Soft Tissue Sarcomas in Adults – Local treatment after neo-adjuvant therapy

Piotr Rutkowski

Maria Sklodowska-Curie Memorial Cancer Center-Institute of Oncology

Department of Soft Tissue/Bone Sarcoma and Melanoma

Warsaw, POLAND

rutkowskip@coi.waw.pl

Disclosure slide

- **Advisory board: Novartis, MSD, BMS, Bayer**
- **Honoraria: Novartis, Pfizer, MSD, Roche, GSK, Amgen**
- **Travel grants: Novartis**

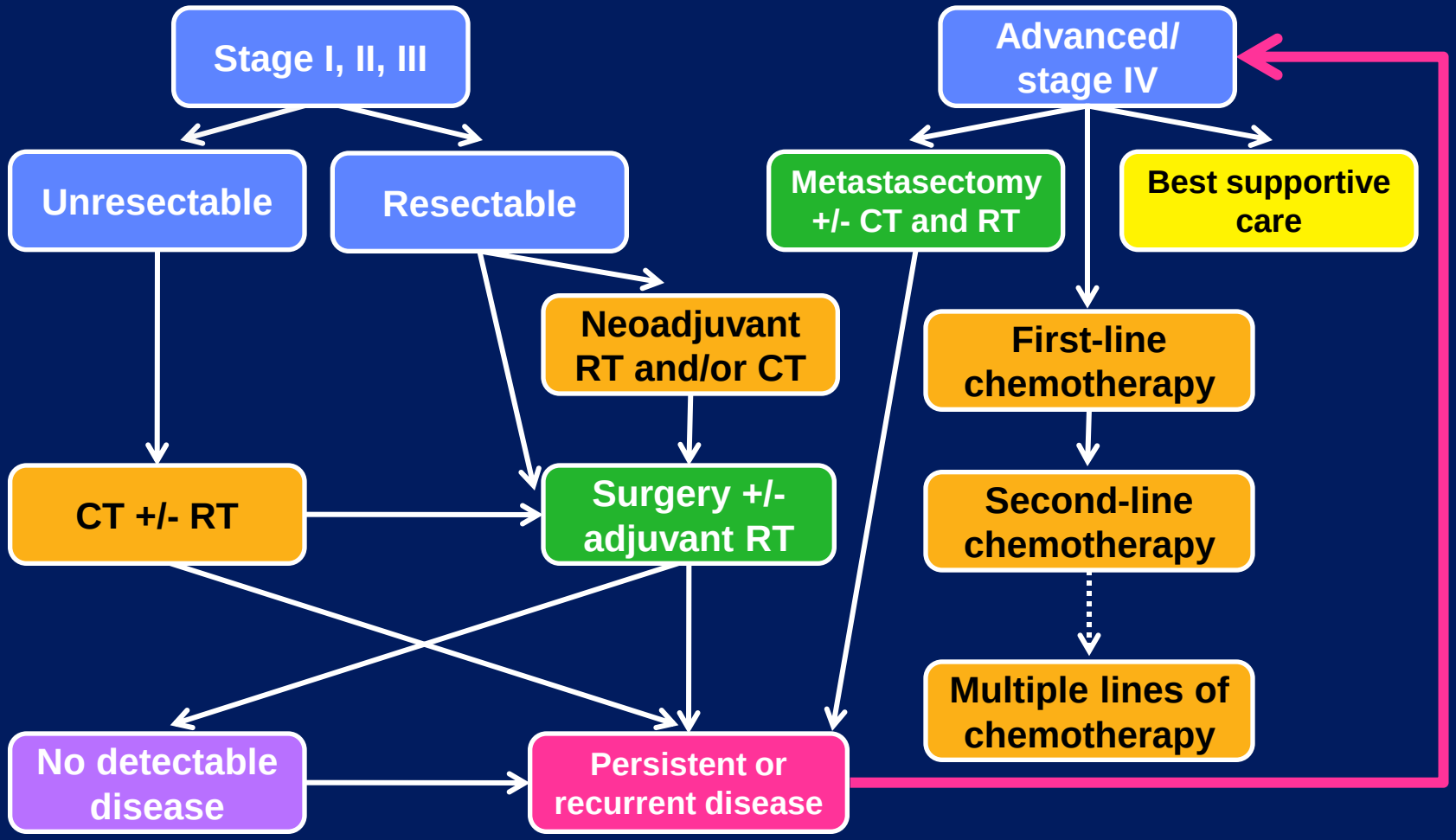
Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

The ESMO/European Sarcoma Network Working Group*

Annals of Oncology 25 (Supplement 3): iii102–iii112, 2014
doi:10.1093/annonc/mdu254

Soft tissue sarcomas (STSs) are ubiquitous in their site of origin and are often managed with multimodality treatment. A multidisciplinary approach is therefore mandatory in all cases (involving pathologists, radiologists, surgeons, radiation therapists, medical oncologists and paediatric oncologists, as well as nuclear medicine specialists, organ-based specialists, as applicable). Management should be carried out in reference centres for sarcomas and/or within reference networks sharing multidisciplinary expertise and treating a high number of patients annually. These centres are involved in ongoing clinical trials, in which sarcoma patients' enrolment is common. This centralised referral should be pursued as early as at the time of the clinical diagnosis of a suspected sarcoma. In practice, referral of all patients with a lesion likely to be a sarcoma would be recommended. This would mean referring all patients with an unexplained deep mass of soft tissues, or with a superficial lesion of soft tissues having a diameter of >5 cm. Quality criteria are needed for sarcoma reference centres and, all the more, reference networks. These criteria may vary from country to country but, among others, should be based on: multidisciplinarity (incorporating tools such as weekly

Summary of current treatment algorithms for soft tissue sarcoma



RT, radiotherapy; CT, chemotherapy

Based on: *NCCN Clinical Practice Guidelines in Oncology: Soft Tissue Sarcoma*, v.1. 2012. http://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf [accessed Mar 2012]; Casali P & Blay JY. *Ann Oncol* 2010;21:198; Grimer R *et al. Sarcoma* 2010;2010:506182

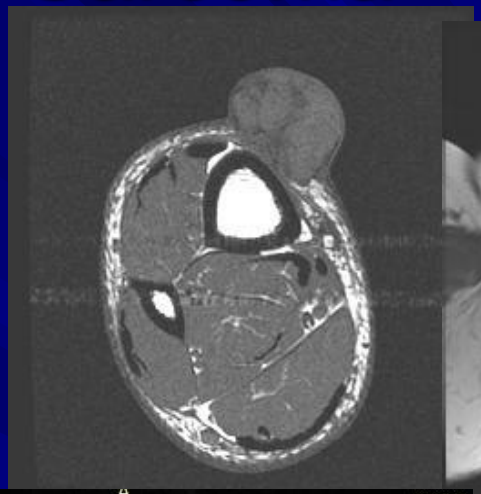
Neoadjuvant therapy

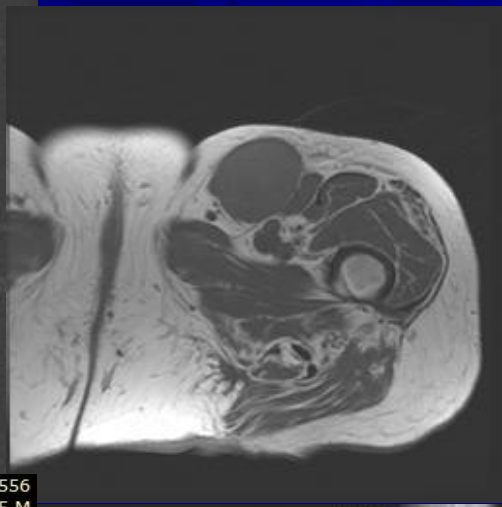
*In high grade, borderline resectable STS the preoperative chemotherapy and radiotherapy or isolated limb perfusion with melphalan/TNF alpha may be applied allowing for limb preservation/function-sparing and radical resection.

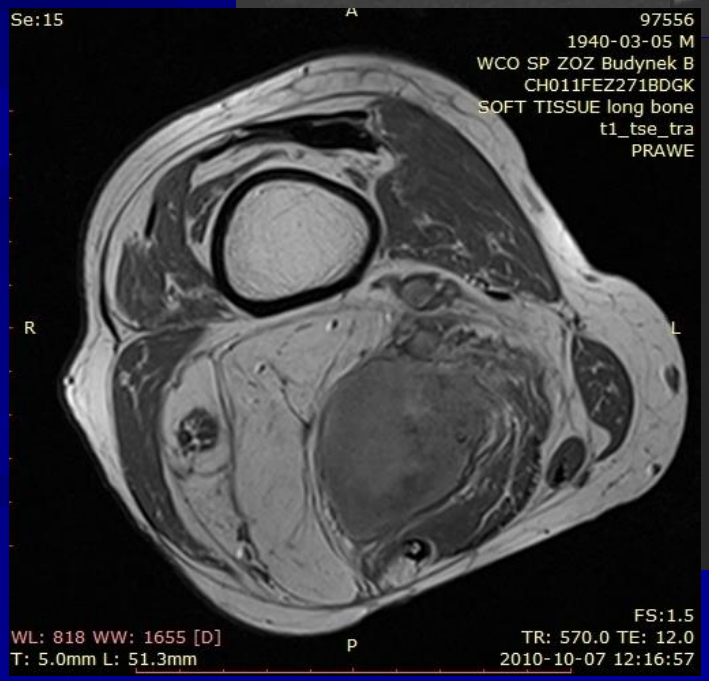
*The potential benefit of neoadjuvant therapy is the determination of tumor sensitivity to therapy gained from examination of the postresection surgical specimen.

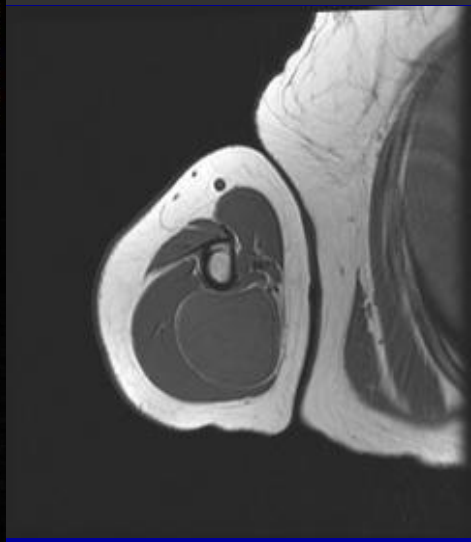
When to consider? - “High risk” Sarcoma

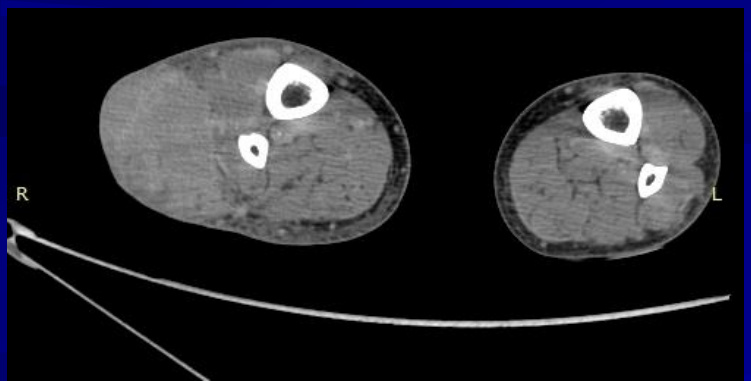
- Greater than 5 cm in diameter
- Deep to fascia
- Adjacent to bone/joints
- Adjacent to neurovascular structures
- Invading skin











Neo-/Adjuvant chemotherapy (2012 ESMO)

- No consensus
- Not a standard option
- « No treatment arm » still a standard
- May be discussed in multidisciplinary setting
  - which objective?
  - Which patients (Size>5, grade 3, histotypes ...)
- Targeted treatment to be explored?
- Some exceptions are RMS, EFT….

Neoadjuvant chemotherapy

Table 3. Recent Randomized Studies of Adjuvant or Neoadjuvant Anthracycline/Ifosfamide-Based Chemotherapy

Study	Year of Publication	N	Median Follow-Up (months)	Treatment	Overall Survival Rate (%)	*P*
Frustaci et al[21]	2003	104	90	EI	NR	.07
				Observation	49	
Petrioli et al[23]	2002	88	94	E or E + I	72	.06
				Observation	47	
Brodawicz et al[22]	2000	59	41	IFADIC	NR	Reported as 0.4, but no data provided
				Observation	NR	
Gortzak et al[24]	2001	134	88	AI	65	.22
				Observation	64	

Abbreviations: EI, epirubicin/ifosfamide; E, epirubicin; I, ifosfamide; IFADIC, ifosfamide/doxorubicin/dacarbazine; AI, doxorubicin/ifosfamide; NR, not reached.

Short, Full-Dose Adjuvant Chemotherapy in High-Risk Adult Soft Tissue Sarcomas: A Randomized Clinical Trial From the Italian Sarcoma Group and the Spanish Sarcoma Group

Alessandro Gronchi, Sergio Frustaci, Mario Mercuri, Javier Martin, Antonio Lopez-Pousa, Paolo Verderio, Lidia Mariani, Pinuccia Valagussa, Rosalba Miceli, Silvia Stacchiotti, Angelo Paolo Dei Tos, Antonino De Paoli, Alessandra Longhi, Andres Poveda, Vittorio Quagliuolo, Alessandro Comandone, Paolo Giovanni Casali, and Piero Picci

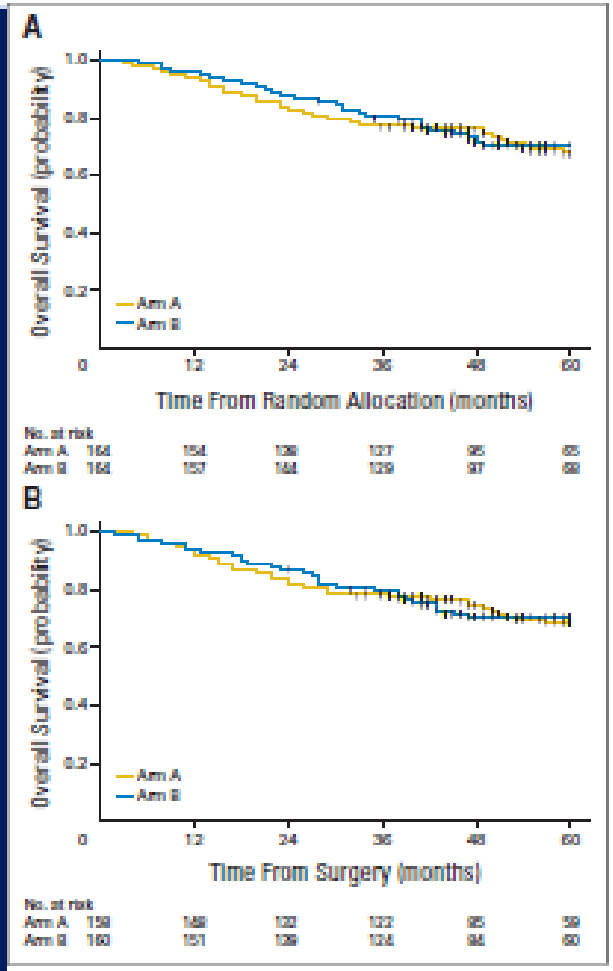
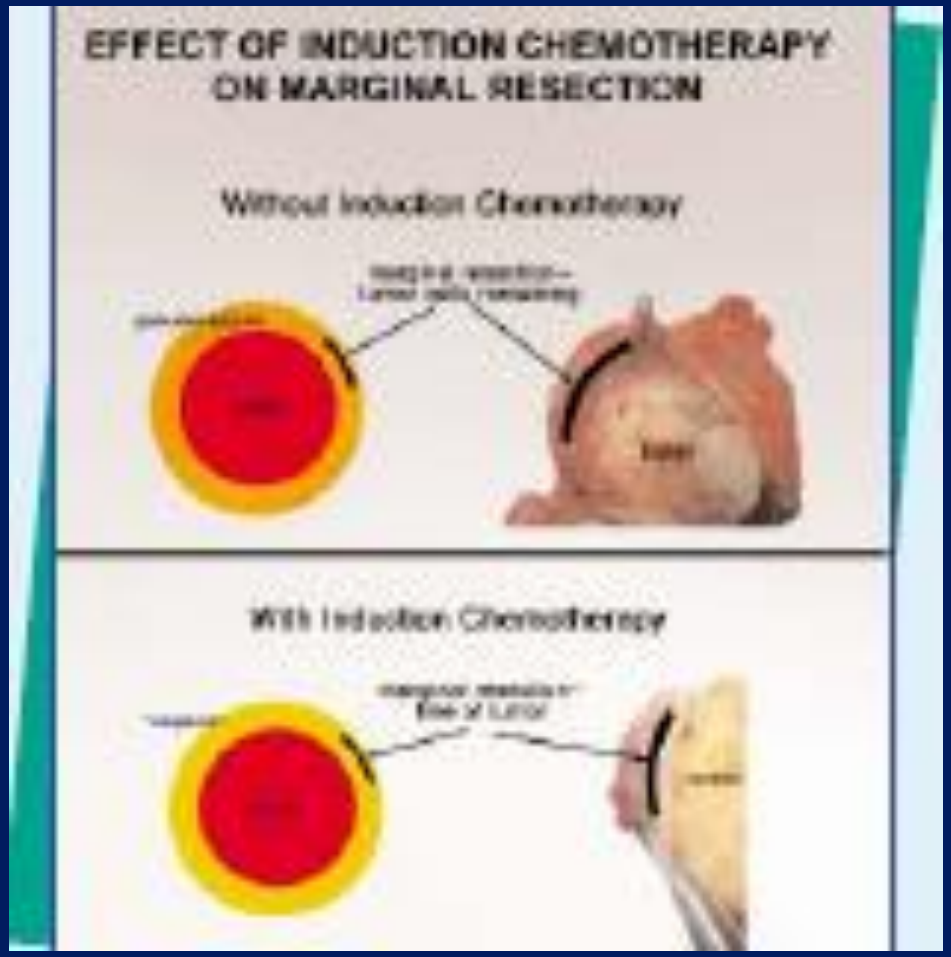
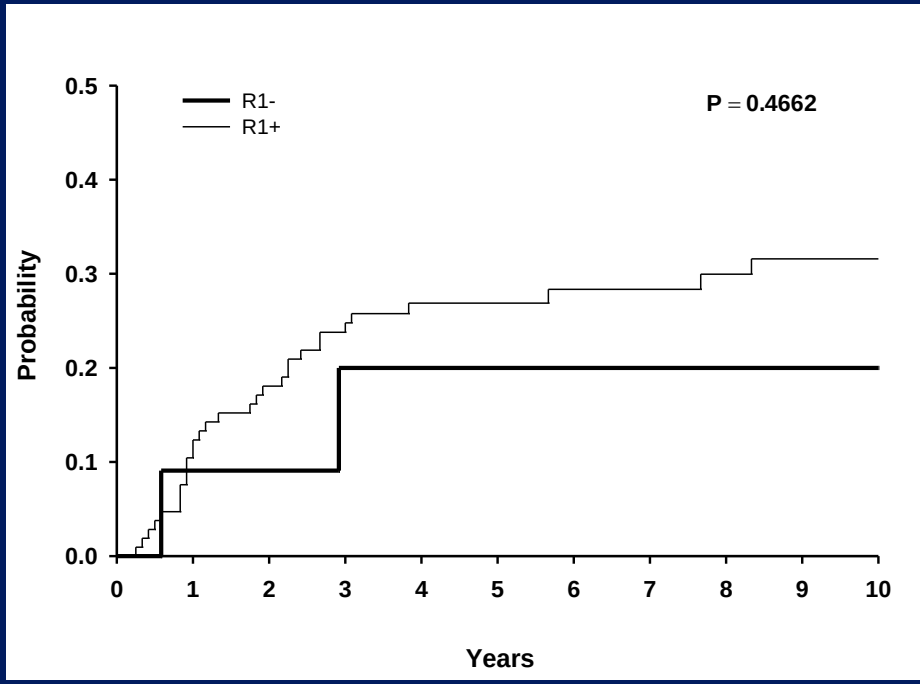


Fig 2. Five-year probability of overall survival (A) from random assignment and (B) from surgery according to study arm.

