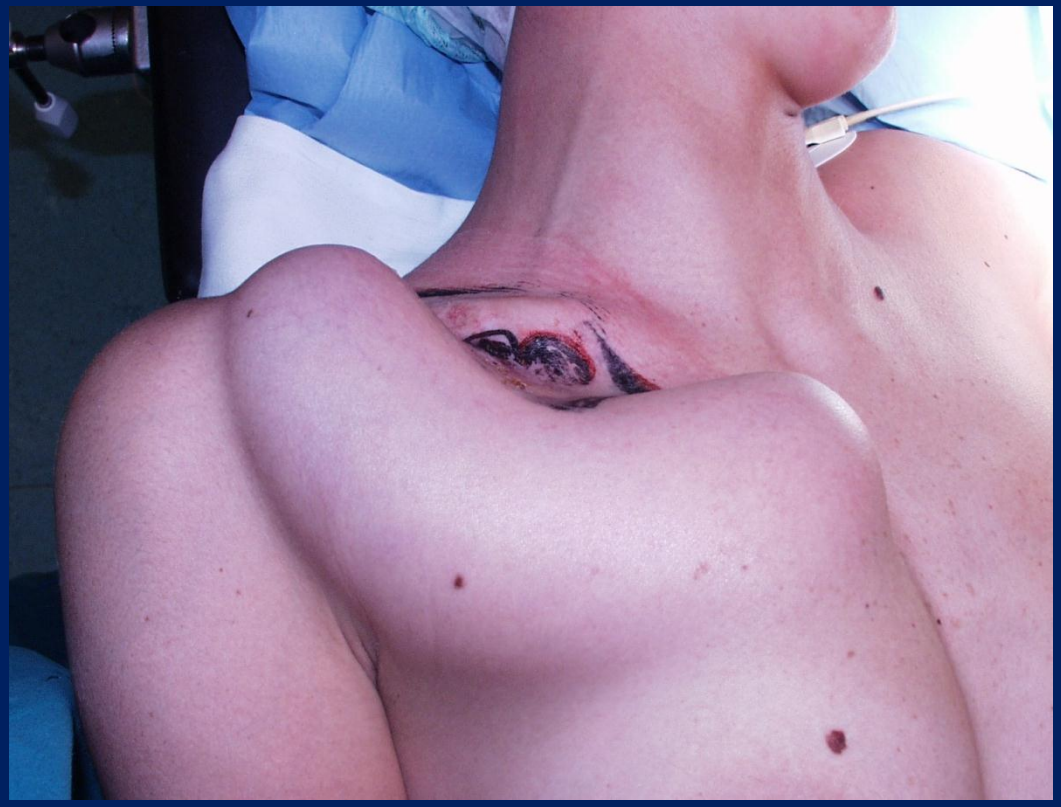


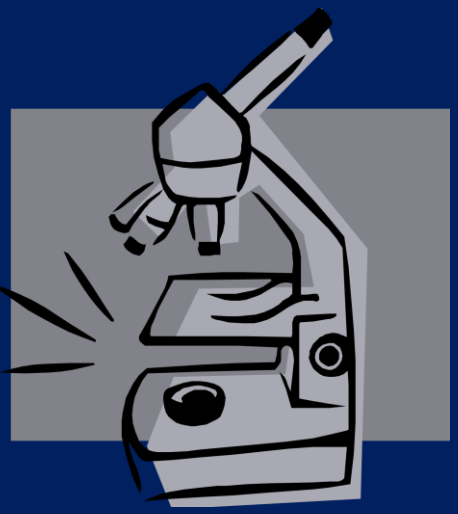




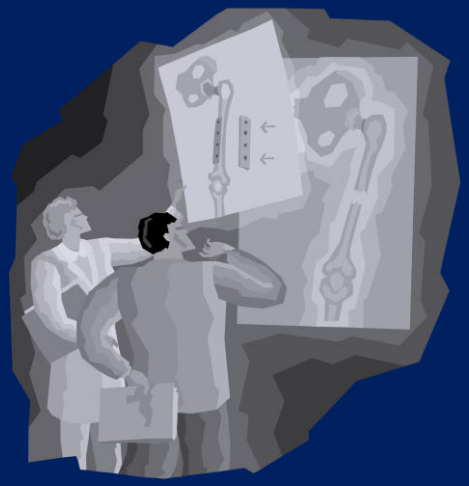


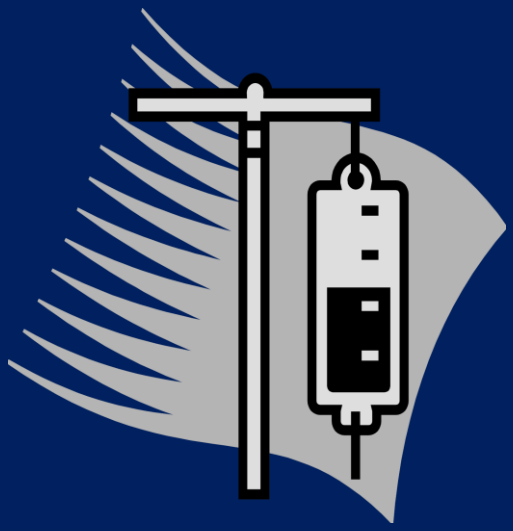


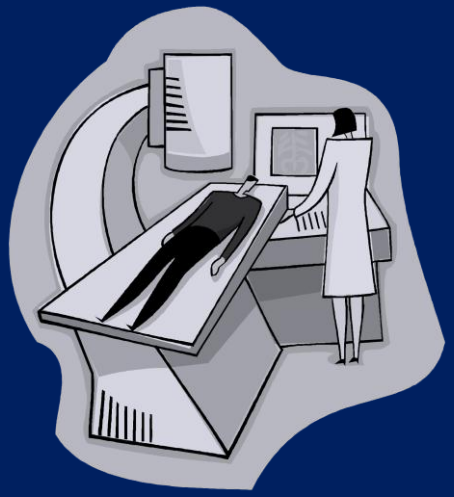
IM 400 mg/d x 8 mos











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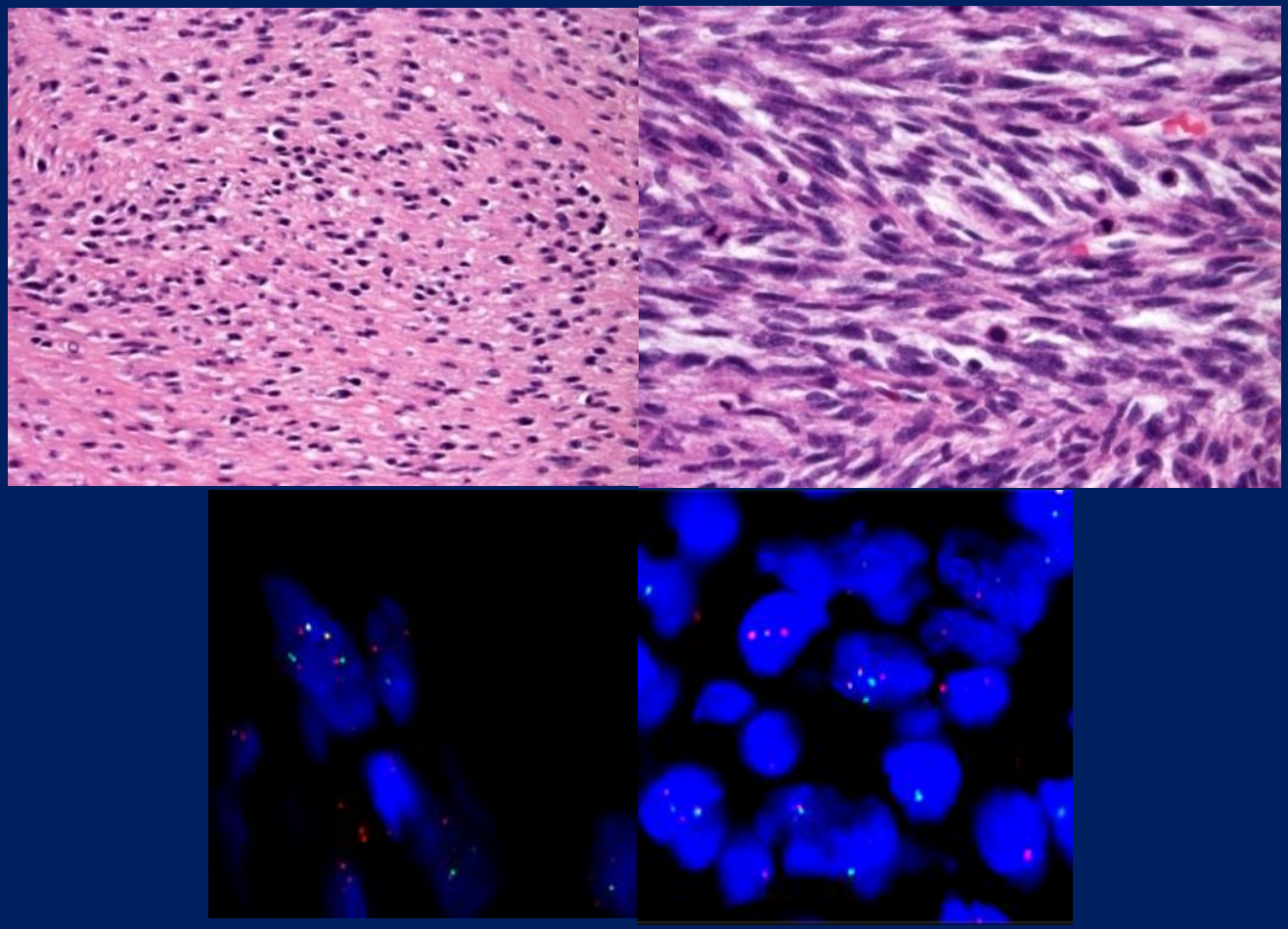

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Dermatofibrosarcoma protuberans-derived fibrosarcoma: clinical history, biological profile and sensitivity to imatinib

Silvia Stacchiotti[1], Florence Pedeutour[2], Tiziana Negri[3], Elena Conca[3], Andrea Marrari[1], Elena Palassini[1], Paola Collini[3], Frederique Keslair[2], Carlo Morosi[4], Alessandro Gronchi[5], Silvana Pilotti[2] and Paolo G. Casali[1]

[1] Adult Sarcoma Medical Oncology Unit, Department of Cancer Medicine, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy
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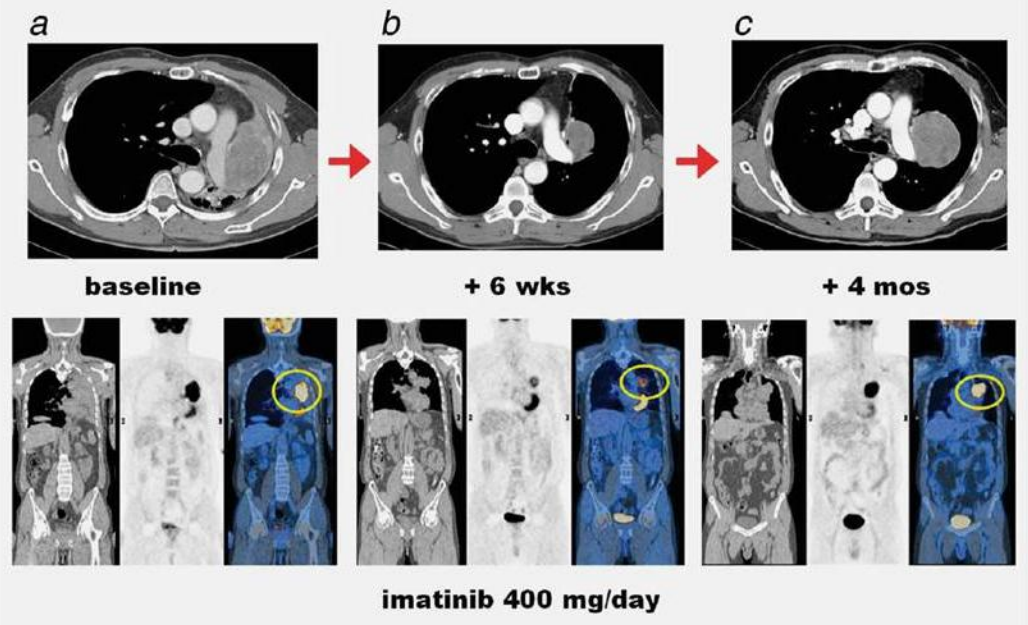

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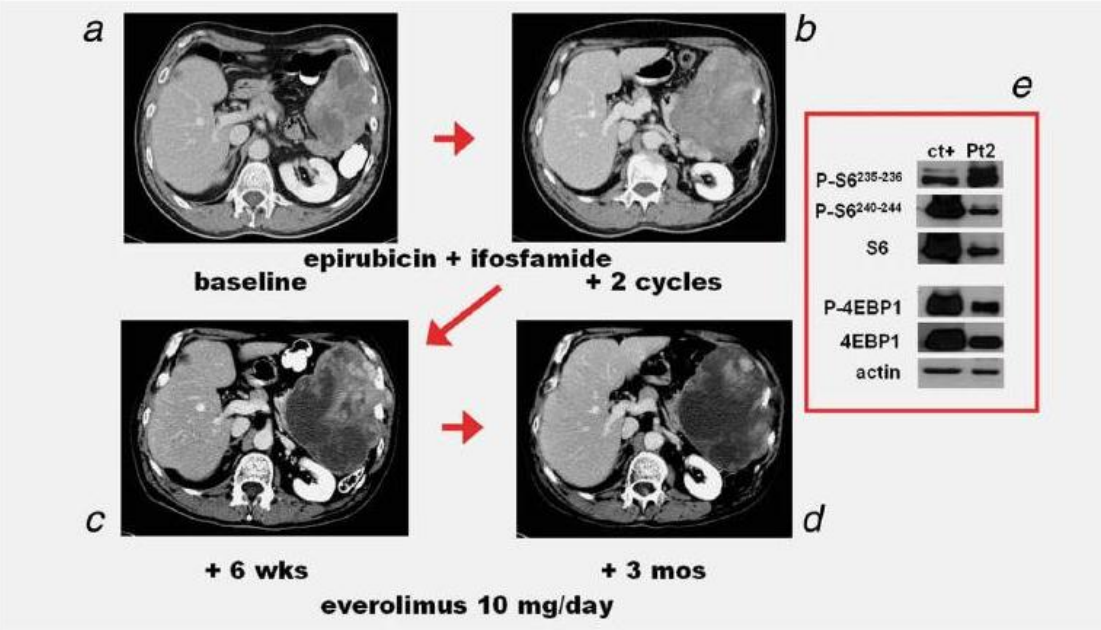
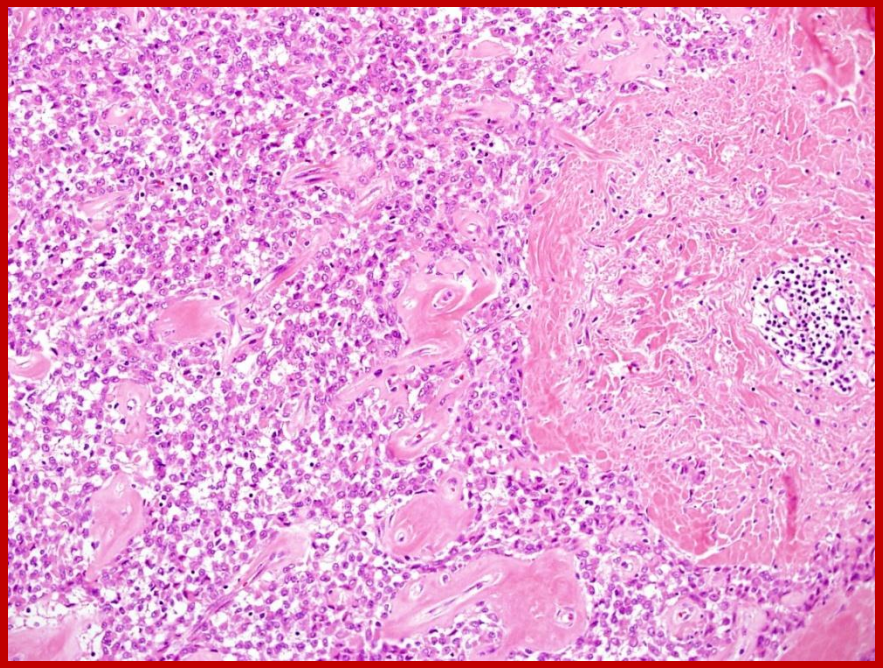


PEComas

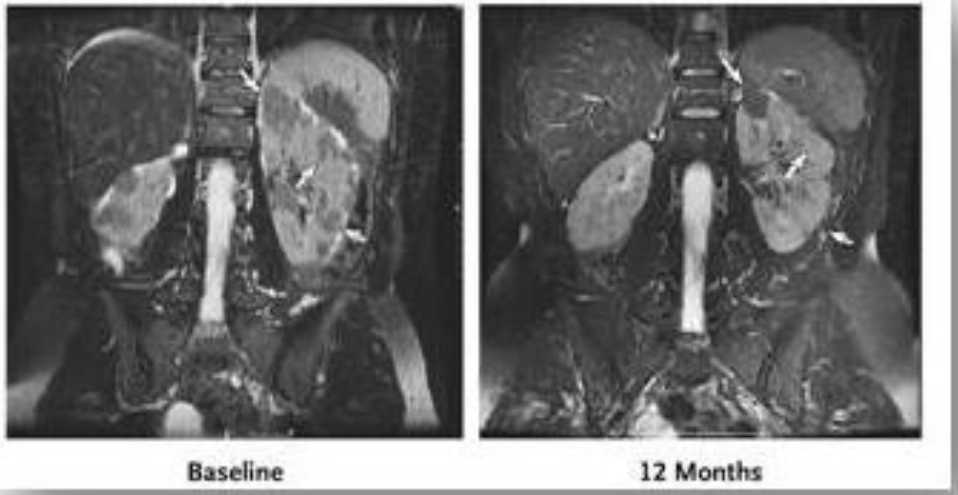


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sirolimus for Angiomyolipoma in Tuberous Sclerosis Complex or Lymphangioleiomyomatosis

John J. Bissler, M.D., Francis X. McCormack, M.D., Lisa R. Young, M.D., Jean M. Elwing, M.D., Gail Chuck, L.M.T., Jennifer M. Leonard, R.N., Vincent J. Schmithorst, Ph.D., Tal Laor, M.D., Alan S. Brody, M.D., Judy Bean, Ph.D., Shelia Salisbury, M.S., and David N. Franz, M.D.



From the Divisions of Nephrology and Hypertension (J.J.B.), Pulmonary Medicine (L.R.Y.), Neurology (G.C., J.M.E., D.N.F.), Radiology (V.J.S., T.L., A.S.B.), and Biostatistics (J.B., S.S.), Cincinnati Children's Hospital Medical Center; and the Division of Pulmonary and Critical Care, University of Cincinnati College of Medicine (F.X.M., L.R.Y., J.M.E.) — both in Cincinnati. Address reprint requests to Dr. Bissler at Cincinnati Children's Hospital Medical Center, MLC 7022, 3333 Burnet Ave., Cincinnati, OH 45229-3039, or at john.bissler@cchmc.org.

Drs. McCormack, Young, and Franz contributed equally to the article.

N Engl J Med 2008;358:140-51.

mount height and radius estimates.
20. The marine portions of the ETOPO5 data set derive from SYNPAPS [R. J. Van Wyckhouse, Tech. Rep. TR-233 (U.S. Naval Oceanographic Office, NOO-Washington, DC, 1973)] and contain numerous artifacts caused by the combination of poor data coverage, gridding of contours instead of depth soundings, and inappropriate gridding methodology [W. H. F. Smith, *J. Geophys. Res.* **99**, 9591 (1994)].
21. R. A. Duncan and D. A. Clague, in *The Ocean Basins and Margins*, A. E. M. Nairn, F. G. Stehli, S. Uyeda, Eds. (Plenum, New York, 1985), pp. 89–121; R. D. Jarrard and D. A. Clague, *Rev. Geophys.* **15**, 57 (1977); C. Y. Yan and L. W. Kroenke, *Proc. ODP Sci. Results* **130**, 697 (1993).
22. J. P. Morgan, W. J. Morgan, E. Price, *J. Geophys. Res.* **100**, 8045 (1995).
23. U. S. ten Brink, *Geology* **19**, 397 (1991).
24. P. Wessel and L. W. Kroenke, *Nature* **387**, 365 (1997).
25. R. D. Müller, W. R. Roest, J. Y. Royer, L. M. Gahagan, J. G. Sclater, *J. Geophys. Res.* **102**, 3211 (1997).
26. Robust regression of the envelope in Fig. 3 gives $VGG/\Delta t = 61.8 + 10.5\sqrt{2}$. This is inverted to yield the empirical relation

$$\text{pseudo age} = \text{seafloor age} - \left[\frac{VGG/\Delta t - 61.8}{10.5}\right]^2 \quad (2)$$

27. The flexural modeling also allowed numerical estimation of most volumes.
28. R. Bilham, *Earth Planet. Sci. Lett.* **80**, 105 (1982).
29. W. H. F. Smith, thesis, Columbia University (1988).
30. The Ontong Java plateau was emplaced during two distinct episodes at ~121 Ma and ~89 Ma [D. Gaboveki and J. Mahoney, *Science* **268**, 1327 (1995)]; the Manihiki plateau also formed at ~123 Ma, whereas the Hess rise (90 to 100 Ma) and the Mid-Pacific Mountains (75 to 130 Ma) have longer ranges of ages. The oldest plateau is Shatsky rise (135 to 145 Ma) [R. Larson and P. Olson, *Earth Planet. Sci. Lett.* **107**, 437 (1991)].
31. I thank W. Smith for providing the WGG grid. Supported by NSF grant EAR-9303402, School of Ocean and Earth Science and Technology, University of Hawaii, contribution no. 4517.

17 April 1997; accepted 13 June 1997

Identification of the Tuberous Sclerosis Gene *TSC1* on Chromosome 9q34

Marjon van Slegtenhorst, Ronald de Hoogt, Caroline Hermans, Mark Nellist, Bart Janssen, Senno Verhoef, Dick Lindhout, Ans van den Ouweland, Dicky Halley • Janet Young, Mariwyn Burley, Steve Jeremiah, Karen Woodward, Joseph Nahmias, Margaret Fox, Rosemary Ekong, John Osborne, Jonathan Wolfe, Sue Povey • Russell G. Snell, Jeremy P. Cheadle, Alistair C. Jones, Maria Tachataki, David Ravine, Julian R. Sampson • Mary Pat Reeve, Paul Richardson, Friederike Wilmer, Cheryl Munro, Trevor L. Hawkins • Tiina Sepp, Johari B. M. Ali, Susannah Ward, Andrew J. Green, John R. W. Yates • Jolanta Kwiatkowska, Elizabeth P. Henske, M. Priscilla Short, Jonathan H. Haines, Sergiusz Jozwiak, David J. Kwiatkowski*

Tuberous sclerosis complex (TSC) is an autosomal dominant disorder characterized by the widespread development of distinctive tumors termed hamartomas. TSC-determining loci have been mapped to chromosomes 9q34 (*TSC1*) and 16p13 (*TSC2*). The *TSC1* gene was identified from a 900-kilobase region containing at least 30 genes. The 8.6-kilobase *TSC1* transcript is widely expressed and encodes a protein of 130 kilodaltons (hamartin) that has homology to a putative yeast protein of unknown function. Thirty-two distinct mutations were identified in *TSC1*, 30 of which were truncating, and a single mutation (2105delAAAG) was seen in six apparently unrelated patients. In one of these six, a somatic mutation in the wild-type allele was found in a TSC-associated renal carcinoma, which suggests that hamartin acts as a tumor suppressor.

TSC is a systemic disorder in which hamartomas occur in multiple organ systems, particularly the brain, skin, heart, lungs, and kidneys (*1*, *2*). In addition to its distinct clinical presentation, two features serve to distinguish TSC from other familial tumor syndromes. First, the tumors that occur in TSC are very rare in the general population, such that several TSC lesions are, by themselves, diagnostic of TSC. Second, TSC hamartomas rarely progress to malignancy. Only renal cell carcinoma occurs at increased frequency in TSC (~2.5%) and with earlier age of onset; it appears to arise in TSC renal hamartomas, termed angiomyolipomas (*3*). Nonetheless, TSC can be a devastating condition, as the cortical tubers (brain hamartomas) frequently cause epilepsy, mental retardation, autism, or attention deficit–hyperactive disorder, or a combination of these conditions (*1*, *4*).

TSC affects about 1 in 6000 individuals, and ~65% of cases are sporadic (*5*). Linkage of TSC to chromosome 9q34 was first reported in 1987, and this locus was denoted *TSC1* (*6*). Later studies provided strong evidence for locus heterogeneity (*7*) and led to the identification of chromosome 16p13 as the site of a second TSC locus (denoted *TSC2*) (*8*). The *TSC2* gene was identified by positional cloning, and the encoded protein, denoted tuberin, contains a domain near the COOH-terminus with homology to a guanosine triphosphatase (GTPase) activating protein (GAP) for rap1, a Ras-related GTPase (*9*).

The focal nature of TSC-associated hamartomas has suggested that *TSC1* and *TSC2* may function as tumor suppressor genes. The occurrence of inactivating germline mutations of *TSC2* in patients with tuberous sclerosis (*9–11*) and of loss of heterozygosity (LOH) at the *TSC2* locus in about 50% of TSC-associated hamartomas (*12–14*) supports a tumor suppressor function for *TSC2*. In contrast, LOH at the *TSC1* locus has been detected in <10% of TSC-associated hamartomas (*13*, *14*), suggesting the possibility of an alternative pathogenic mechanism for lesion development in patients with *TSC1* disease.

As part of a comprehensive strategy to identify *TSC1*, we identified 11 microsatellite markers from the 1.4-Mb *TSC1* region and developed an overlapping contig (with only a single gap of 20 kb) of cosmid, P1

The TSC1 Consortium:
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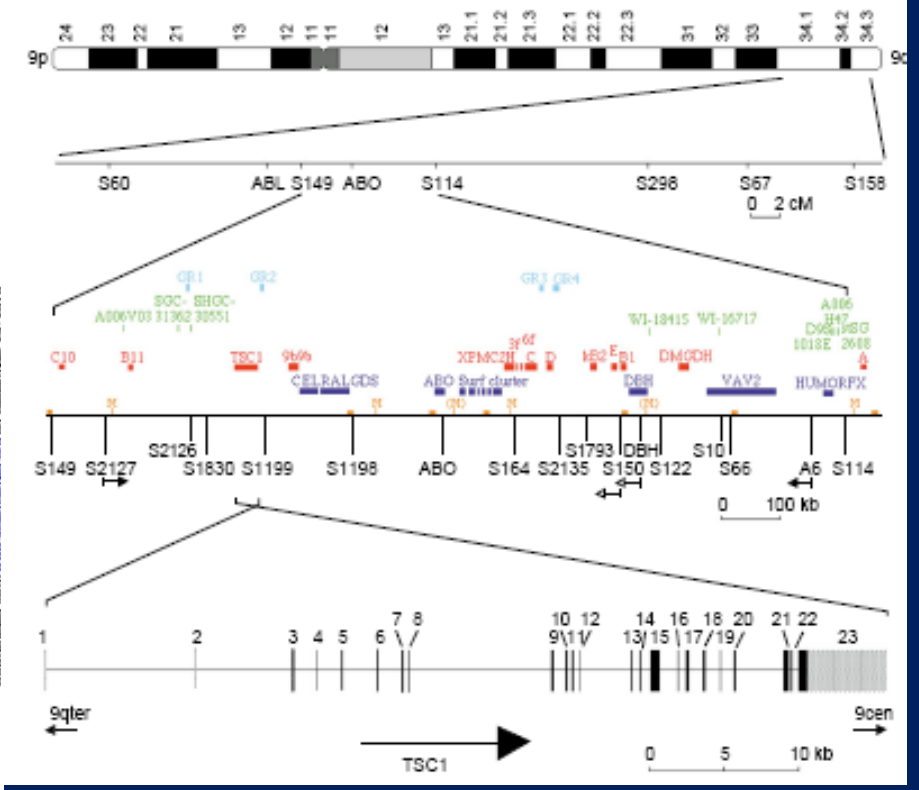
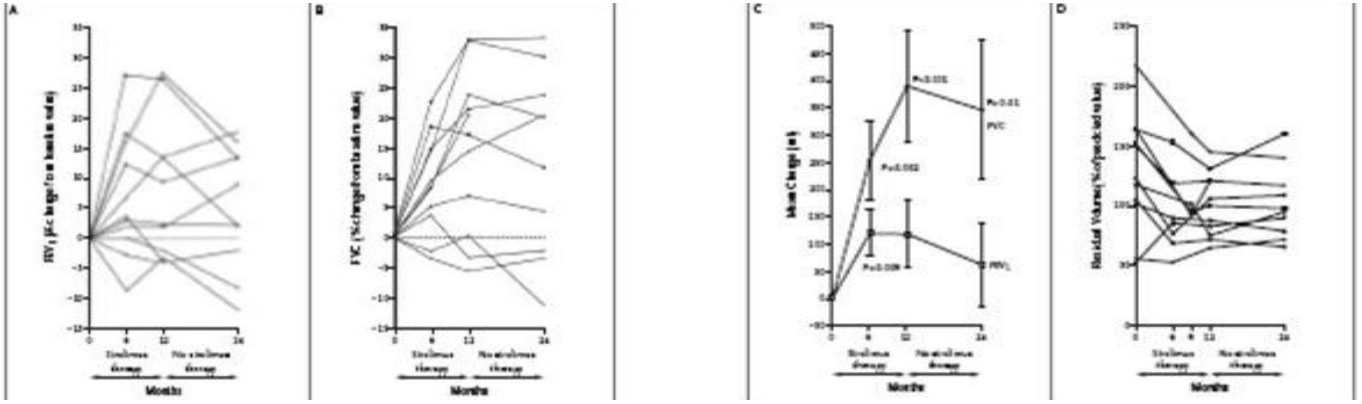


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sirolimus for Angiomyolipoma in Tuberous Sclerosis Complex or Lymphangioleiomyomatosis

John J. Bissler, M.D., Francis X. McCormack, M.D., Lisa R. Young, M.D., Jean M. Elwing, M.D., Gail Chuck, L.M.T., Jennifer M. Leonard, R.N., Vincent J. Schmithorst, Ph.D., Tal Laor, M.D., Alan S. Brody, M.D., Judy Bean, Ph.D., Shelia Salisbury, M.S., and David N. Franz, M.D.



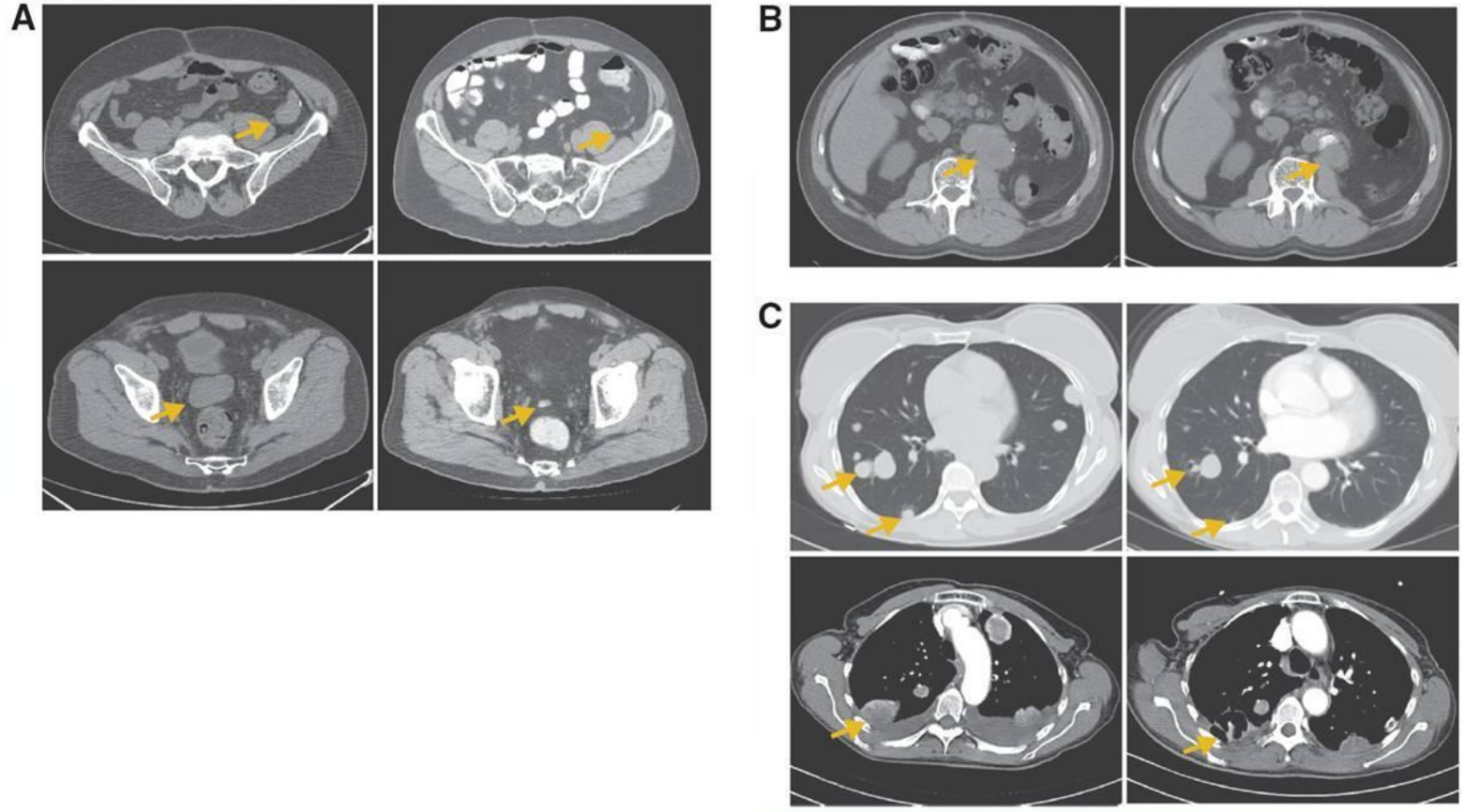
VOLUME 28 · NUMBER 5 · FEBRUARY 10 2010

JOURNAL OF CLINICAL ONCOLOGY

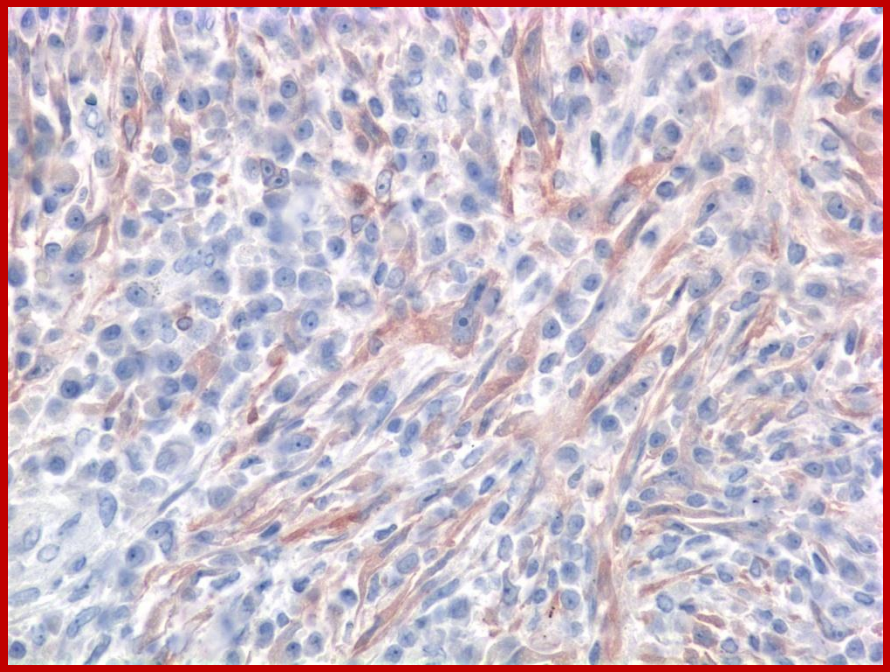
ORIGINAL REPORT

Clinical Activity of mTOR Inhibition With Sirolimus in Malignant Perivascular Epithelioid Cell Tumors: Targeting the Pathogenic Activation of mTORC1 in Tumors

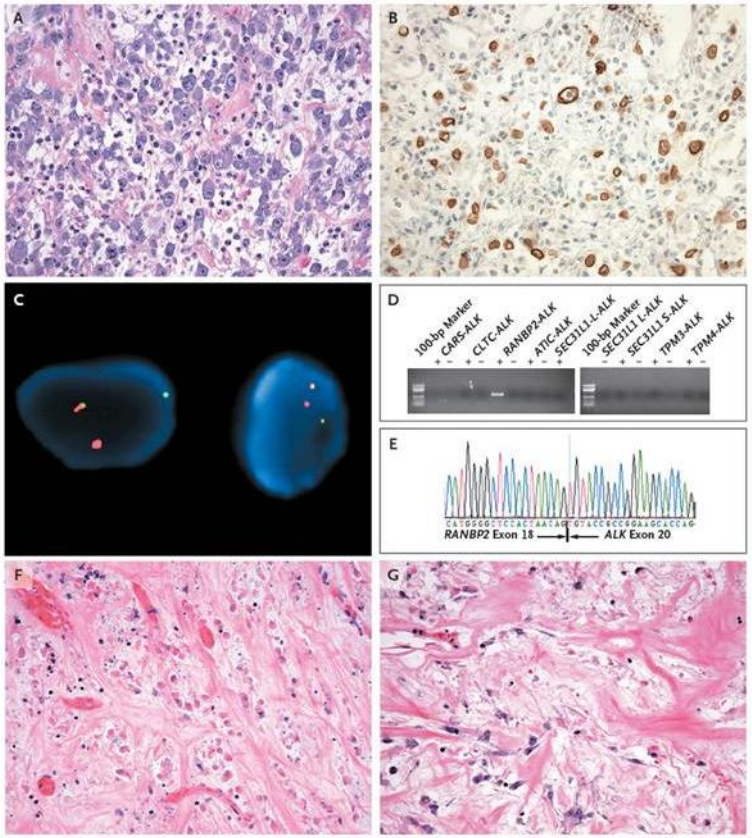
Andrew J. Wagner, Izabela Malinowska-Kolodziej, Jeffrey A. Morgan, Wei Qin, Christopher D.M. Fletcher, Natalie Vena, Azra H. Ligon, Cristina R. Antonescu, Nikhil H. Ramaiya, George D. Demetri, David J. Kwiatkowski, and Robert G. Maki



Myofibroblastic inflammatory tumor



The NEW ENGLAND JOURNAL of MEDICINE

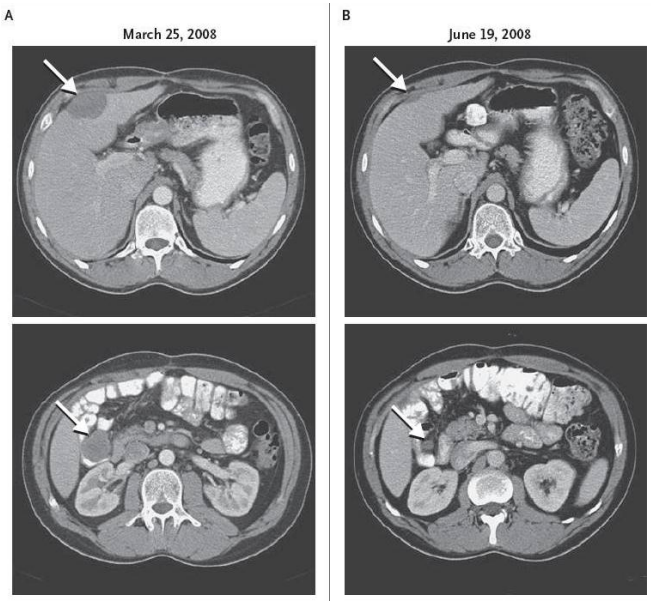


N Engl J Med 2010;363:1727-33.

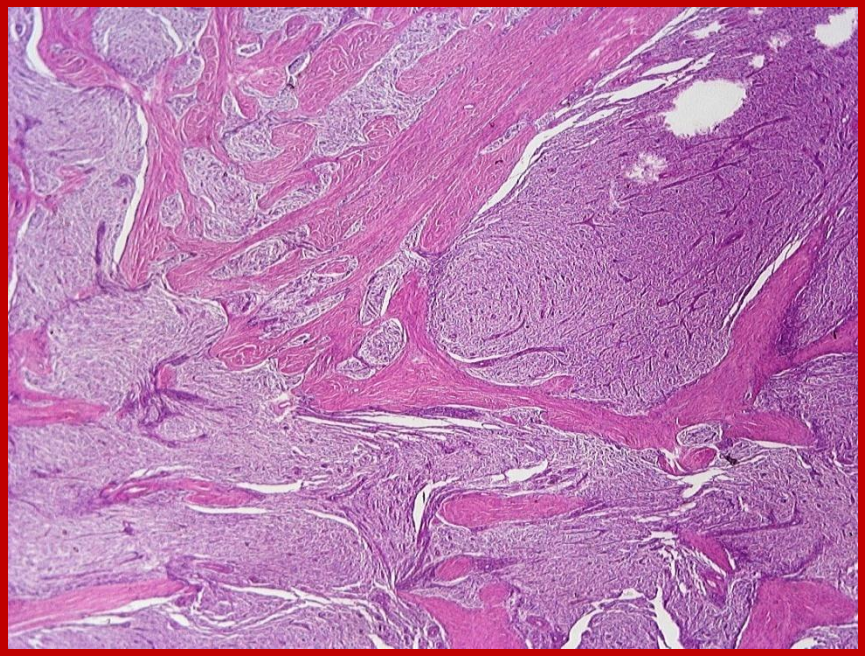
BRIEF REPORT

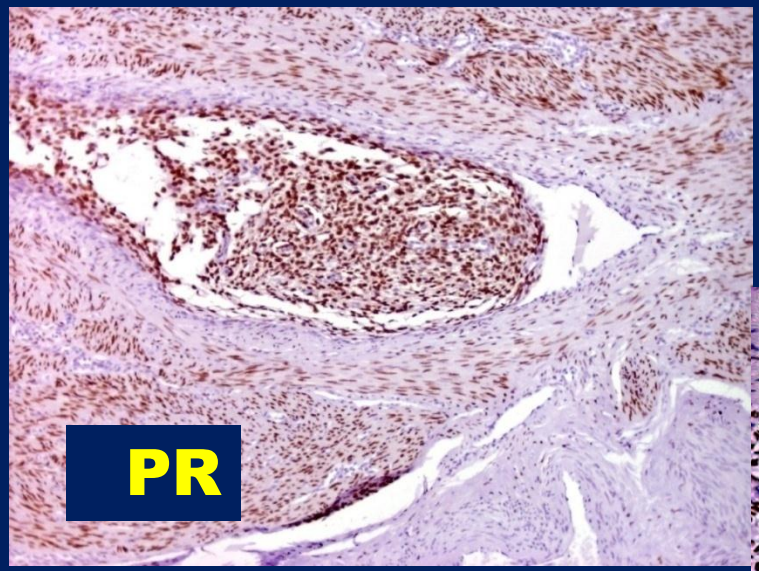
Crizotinib in *ALK*-Rearranged Inflammatory Myofibroblastic Tumor

James E. Butrynski, M.D., David R. D'Adamo, M.D., Ph.D., Jason L. Hornick, M.D., Ph.D., Paola Dal Cin, Ph.D., Cristina R. Antonescu, M.D., Suresh C. Jhanwar, Ph.D., Marc Ladanyi, M.D., Marzia Capelletti, Ph.D., Scott J. Rodig, M.D., Ph.D., Nikhil Ramaiya, M.D., Eunice L. Kwak, M.D., Jeffrey W. Clark, M.D., Keith D. Wilner, Ph.D., James G. Christensen, Ph.D., Pasi A. Jänne, M.D., Ph.D., Robert G. Maki, M.D., Ph.D., George D. Demetri, M.D., and Geoffrey I. Shapiro, M.D., Ph.D.