Close Surgical Margins in Soft Tissue Sarcoma Resection Do Not Predict Local Recurrence When Induction (Neoadjuvant) Chemotherapy is Used in the Treatment of High Grade Extremity Soft Tissue Sarcoma

Felasfa M. Wodajo, MD • James Wittig, MD • Kari Mansour • Dennis Priebat, MD • Robert M. Henshaw, MD • Martin M. Malawer, MD
Orthopedic Oncology • Washington Cancer Institute at Washington Hospital Center • Washington DC





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Preop RT – smaller target volume and dose, better defined tumor volume but higher rate of early postop complications (less late complications)

Table 1 Wound complication probabilities with respect to RT schedule and timing in ESTS

Investigator	Patients (*n*)	Preoperative RT (Gy)	Preoperative WC (%)	Postoperative RT (Gy)	Postoperative WC (%)	*p*	Comment
O'Sullivan et al. (3)	182	25 × 2	35	33 × 2	17	.01	Excess in WC predominantly seen in thigh tumors
Cannon et al. (11)	412	50 (44-70)	34	60 (50-72)	16	<.001	
Virkus et al. (12)	209	28 × 1.8	22	-	-	-	
Pisters et al. (13)	26	25 × 2	23	-	-	-	Concurrent with continuous doxorubicin
Jakob et al. (14)	15	28 × 1.8	40	-	-	-	Concurrent with temozolomide
Tseng et al. (15)	173	25 × 2	32	-	-	-	Surgery performed with particular focus on reconstructive surgical techniques
Mack et al. (16)	75	10 × 3	15	-	-	-	3 days of preoperative doxorubicin (30 mg/d) and sequential RT of 10 × 3 Gy
Kraybill et al. (17)	61	22 × 2	11	-	-	-	RTOG 9514 phase II trial: 44 Gy split course interdigitated RT with mesna, doxorubicin, ifosfamide, and dacarbazine
Temple et al. (18)	53	10 × 3	11	-	-	-	Surgery performed with particular focus on reconstructive surgical techniques

Abbreviations: RT = radiotherapy; ESTS = extremity soft tissue sarcoma; WC = wound complications.

Critical Review

Radiotherapy for Management of Extremity Soft Tissue Sarcomas: Why, When, and Where?

Rick L.M. Haas, MD, PhD,* Thomas F. DeLaney, MD, PhD,† Brian O'Sullivan, MD, PhD,‡ Ronald B. Keus, MD,§ Cécile Le Pechoux, MD, PhD,|| Patricia Olmi, MD, PhD,¶ Jan-Peter Poulsen, MD, PhD,# Beatrice Seddon, MD, PhD,** and Dian Wang, MD, PhD††

International Journal of Radiation Oncology biology • physics

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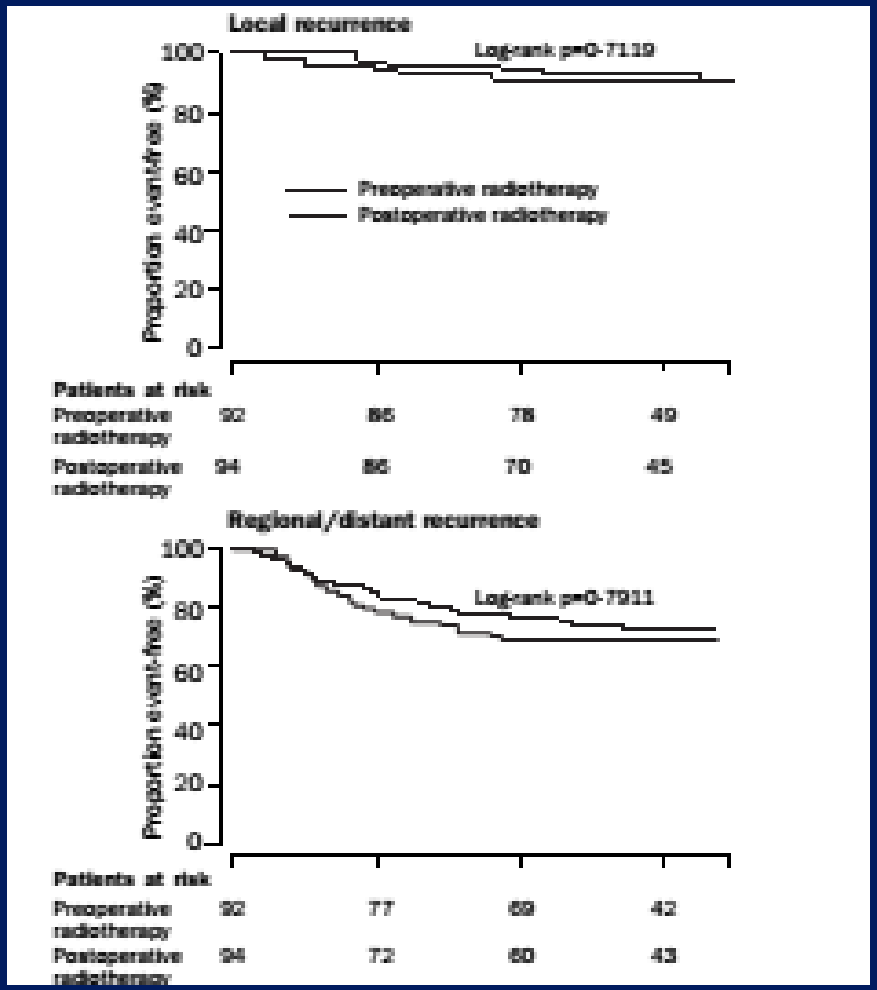
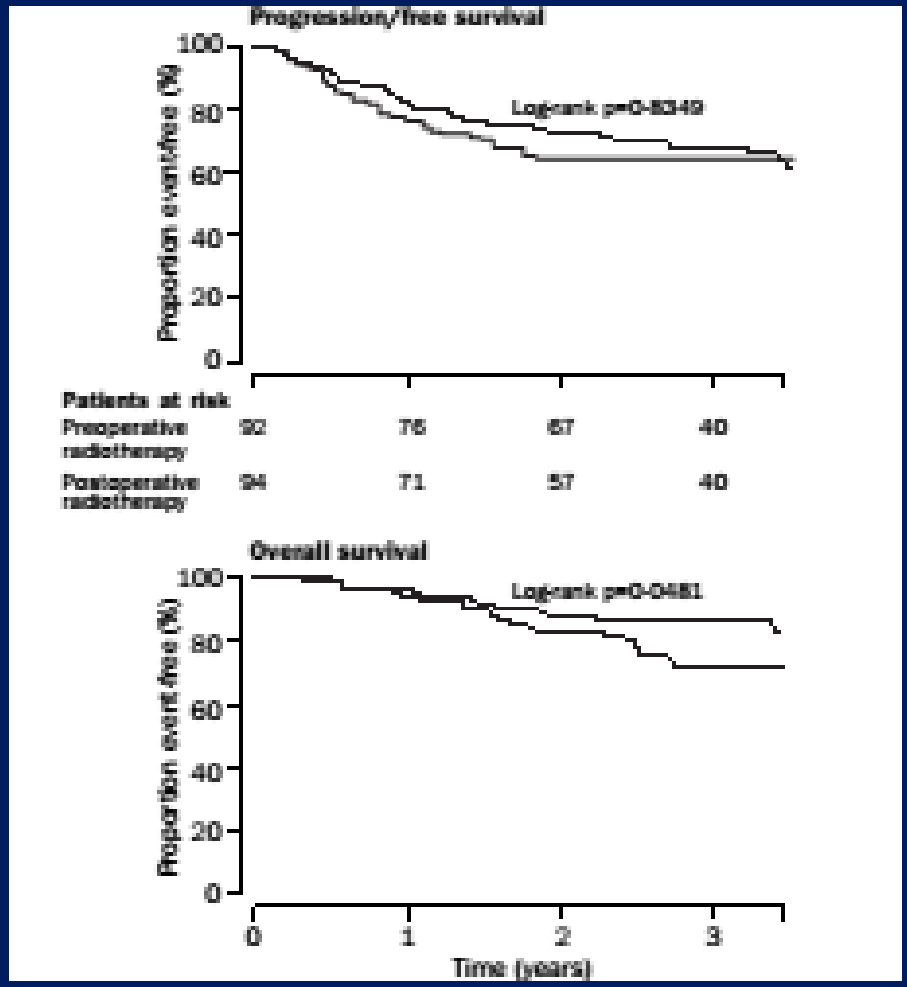
Preoperative versus postoperative radiotherapy in soft-tissue sarcoma of the limbs: a randomised trial

Lancet 2002, 359: 2235–41.

Brian O'Sullivan, Aileen M Davis, Robert Turcotte, Robert Bell, Charles Catton, Pierre Chabot, Jay Wunder, Rita Kandel, Karen Goddard, Anna Sadura, Joseph Pater, Benny Zee





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PREOPERATIVE VERSUS POSTOPERATIVE RADIOTHERAPY IN SOFT-TISSUE SARCOMA: MULTI-INSTITUTIONAL ANALYSIS OF 821 PATIENTS

Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 2, pp. 498–505, 2011

SAGUS SAMPATH, M.D.,* TIMOTHY E. SCHULTHEISS, PH.D.,† YING J. HITCHCOCK, M.D.,* R. LOR RANDALL, M.D.,‡ DENNIS C. SHRIEVE, M.D., PH.D.,* AND JEFFREY Y. C. WONG, M.D.†

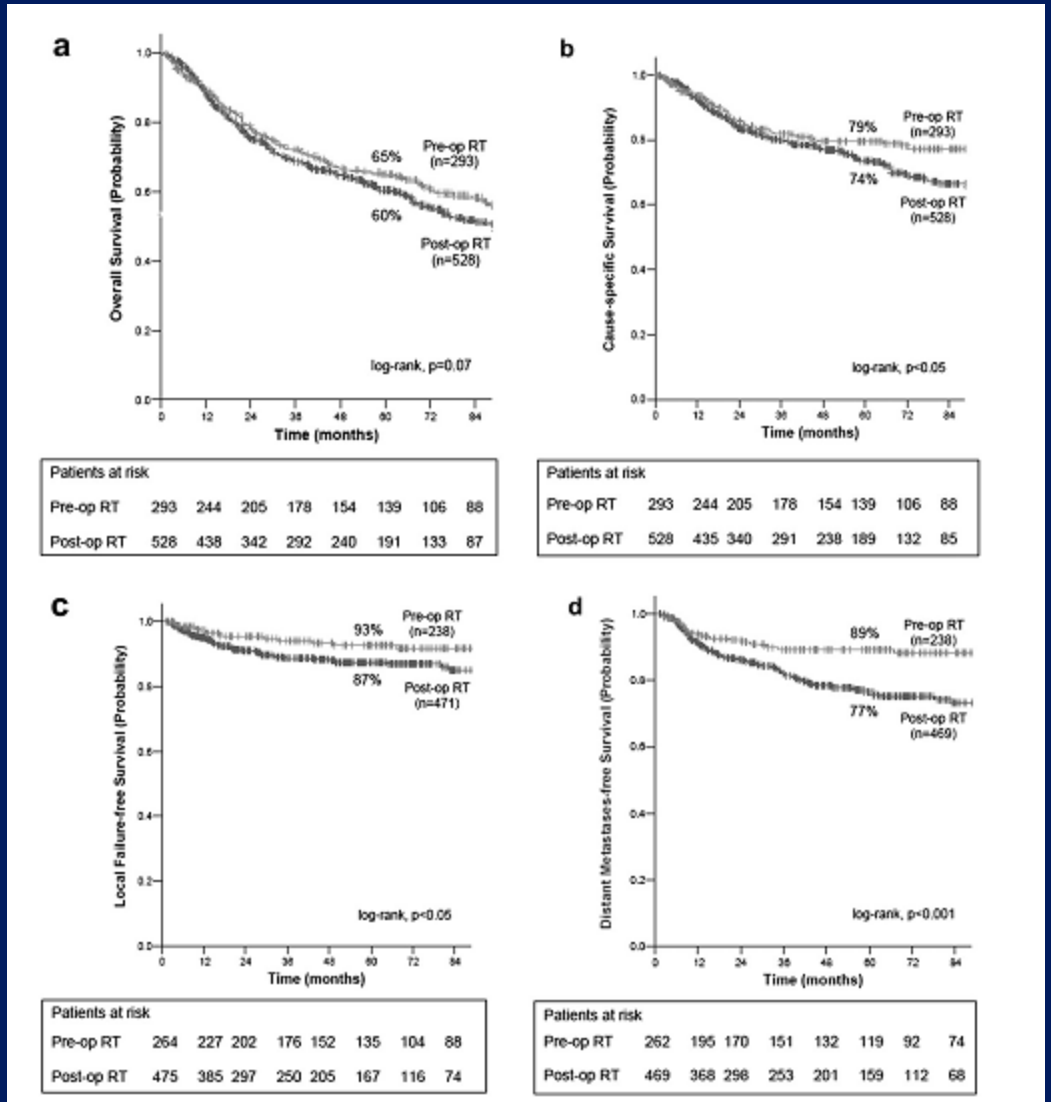
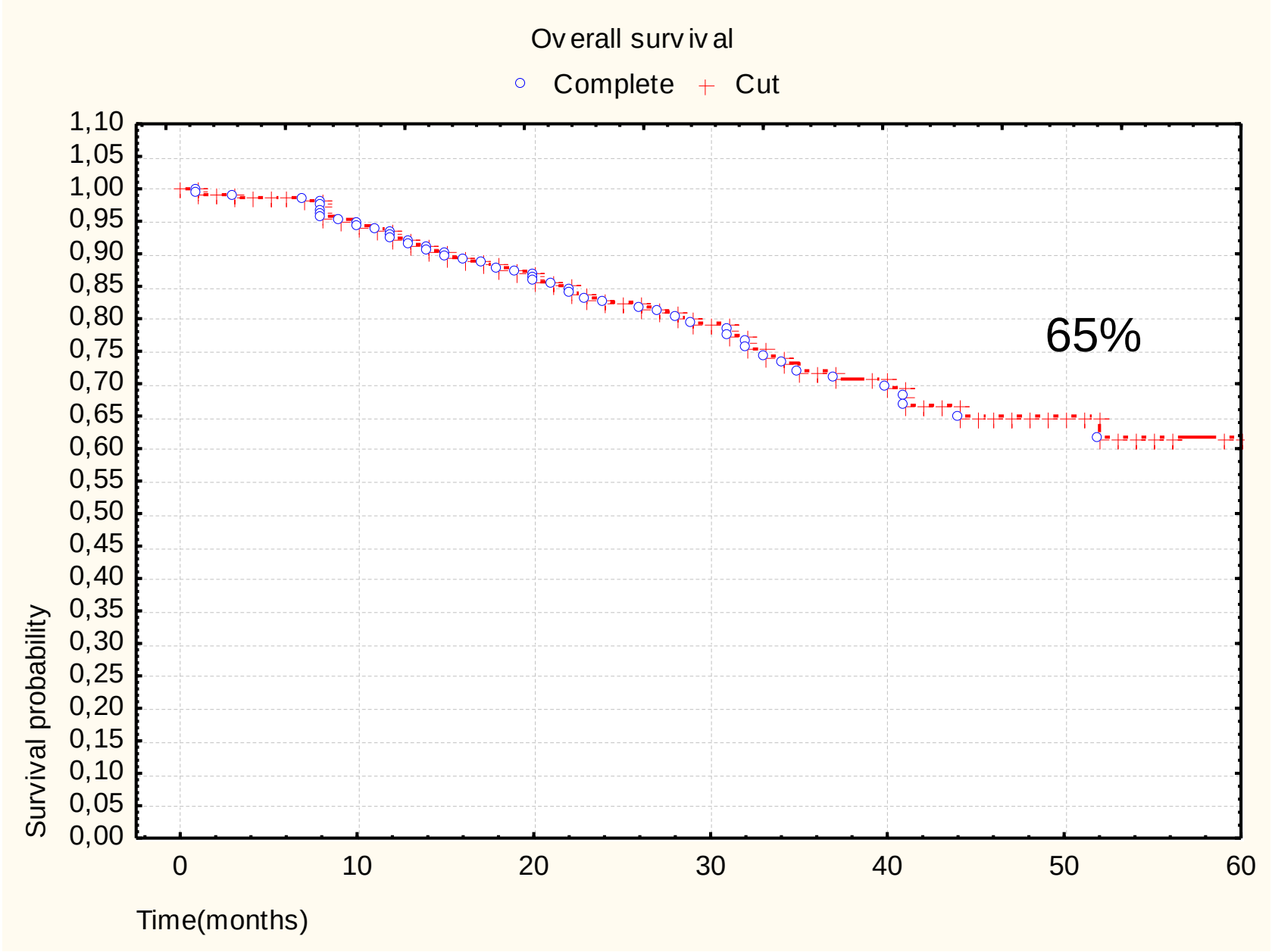
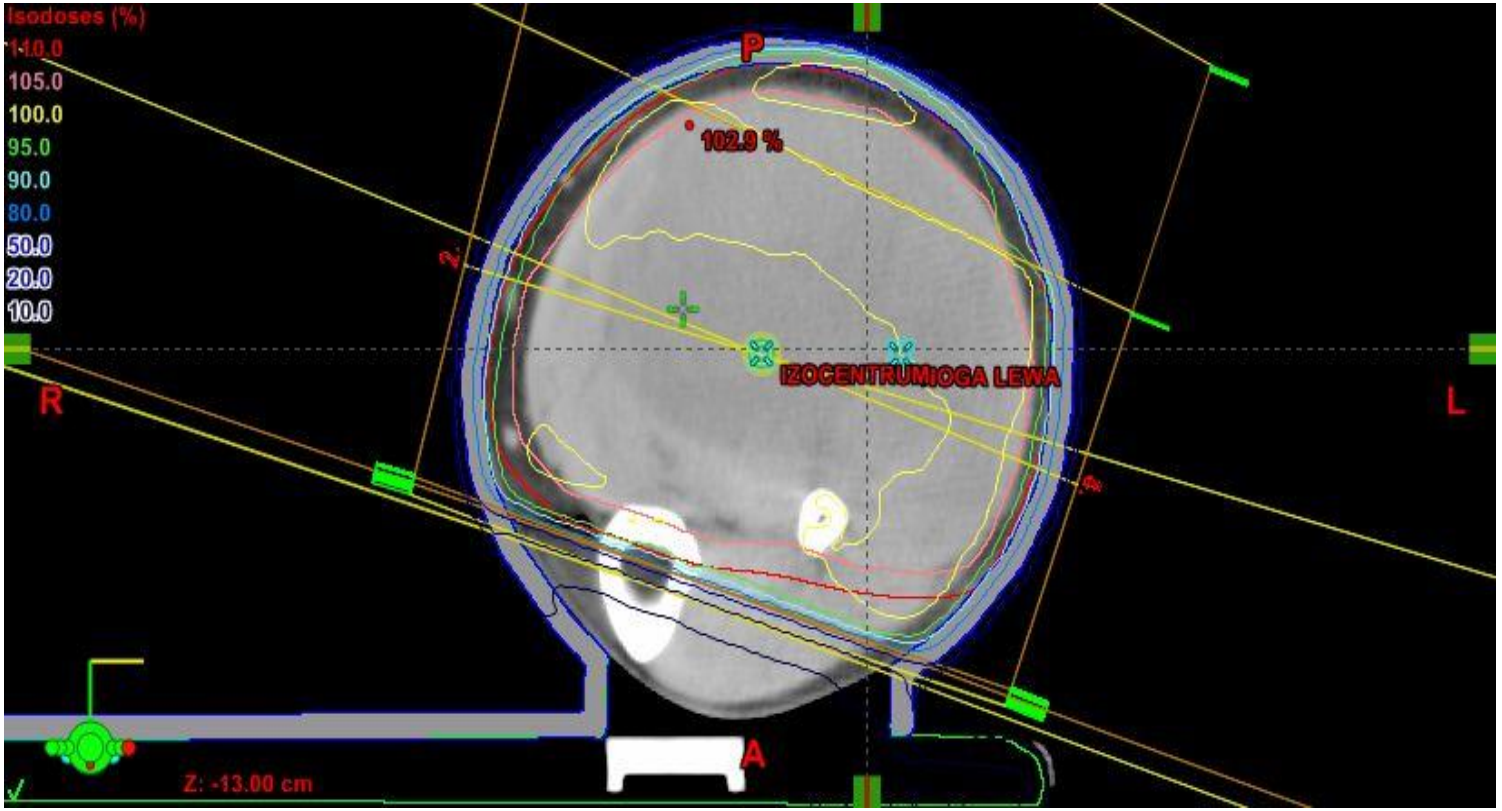


Fig. 1. Kaplan-Meier estimates comparing preoperative radiotherapy (preop RT) and postoperative radiotherapy (postop RT) for: (a) overall survival; (b) cause-specific survival; (c) local failure-free survival; (d) distant metastases-free survival.