Endometrial stromal sarcoma

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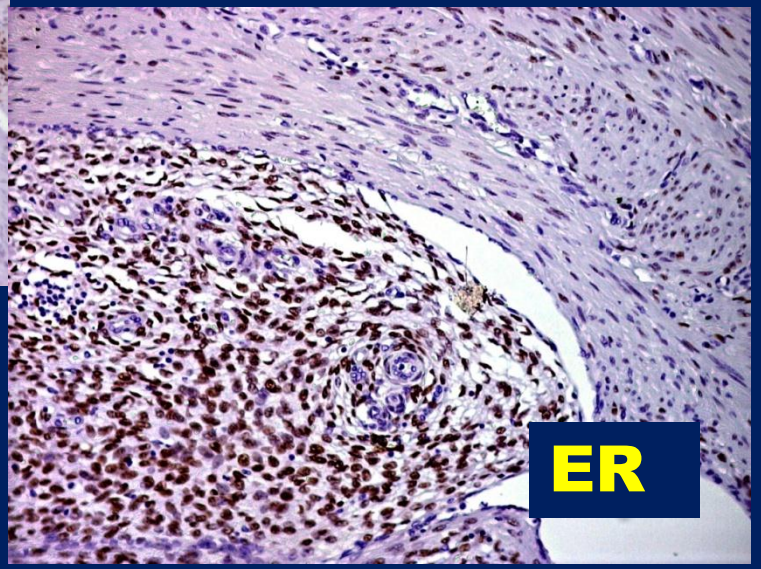
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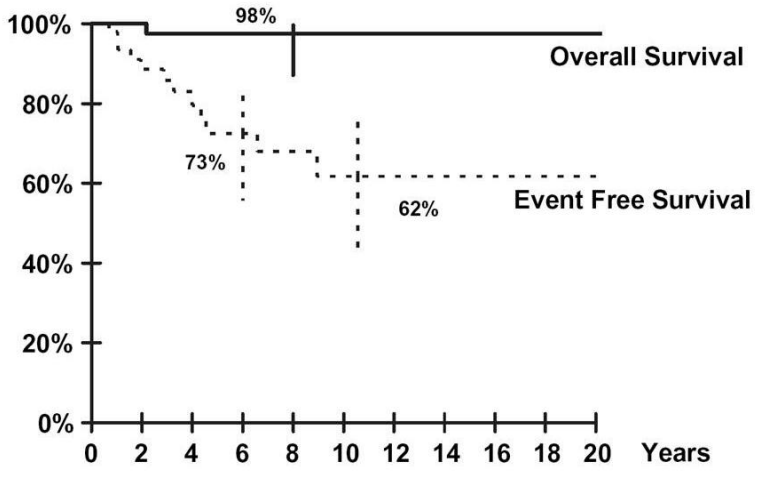
original article

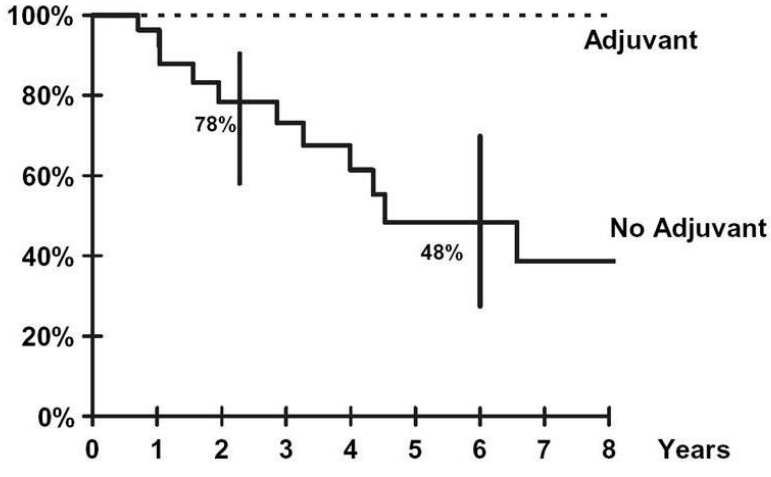
Annals of Oncology 21: 2102–2106, 2010
doi:10.1093/annonc/mdq064
Published online 19 March 2010

Impact of adjuvant treatment modalities on the management of patients with stages I–II endometrial stromal sarcoma

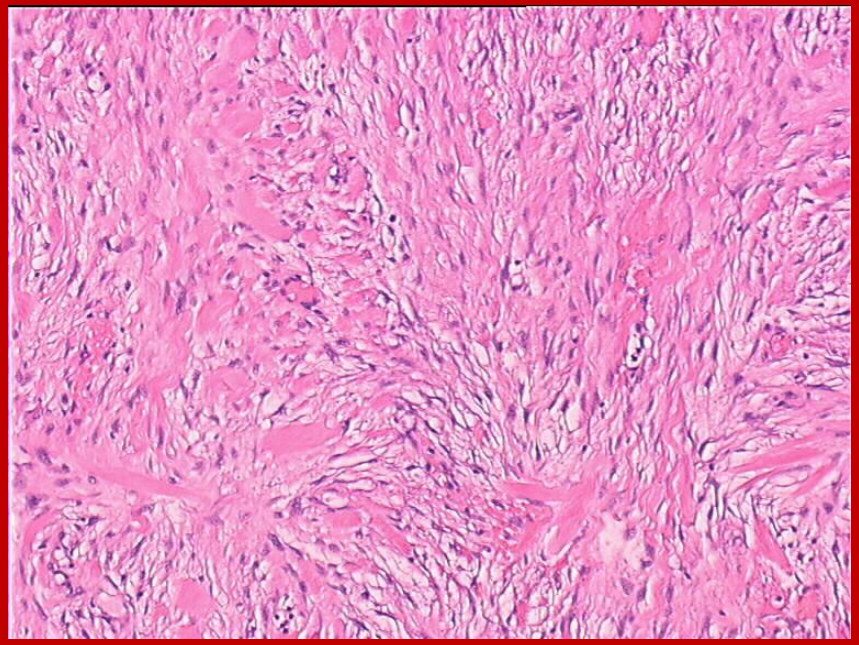
G. G. Malouf[1], J. Duclos[2], A. Rey[3], P. Duvillard[2], V. Lazar[4], C. Haie-Meder[5], C. Balleyguier[6], P. Morice[7], C. Lhommé[1] & P. Pautier[1]*

Departments of [1]Medicine; [2]Pathology; [3]Biostatistics; [4]Platform of Genomics, Departments of [5]Radiotherapy; [6]Radiology; [7]Surgery, Institut Gustave-Roussy, Villejuif, France





Aggressive fibromatosis (desmoid tumors)



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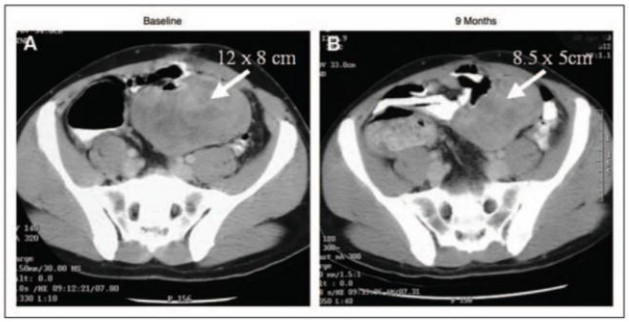
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT



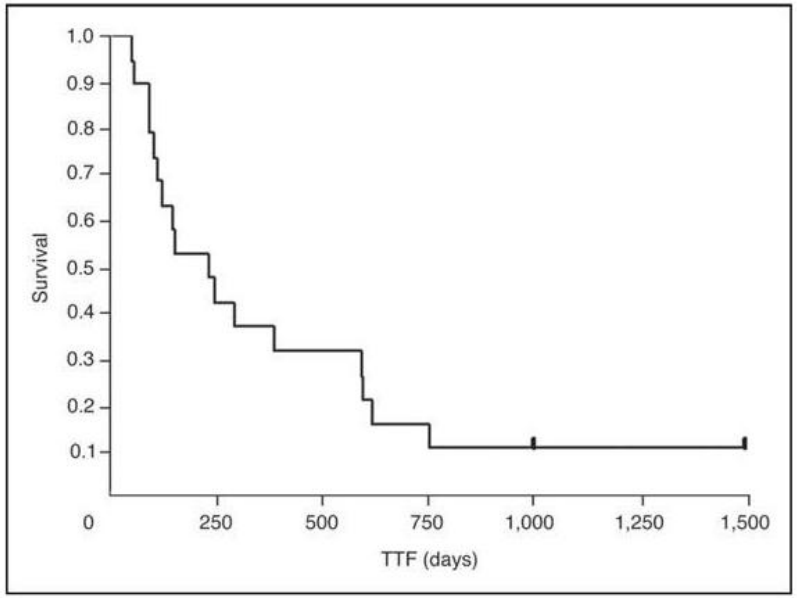
Clinical and Molecular Studies of the Effect of Imatinib on Advanced Aggressive Fibromatosis (desmoid tumor)

Michael C. Heinrich, Grant A. McArthur, George D. Demetri, Heikki Joensuu, Petri Bono, Richard Herrmann, Hal Hirte, Sara Cresta, D. Bradley Koslin, Christopher L. Corless, Stephan Dirnhofer, Allan T. van Oosterom, Zariana Nikolova, Sasa Dimitrijevic, and Jonathan A. Fletcher

Table 3. Plasma Levels of Soluble PDGF Ligands and Correlation With Clinical Response to Imatinib

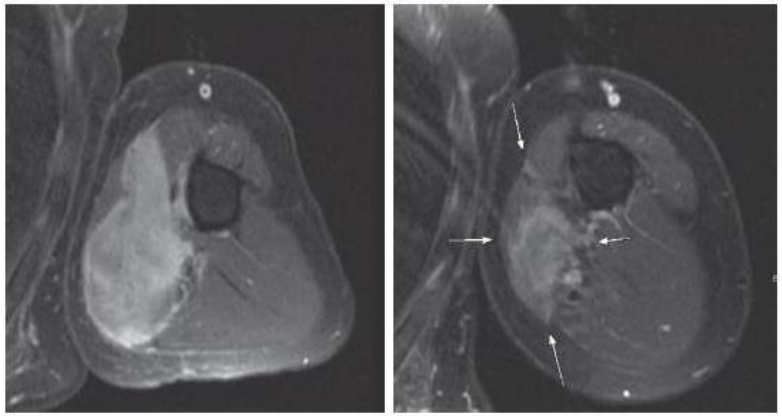
Patient ID	Age	Sex	Primary Site	Response	TTF (days)	PDGF-AA at BL	PDGF-AA After 1 Month	PDGF-BB at BL	PDGF-BB After 1 Month
1	25	F	ABD	PR	1,494+	310	62	330	41
2	63	F	ABD	PD	90	725	1,800	450	2,000
3	25	F	EXT	PD	110	270	118	350	110
4	24	M	EXT	SD	99	350	970	560	370
5	31	F	ABD	SD	592	230	245	330	235
6	30	M	EXT	SD	49	56	105	90	300
7	32	M	ABD	SD	292	ND	ND	ND	ND
8	33	M	ABD	SD	151	1,310	490	875	290
9	17	F	EXT	SD	245	ND	ND	ND	ND
10	22	F	ABD	SD	144	340	200	290	260
11	30	M	ABD	PR	750	250	410	145	180
12	25	M	ABD	PR	594	19	43	75	62
13	24	M	EXT	SD	994+	ND	ND	ND	ND
14	31	M	ABD	SD	386	415	265	720	400
15	26	M	ABD	SD	88	260	77	490	245
16	20	M	EXT	SD	118	ND	ND	ND	ND
17	23	M	ABD	SD	228	190	825	190	520
18	18	F	EXT	SD	516+	410	190	775	370
19	20	F	ABD	PD	56	ND	ND	ND	ND

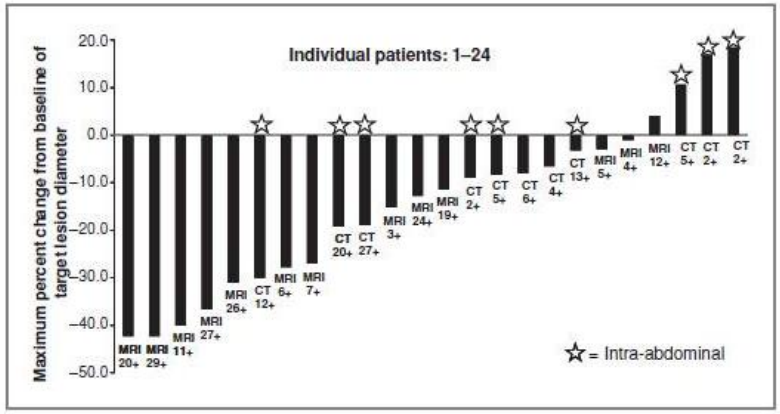
Abbreviations: PDGF-AA, platelet derived growth factor AA homodimer; PDGF-BB, platelet derived growth factor BB homodimer; TTF, time to treatment failure; BL, baseline; ABD, abdominal primary site; PR, partial response; PD, progressive disease; EXT, extra-abdominal primary site; SD, stable disease; ND, not done.



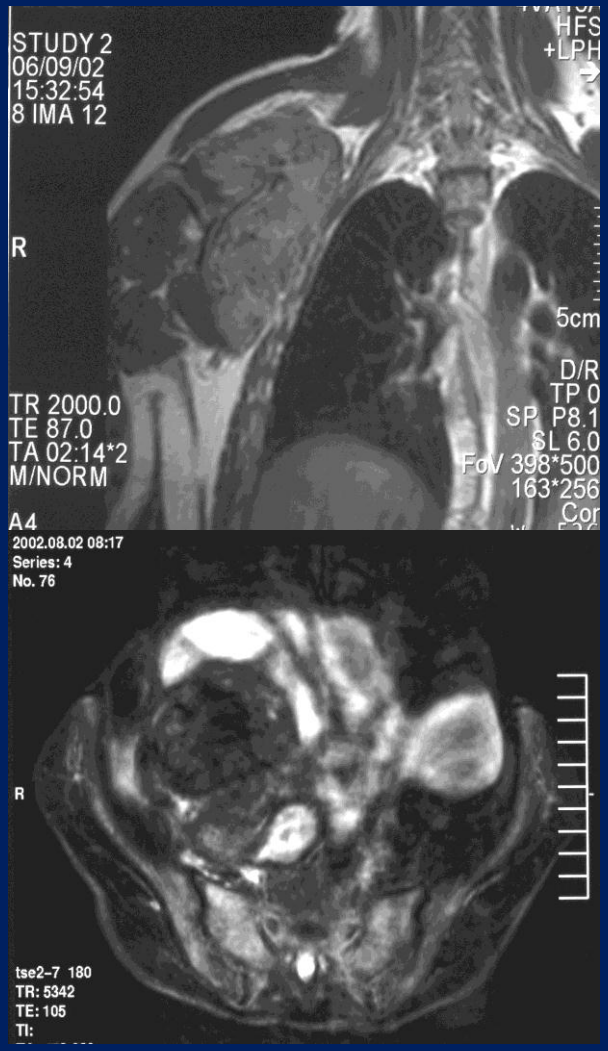
Activity of Sorafenib against Desmoid Tumor/Deep Fibromatosis

Mrinal M. Gounder[1], Robert A. Lefkowitz[2], Mary Louise Keohan[1], David R. D'Adamo[1], Meera Hameed[3], Cristina R. Antonescu[3], Samuel Singer[4], Katherine Stout[1], Linda Ahn[1], and Robert G. Maki[1]



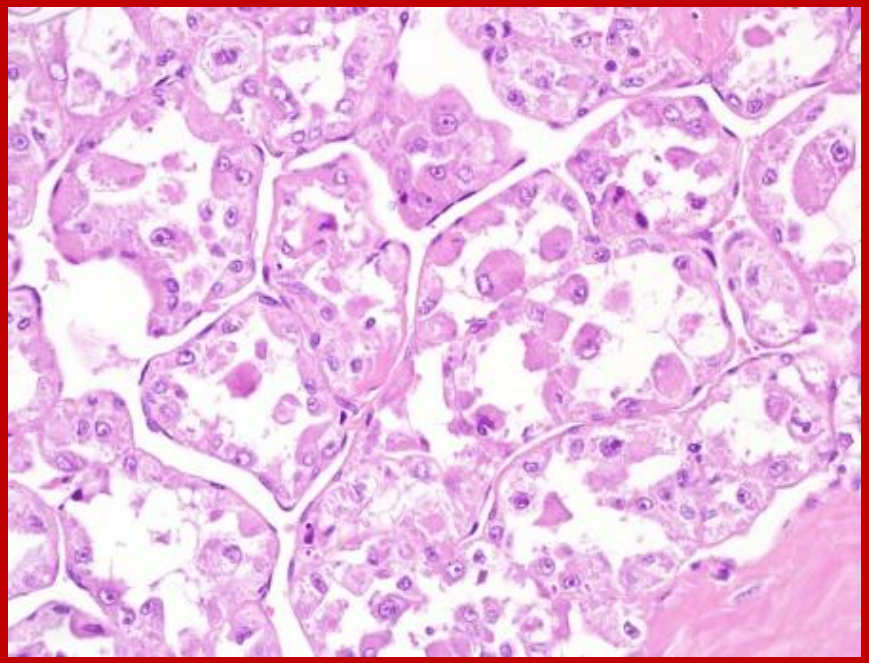


Clin Cancer Res 2011;17:4082



- **Antiestrogens ± FANS**
- **MTX + VNB**
- **Imatinib**
- **Sorafenib**
- **ADM ± IFX**
- **.....**

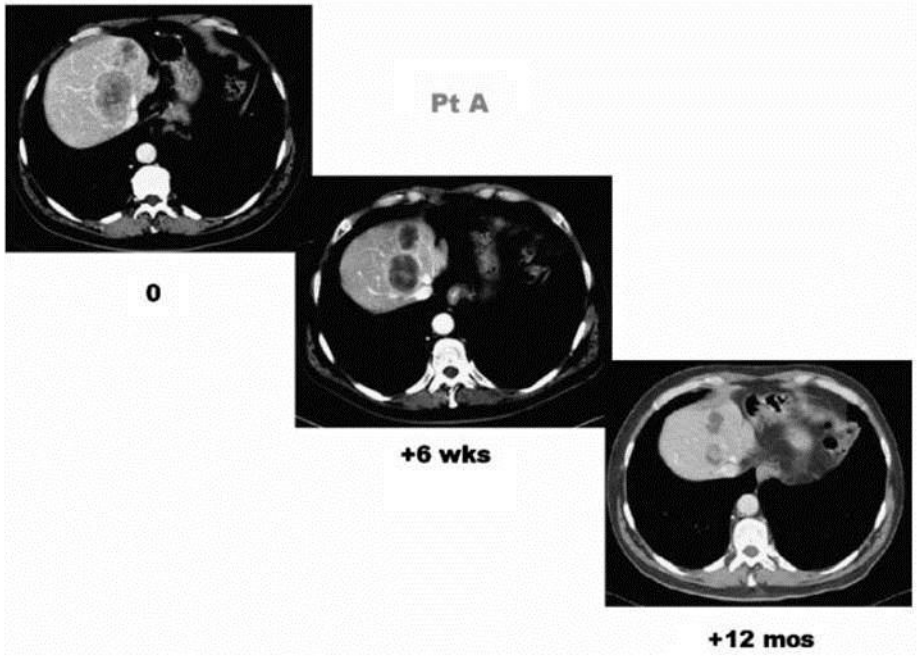
Alveolar soft part sarcoma

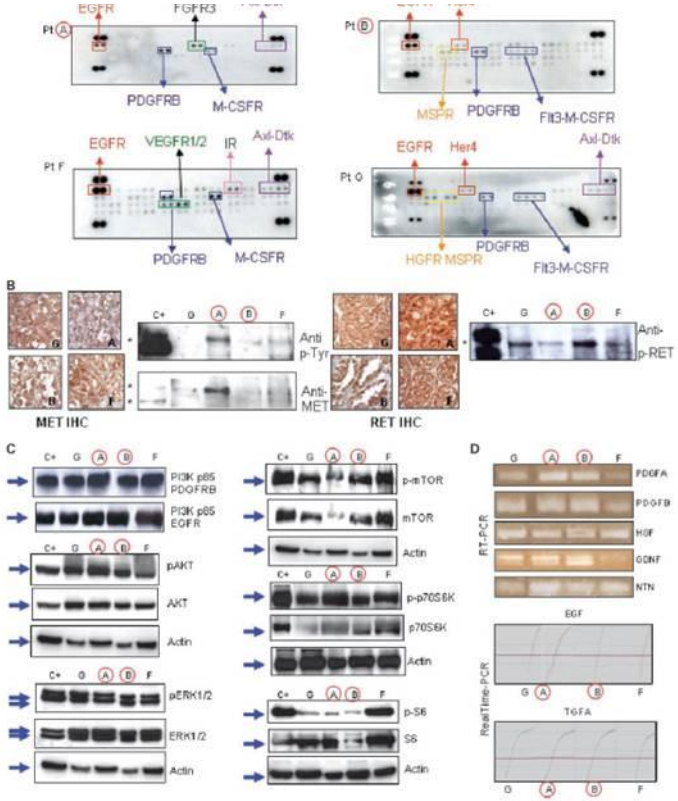


Cancer Therapy: Clinical

Response to Sunitinib Malate in Advanced Alveolar Soft Part Sarcoma

Silvia Stacchiotti,[1] Elena Tamborini,[2] Andrea Marrari,[1] Silvia Brich,[2] Sara Arisi Rota,[2] Marta Orsenigo,[2] Flavio Crippa,[3] Carlo Morosi,[4] Alessandro Gronchi,[5] Marco A. Pierotti,[2] Paolo G. Casali,[1] and Silvana Pilotti[2]





original article

Annals of Oncology
doi:10.1093/annonc/mdq644

Sunitinib in advanced alveolar soft part sarcoma: evidence of a direct antitumor effect

S. Stacchiotti[1]*, T. Negri[2], N. Zaffaroni[3], E. Palassini[1], C. Morosi[4], S. Brich[2], E. Conca[2], F. Bozzi[2], G. Cassinelli[3], A. Gronchi[5], P. G. Casali[1] & S. Pilotti[2]

Departments of [1]Cancer Medicine; [2]Pathology, Laboratory of Experimental Molecular Pathology; [3]Experimental Oncology and Molecular Medicine; [4]Radiology; [5]Surgery, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

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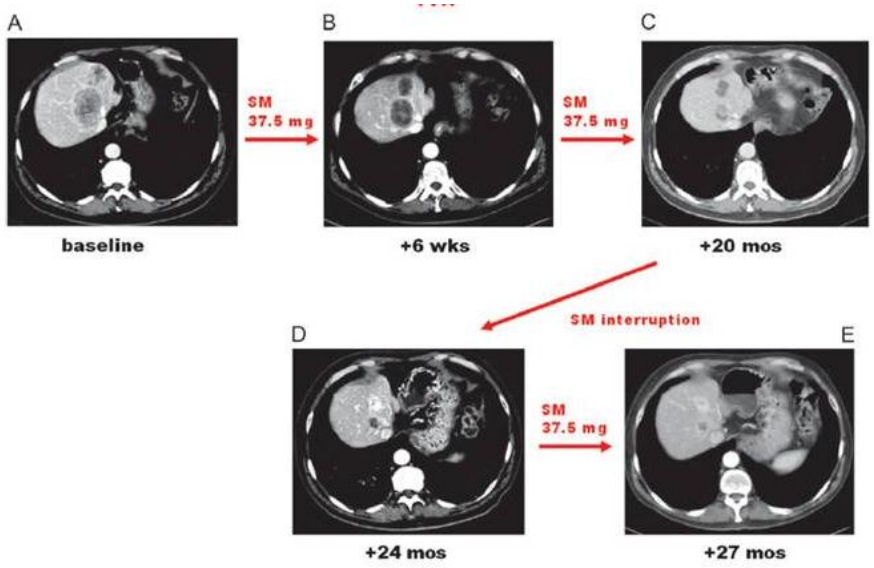

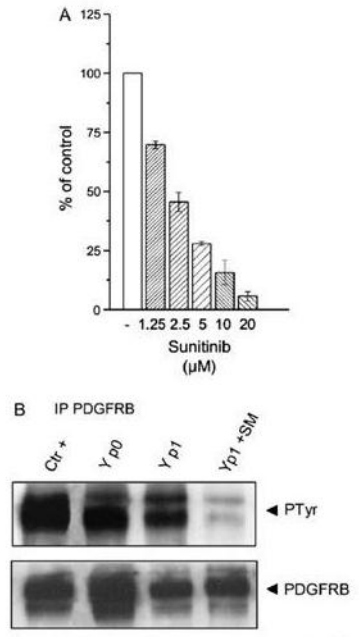

ASPS: Cediranib

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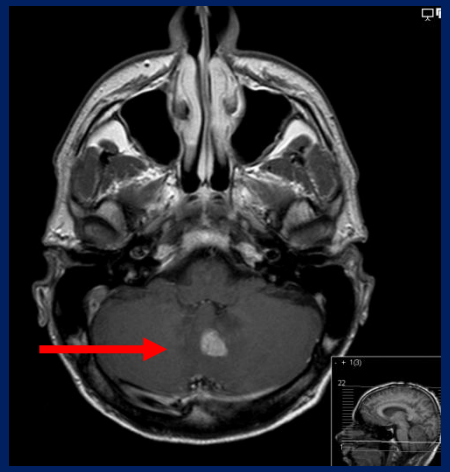
Activity of cediranib, a highly potent and selective VEGF signaling inhibitor, in ASPS

7 pts: 4 PR RECIST
2 minor responses
1 SD



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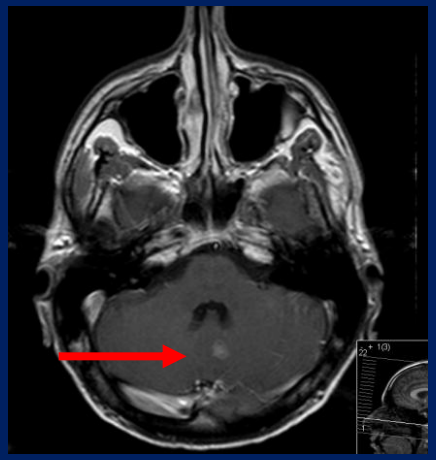

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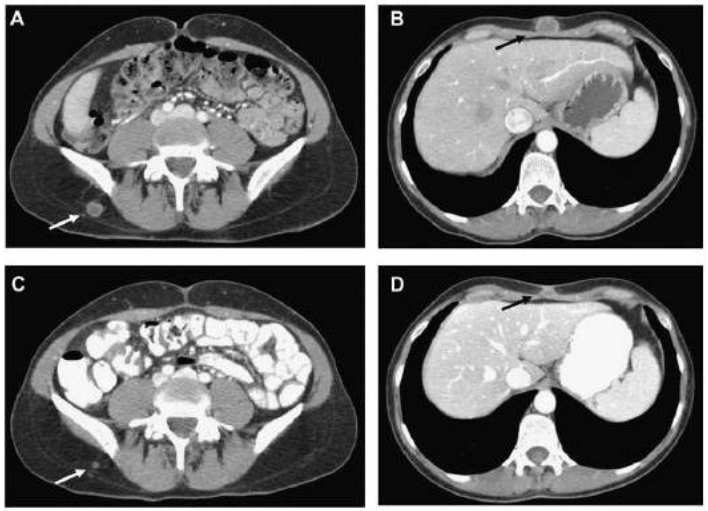
Gardner K, ASCO2009, Abs #10523

Annals of Oncology

Tumor response to sunitinib malate observed in clear-cell sarcoma



We report on a tumor response to sunitinib malate (SM) in a 46-year-old female patient with metastatic clear-cell sarcoma (CCS).

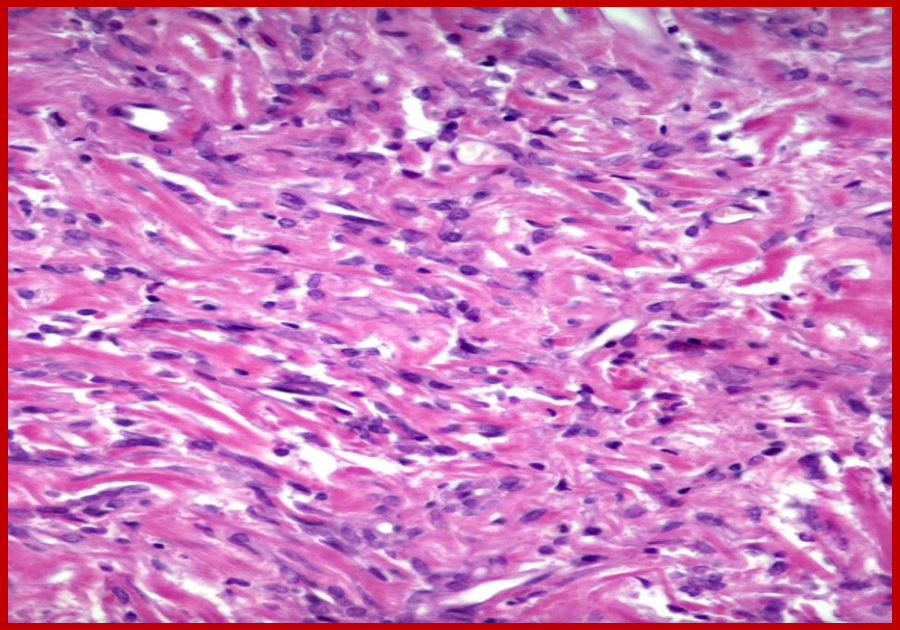
We already described the activity of SM in alveolar soft part sarcoma [2]. There are similarities between this sarcoma and CCS (both are translocation related, belong to the MITF-family tumors, and show activation of PDGFRB). The tumor response observed in this case suggests that this may be clinically relevant.

S. Stacchiotti[1]*, F. Grosso[2], T. Negri[3], E. Palassini[1], C. Morosi[4], S. Pilotti[3], A. Gronchi[5] & P. G. Casali[1]

[1]Adult Sarcoma Medical Oncology Unit, Department of Cancer Medicine, Istituto Nazionale Tumori, Milan, [2]Department of Cancer Medicine, Alessandria General Hospital, Alessandria; Departments of [3]Pathology and Molecular Biology, [4]Radiology and [5]Surgery, Istituto Nazionale Tumori, Milan, Italy
(*E-mail: silvia.stacchiotti@istitutotumori.mi.it)

Stacchiotti S et al, Ann Oncol 2010, 21:1130

Solitary fibrous tumor



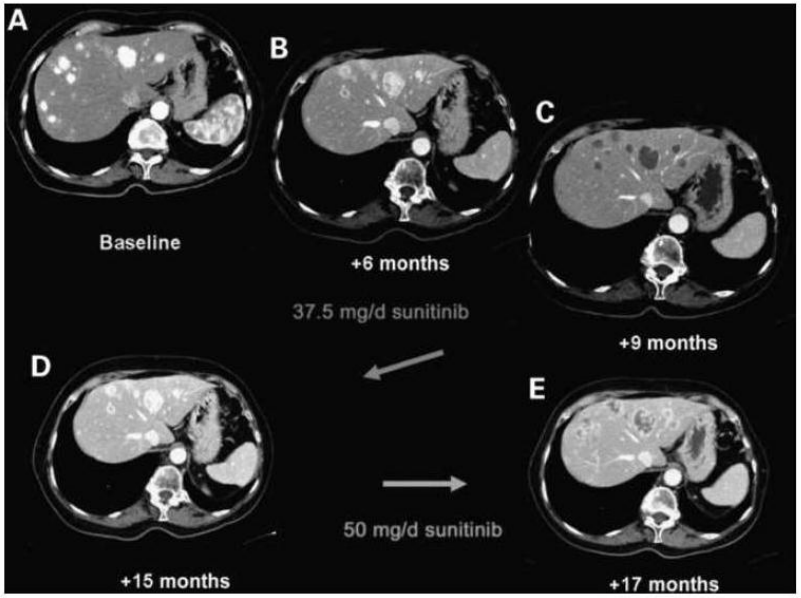
Mol Cancer Ther; 9(5) May 2010

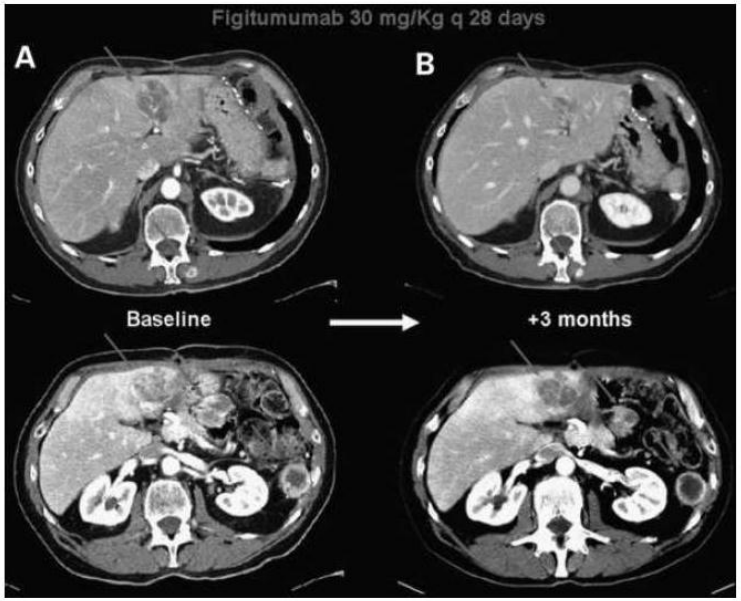
Research Article

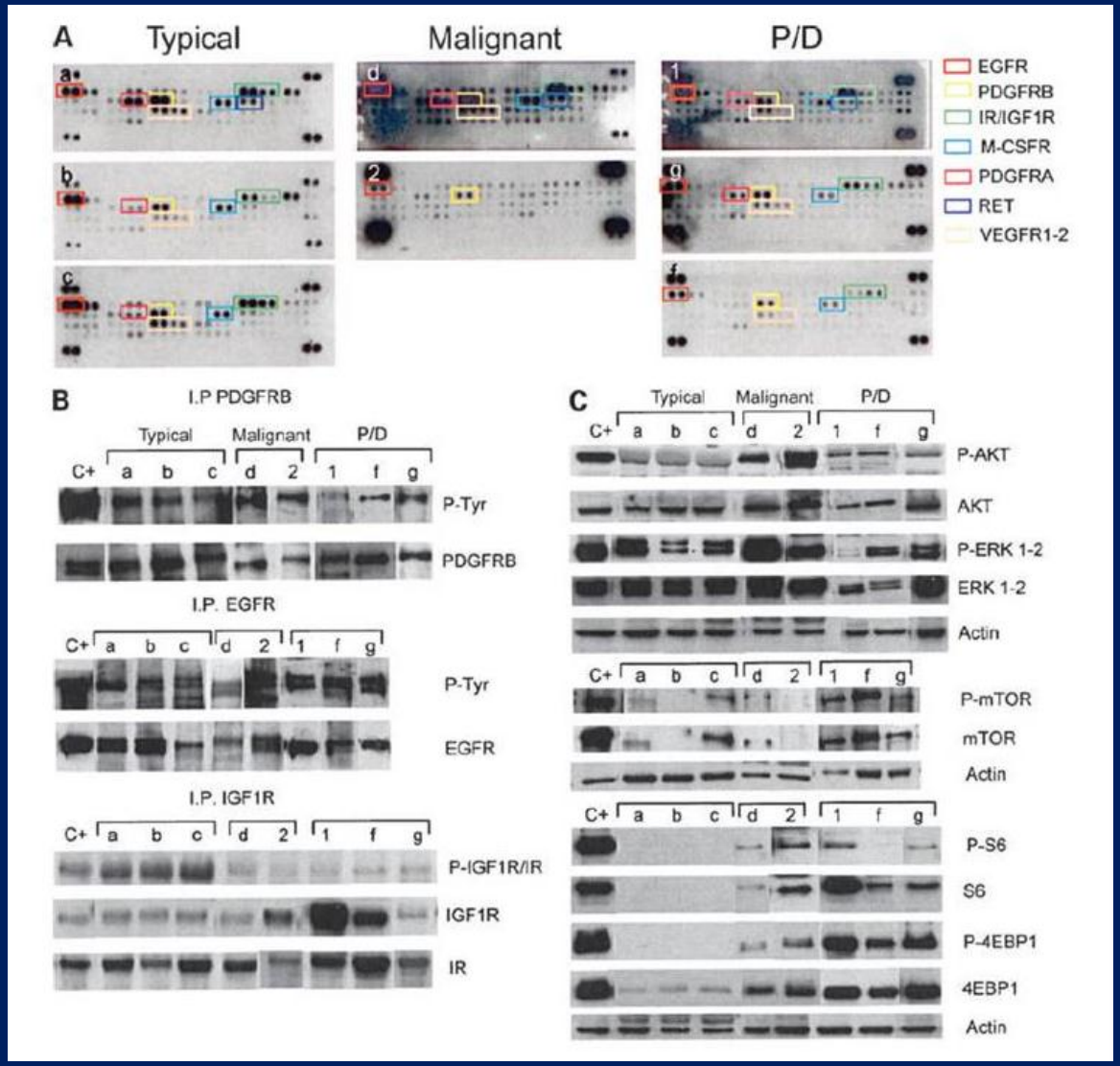
Molecular Cancer Therapeutics

Sunitinib Malate and Figitumumab in Solitary Fibrous Tumor: Patterns and Molecular Bases of Tumor Response

Silvia Stacchiotti[1], Tiziana Negri[2], Elena Palassini[1], Elena Conca[2], Alessandro Gronchi[3], Carlo Morosi[4], Antonella Messina[4], Ugo Pastorino[3], Marco A. Pierotti[5], Paolo G. Casali[1], and Silvana Pilotti[2]





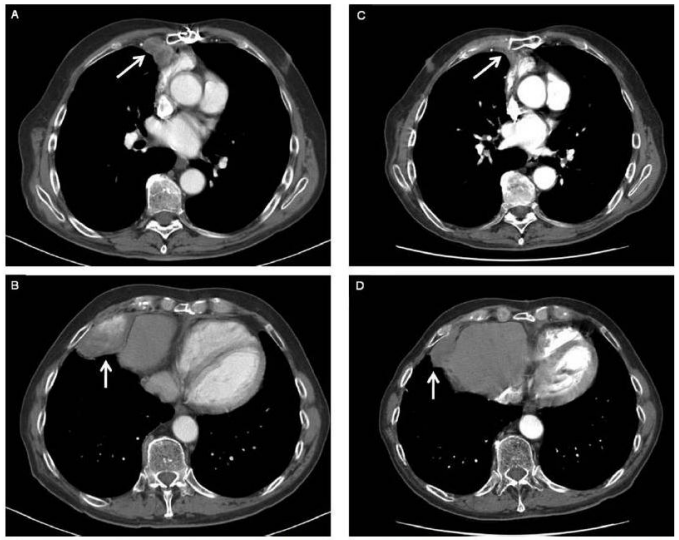


Stacchiotti S et al, Mol Cancer Ther 2010;9:1286

Original Article

Activity of Temozolomide and Bevacizumab in the Treatment of Locally Advanced, Recurrent, and Metastatic Hemangiopericytoma and Malignant Solitary Fibrous Tumor

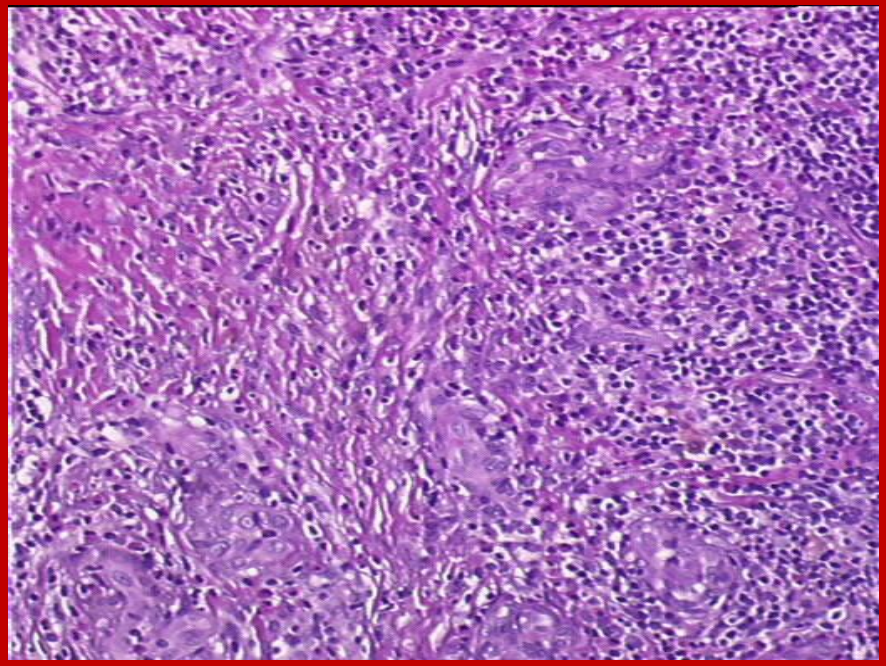
Min S. Park, MD[1]; Shreyaskumar R. Patel, MD[1]; Joseph A. Ludwig, MD[1]; Jonathan C. Trent, MD, PhD[1]; Charles A. Conrad, MD[2]; Alexander J. Lazar, MD, PhD[3]; Wei-Lien Wang, MD[3]; Piyaporn Boonsirikamchai, MD[4]; Haesun Choi, MD[4]; Xuemei Wang, MS[5]; Robert S. Benjamin, MD[1]; and Dejka M. Araujo, MD[1]



Patient No.	Tumor	Maximum Change in Tumor Size (%)	Maximum Change in Density (%)	Best Response (Choi Criteria)			Best Response (RECIST)
1	HPC	−56.2	−41.3	PR	↓Size	↓HU	PR
2	SFT	−42.1	−67.6	PR	↓Size	↓HU	PR
3	SFT	−26.7	−16.2	PR	↓Size	↓HU	SD
4	HPC	−19.5	−19.1	PR	↓Size	↓HU	SD
5	HPC	−18.5	−39.4	PR	↓Size	↓HU	SD
6	SFT	−13.7	−83.1	PR	↓Size	↓HU	SD
7	SFT	−6.5	−23.7	PR	↓Size	↓HU	SD
8	HPC	−26.9	ND[a]	PR	↓Size		SD
9	HPC	−6.1	−28.7	PR		↓HU	SD
10	HPC	−3.4	−60.5	PR		↓HU	SD
11	HPC	4.9	−15.5	PR		↓HU	SD
12	HPC	0	ND[a]	SD			SD
13	HPC	4.6	4.4	SD			SD
14	HPC	15.5	5.4	PD			SD
Median		−10.1	−26.2				

Cancer 2011;117:4939

Angiosarcoma



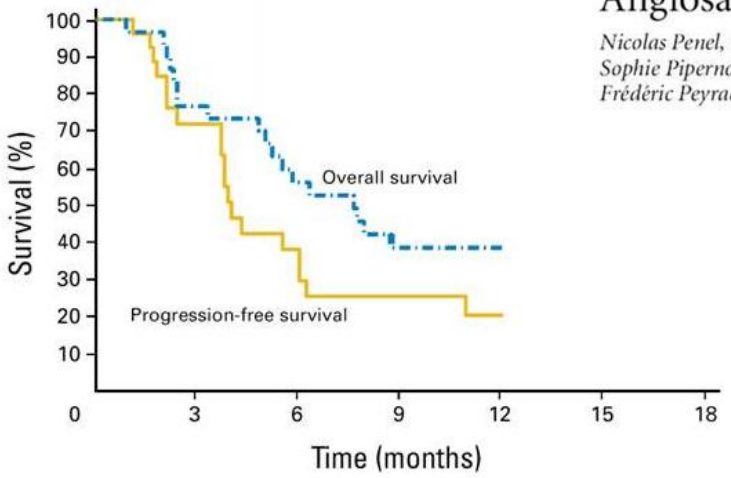
VOLUME 26 · NUMBER 32 · NOVEMBER 10 2008

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

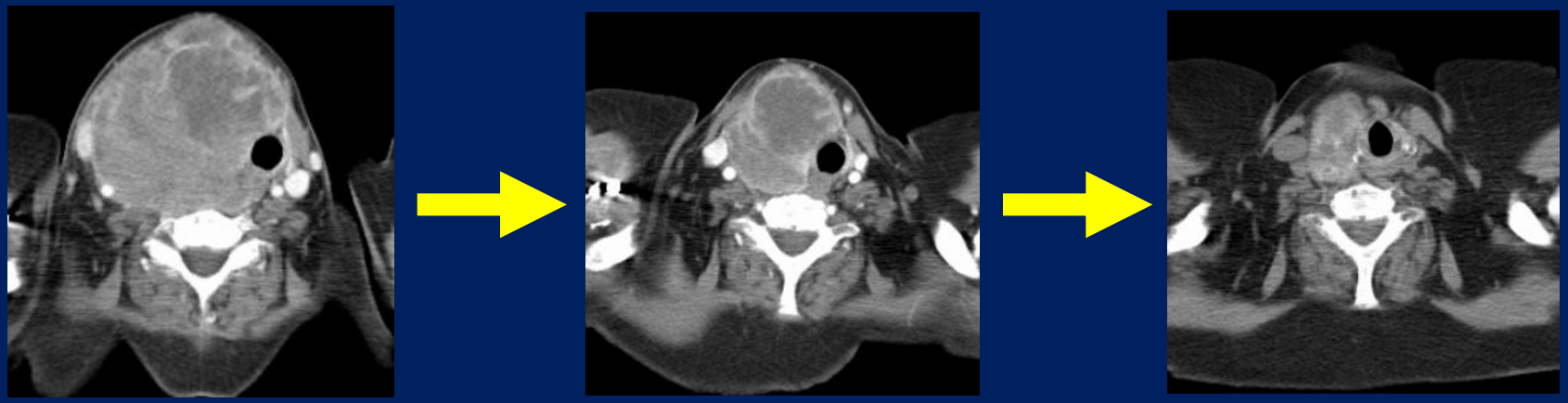
Phase II Trial of Weekly Paclitaxel for Unresectable Angiosarcoma: The ANGIOTAX Study

Nicolas Penel, Binh Nguyen Bui, Jacques-Olivier Bay, Didier Cupissol, Isabelle Ray-Coquard, Sophie Piperno-Neumann, Pierre Kerbrat, Charles Fournier, Sophie Taieb, Marta Jimenez, Nicolas Isambert, Frédéric Peyrade, Christine Chevreau, Emmanuelle Bompas, Etienne G.C. Brain, and Jean-Yves Blay



Patient	Baseline Disease Characteristics	Clinical and Histologic Response	Outcome
11	Relapsed multinodular radiation-induced angiosarcoma	Partial response after 6 cycles Mastectomy Complete histologic response	Disease-free survival, 19 months after inclusion
13	Primary multinodular angiosarcoma with rapid evolution	Partial response after 4 cycles Mastectomy Complete histologic response	Disease-free survival, 17 months after inclusion
17	Multinodular radiation-induced angiosarcoma with skin ulceration and rapid progression	Stable disease after 5 cycles Mastectomy Complete histologic response in 2 nodules but persistent disease in third nodule (10 mm, grade 3)	Diagnosis of glioblastoma at 8 months, death at 9 months