Own data 2005-2010 OS (preop RTH)



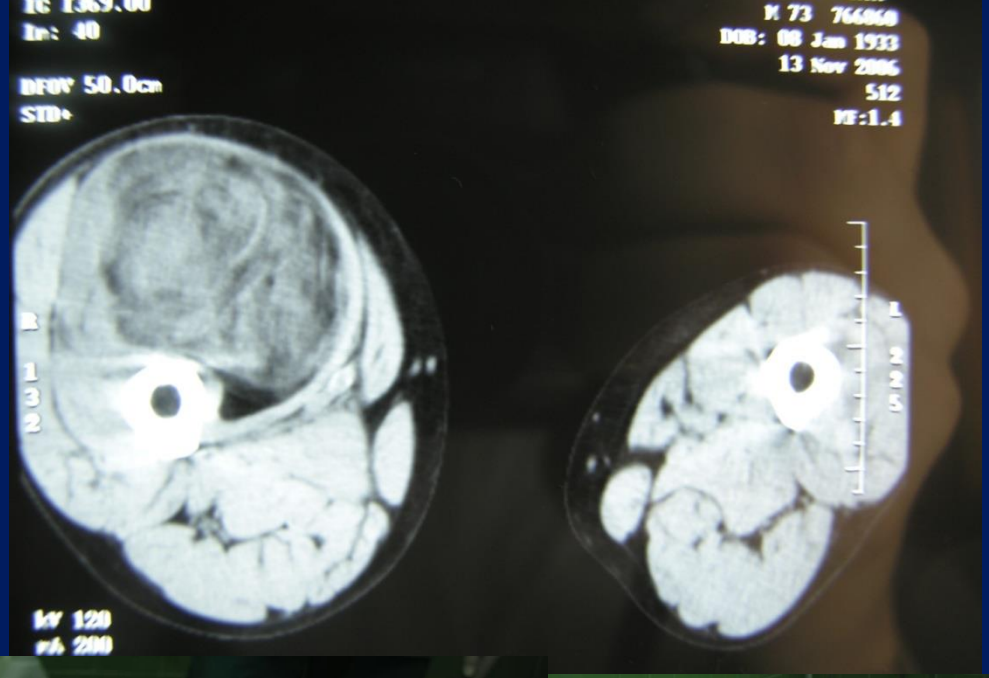

Isodoses (%)
110.0
105.0
100.0
95.0
90.0
80.0
50.0
20.0
10.0
P
102.9 %
IZOCENTRUM;OGA LEWA
R
L
A
Z: -13.00 cm

FACTOR (N)	ACUTE TREATMENT TOXICITY				LATE TREATMENT TOXICITY		
	ALL% (N) 32.4%(88)	Inflammation requiring oral antibiotics % (N) All 11.8% (32)	Wound dehiscence % (N) All11.8%(32)	Prolonged wound healing % (N) All 16.5% (45)	ALL %(N) 14.7%(40)	Prolonged edema % (N) All 9.2%(25)	Increased tissue fibrosis % (N) All 3.7%(10)
Anatomic site of primary tumour	**P= <0.002**	**P=0.021**	**P=0.072**	**P=0.001**	**P=0.154**	**P=0.428**	**P=0.074**
Trunk (37)	13.5%(5)	5.4% (2)	5.4%(2)	2.7%(1)	5.4% (2)	5.4% (2)	0
Upper extremity(44)	9.1%(4)	2.3% (1)	4.5% (2)	4.5%(2)	20.5%(9)	13.6% (6)	9.1%(4)
Lower extremity(191)	41.4%(79)	15.2%(29)	14.7%(28)	22%(42)	15.2%(29)	8.9%(17)	3.1%(6)
Neoadjuvant chemotherapy	**P <0.001**	**P=0.084**	**P=0.009**	**P=0.021**	**P=0.039**	**P=0.088**	**P=0.559**
Yes (61)	52.5%(32)	18% (11)	21.3%(13)	26.2%(16)	23% (14)	14.8% (9)	4.9%(3)
No(211)	26.5%(56)	10% (21)	9.0%(19)	13.7%(29)	12.3%(26)	7.6% (16)	3.3%(7)
Postoperative radiotherapy	**P=0.005**	**P=0.082**	**P=0.082**	**P=0.034**	**P <0.001**	**P=0.016**	**P<0.001**
Yes (21)	4.8%(1)	0	0	0	42.9%(9)	23.8%(5)	23.8%(5)
No(251)	34.7%(87)	12.7% (32)	12.7% (32)	17.9% (45)	12.4%(31)	8.0%(20)	2.0%(5)

EJSO 2014

Major series of preop RT

Study	Radiotherapy sequence	Patients number	Tumor grade	Local control rate	Overall survival	Wound complication rate		Surgery for treatment of the complications
						Early toxicity	Late toxicity	
5x5 Gy	preoperative radiotherapy	272	65% G3	81%	Estimated 5-years 60%	32.4%	12.4%	7%
O'Sullivan et al. 2002	preoperative radiotherapy	94	83% G2+G3	Not analyzed	3-years follow up 85%	35%	Approximately 50%[28]	16%
	postoperative radiotherapy	96	83% G2+G3			17%		5.3%
Pollack et al. 1998	preoperative radiotherapy	128	67%	82%	Not analyzed	25%	6%	Not analyzed
	postoperative radiotherapy	165	73%	81% p=0.07		6%		
Zagars et al. 2003	preoperative radiotherapy	271	74% G3	83%	Estimated 5-years 63%	Not analyzed	5%	1.5% (eight patients from the whole study group)
	postoperative radiotherapy	246	70% G3	72% P=0.491			9% P=0.03	
Hui et al[i]. 2006	preoperative radiotherapy	67	69% G3	93%	Estimated 5-years 73%	41%	7.4%	18%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STD+
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13 Nov 2006
512
WF:1.4
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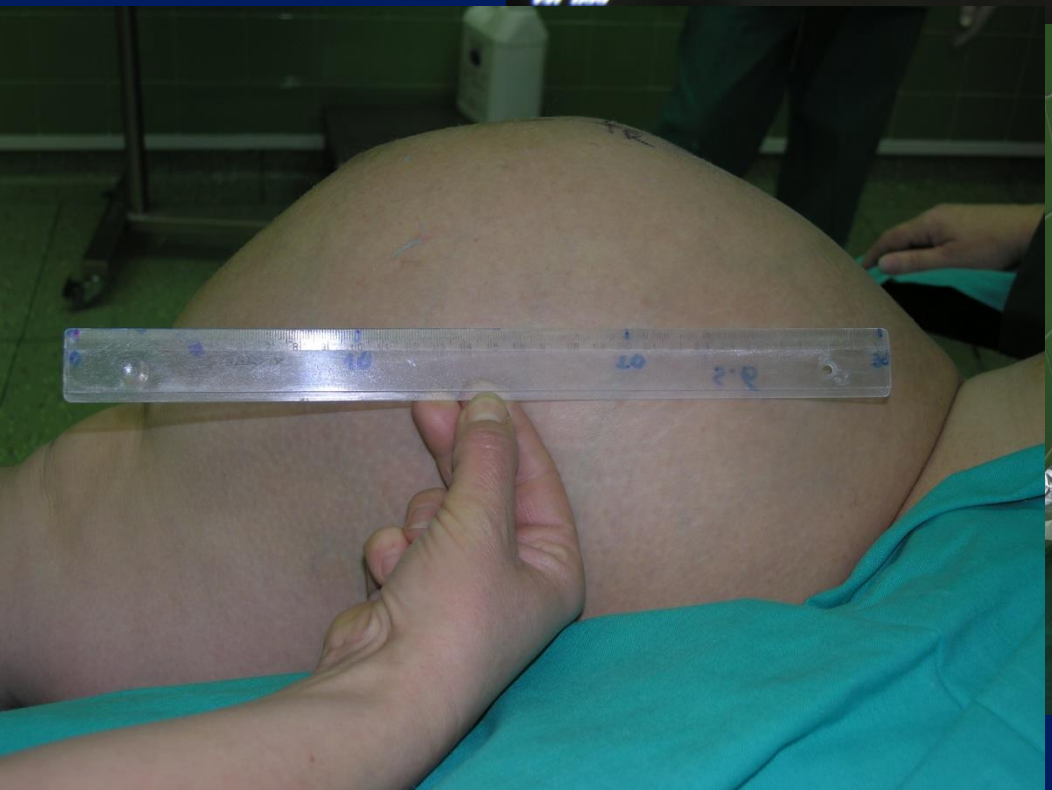
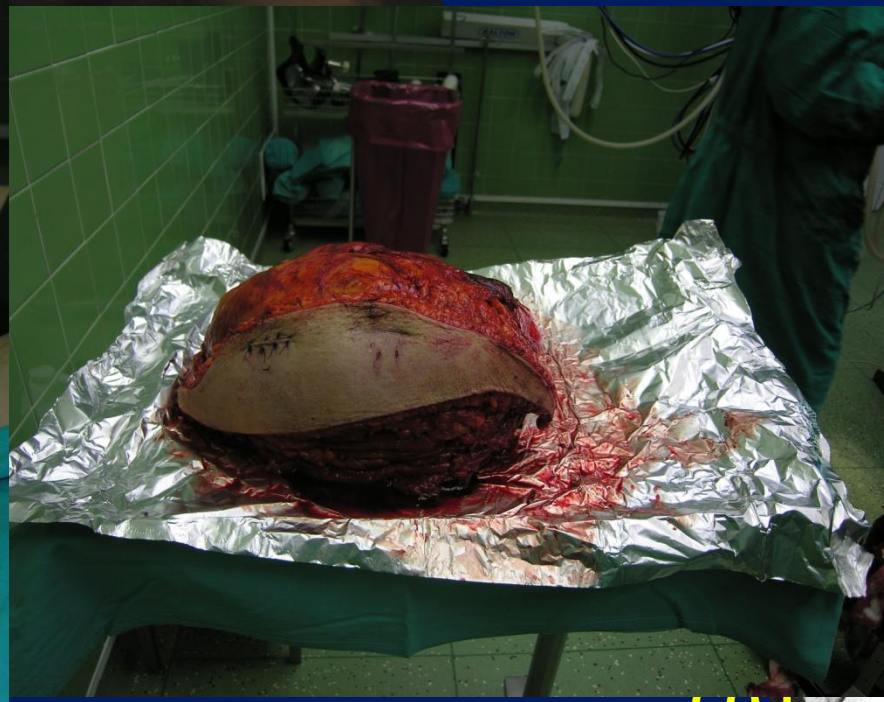
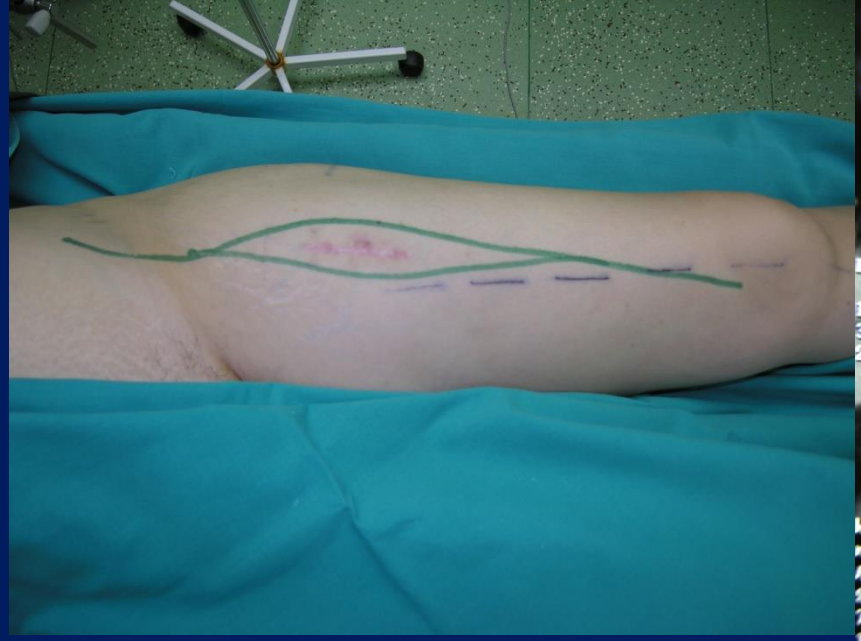
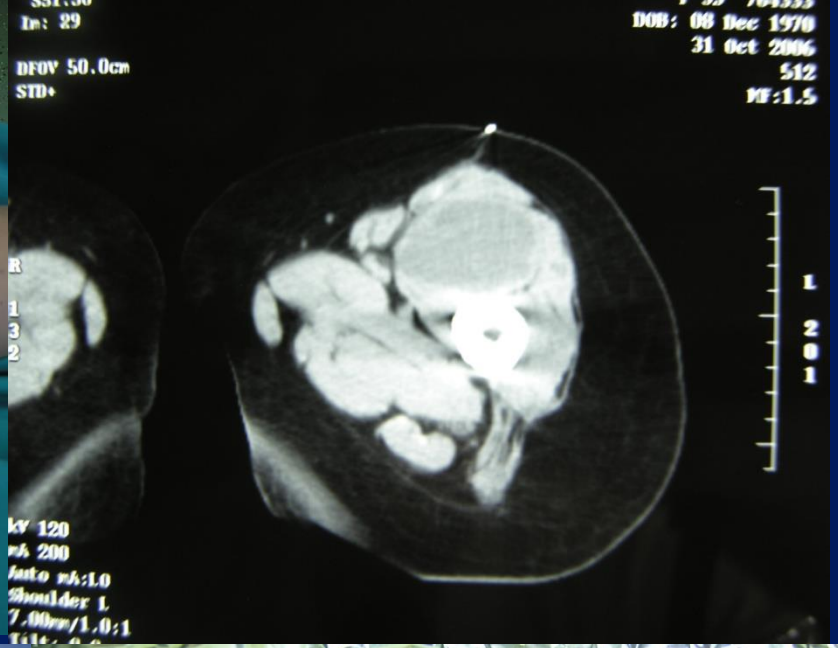
mA 280