Gemcitabine



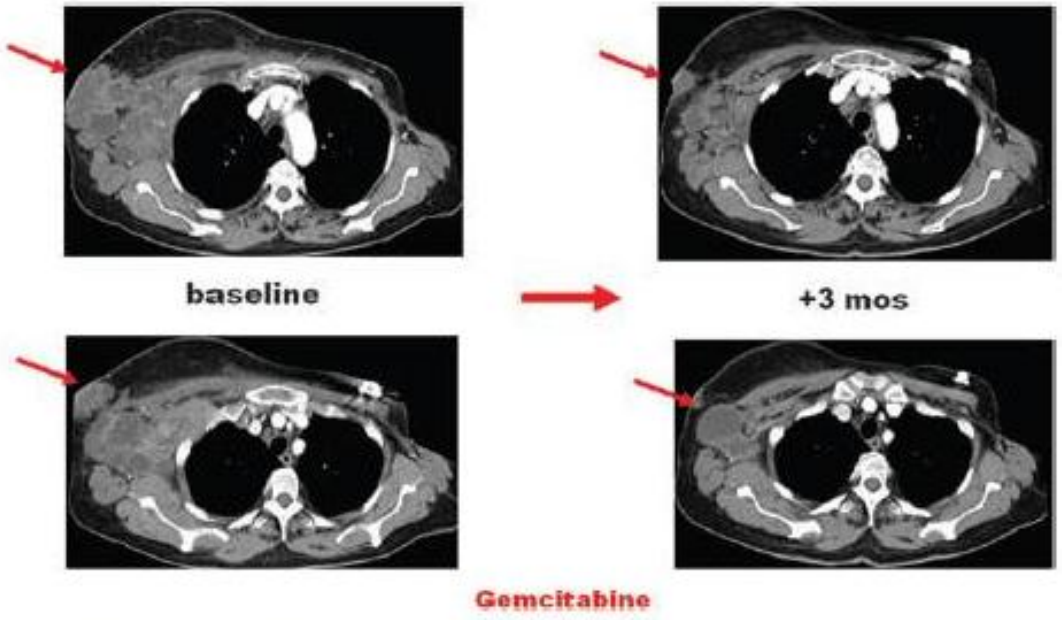
0 +1 mos +4 mos

original article

Annals of Oncology
doi:10.1093/annonc/mdr066

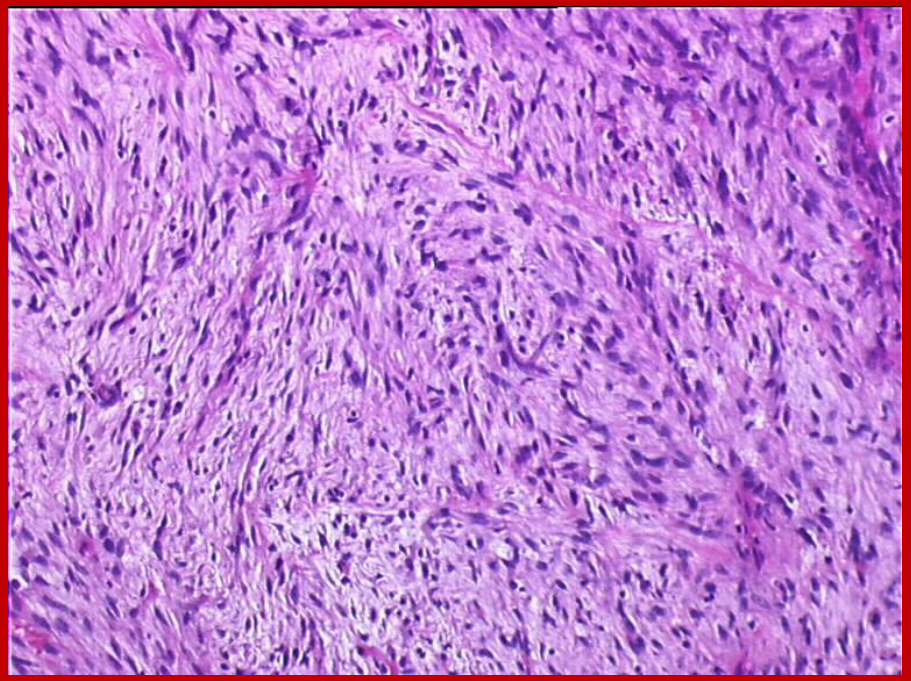
Gemcitabine in advanced angiosarcoma: a retrospective case series analysis from the Italian Rare Cancer Network

S. Stacchiotti[1], E. Palassini[1], R. Sanfilippo[1], B. Vincenzi[2], M. G. Arena[3], A. M. Bochicchio[4], P. De Rosa[5], A. Nuzzo[6], S. Turano[7], C. Morosi[8], A. P. Dei Tos[9], S. Pilotti[9] & P. G. Casali[10]



Ann Oncol 2012;23:501

Leiomyosarcoma



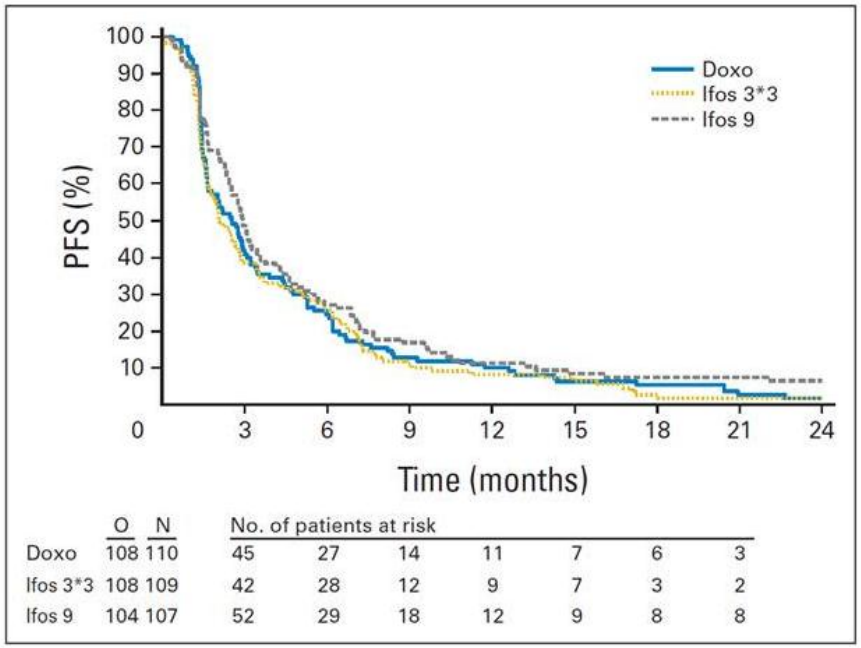
VOLUME 25 · NUMBER 21 · JULY 20 2007

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

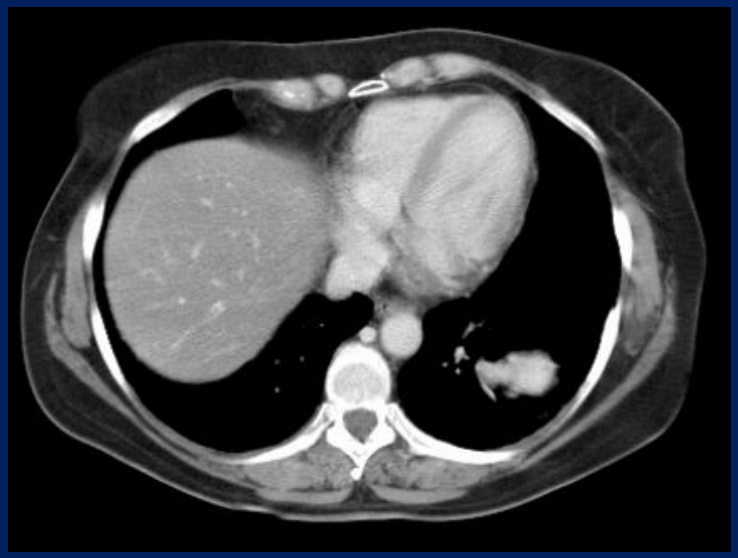
Phase III Trial of Two Investigational Schedules of Ifosfamide Compared With Standard-Dose Doxorubicin in Advanced or Metastatic Soft Tissue Sarcoma: A European Organisation for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group Study

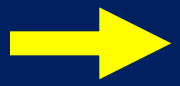
Paul Lorigan, Jaap Verweij, Zsuzsa Papai, Sjoerd Rodenhuis, Axel Le Cesne, Michael G. Leahy, John A. Radford, Martine M. Van Glabbeke, Anne Kirkpatrick, Pancras C.W. Hogendoorn, and Jean-Yves Blay

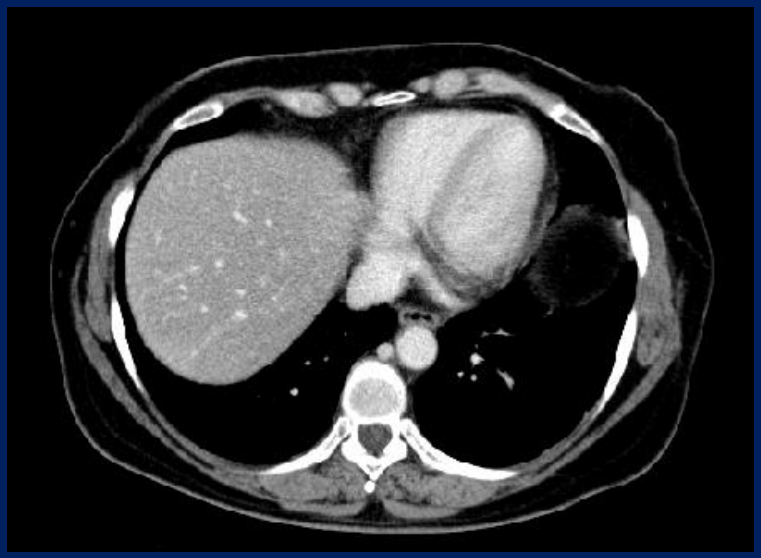


	Dox		Ifos 3*3		Ifos 9		Total		3-Year Survivors	
Condition	No.	%	No.	%	No.	%	No.	%	No.	%
Leiomyosarcoma									8/58	13.8
PR	2	13.3	1	4.8	1	4.5	4	6.9		
NC	10	66.7	10	47.6	10	45.5	30	51.7		
PD	3	20	8	38.1	7	31.8	18	31		
Synovial									2/23	8.7
PR	2	25	3	37.5	3	42.9	8	34.8		
NC	2	25	3	37.5	3	42.9	8	34.8		
PD	4	50	1	12.5	1	14.3	6	26.1		
Liposarcoma									5/32	15.5
PR	2	15.4			1	8.3	3	9.4		
NC	4	30.8	1	14.3	7	58.3	12	37.5		
PD	7	53.8	5	71.4	3	25	15	46.9		
GIST									3/28	10.7
PR			1	7.7			1	3.6		
NC	2	20	4	30.8	3	60	9	32.1		
PD	8	80	7	53.8	2	40	17	60.7		
Neurogenic									3/19	15.8
CR	1	12.5					1	5.3		
NC	3	37.5	3	50			6	31.6		
PD	4	50	3	50	3	60	10	52.6		

Leiomyosarcoma: Dacarbazine







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DTIC x 2

A Phase II Trial of Temozolomide in Patients with Unresectable or Metastatic Soft Tissue Sarcoma

Susan M. Talbot, M.D.[1]
Mary Louise Keohan, M.D.[1]
Mary Hesdorffer, B.S.N.[1]
Russell Orrico, B.S.[1]
Emilia Bagiella, Ph.D.[2]
Andrea B. Troxel, Sc.D.[2]
Robert N. Taub, M.D., Ph.D.[1]

[1] Department of Medicine, Columbia University, College of Physicians and Surgeons, New York, New York.

[2] Department of Biostatistics, Columbia University, College of Physicians and Surgeons, New York, New York.

Response

Among the 25 evaluable patients, there were 2 objective responses (partial responses), 2 mixed responses, and 3 patients with stable disease that lasted > 6 months, for an overall objective response rate of 8%. All of these patients had leiomyosarcoma (of uterine and nonuterine origin).

CONCLUSIONS. Temozolomide at the dose schedule employed in the current study was tolerated well and had modest activity against previously treated unresectable or metastatic leiomyosarcoma of both uterine and nonuterine origin. ***Cancer*** **2003; 98:1942–6.**

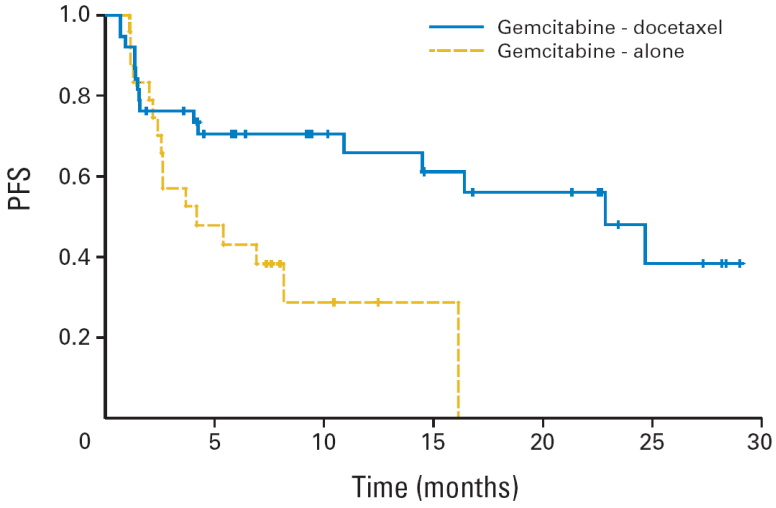
VOLUME 25 · NUMBER 19 · JULY 1 2007

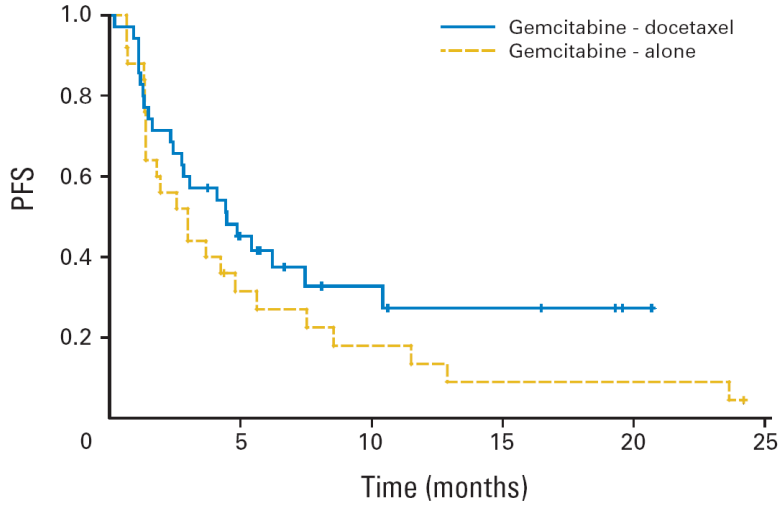
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

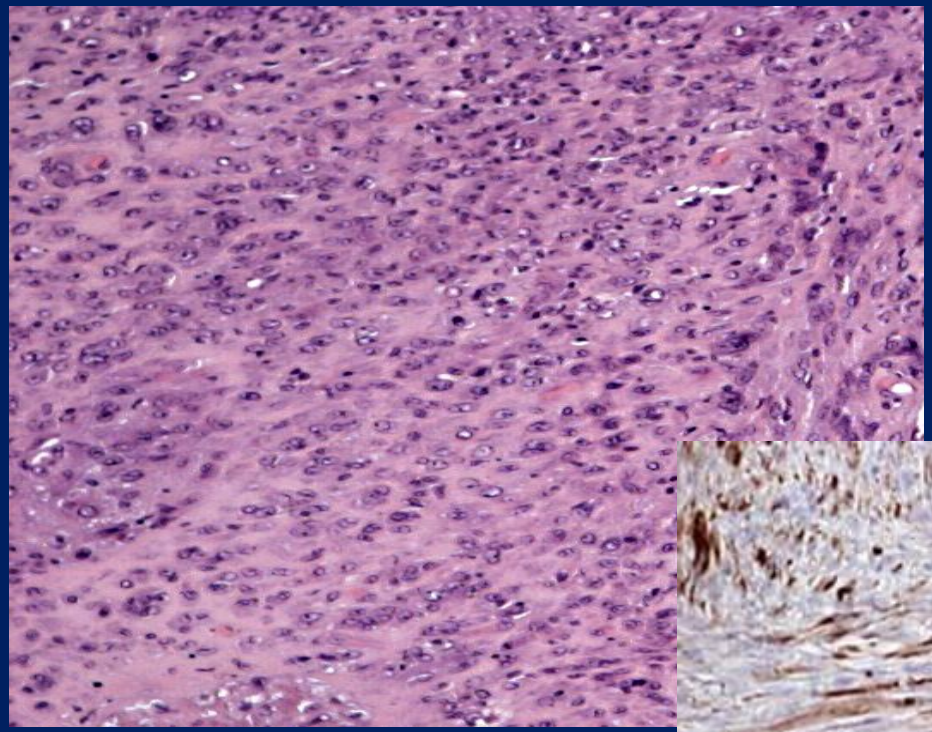
Randomized Phase II Study of Gemcitabine and Docetaxel Compared With Gemcitabine Alone in Patients With Metastatic Soft Tissue Sarcomas: Results of Sarcoma Alliance for Research Through Collaboration Study 002

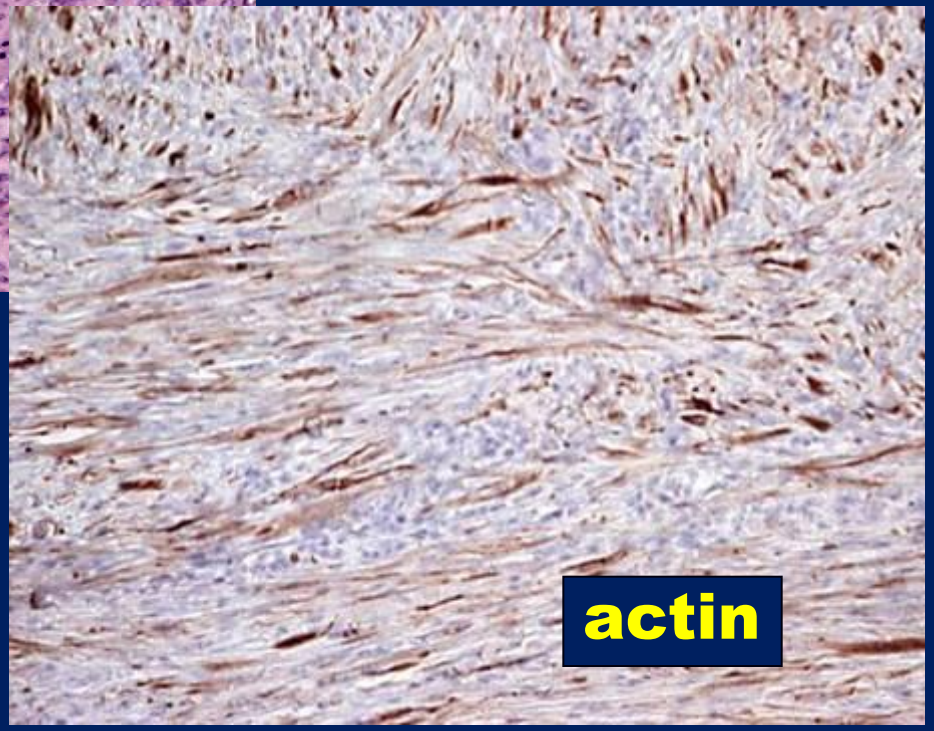
Robert G. Maki, J. Kyle Wathen, Shreyaskumar R. Patel, Dennis A. Priebat, Scott H. Okuno, Brian Samuels, Michael Fanucchi, David C. Harmon, Scott M. Schuetze, Denise Reinke, Peter F. Thall, Robert S. Benjamin, Laurence H. Baker, and Martee L. Hensley





Histology	Gemcitabine						Gemcitabine-Docetaxel					
	CR	PR	Stable Disease ≥ 24 Weeks	Stable Disease < 24 Weeks	Progressive Disease	Not Assessable	CR	PR	Stable Disease ≥ 24 Weeks	Stable Disease < 24 Weeks	Progressive Disease	Not Assessable
Leiomyosarcoma		1	2	5	1			5	3	13	8	
MFH/HGUPS		2	2	1	3		1	3	3	2	1	1
Liposarcoma												
Well differentiated/dedifferentiated			2	3	3					4		1
Myxoid-round cell				2	1	1						
Pleomorphic								2		1		
Synovial sarcoma			1	1	2				1	1	2	1
Malignant peripheral nerve sheath tumor				1	1				1		3	
Unclassified sarcoma			1	2	1					1		
Fibrosarcoma			1		2				1	2		
Rhabdomyosarcoma							1				1	
Other sarcoma histology	1			2	4				2	4	4	

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Sarcomas

Randomized Multicenter and Stratified Phase II Study of Gemcitabine Alone Versus Gemcitabine and Docetaxel in Patients with Metastatic or Relapsed Leiomyosarcomas: A Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) French Sarcoma Group Study (TAXOGEM study)

PATRICIA PAUTIER,[a] ANNE FLOQUET,[c] NICOLAS PENEL,[d] SOPHIE PIPERNO-NEUMANN,[e] NICOLAS ISAMBERT,[g] ANNIE REY,[b] EMMANUELLE BOMPAS,[h] ANGELA CIOFFI,[a] CORINNE DELCAMBRE,[i] DIDIER CUPISSOL,[j] FRANCOISE COLLIN,[f] JEAN-YVES BLAY,[k] MARTA JIMENEZ,[l] FLORENCE DUFFAUD[m]

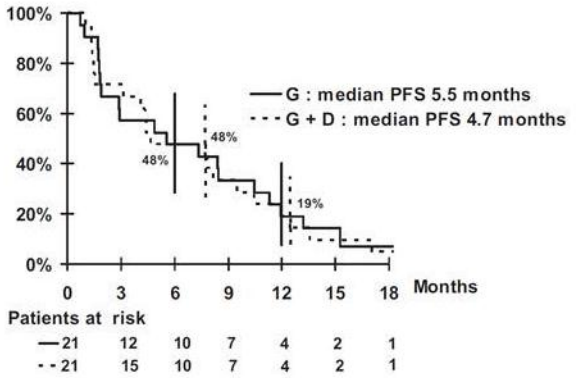


Figure 1. Kaplan–Meier curve of progression-free survival for the uterine leiomyosarcoma group.

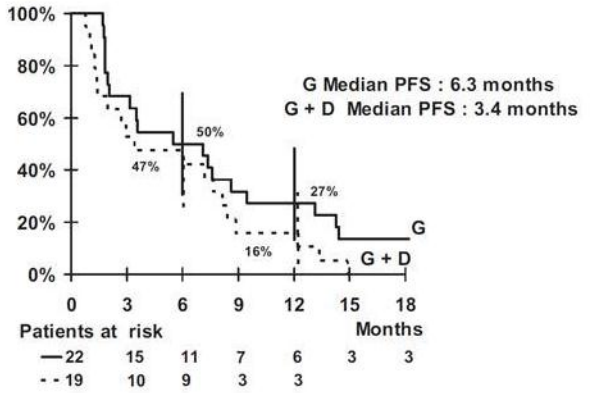
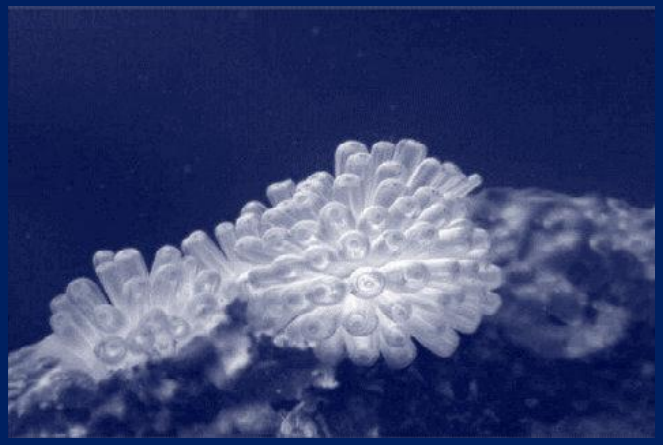
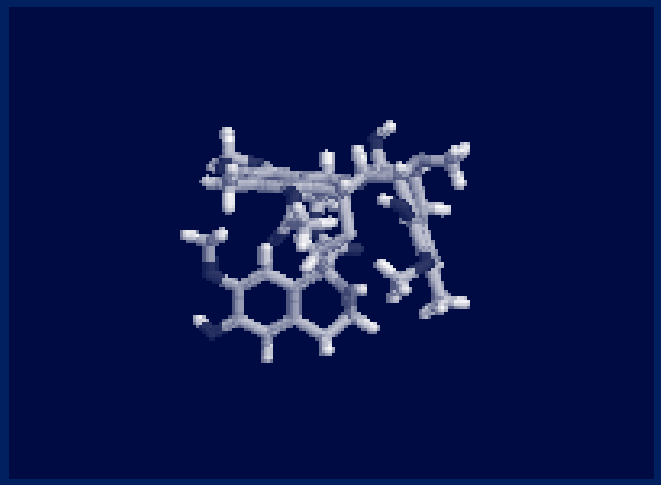


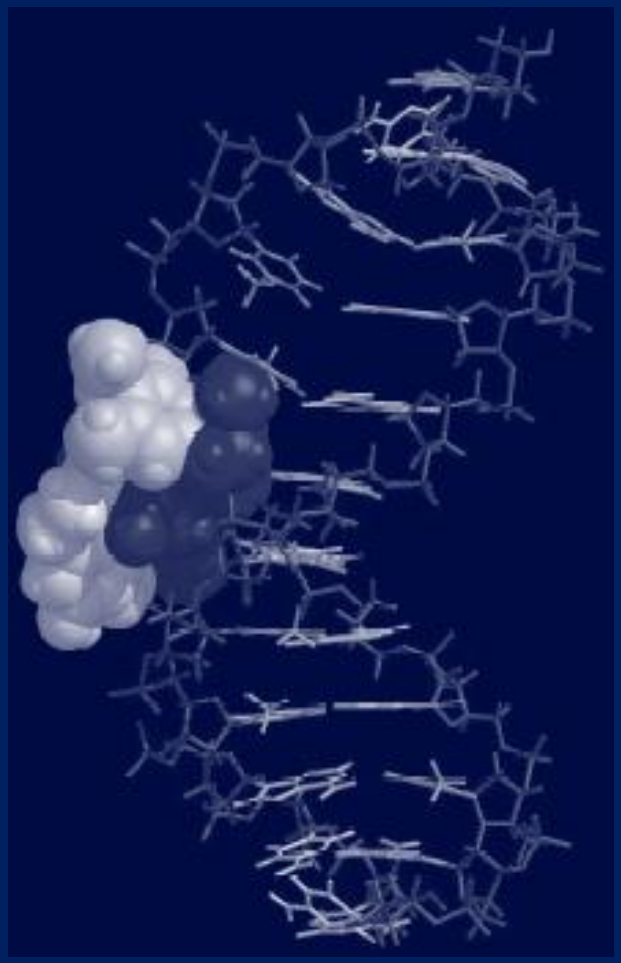
Figure 2. Kaplan–Meier curve of progression-free survival for the nonuterine leiomyosarcoma group.

The Oncologist 2012;17:1213

Trabectedin (ET-743)







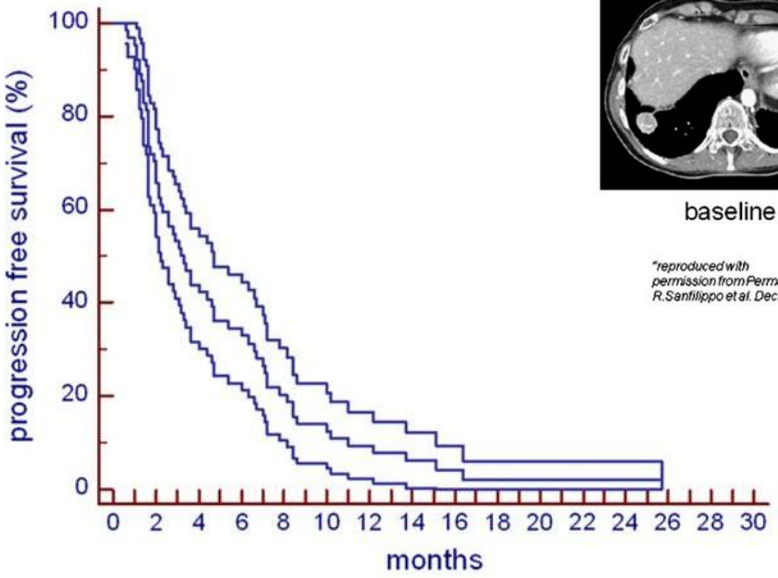
Contents lists available at SciVerse ScienceDirect

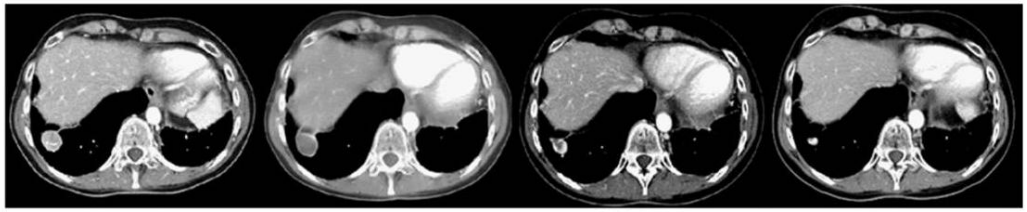
Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Trabectedin in advanced uterine leiomyosarcomas: A retrospective case series analysis from two reference centers ☆

Roberta Sanfilippo [a,*,1], Federica Grosso [a,1,2], Robin L. Jones [b,3], Susana Banerjee [b], Silvana Pilotti [c], Maurizio D'Incalci [d], Angelo Paolo Dei Tos [e], Francesco Raspagliesi [f], Ian Judson [b], Paolo Giovanni Casali [a]





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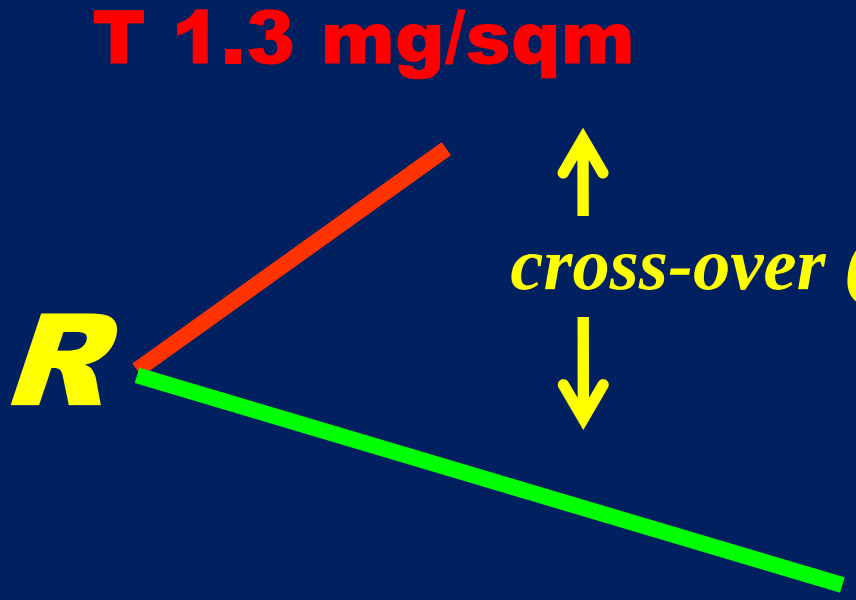
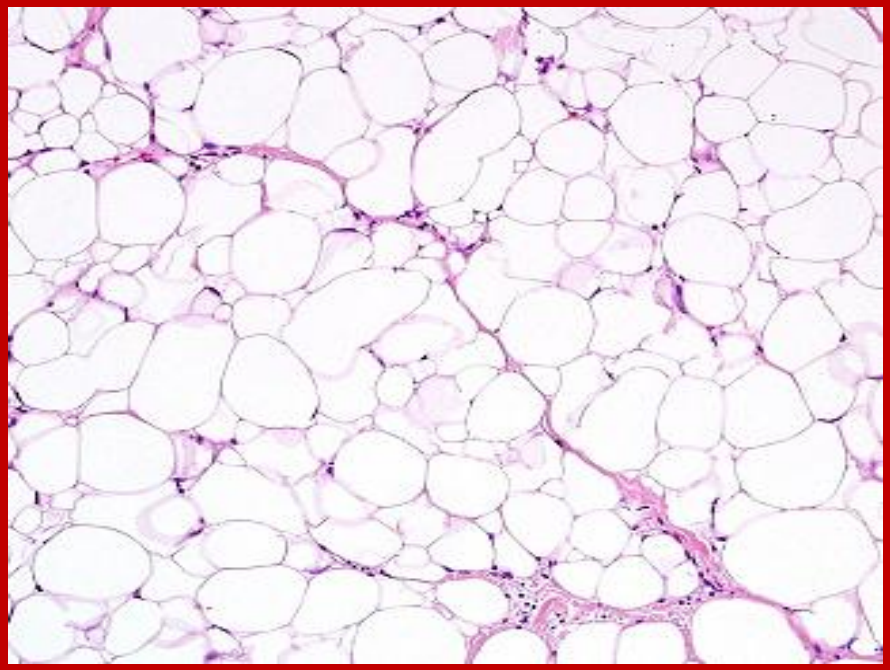
R.Sanfilippo et al. Decrease in tumor density with Yondelis® as a prelude to tumor response

Fig. 3. Tumor shrinkage preceded by a decrease in tumor density.

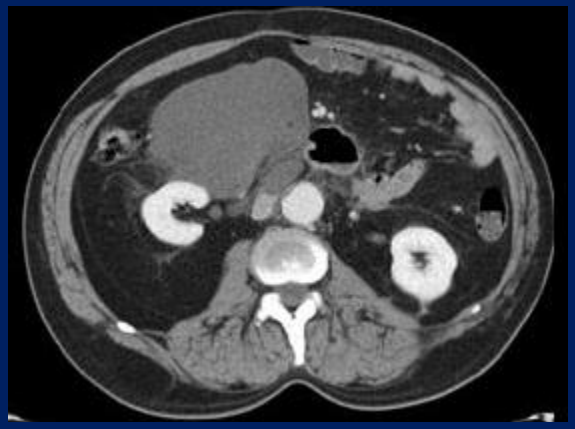
Uterine leiomyosarcoma: Phase 2 randomized study

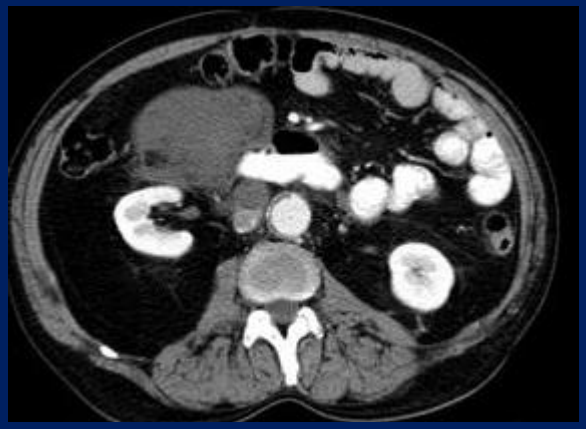


Liposarcoma



Dedifferentiated liposarcoma: Trabectedin





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ET743 x 16 mos

Annals of Oncology 9: 1047–1052, 1998.

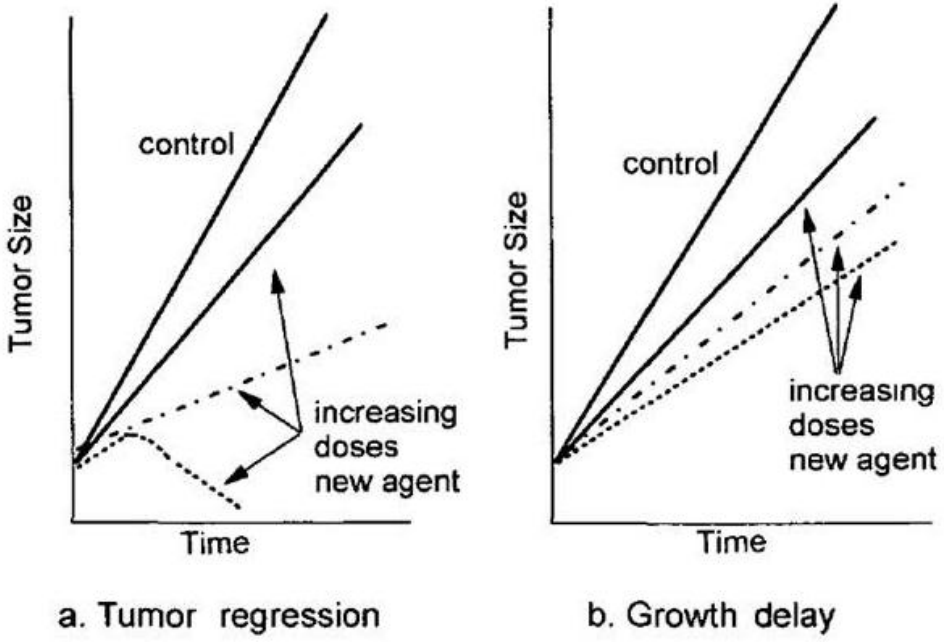
Special article

Phase I and II trials of novel anti-cancer agents: Endpoints, efficacy and existentialism

The Michel Clavel lecture, held at the 10th NCI-EORTC Conference on New Drugs in Cancer Therapy, Amsterdam, 16–19 June 1998

E. A. Eisenhauer

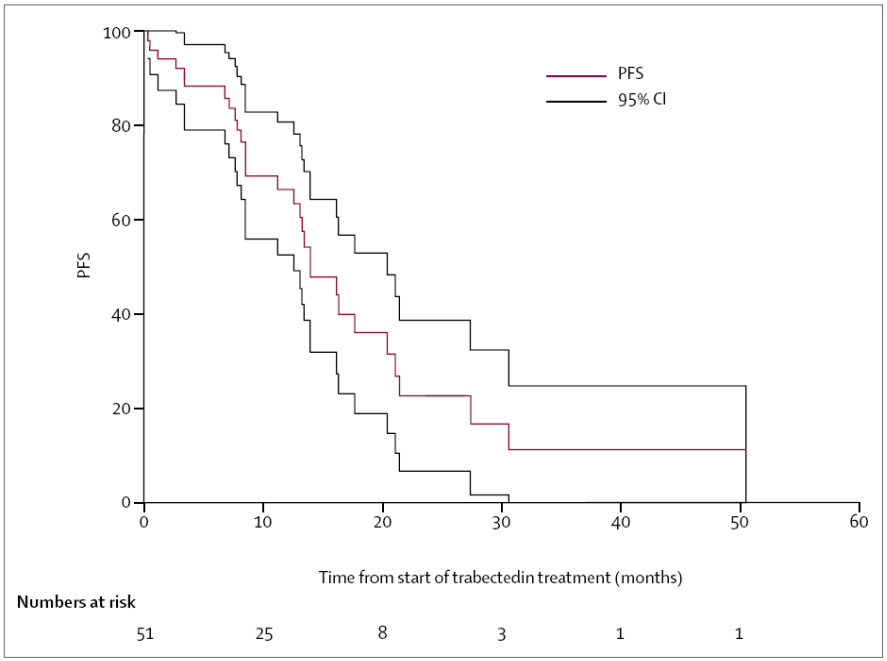
Investigational New Drug Program, NCIC Clinical Trials Group, Queen's University, Kingston, Ontario, Canada

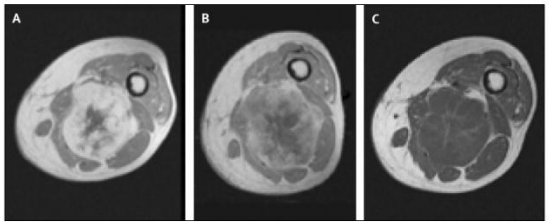


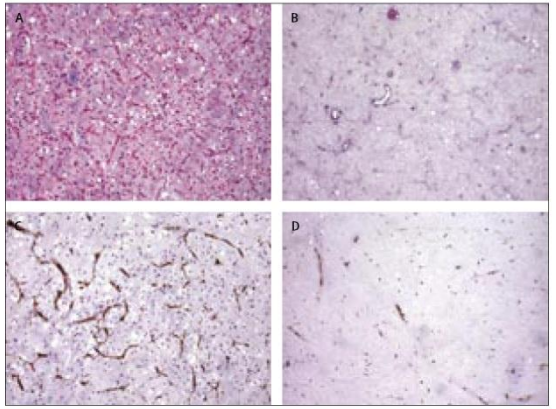
Efficacy of trabectedin (ecteinascidin-743) in advanced pretreated myxoid liposarcomas: a retrospective study

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

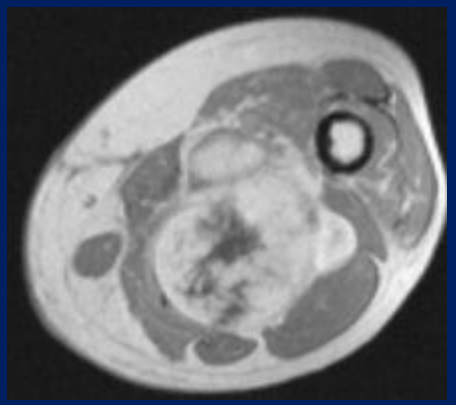






Trabectedin—a targeted chemotherapy?

Margaret von Mehren
Sarcoma Oncology, Fox Chase Cancer Center, Philadelphia, PA, USA
m_vonmehren@fccc.edu



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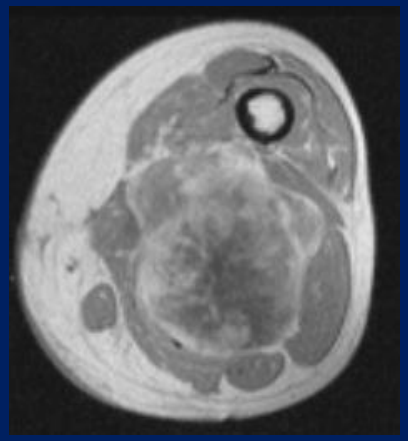

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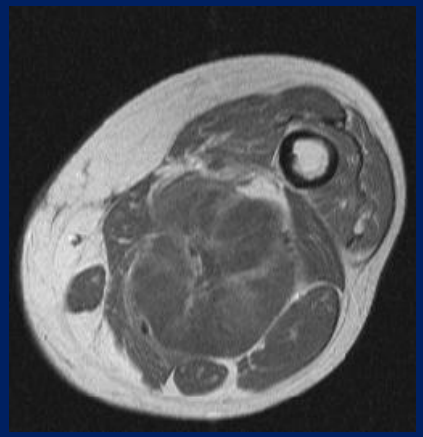

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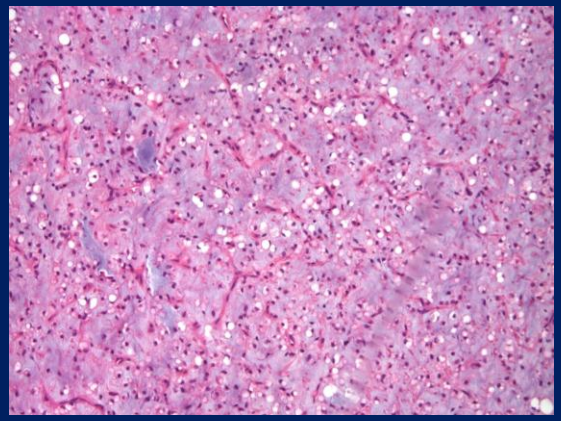

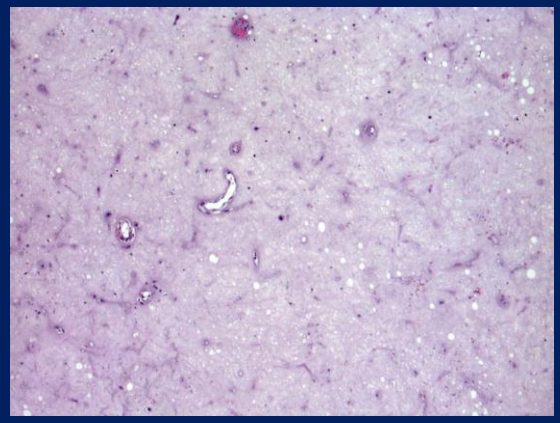

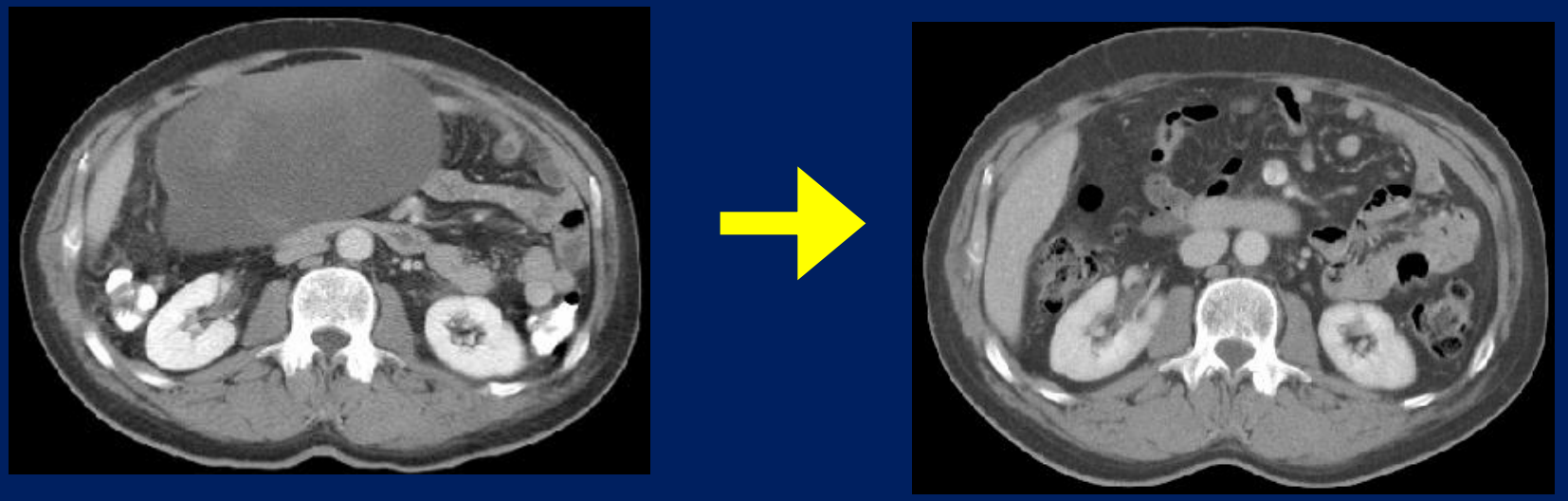

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ET743 x 3

Trabectedin (ET-743) promotes differentiation in myxoid liposarcoma tumors

Claudia Forni,[1] Mario Minuzzo,[1] Emanuela Virdis,[2] Elena Tamborini,[2] Matteo Simone,[3] Michele Tavecchio,[3] Eugenio Erba,[3] Federica Grosso,[2] Alessandro Gronchi,[2] Pierre Aman,[4] Paolo Casali,[2] Maurizio D'Incalci,[3] Silvana Pilotti,[2] and Roberto Mantovani[1]

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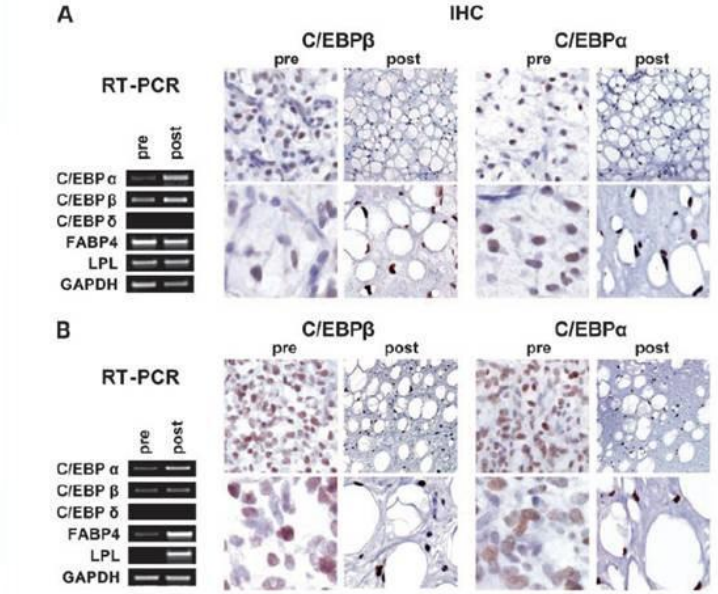