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STD+
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31 Oct 2006
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2
L
2
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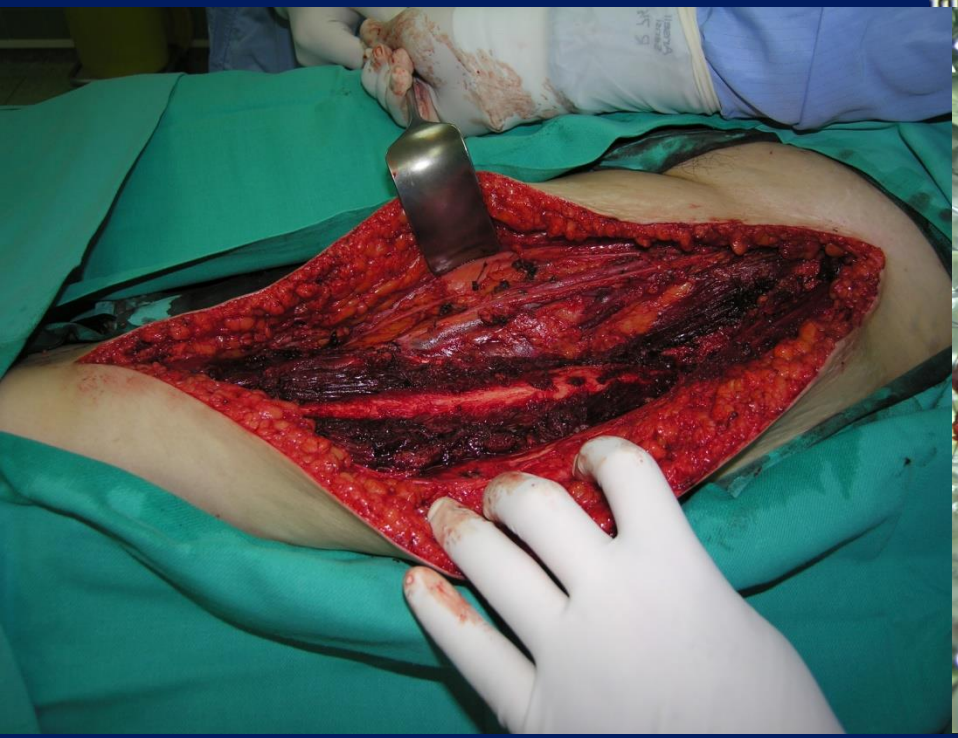
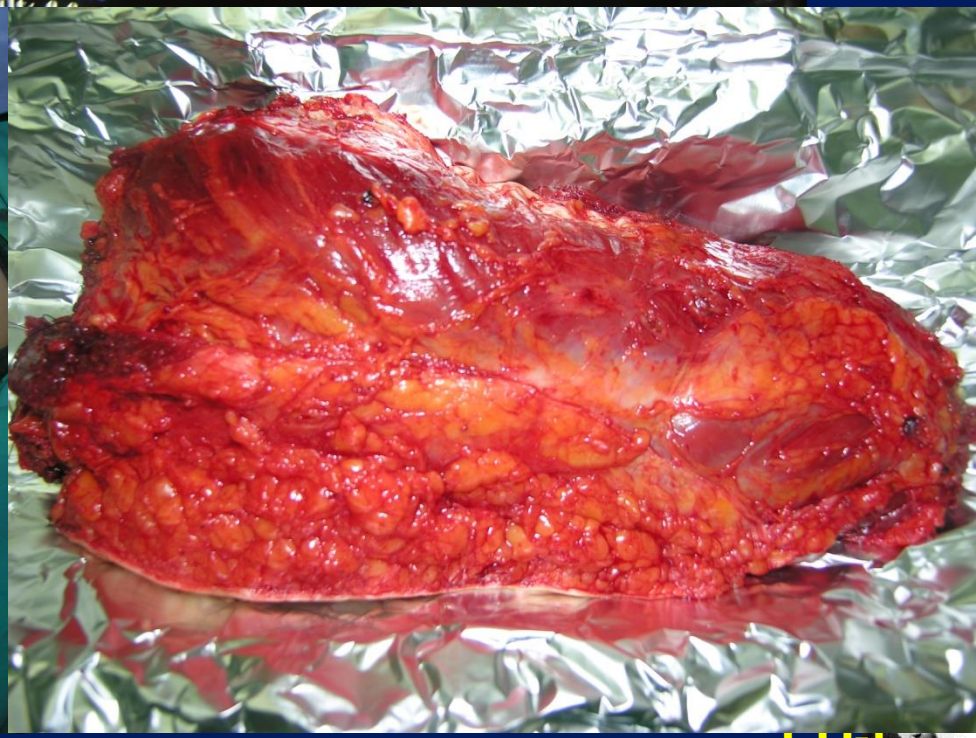
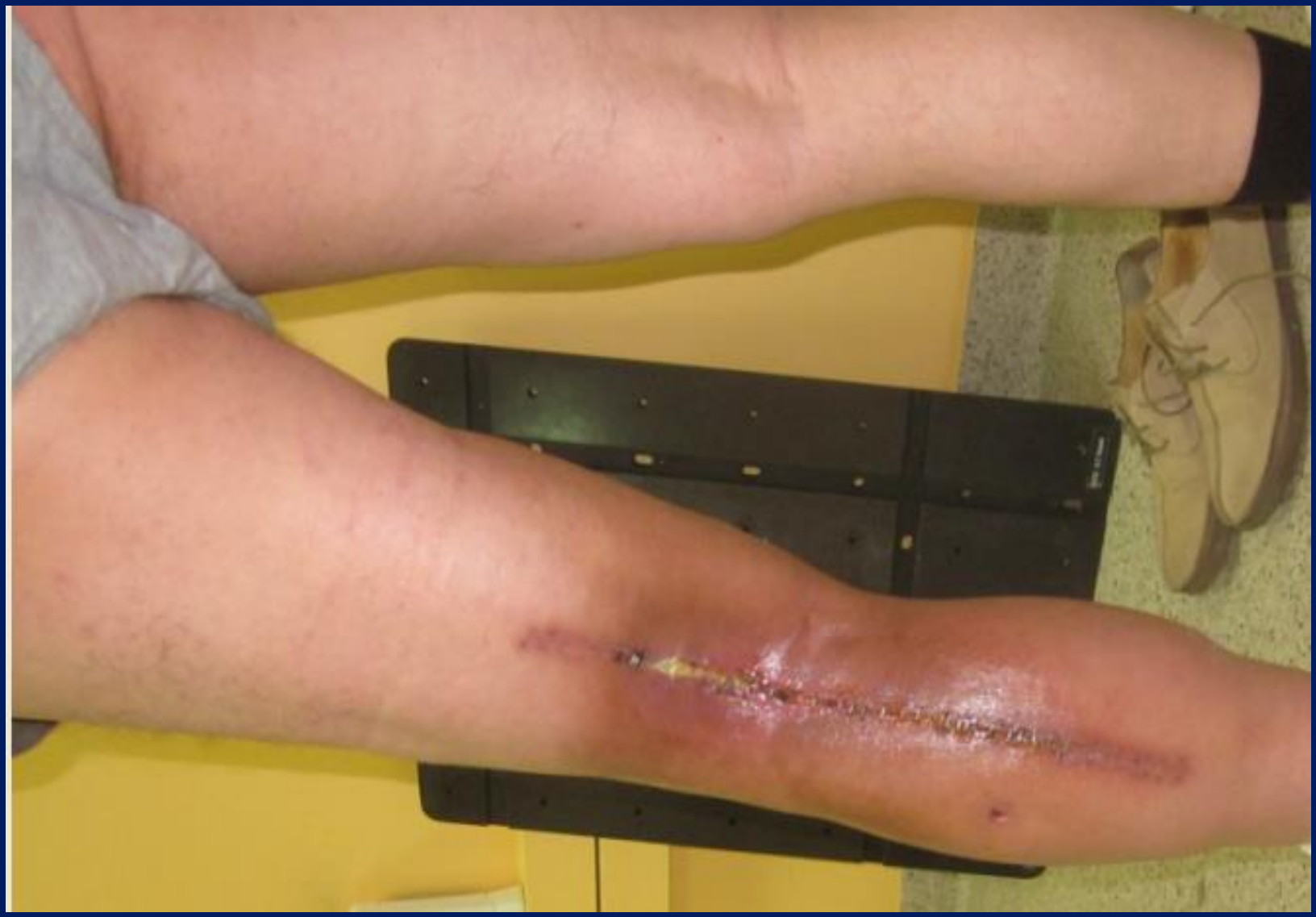
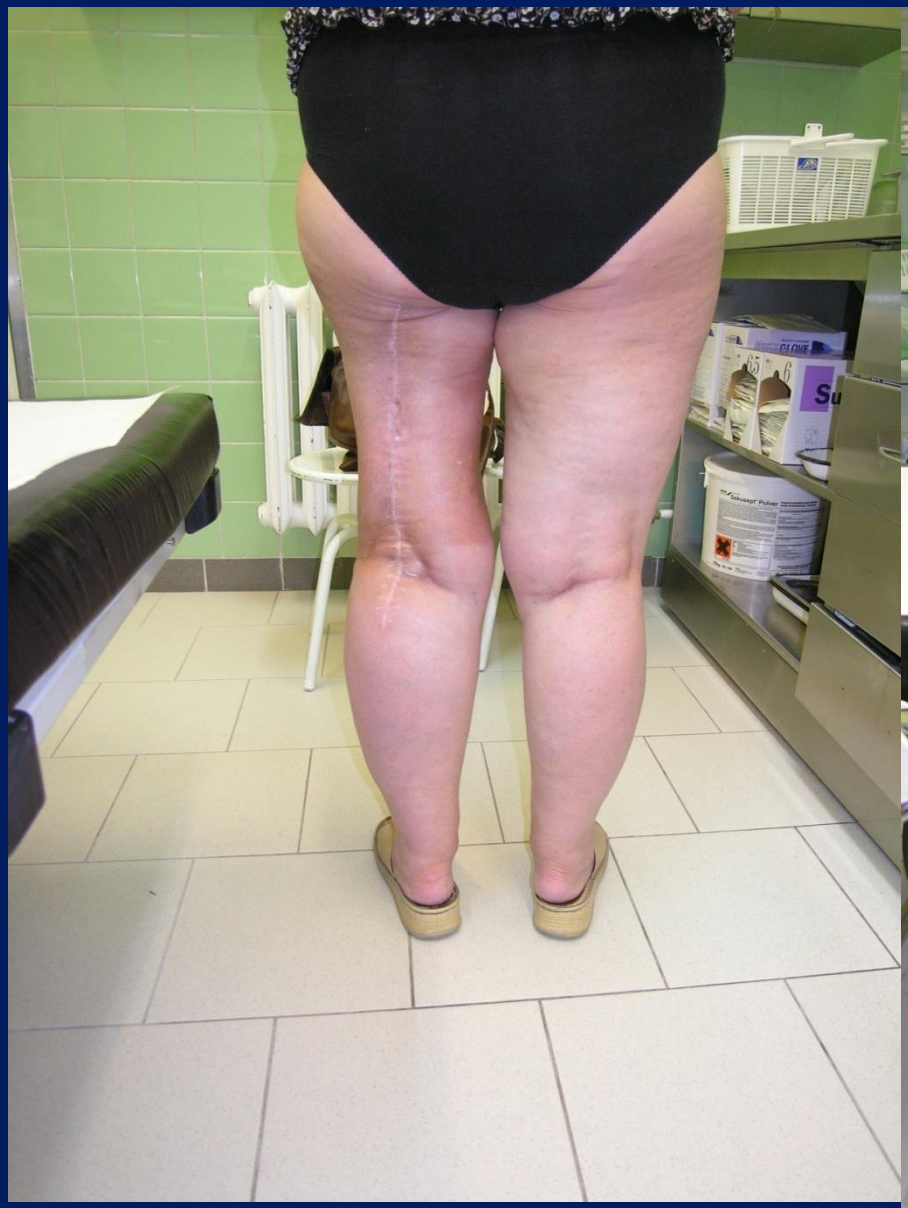
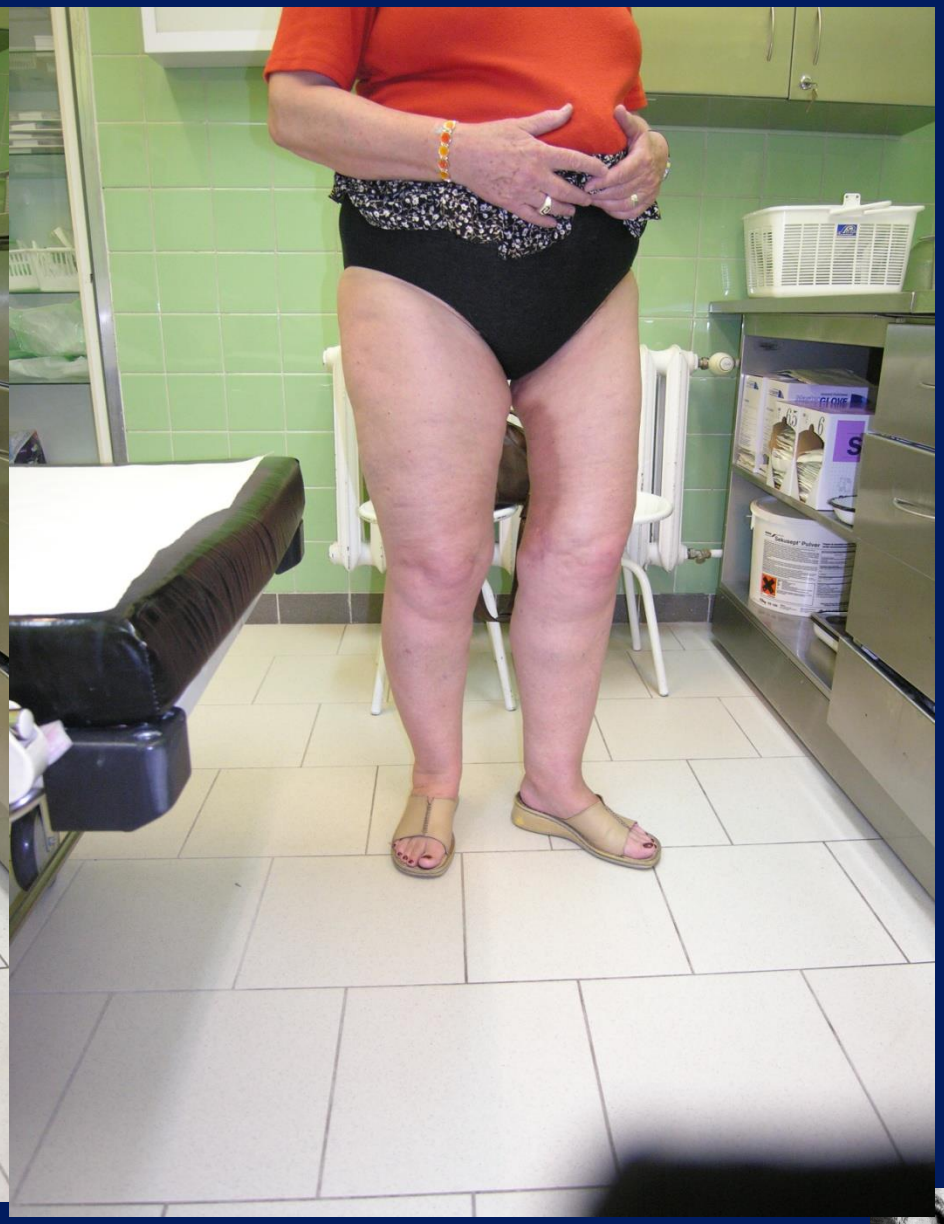
1
kV 120
mA 200
Shoulder L

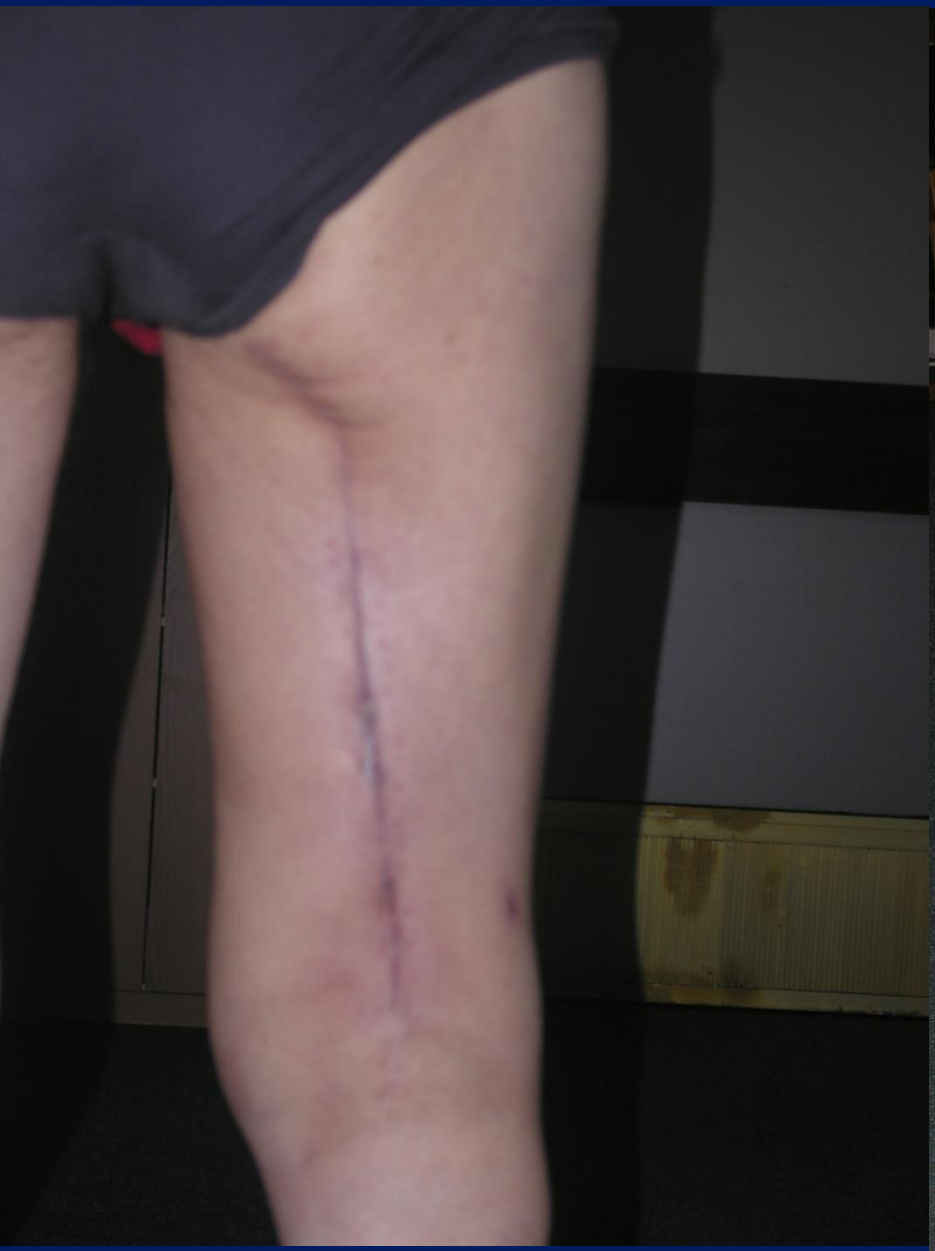


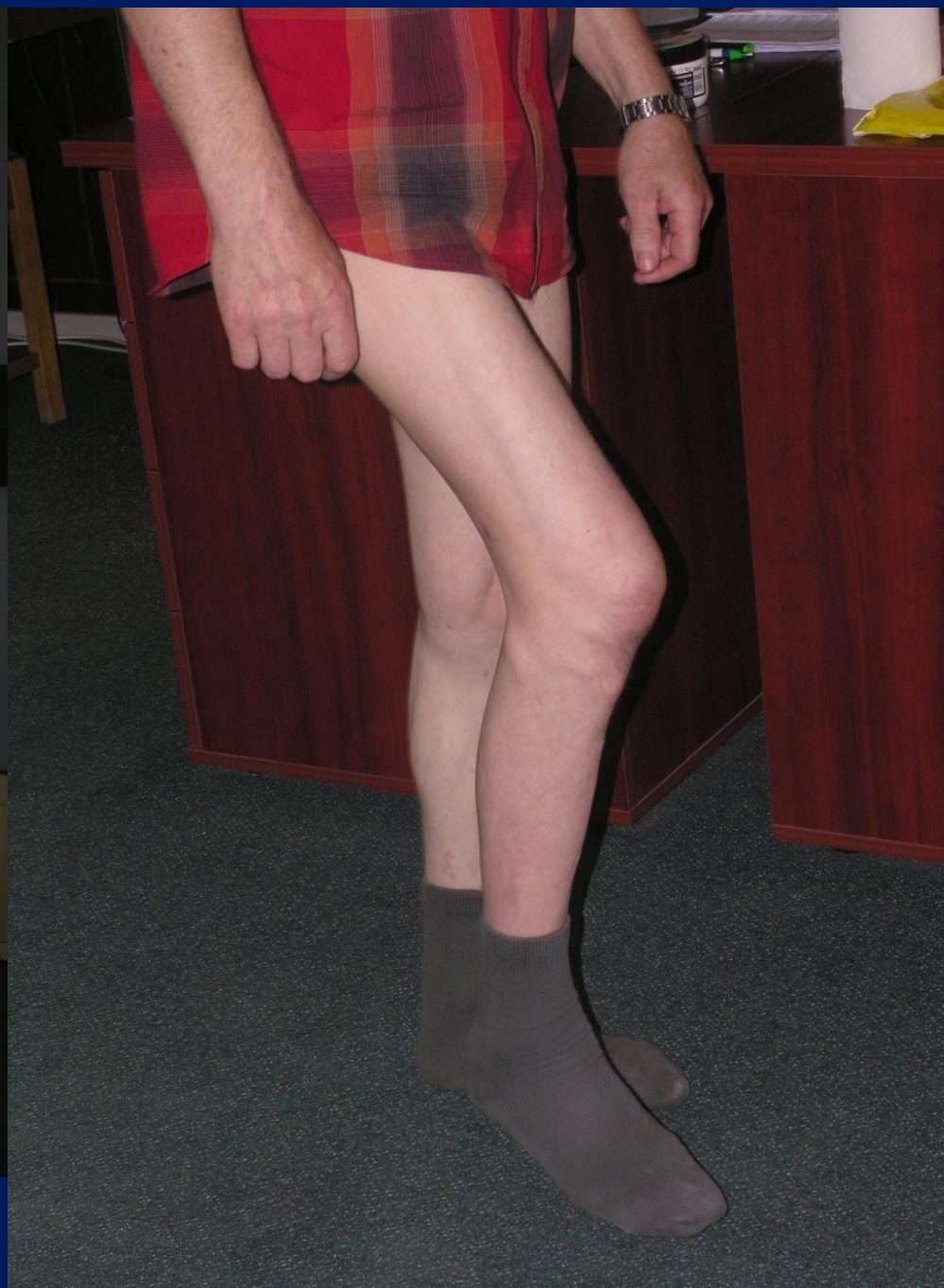












Synovial sarcoma – multimodal therapy

Preoperative chemo- and radiotherapy in *synovial sarcoma*. A phase II study - Cancer Center-Institute, Warsaw

Dates of accrual: - February 1996 - ongoing
Patients #: - > 100

Results: - 5-year OS 71%,

Conclusion: the very aggressive treatment schedule is manageable

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Dane pacjenta:

Schemat postępowania
u chorych na SARCOMA SYNOVIALE leczonych w sposób skojarzony
Klinika Nowotworów Tkanek Miękkich i Kości, Centrum Onkologii – Instytut Warszawa

Wypełnia pierwszy lekarz prowadzący (badacz): ……

imię i nazwisko

Tydzień leczenia	POSTĘPOWANIE	Data planowana	Data wykonania
0	BIOPSJA, BADANIA (1,2,3,4,5)		
1	CHTH **1-szy kurs**: HD-IFO 1,7g/m^2 7 dni		
2			
3	Badania (1, 4)		
4	CHTH **2-gi kurs**: HD-IFO 1,7g/m^2 7 dni		
5			
6	Badania (4, 5)		
7	**Radioterapia** przedoperacyjna: 5 dni po 500cGy		
8	**OPERACJA**		
9			
10	Badania (1, 4)		
11	CHTH **1-szy kurs poop**: ADM 60mg/m^2; DDP 30mg/m^2 3 dni		
12			
13	Badania (4, 5)		
14	CHTH 2-**gi kurs poop**: HD-IFO 1,7g/m^2 7dni		
15			
16	Badania (1, 4)		
17	CHTH **3-ci kurs poop**: HD–IFO 1,7g/m^2 7dni		
18			
19	Badania (4)		
20	CHTH **4-ty kurs poop**: ADM 60mg/m^2; DDP 30mg/m^2 3 dni		

Chory przechodzi do kontroli ambulatoryjnej w gabinecie chemioterapii.