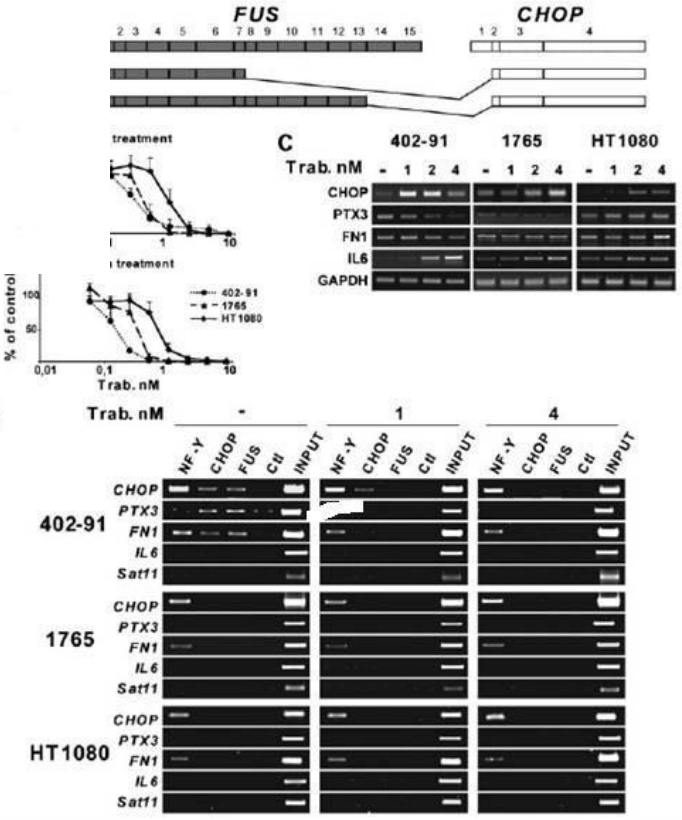

Mol Cancer Therap 2009;8:449

original article

Annals of Oncology
doi:10.1093/annonc/mdp004

Trabectedin in myxoid liposarcomas (MLS): a long-term analysis of a single-institution series

F. Grosso[1]*, R. Sanfilippo[1], E. Virdis[2], C. Piovesan[1], P. Collini[2], P. Dileo[1], C. Morosi[3], J. C. Tercero[4], J. Jimeno[4], M. D'Incalci[5], A. Gronchi[6], S. Pilotti[2] & P. G. Casali[1]

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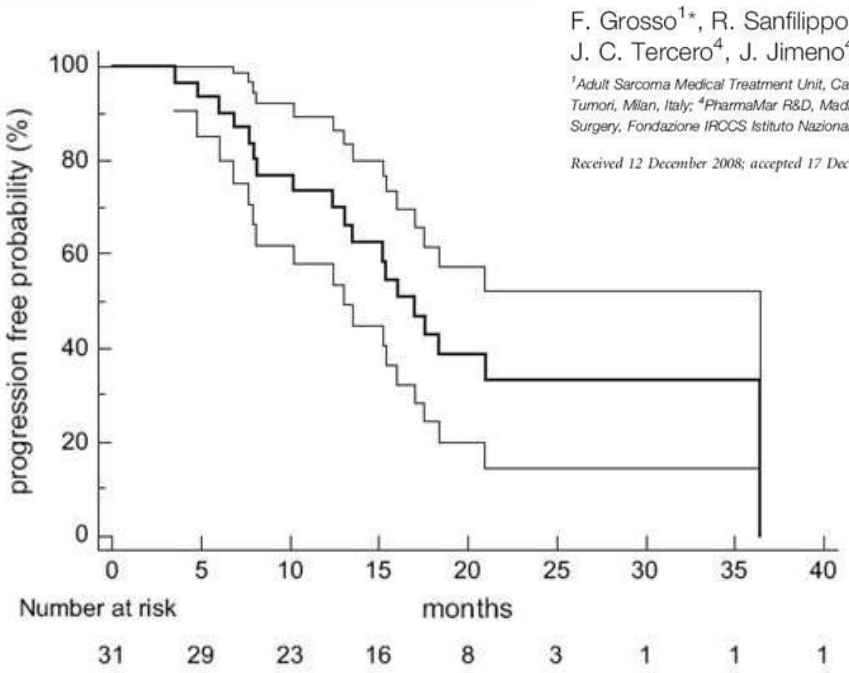
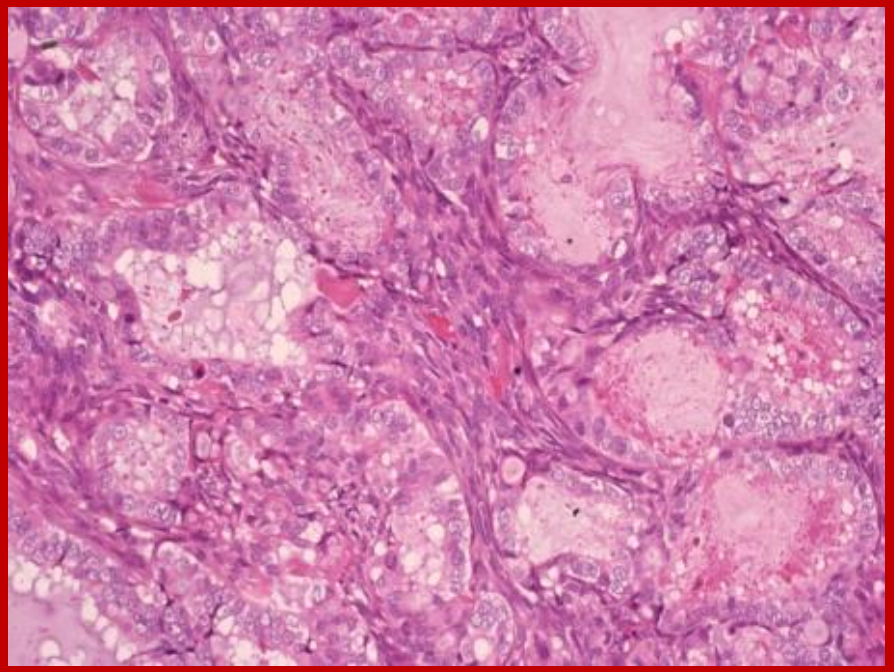
Received 12 December 2008; accepted 17 December 2008

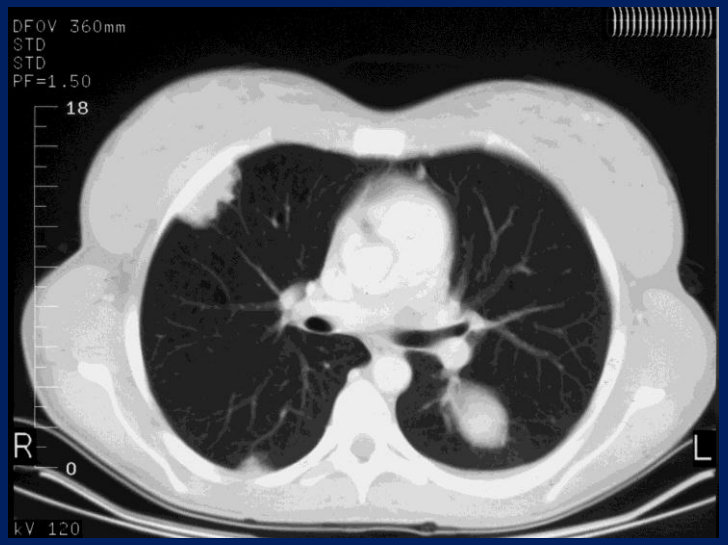


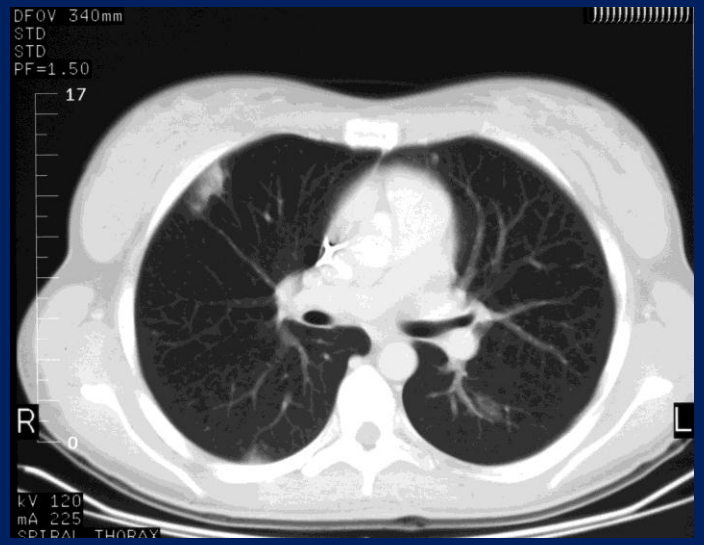
Age (years)	Sex	Location	Grade	*TLS-DDIT3*	Metastatic sites	T courses (*n*)	BR	STOP T	PFS (months)	PFS-end (months)	Status
59.7	M	Thigh	RC	I del	Abdominal cavity, bone	16	MR	Surgery	24.6	10.5	NED
36.0	F	Thigh	RC	II	Soft part, pericardium	13	PR	Surgery	22.0	11.9	NED
32.5	M	Pelvis	MLS	II	Abdominal cavity	13	PR	Surgery	24.6	13.7	AWD
44.6	M	Thigh	RC	II	Abdominal cavity	15	PR	Surgery	27.5	16.8	AWD
56.4	M	Thigh	MLS	II	Local relapse (soft part)	6	SD	Surgery	12.0	8.5	NED
47.3	M	Thigh	MLS	II	Local relapse (soft part)	5	SD	Surgery	26.4	17.6	NED
53.0	M	Leg	RC	ND	Pericardium, mediastinum	9	CR	Medical decision	36.4	19.0	AWD
48.3	M	Thigh	RC	ND	Bone	7	SD	RT	13.6	7.5	AWD
42.2	M	Thigh	RC	II	Lung	13	CR	Patient decision	19.5	20.2	AWD
54.8	F	Thigh	RC	I	Abdominal cavity	10	MR	Surgery	18.1	12.8	AWD

Synovial sarcoma



Synovial sarcoma: HD-ci-IFX





0

HD-ci-IFX x 3 mos

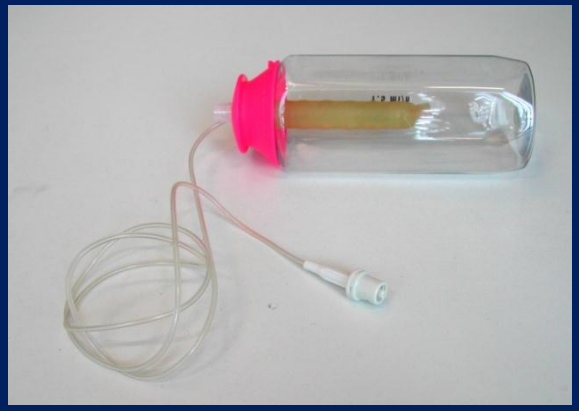
HD-ci-IFX

IFOSFAMIDE
7 g/sqm

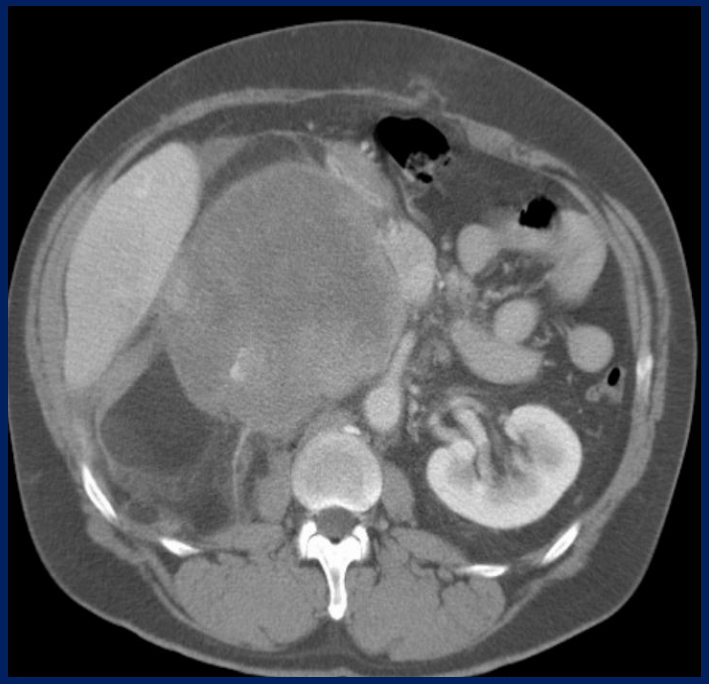
Mesna
7 g/sqm

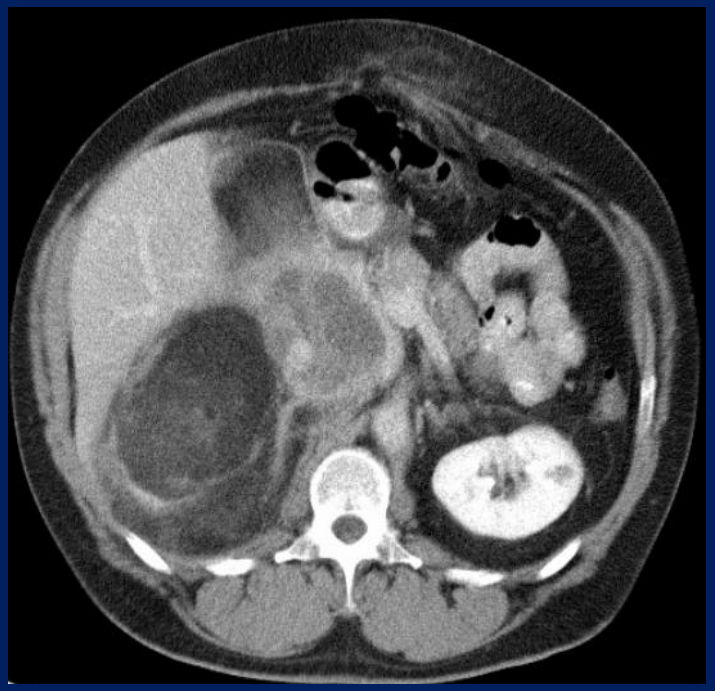
in Saline up to 250 mL (1,5 mL/h)

x 2 (14 g/sqm in 14 d) / 28 d



Dedifferentiated liposarcoma





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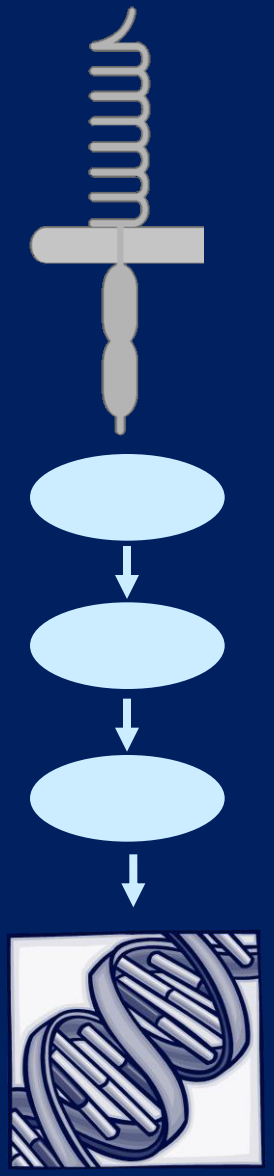
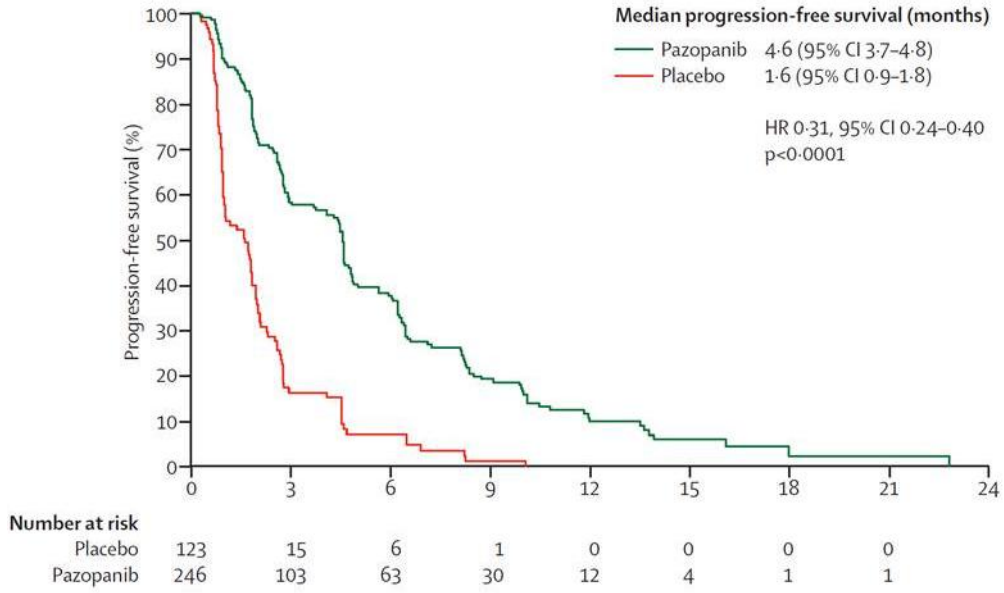
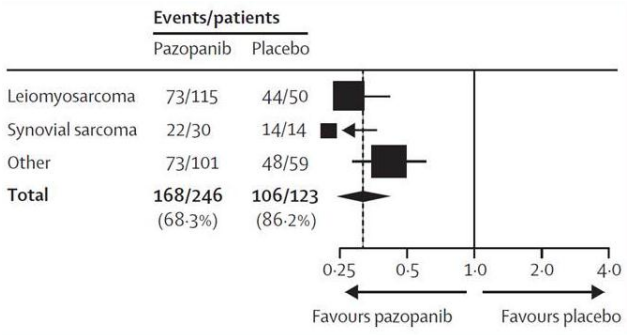
HD-ci-IFX x 5



Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double-blind, placebo-controlled phase 3 trial

Winette T A van der Graaf, Jean-Yves Blay, Sant P Chawla, Dong-Wan Kim, Binh Bui-Nguyen, Paolo G Casali, Patrick Schöffski, Massimo Aglietta, Arthur P Staddon, Yasuo Beppu, Axel Le Cesne, Hans Gelderblom, Ian R Judson, Nobuhito Araki, Monia Ouali, Sandrine Marreaud, Rachel Hodge, Mohammed R Dewji, Corneel Coens, George D Demetri, Christopher D Fletcher, Angelo Paolo Dei Tos, Peter Hohenberger, on behalf of the EORTC Soft Tissue and Bone Sarcoma Group and the PALETTE study group





Van Der Graaf WTA et al, Lancet 2012;379:1879

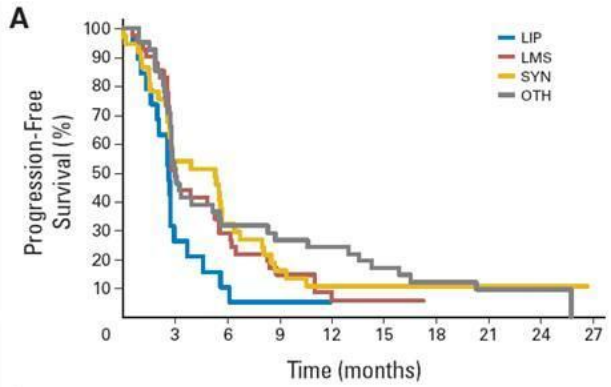
VOLUME 27 · NUMBER 19 · JULY 1 2009

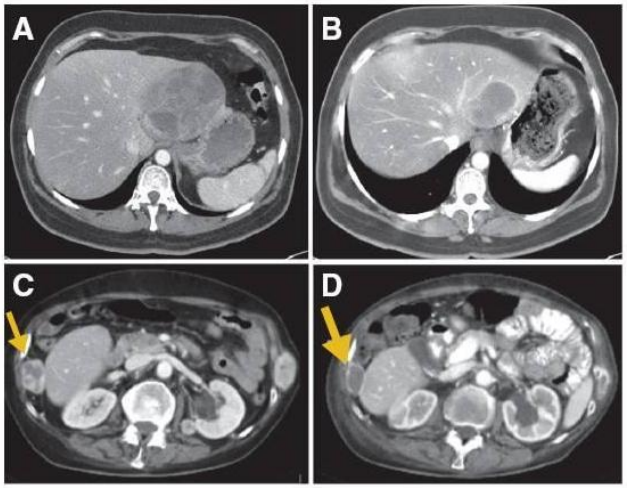
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

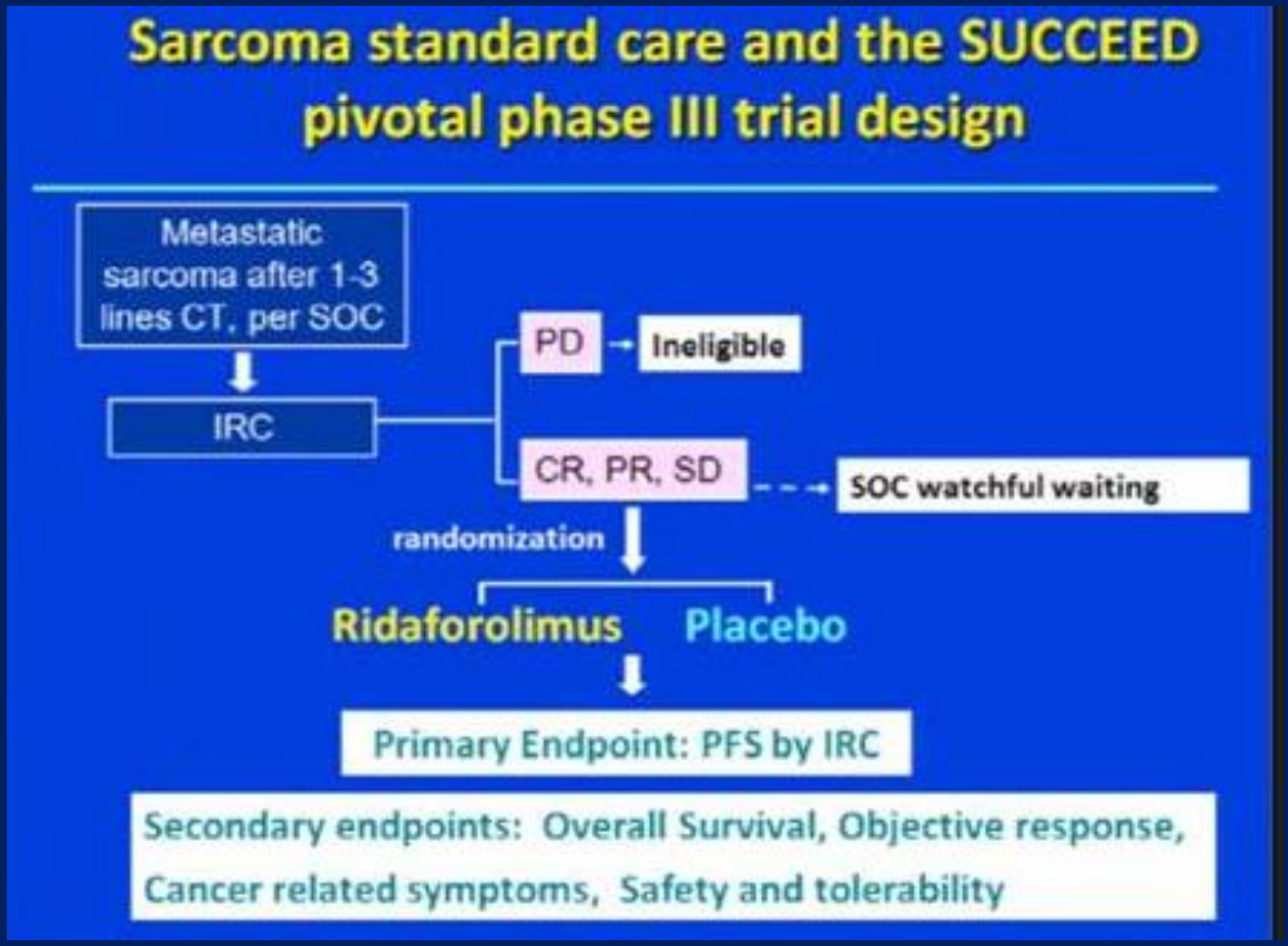
Pazopanib, a Multikinase Angiogenesis Inhibitor, in Patients With Relapsed or Refractory Advanced Soft Tissue Sarcoma: A Phase II Study From the European Organisation for Research and Treatment of Cancer–Soft Tissue and Bone Sarcoma Group (EORTC Study 62043)

Stefan Sleijfer, Isabelle Ray-Coquard, Zsuzsa Papai, Axel Le Cesne, Michelle Scurr, Patrick Schöffski, Françoise Collin, Lini Pandite, Sandrine Marreaud, Annick De Brauwer, Martine van Glabbeke, Jaap Verweij, and Jean-Yves Blay





LMS



from: ASCO 2011 Virtual Meeting

Chawla SP et al, ASCO 2011

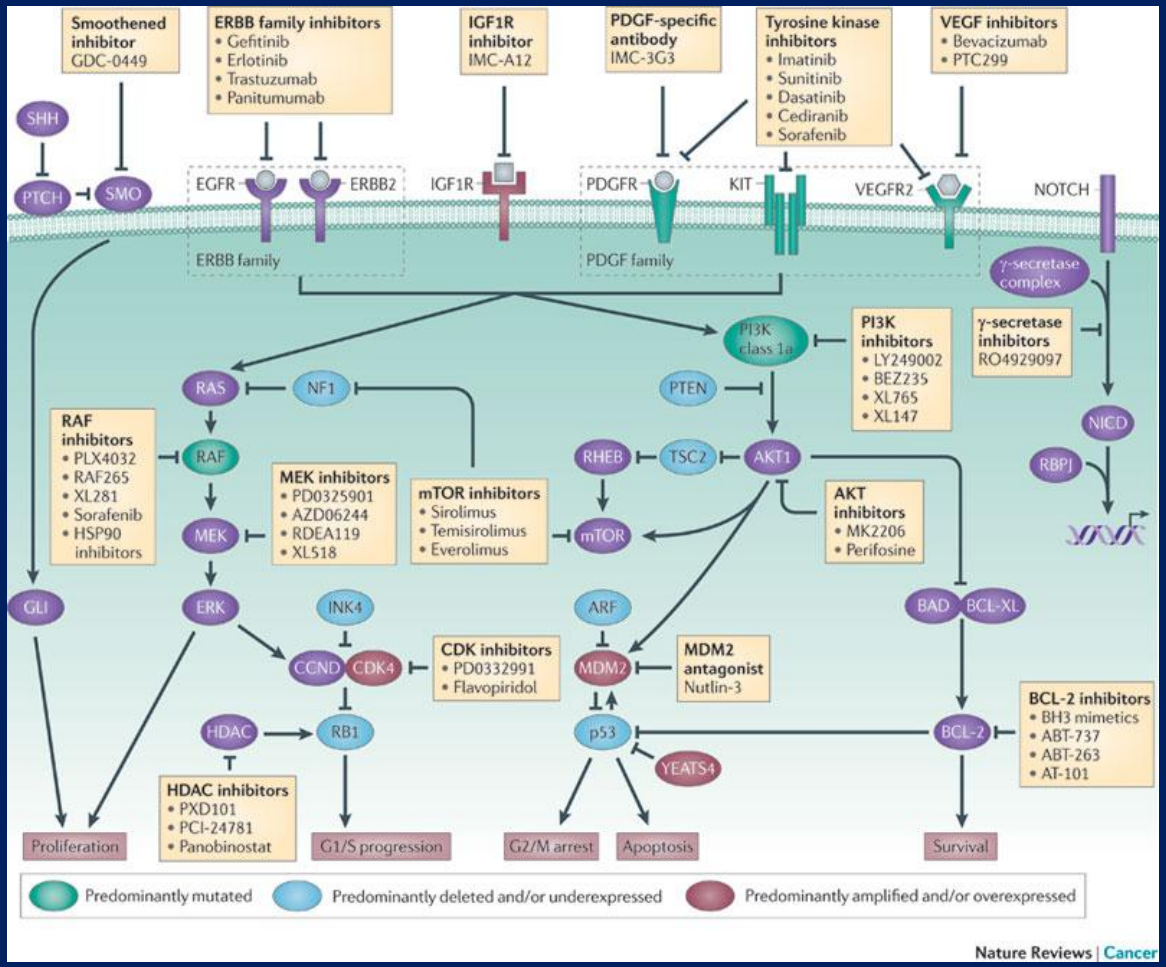
PFS per independent radiology review

(Data cut-off date 10-25-2010)

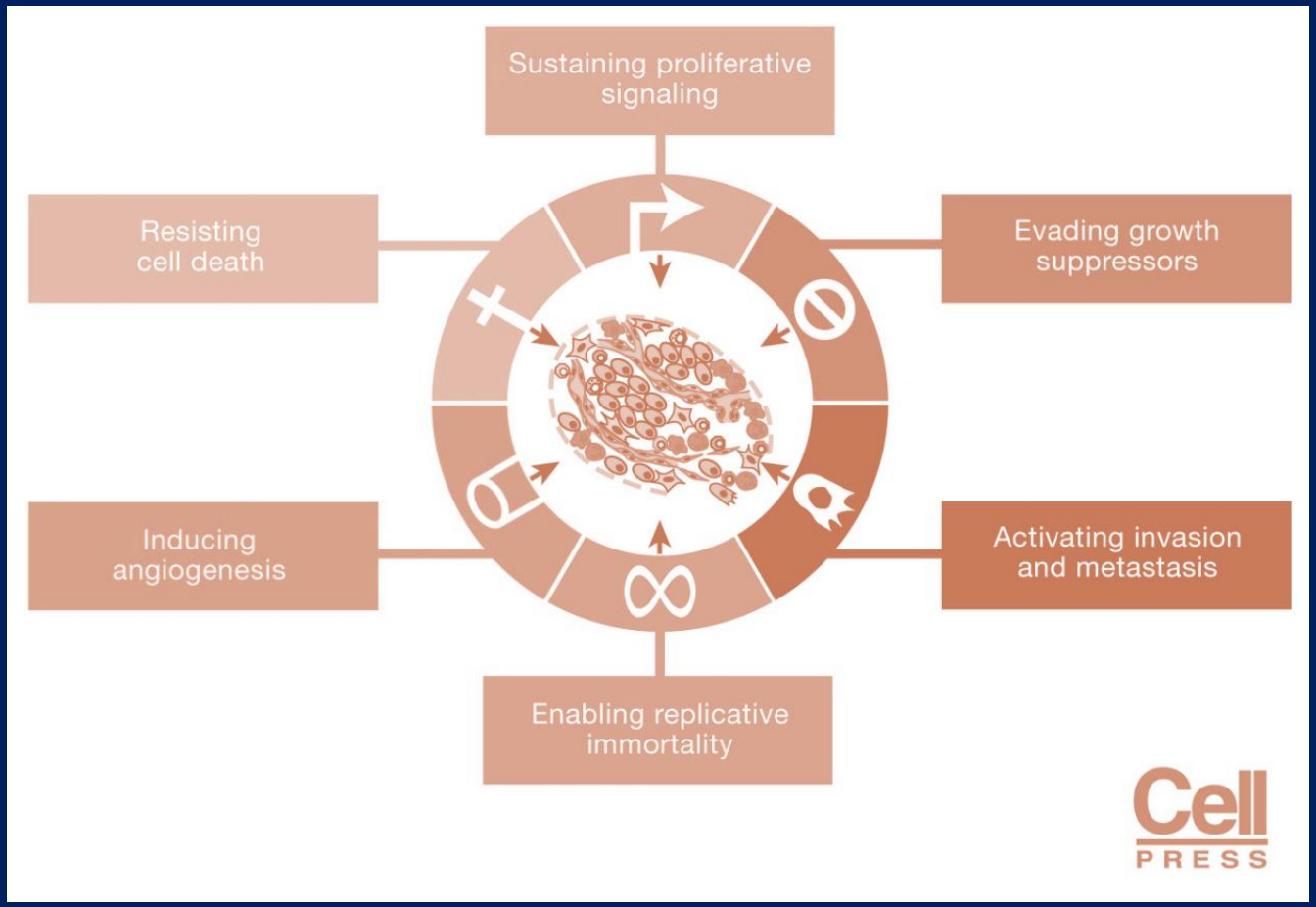
from: ASCO 2011 Virtual Meeting

Chawla SP et al, ASCO 2011

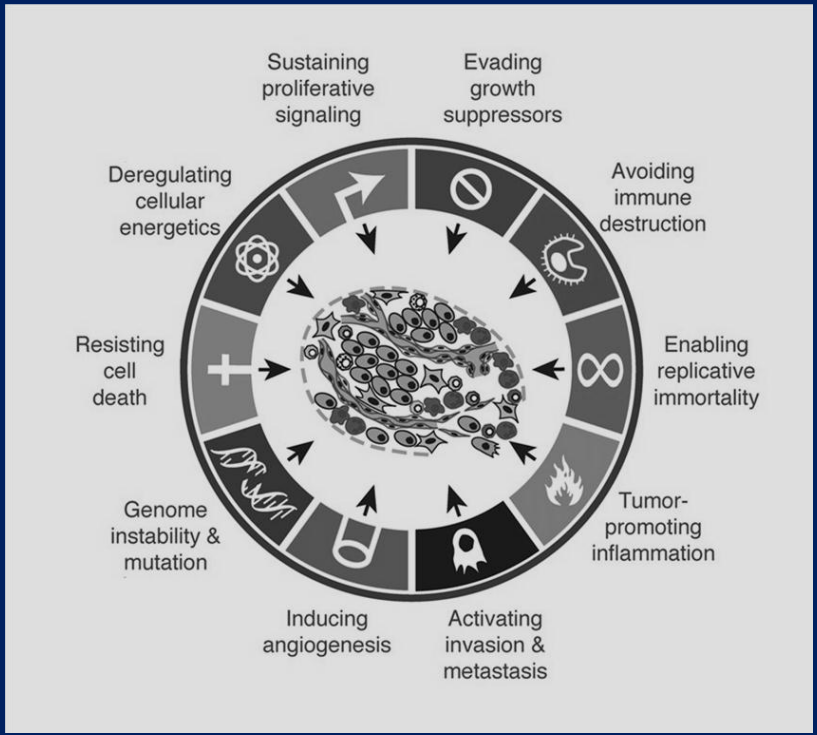
The Sarcoma family of tumors



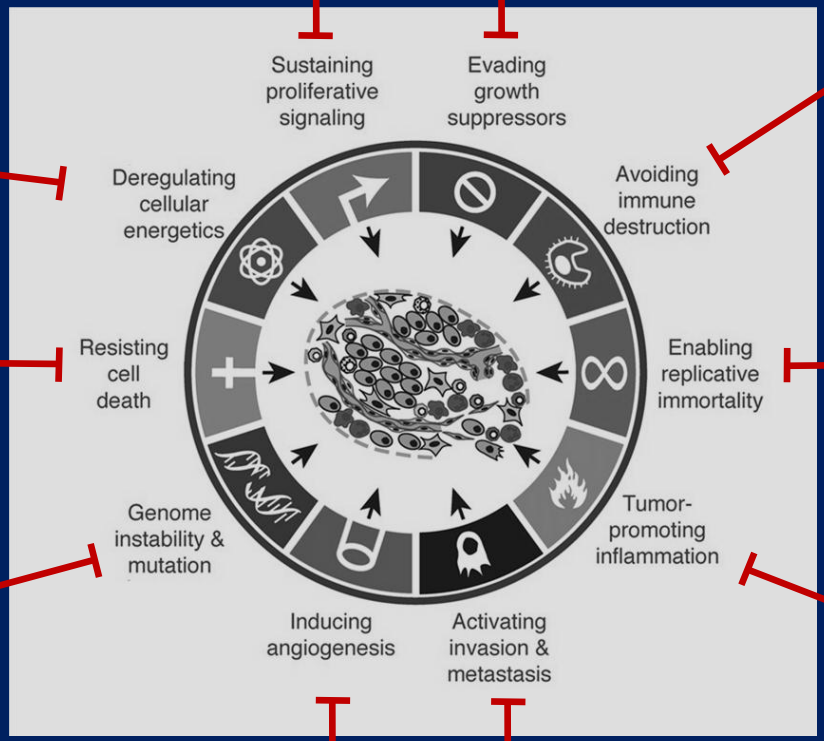
Taylor BS, Nat Rev Cancer 2011;11:541



Hanahan D and Weinberg RA, Cell 2011;144:646



Hanahan D and Weinberg RA, Cell 2011;144:646



imatinib
IGFR inhibitors
PI3K inhibitors
MAPK inhibitors
mTOR inhibitors
hedgehog inhibitors
RANK-RANKL inhibitors

MAPK inhibitors
PI3K inhibitors
mTOR inhibitors
sorafenib
regorafenib

trabectedin
imatinib
mTOR inhibitors

IGFR inhibitors
mTOR inhibitors

MDM2 inhibitors
hsp inhibitors

eribulin
trabectedin
PI3K inhibitors
MAPK inhibitors
sorafenib
regorafenib
hedgehog inhibitors

eribulin
imatinib
trabectedin
hsp inhibitors
anti PDGFRa MoAb

trabectedin
mTOR inhibitors

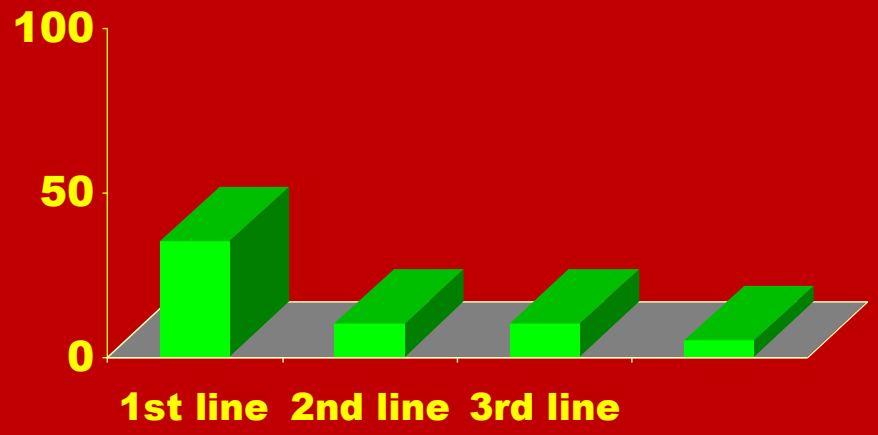
sunitinib
sorafenib
dovitinib
pazopanib
regorafenib
anti PDGFRa MoAb

MAPK inhibitors
PI3K inhibitors
hedgehog inhibitors
sunitinib
sorafenib
dovitinib
pazopanib
regorafenib
anti PDGFRa MoAb

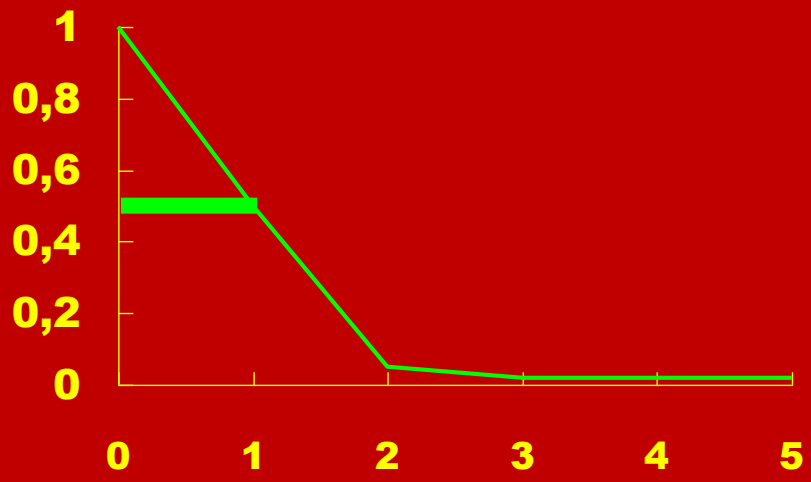
Hanahan D and Weinberg RA, Cell 2011;144:646

Advanced disease: chemo

OR



OS

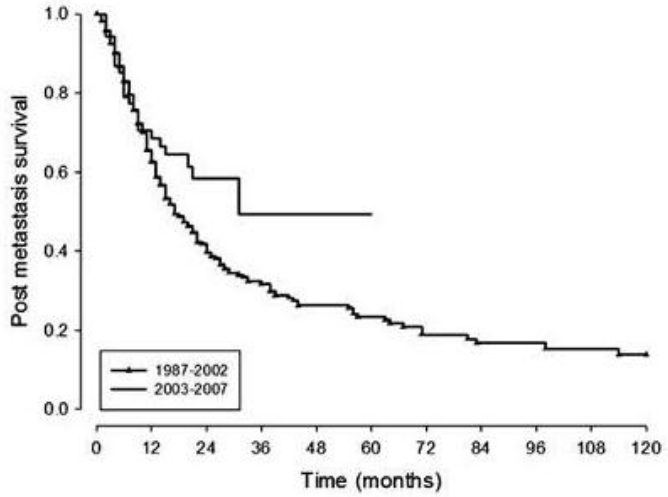


original article

Annals of Oncology 22: 1675–1681, 2011
doi:10.1093/annonc/mdq643
Published online 17 January 2011

Primary extremity soft tissue sarcomas: outcome improvement over time at a single institution

A. Gronchi[1*], R. Miceli[2], C. Colombo[1], P. Collini[3], S. Stacchiotti[4], P. Olmi[5], L. Mariani[2], R. Bertulli[4], M. Fiore[1] & P. G. Casali[4]



Gronchi a et al, Ann Oncol 2011;22:1675

Histology-driven chemotherapy

- **Leiomyosarcoma: GEM, Trabectedin, DTIC (& Temozolomide), ...**
- **Liposarcoma, dediff: Trabectedin, HD-IFX .....**
- **Liposarcoma, myxoid: Trabectedin, ...**
- **Angiosarcoma: taxanes, GEM, HD-IFX, ...**
- **Synovial sa: HD-IFX, Trabectedin, ...**
- **MPNST: HD-IFX, VP16 + ...**
- **.....**

Histology-driven targeted therapy

- Dermatofibrosarcoma: Imatinib
- Desmoids: hormones, Imatinib, Sorafenib, ...
- PVNS: Imatinib, ...
- Alveolar soft part sa: Sunitinib, Cediranib
- Solitary fibrous tumor: Sunitinib, ...
- Angiosarcoma: Sorafenib, ...
- Inflammatory myofibroblastic tumor: Crizotinib, ...
- LAM and Pecomas: m-TOR inhibitors
- .....

The quality of evidence…


RARE
CANCERS
EUROPE
Joining forces for action

ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
European Society for Medical Oncology

EURORDIS
Rare Diseases Europe

EUROPEAN
CANCER
PATIENT
COALITION

EORTC
European Organisation for Research and Treatment of Cancer

Conticanet

EuroBoNeT

ECL
Association of European Cancer Leagues

cmlsupport
chronic myeloid leukaemia support group

IBTA
INTERNATIONAL
BRAIN TUMOUR
ALLIANCE

orphanet

FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

CML AdvocatesNetwork

IEO
European Institute of Oncology

SIOPE
SIOP Europe

ESO
European
School
of
Oncology
Learning to care

EUROPEAN ONCOLOGY NURSING SOCIETY

European
Society of
Pathology

NOVARTIS
ONCOLOGY

Pfizer Oncology

sanofi aventis
Because health matters

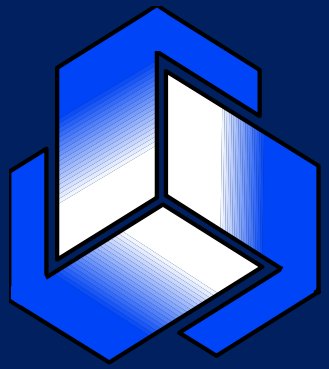
www.rarecancerseurope.org

STS: advanced disease

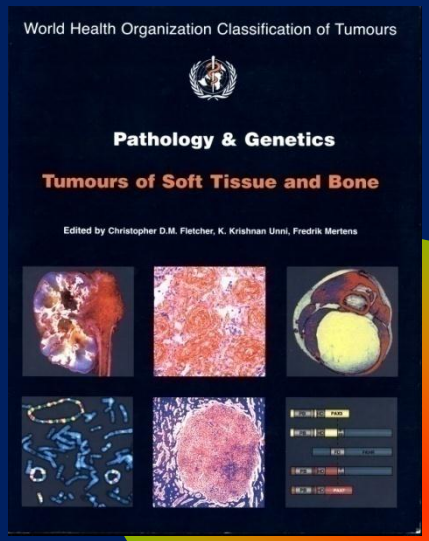
R <

ADM 75 mg/sqm

ADM 75 mg/sqm + IFX 7.5 g/sqm



EORTC
Soft Tissue & Bone Sarcoma Group



Adipocytic tumours
- Well deifferentiated / dedifferentiated liposarcoma
- Myxoid / round cell liposarcoma
- Pleomorphic liposarcoma
- .....

Fibroblastic / myofibroblastic tumours
- Fibromatosis (desmoid)
- Solitary fibrous tumour / haemangiopericytoma
- Low grade myofibroblastic tumour
- Infantile fibrosarcoma
- Adult fibrosarcoma
- Mixofibrosarcoma
- .....

So-called fibrohistiocytic tumours
- Pleomorphic MFH / Undifferentiated pleomorphic sarcoma
- .....

Smooth muscle tumours
- Leiomyosarcoma
- .....

Skeletal muscle tumours
- Embryonal rhabdomyosarcoma
- Alveolar rhabdomyosarcoma
- Pleomorphic rhabdomyosarcoma

Vascular tumours
- Epithelioid haemangioendothelioma
- Angiosarcoma of soft tissue
- .....

Chondro-osseous tumours
- Mesenchymal chondrosarcoma
- Extraskeletal osteosarcoma

Tumours of uncertain differentiation
- Synovial sarcoma
- Epithelioid sarcoma
- Alveolar soft part sarcoma
- Clear cell sarcoma of soft tissue
- Extraskeletal myxoid chondrosarcoma
- Extraskeletal Ewing tumour
- Desmoplastic small round cell tumour
- Extra-renal rhabdoid tumour
- Malignant mesenchymoma
- Neoplasms with perivascular epithelioid cell differentiation (PEComa)
- Intimal sarcoma

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