Badania:
1. RTG klatki piersiowej
2. RTG okolicy objętej chorobą
3. TK i/lub RM okolicy objętej chorobą
4. Badania laboratoryjne
5. Ew. badania dodatkowe (np. na cytokiny)

Prowadzenie chorego: chirurg – od 1 do 10 tyg. (+informacja chorego, decyzja o rodzaju operacji);
chemioterapeuta - od 11 do 20 tyg.

Treatment schedule

Induction neoadjuvant therapy

IFO 1,7g/m^2/d 7 days 2x (3 weeks)

RTH 5 x 5 Gy

(3 - 4 days) **Surgery**

(3 weeks)

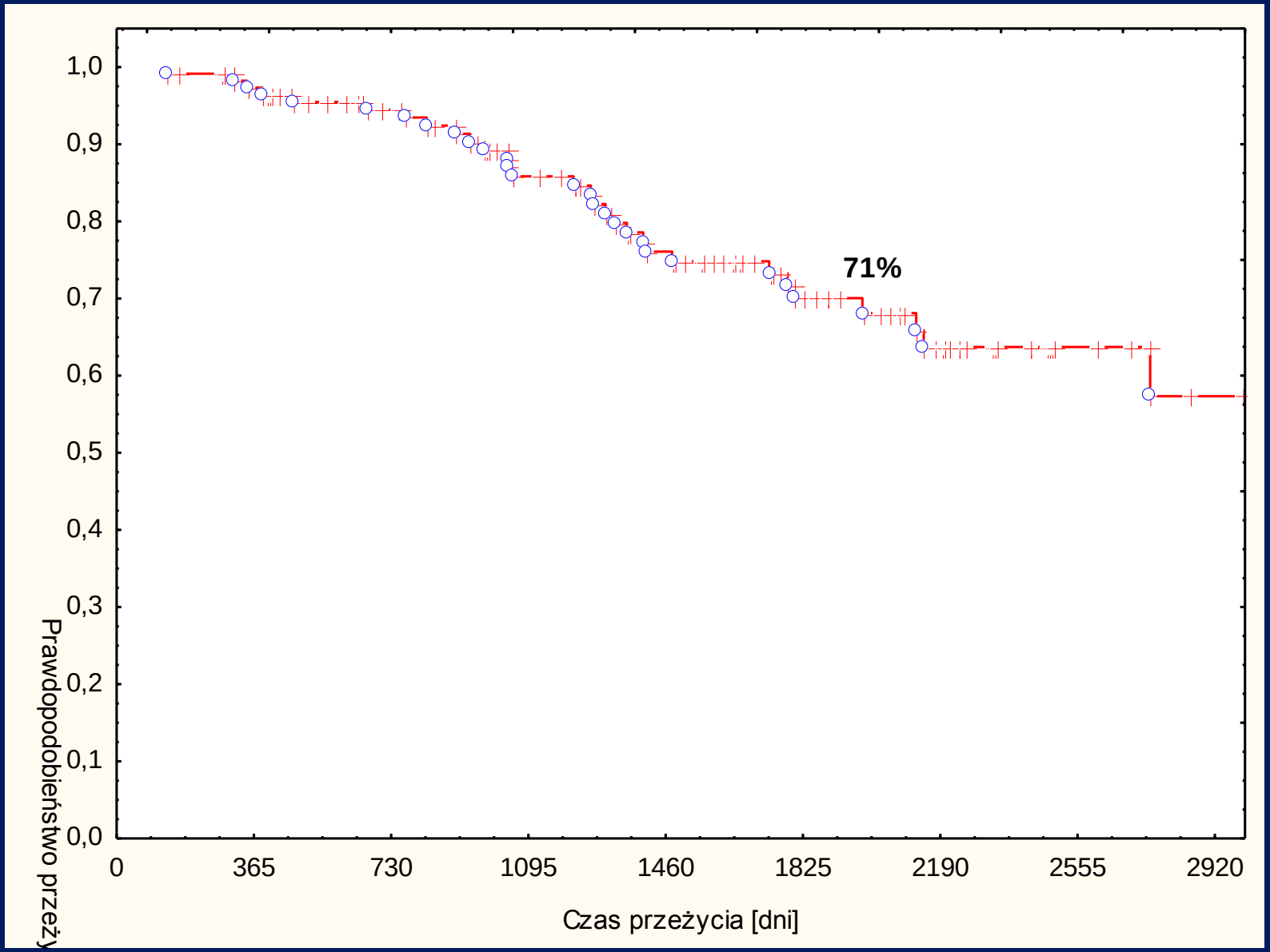
Adjuvant therapy

DOX 60mg/m^2 + DDP 120mg/m^2

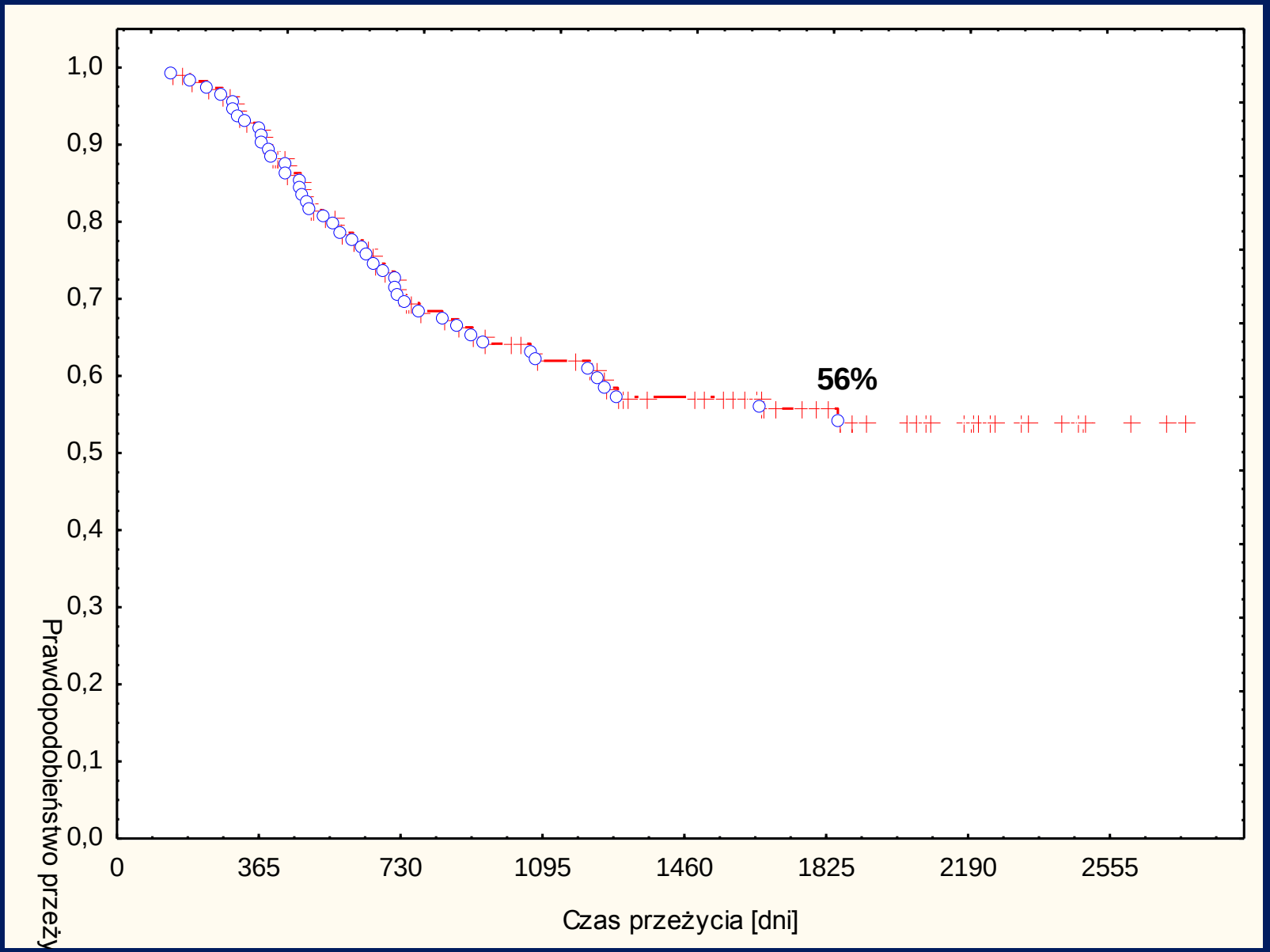
IFO 1,7g/m^2/d 7 days 2x (3 tweeks)

DOX 60mg/m^2 + DDP 120mg/m^2

Overall survival



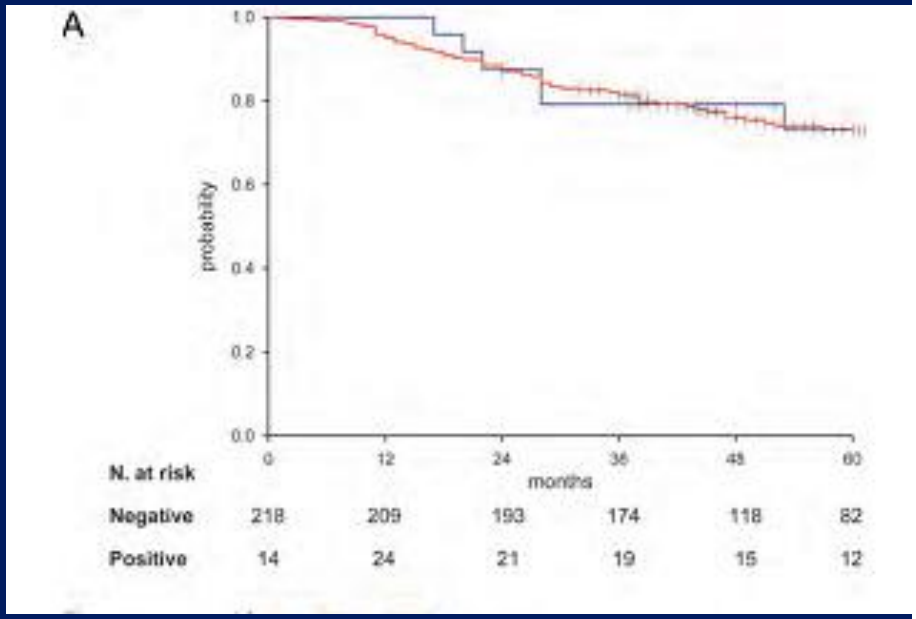
Disease-free survival (DFS) – median 71 months



Quality of surgery and neoadjuvant combined therapy in the ISG-GEIS trial on soft tissue sarcomas of limbs and trunk wall

Annals of Oncology 24: 817–823, 2013

A. Gronchi[1*], P. Verderio[2], A. De Paoli[3], A. Ferraro[4], O. Tendero[5], J. Majò[6], J. Martin[5], A. Comandone[7], G. Grignani[8], S. Pizzamiglio[2], V. Quagliuolo[9], P. Picci[10], S. Frustaci[11], A. P. Dei Tos[12], E. Palassini[13], S. Stacchiotti[13], S. Ferrari[14], M. Fiore[2] & P. G. Casali[13]



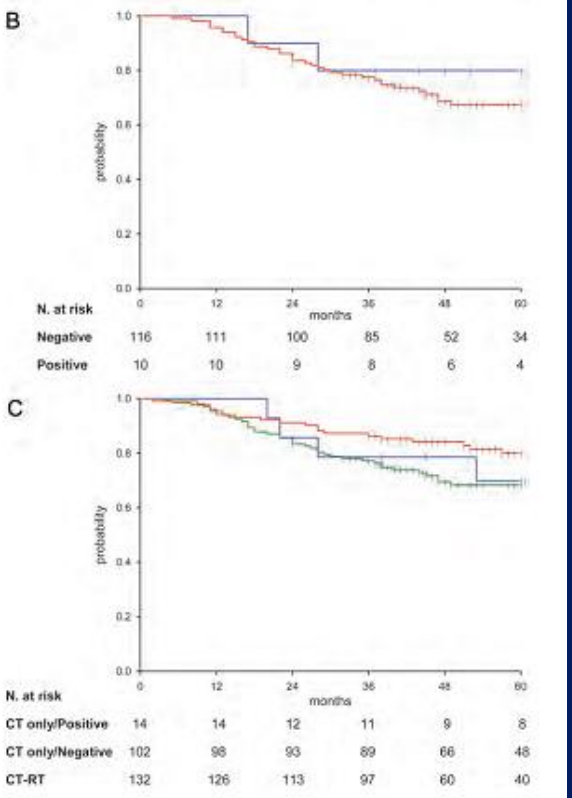


Figure 1. Five-year probability of overall survival (OS) from surgery in the whole series (A) and in patients treated with preoperative concurrent CT–RT (B) according to negative (red lines) and positive (blue lines) microscopic margin status. Five-year probability of OS from surgery in the whole series according to the variable 'treatment/microscopic margin status' categorized as 'preoperative CT only/negative margin' (red lines), 'preoperative CT only/positive margin' (blue lines) and 'preoperative CT–RT' (green lines) (C).

CO-I
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Isolated limb perfusion

Treatment and outcome data for all patients undergoing regional therapy for advanced extremity soft tissue sarcoma

Investigator	Year	N	Modality	Chemo in Perfusate	Median Follow-up (mo)	ORR (%)	CR/PR/SD (%)	Limb Preservation (%)
Eggermont et al[9]	1996	186	HILP	TNF-α IFN-γ (N = 55) Melphalan	22	82	29/53/18	82
Eggermont et al[43]	1996	55	HILP	TNF-α IFN-γ Melphalan	26	87	36/51/13	84
Gutman et al[10]	1997	35	HILP	TNF-α Melphalan	14	91	37/54/8.5	85
Olieman et al[11]	1998	34	HILP	TNF-α IFN-γ Melphalan	34	94	35/59/6	85
Lejeune et al[25]	2000	22	HILP	TNF-α IFN-γ (N = 4) Melphalan	18.7	82	18/64/18	86
Noorda et al[26]	2003	49	HILP	TNF-α, IFN-γ (N = 4) Melphalan	26	63	8/55/35	57
Rossi et al[53]	2005	21	HILP	TNF-α Doxorubicin	30	62	5/57/38	71
Grunhagen et al[8]	2005	53	HILP	TNF-α Melphalan	22	88	42/45/13	82
Bonvalot et al[44]	2005	100	HILP	TNF-α Melphalan	24	65	36/29/35	87
Lans et al[53]	2005	26	HILP	TNF-α Melphalan	22	70	20/50/30	65
Grunhagen et al[14]	2006	197	HILP	TNF-α Melphalan	22	75	26/49/25	87
Hegazy et al[6]	2007	40	ILI	Doxorubicin	15	85	—/85/—	83
Moncrieff et al[29]	2008	21	ILI	Melphalan Actin D	28	90	57/33/10	76
Turaga et al[17]	2011	12	ILI	Melphalan Actin D	8.6	78	14/64/—	78

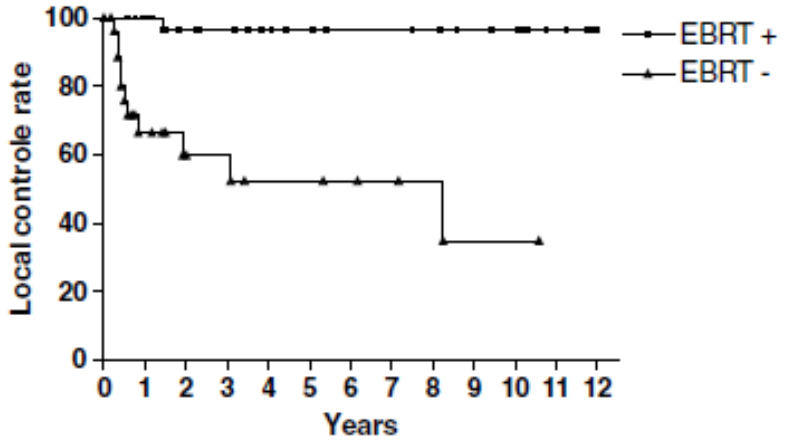
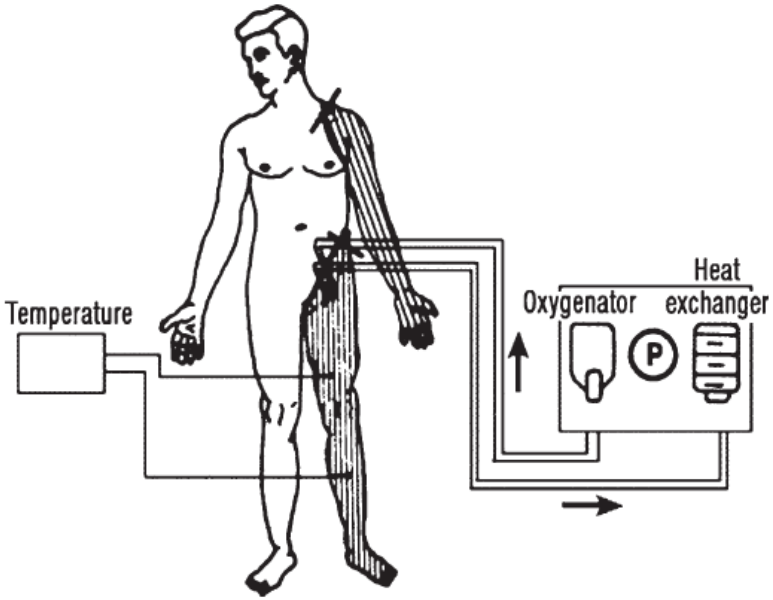
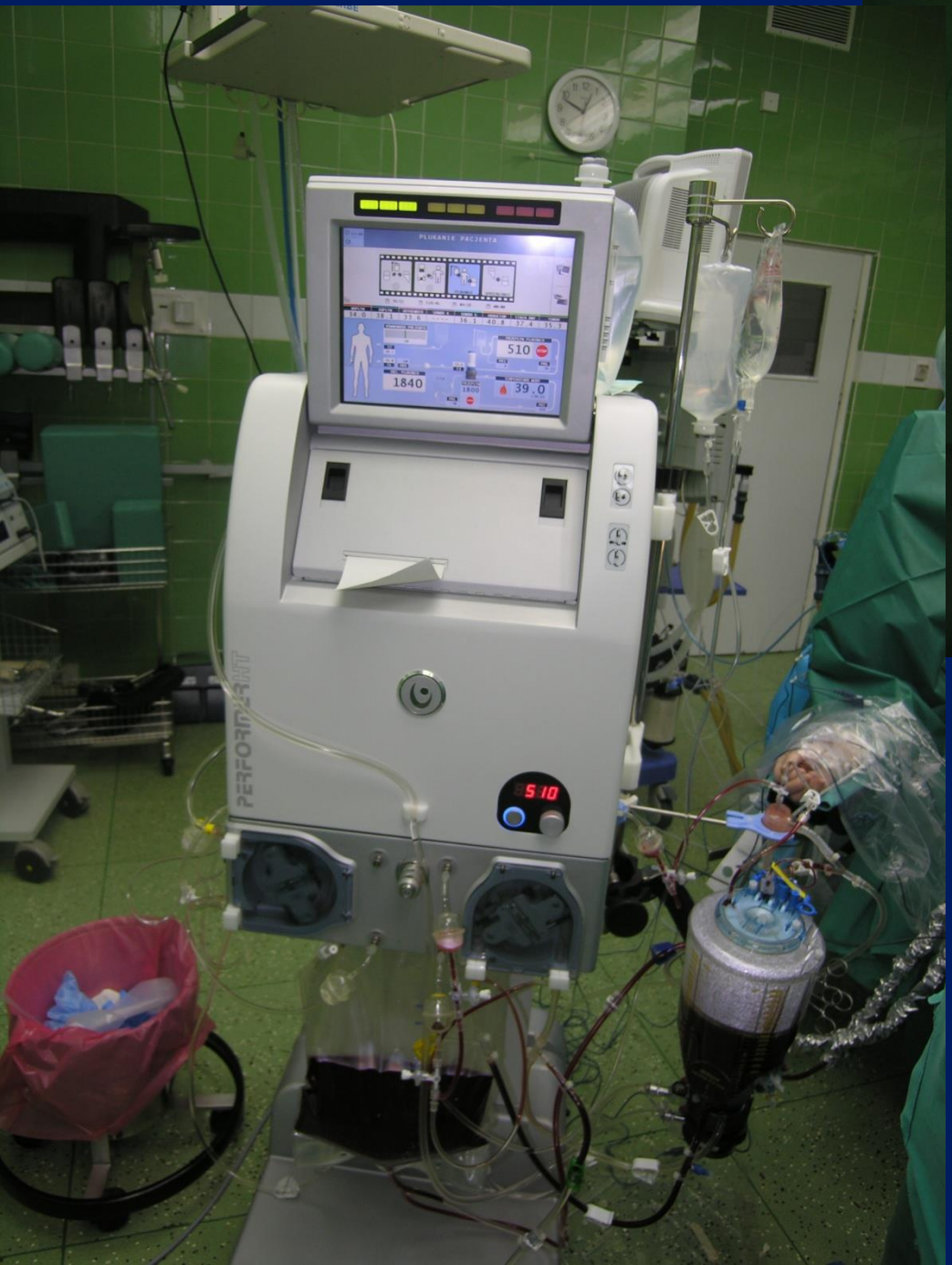
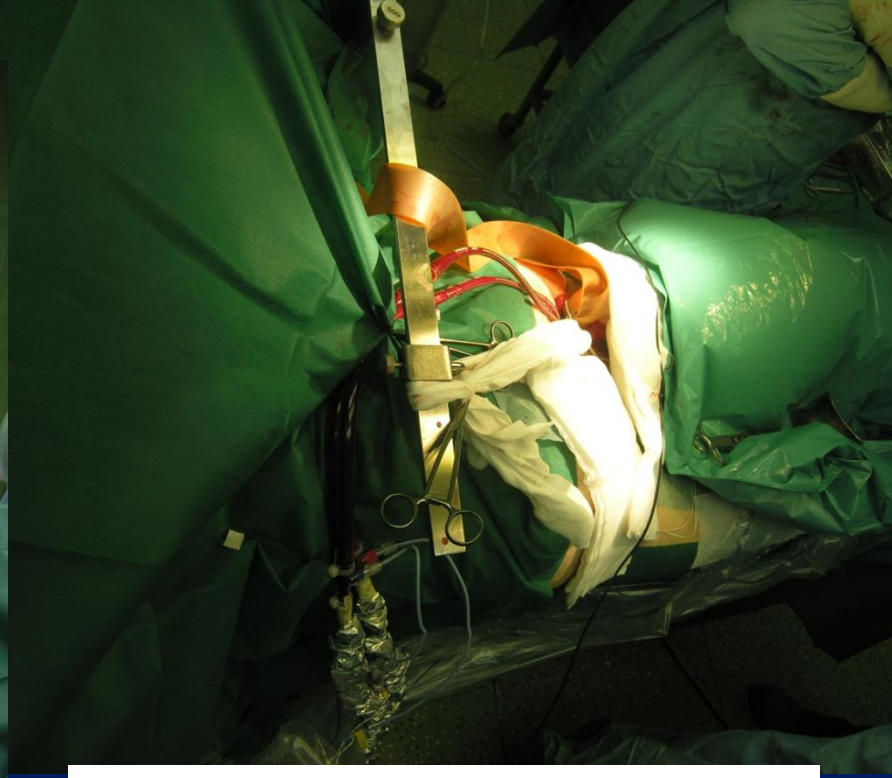


FIG. 2. Local tumor control rate in all patients: the 5-year local control rate in the external beam radiotherapy $(EBRT)^+$ group (n = 37) was 96.5% ± 3.5% vs. 52% ± 23% in the $EBRT^-$ group (n = 20; $P < .0001$). *Ann. Surg. Oncol. Vol. 13, No. 4, 2006*







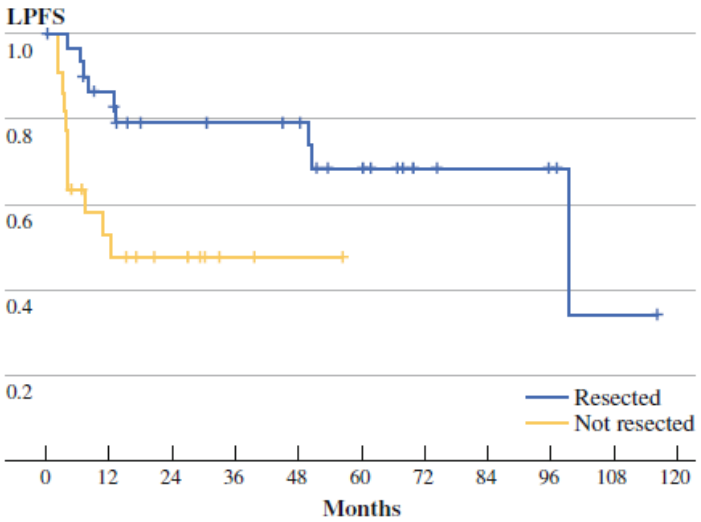
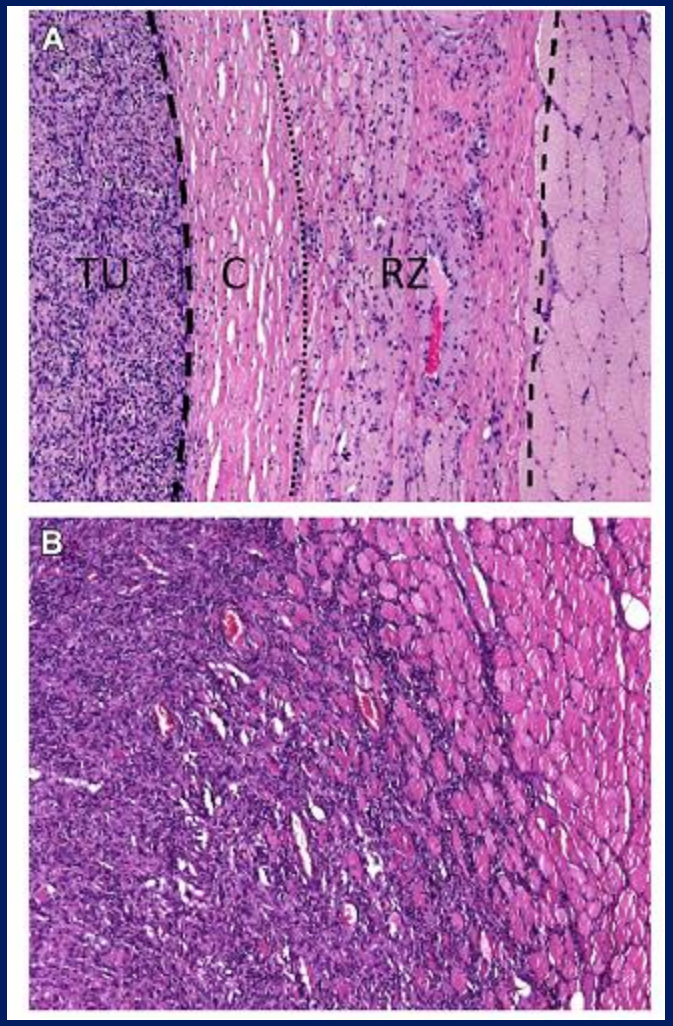


FIG. 3 LPFS for resected ($n = 30$) or nonresected ($n = 24$) STS with a statistically significant difference (median time 99 months vs. 12 months, $P = 0.01$ by log rank test)

Neoadjuvant treatment improves capsular integrity and the width of the fibrous capsule of high-grade soft-tissue sarcomas

EJSO 39 (2013) 61–67

F. Grabellus [a,*], L.E. Podleska [b], S.-Y. Sheu [a], S. Bauer [c], C. Pöttgen [d], C. Kloeters [e], M. Hoiczyk [c], T.C. Lauenstein [e], K.W. Schmid [a], G. Taeger [b]



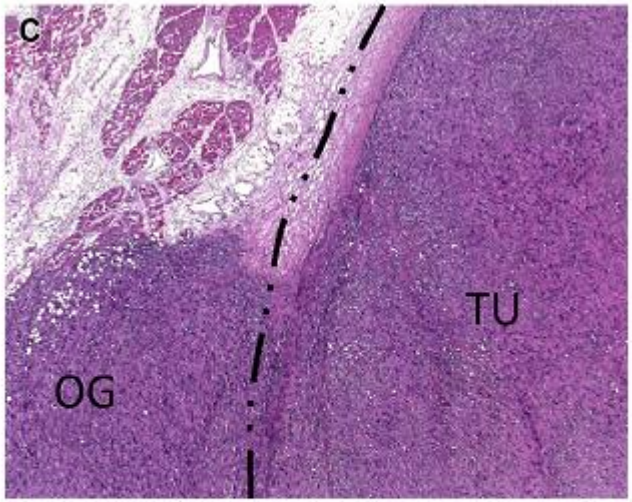


Figure 1. A. Composition of a typical soft-tissue sarcoma margin. TU, tumor; C, fibrous capsule; RZ, reactive zone. B. Histopathology of an untreated sarcoma with diffuse growth into adjacent muscle tissue. C. Histopathology of a neoadjuvant-treated sarcoma with "capsular overgrowth". Remnants of the capsule are seen along the lower portion of the dotted line. TU, tumor; OG, overgrowing part of tumor.

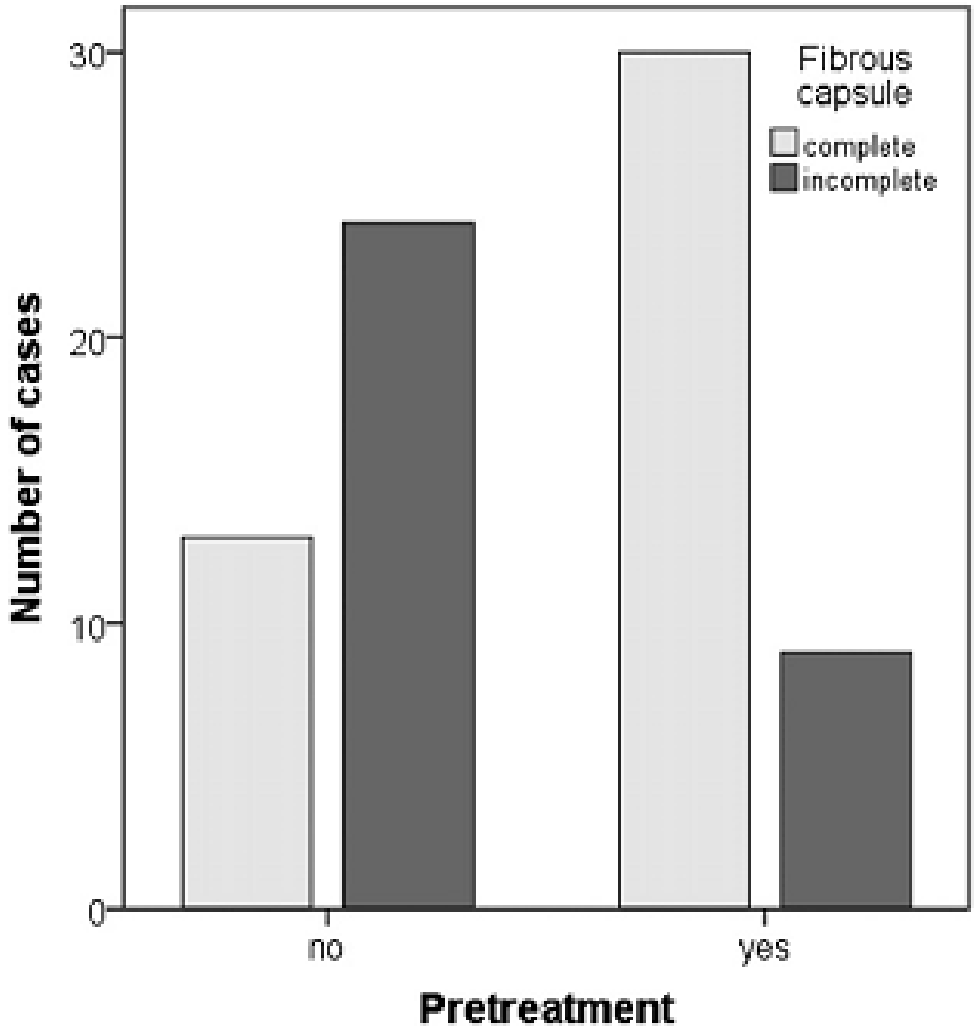
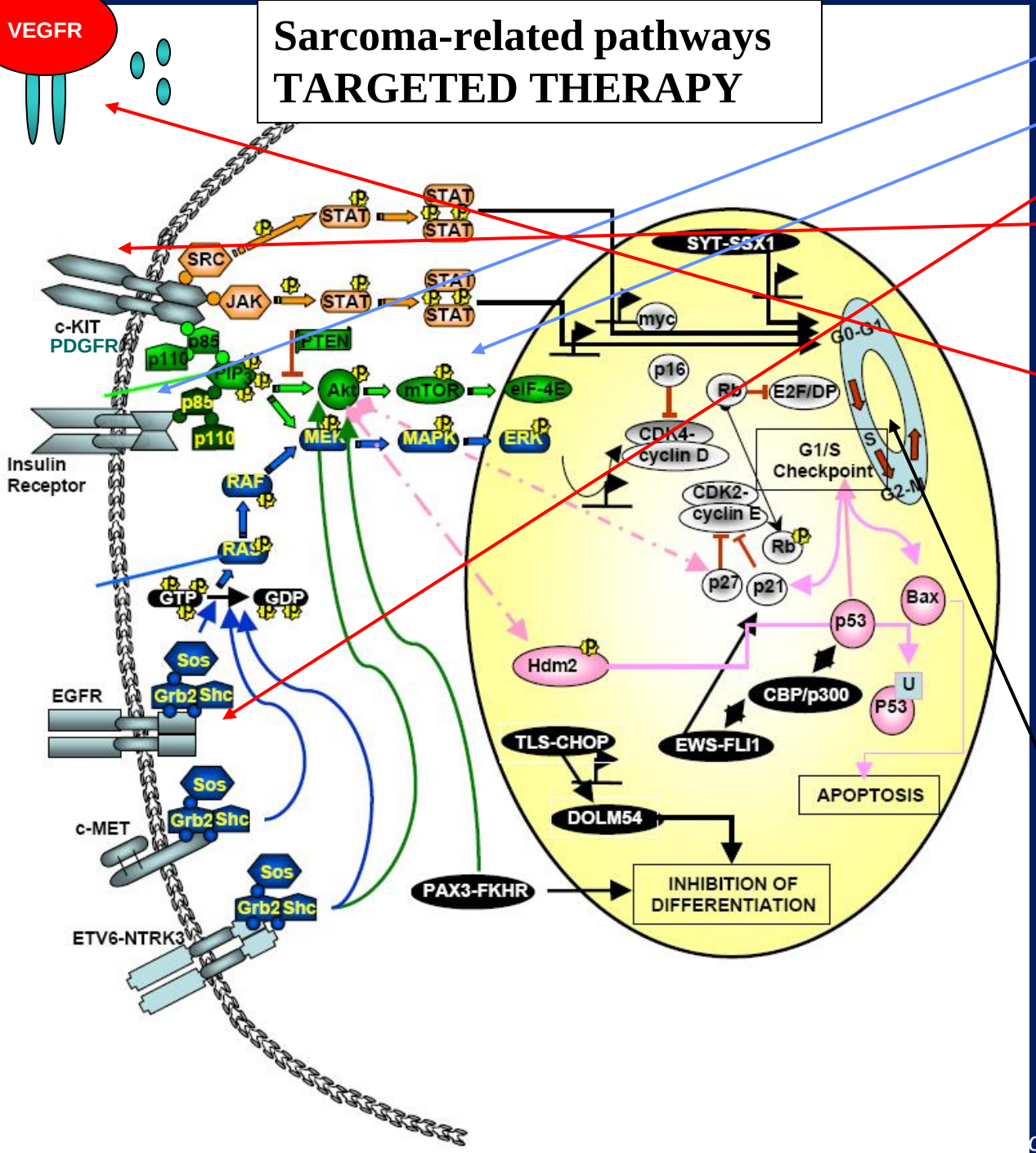


Figure 3. Capsular integrity of tumors (untreated; 35.1%, after pretreatment; 76.9%).

Sarcoma-related pathways
TARGETED THERAPY



- Pathway IGFR-AKT-mTOR
- Pathway EGFR
- Pathway PDGFR
- Pathway MET
- Pathway RB, p53
- **Angiogenesis pathway**
- Fusion proteins
- Heat shock proteins (Hsp)
- Hedgehog Pathway
- Pathway wingless/β-Catenin
- RANKL
- Receptors PPAR
- DNA (minor groove of the spiral)

omagenesis, Hematol Oncol Clin N Am 2005

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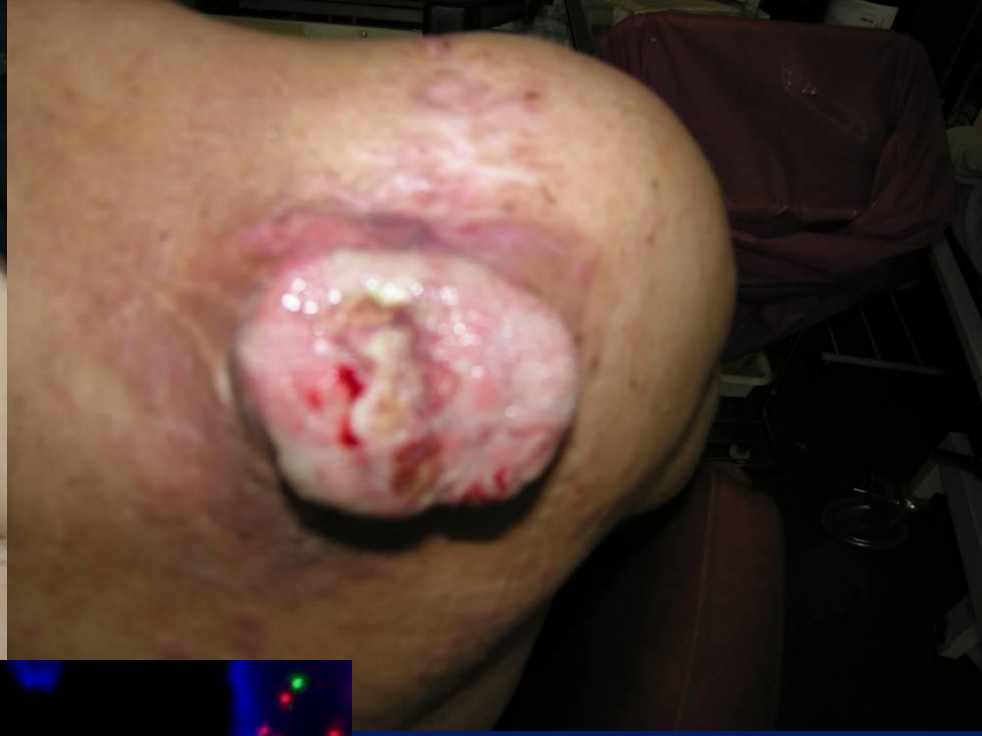
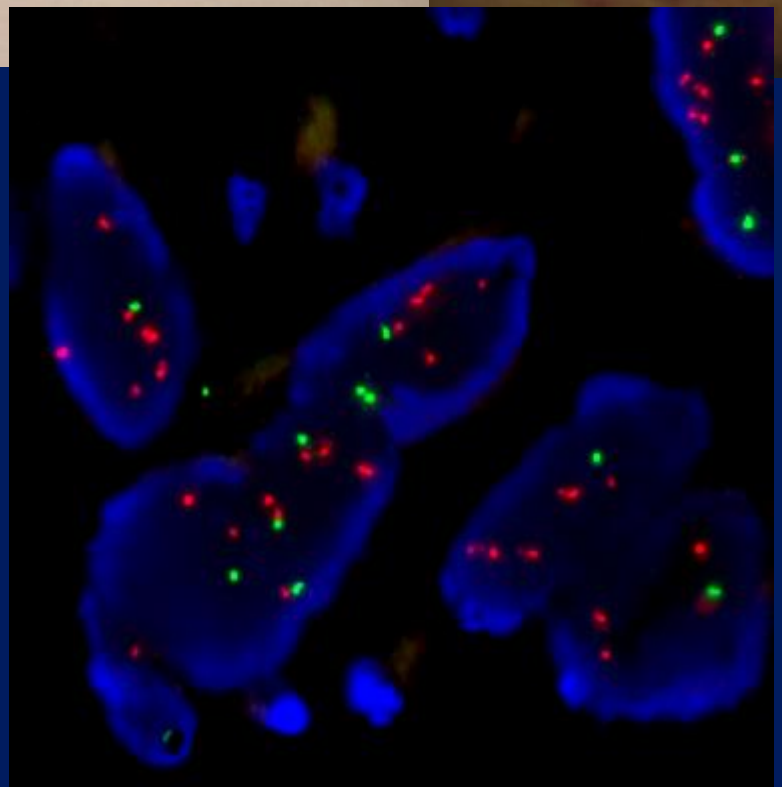
Targeted therapy in STS

Sarcoma type	Drug	Molecular target
Registered indications		
GIST	imatinib	KIT, PDGFRA
GIST	sunitinib	KIT, PDGFR, VEGFR
GIST	regorafenib	KIT, PDGFRA, VEGFR
DFSP	imatinib	PDGFRB
Myxoid/round-cell liposarcoma, leiomyosarcoma	trabectedin	?
STS after previous systemic therapy	pazopanib	neoangiogenesis
Activity of the drugs seen		
Angiosarcoma, hemangioendothelioma, alveolar soft-part sarcoma	sunitinib, sorafenib, bevacizumab, pazopanib, cediranib	VEGFR
Pigmented villo-nodular synovitis	imatinib	CSF1
PEC-oma, rhabdomyosarcoma	mTOR inhibitors	mTOR
Ewing sarcoma, rhabdomyosarcoma	anti-IGFR	IGFRR1
GIST	sorafenib, dasatinib, nilotinib,ponatinib	KIT, PDGFR, VEGFR
ASPS, CCS	ARQ197	Met
Aggressive Fibromatosis	Imatinib	

Targeted therapy in STS

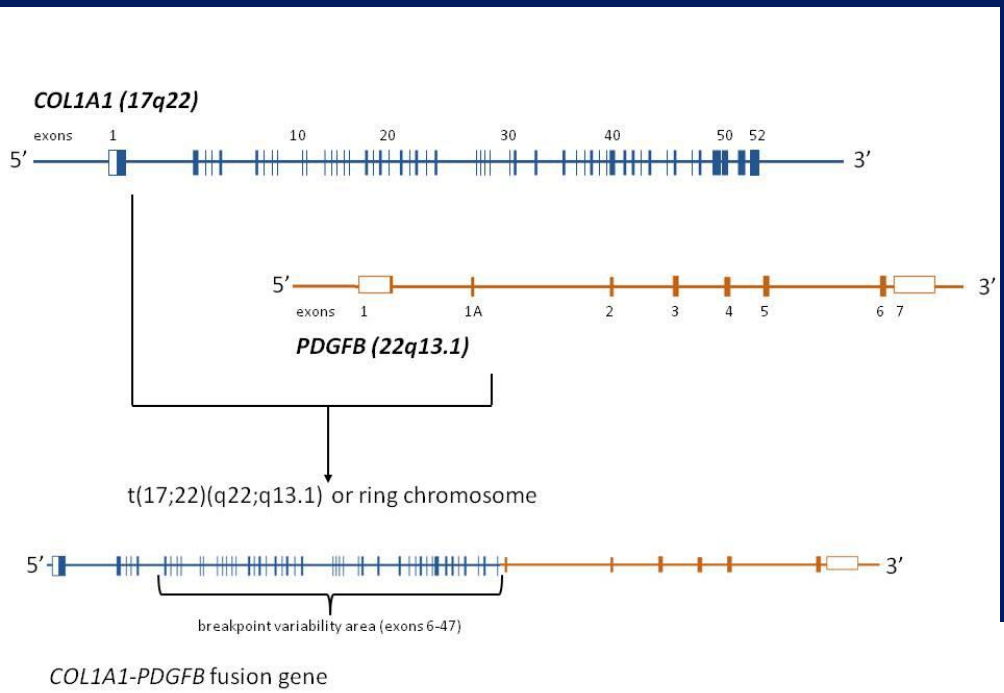
Activity of the drugs seen		
Giant cell tumor of bone	RANKL	denosumab
Inflammatory myofibroblastic tumor	ALK/MET	P02341066
Liposarcoma dedifferentiated		MDM2/CDK4
Chordoma	PDGFR, EGFR, mTOR	Imatinib, imatinib + mTOR, Sunitinib,, EGFR inhibitors
Solitary fibrous tumor	Angiogenesis inhibitors, mTOR inh, anti-IGFR1	Bevacizumab + temozolomide, sunitinib, sorafenib; IGF1R inhibitors

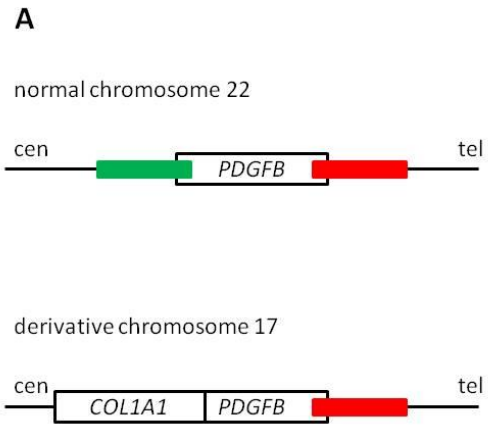


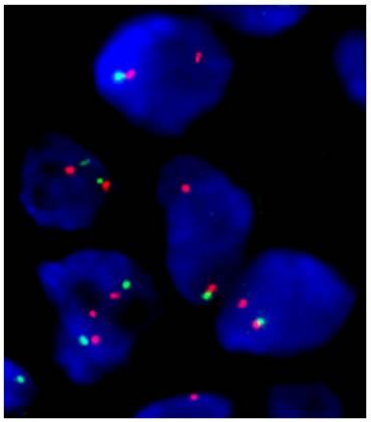


DFSP

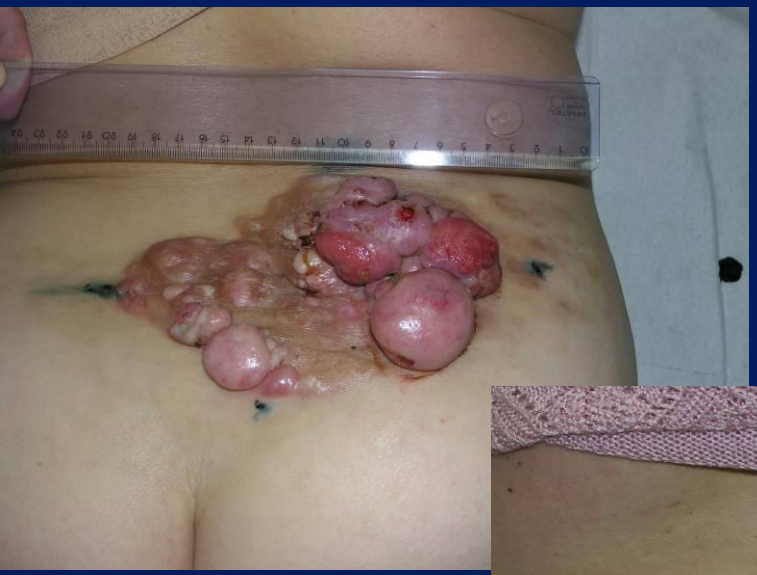
FISH assay confirming *PDGFB* rearrangement (red probe) in dermatofibrosarcoma protuberans (DFSP) cells

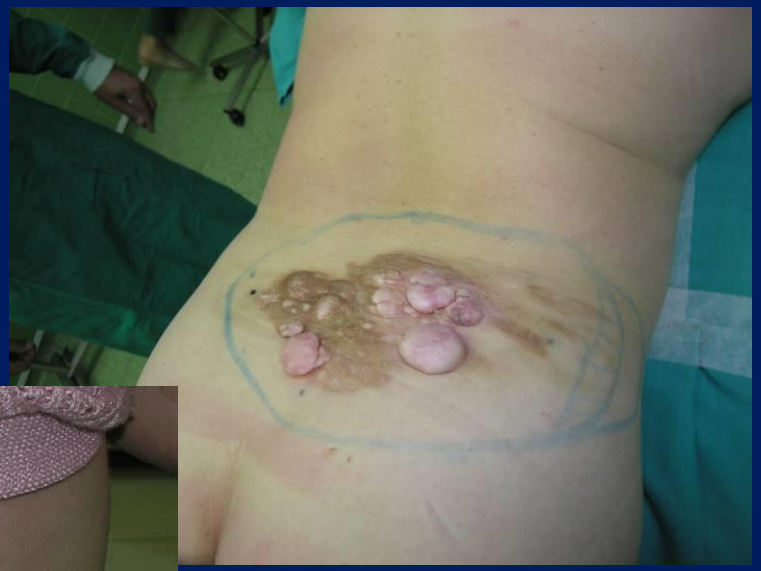


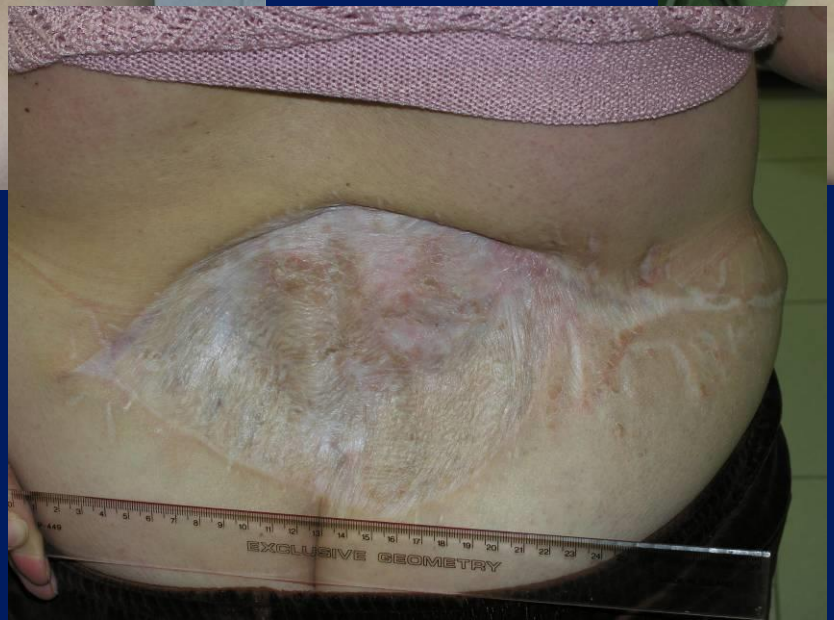




Imatinib (800mg/d) activity in patient with **dermatofibrosarcoma protuberans** t(17;22)(q22;q13) COL1A1/PDGF-B



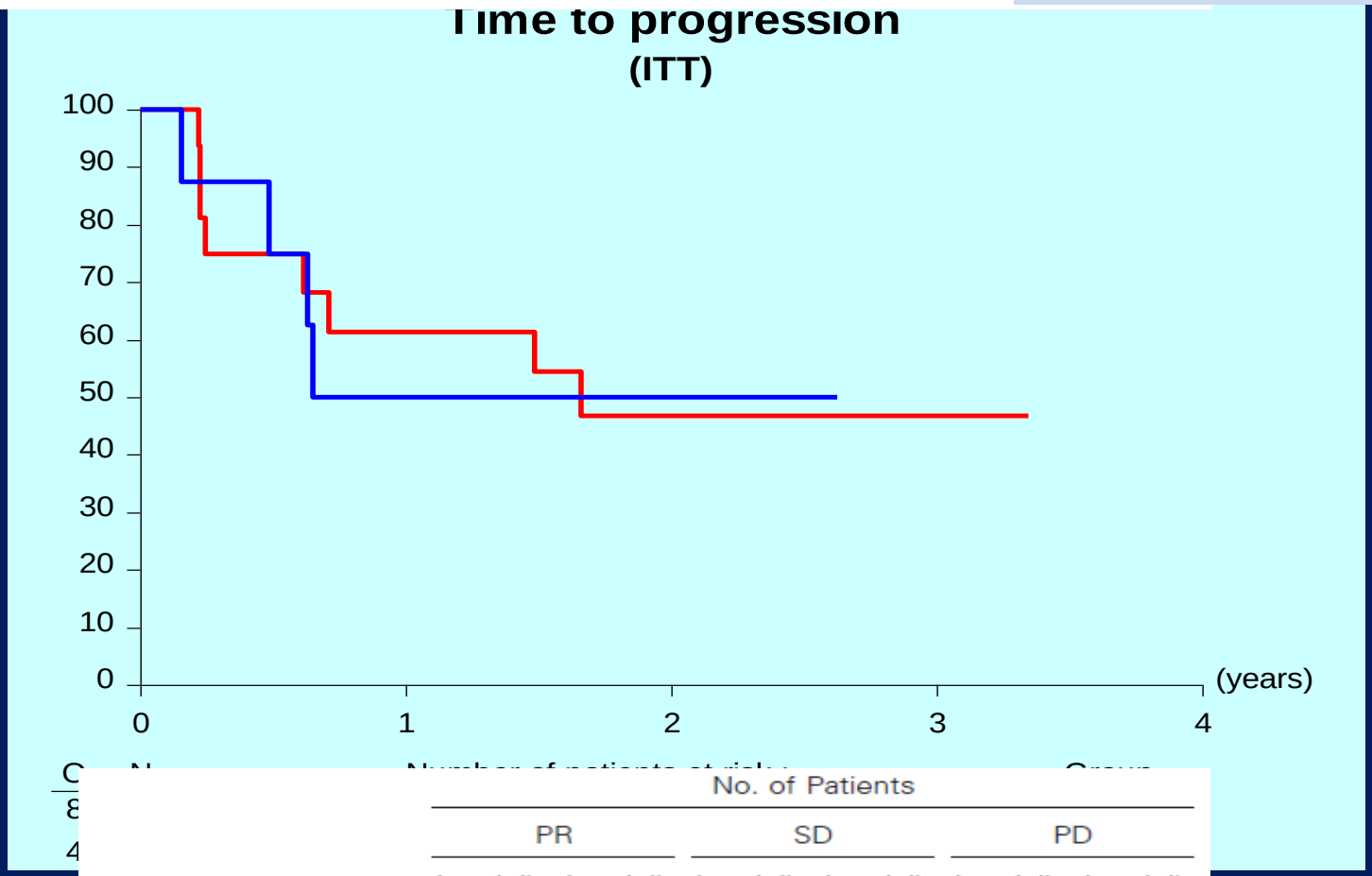




Imatinib Mesylate in Advanced Dermatofibrosarcoma Protuberans: Pooled Analysis of Two Phase II Clinical Trials

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

JOURNAL OF CLINICAL ONCOLOGY



DFSP Subtype	No. of Patients					
	PR		SD		PD	
	Imatinib 400 mg/d	Imatinib 800 mg/d	Imatinib 400 mg/d	Imatinib 800 mg/d	Imatinib 400 mg/d	Imatinib 800 mg/d
DFSP classic	2	4	3	2		
DFSP fibrosarcomatous	2	3		1		2
DFSP pigmented						1
Not DFSP					1	

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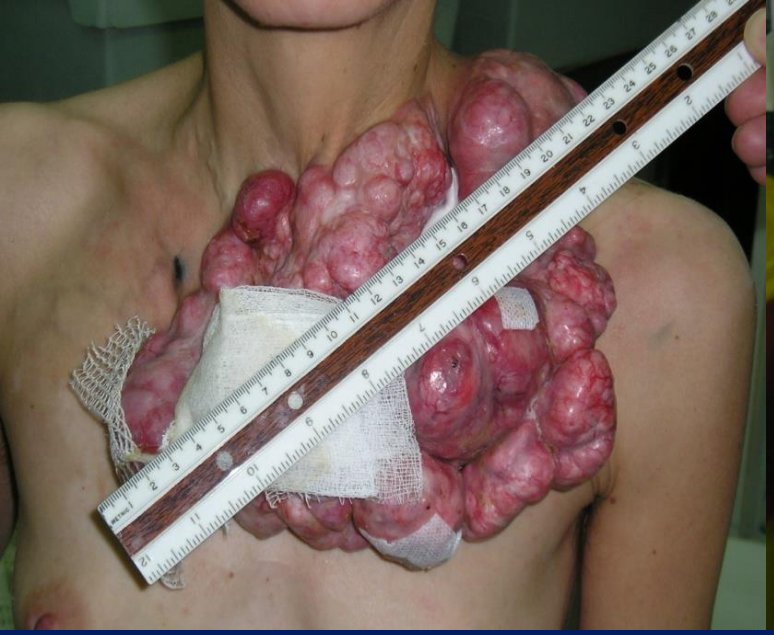

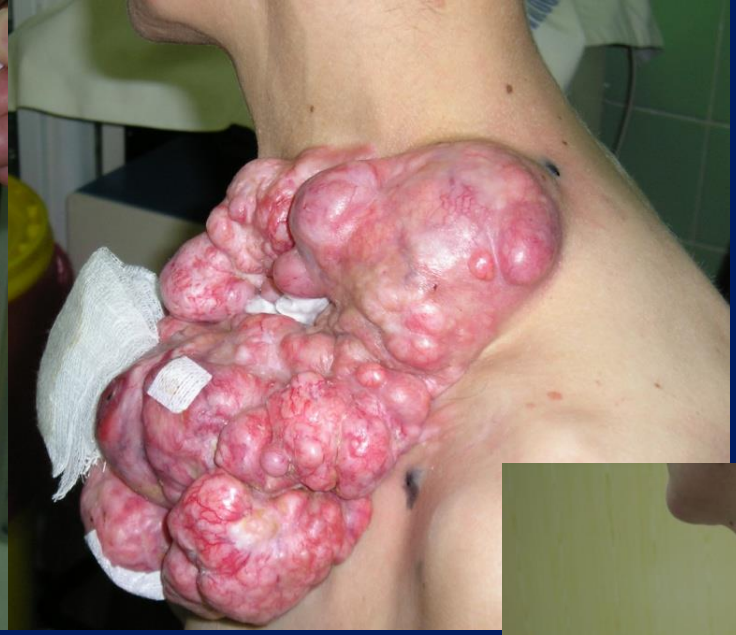

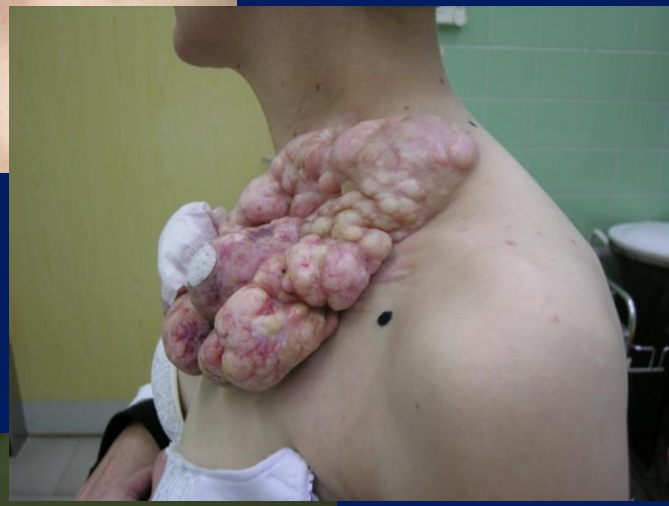

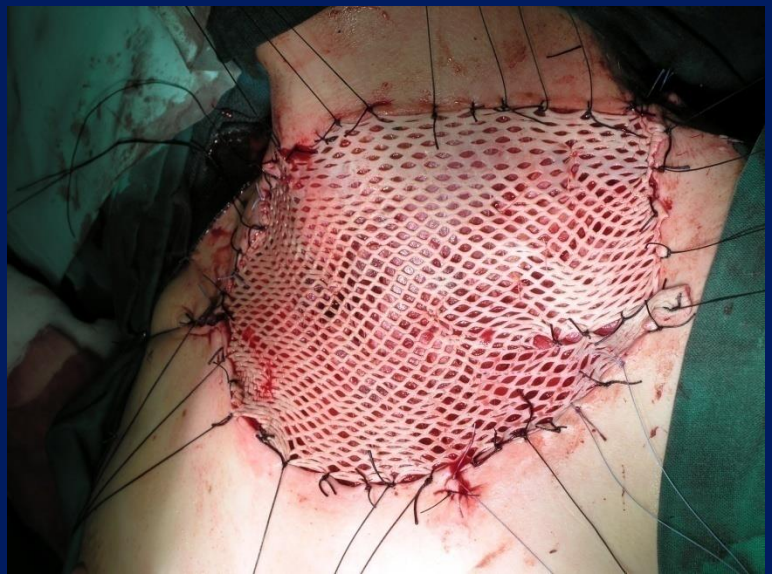

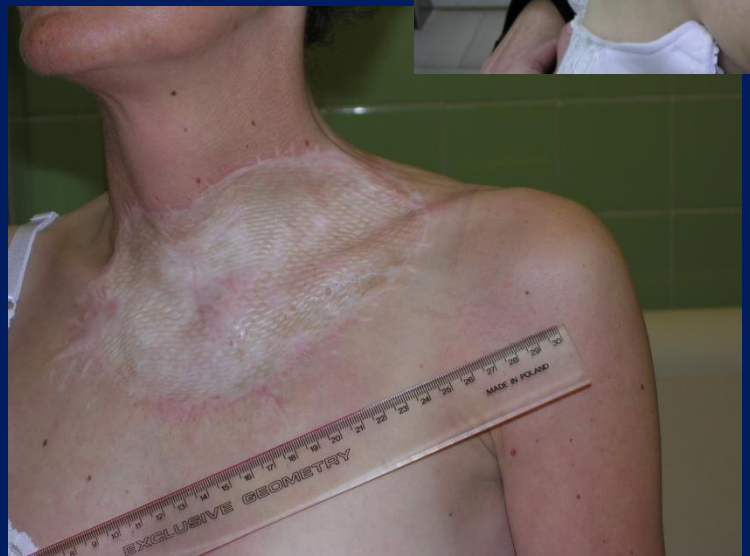

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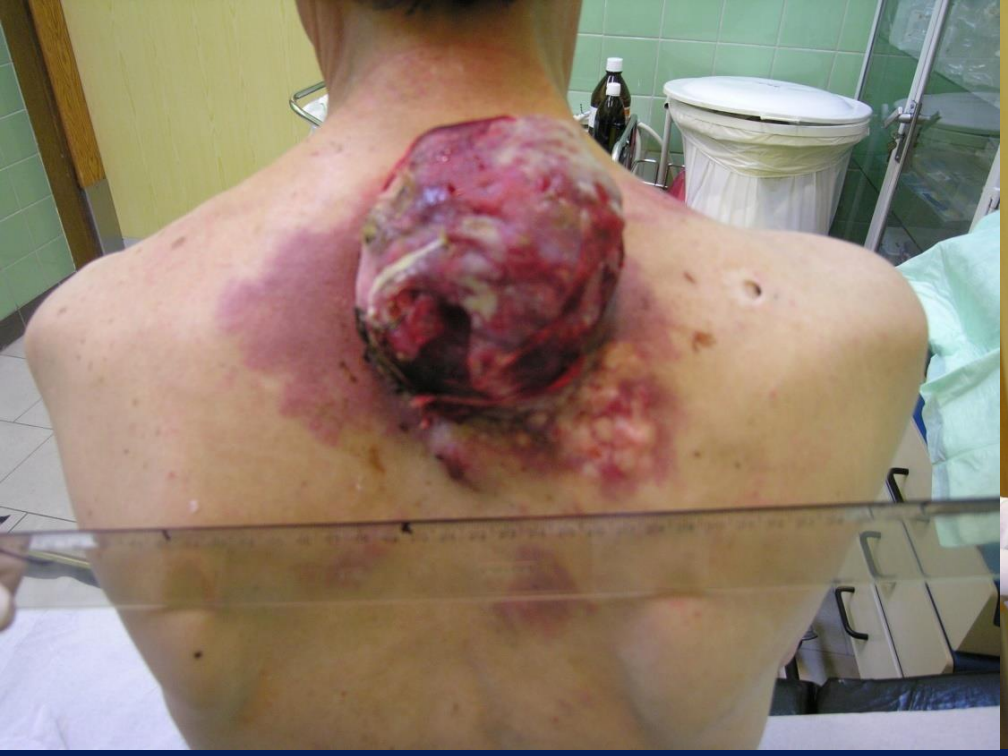
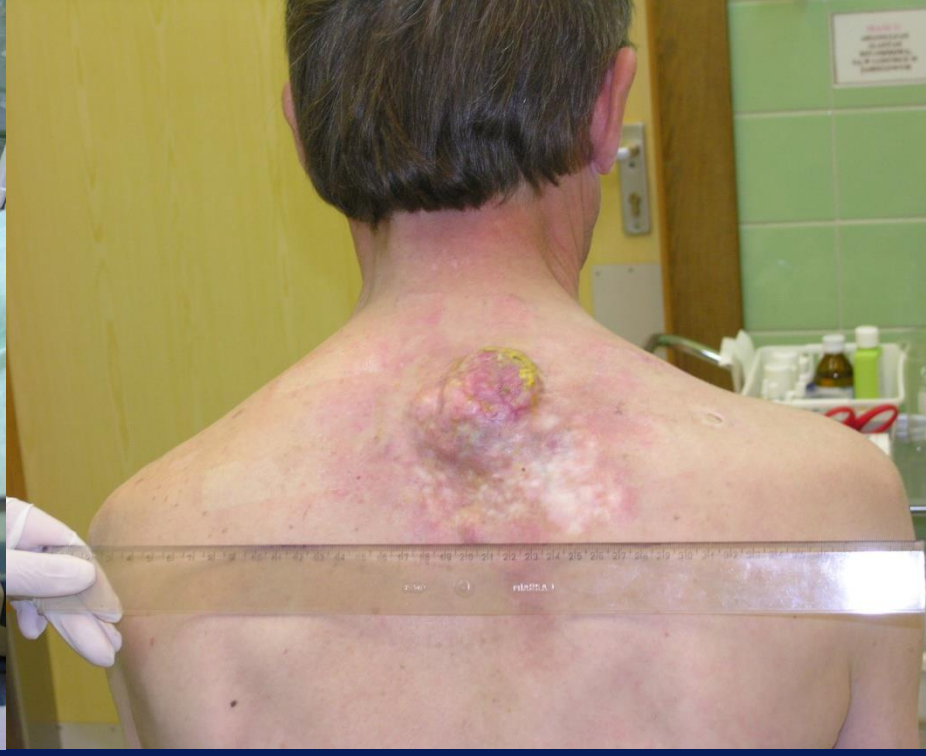
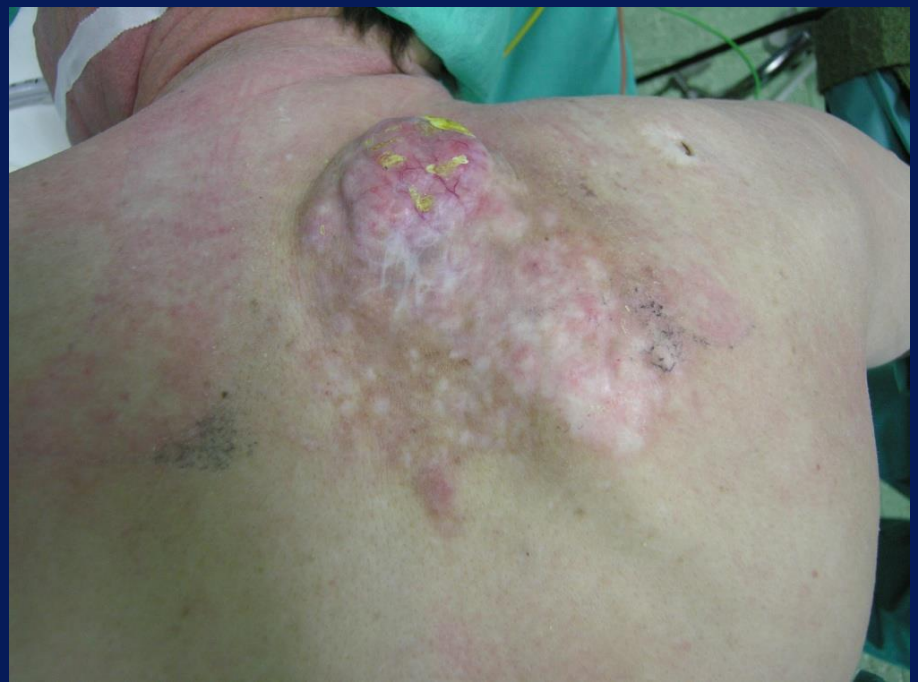
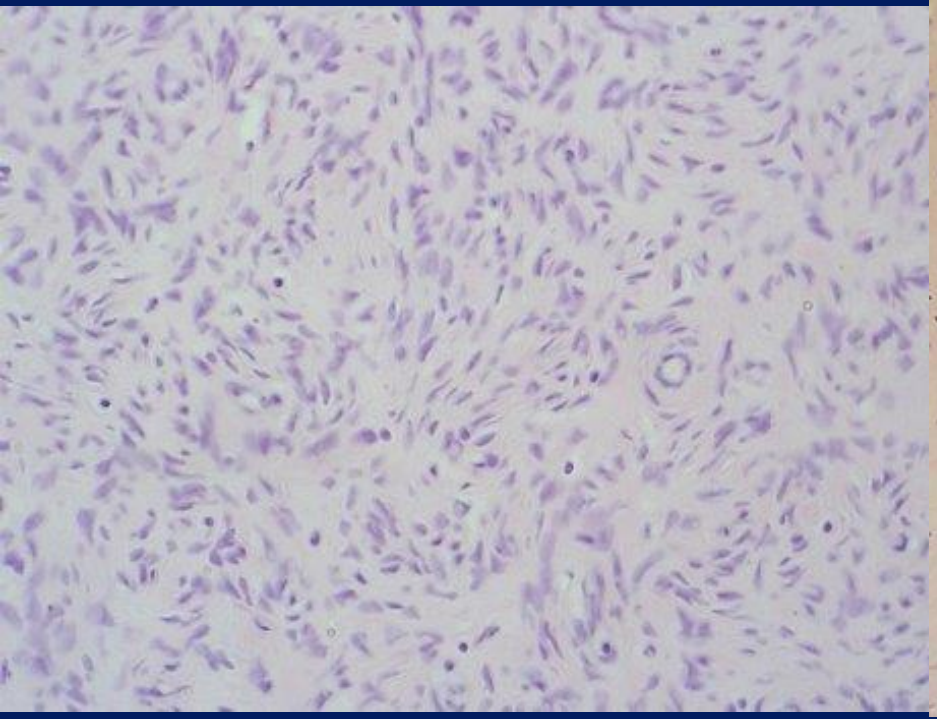
KNTM/K i CzS

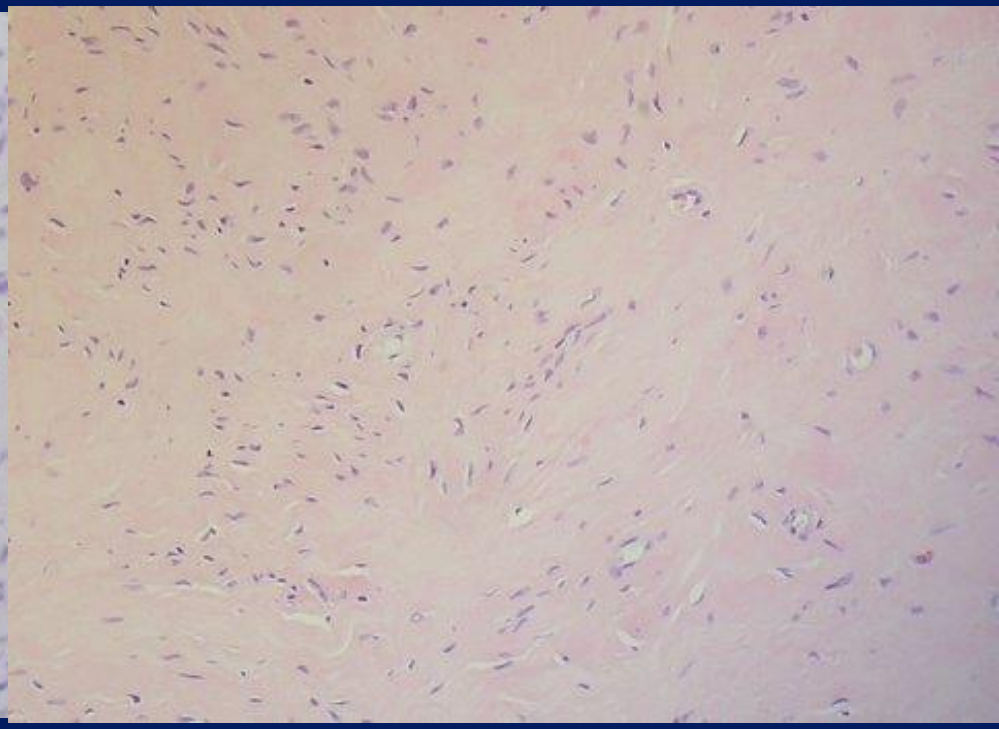






Pathological images before and after imatinib therapy of DFSP





Neoadjuvant imatinib

Imatinib Mesylate as a Preoperative Therapy in Dermatofibrosarcoma: Results of a Multicenter Phase II Study on 25 Patients

Delphine Kérob[1], Raphael Porcher[2], Olivier Vérola[3], Stephane Dalle[9], Eve Maubec[10], François Aubin[11], Michel D'Incan[12], Isaak Bodokh[13], Serge Boulinguez[14], Isabelle Madelaine-Chambrin[4], Anne Mathieu-Boue[15], Jean-Marie Servant[5], Eric de Kerviler[6], Anne Janin[3], Fabien Calvo[7,8], Florence Pedeutour[16], and Celeste Lebbe[1]

Neoadjuvant Imatinib in Advanced Primary or Locally Recurrent Dermatofibrosarcoma Protuberans: A Multicenter Phase II DeCOG Trial with Long-term Follow-up

Selma Ugurel, Thomas Mentzel, Jochen Utikal, et al.

Clin Cancer Res 2014;20:499-510. Published OnlineFirst October 30, 2013.

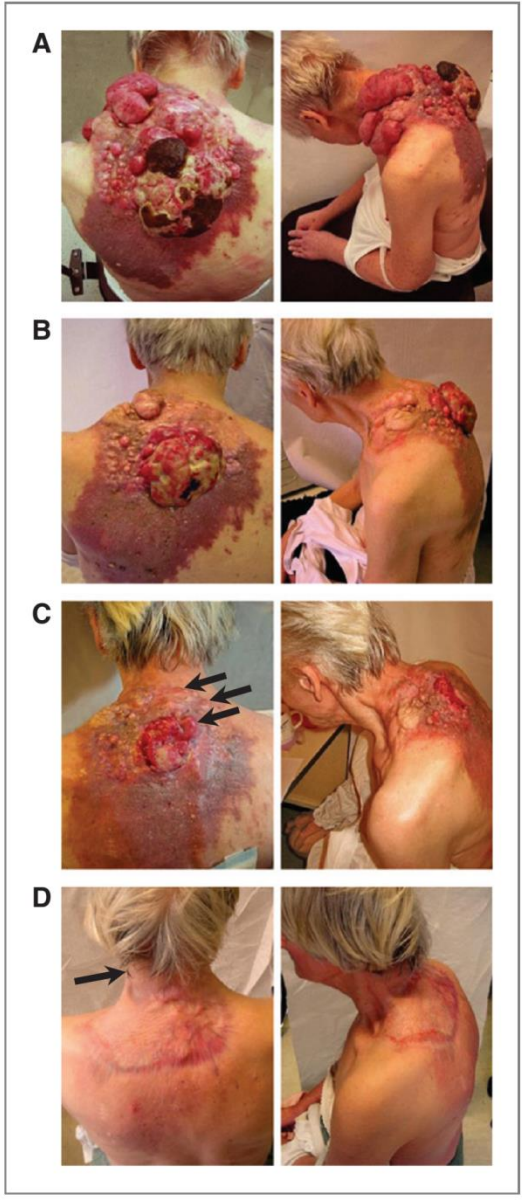


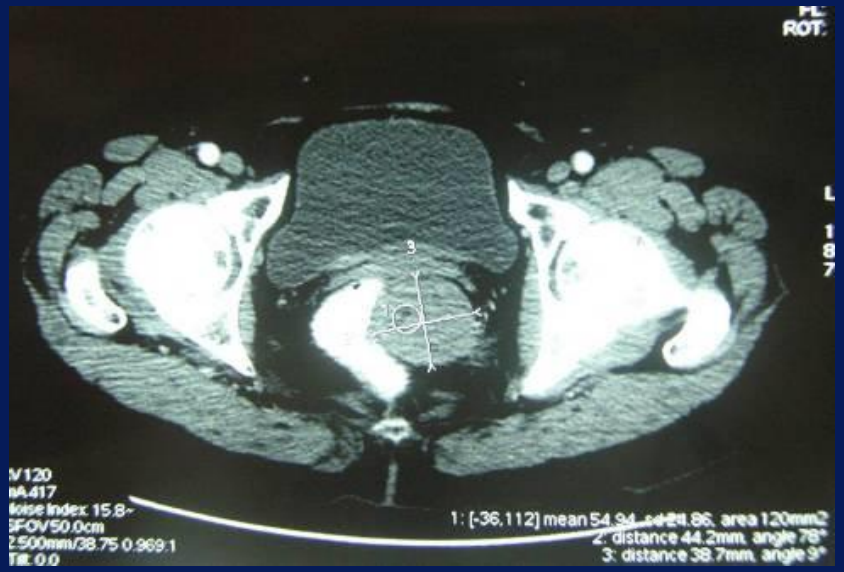
Figure 1. Clinical presentation of patient ADO-06 (A) before treatment; B, at 3 months of imatinib showing marked tumor shrinkage (PR); C, at 6 months of imatinib showing ongoing tumor shrinkage, but also secondary resistance with outgrowth of new tumor lesions (arrows); D, at 13.5 months after onset of imatinib, 7 months after imatinib discontinuation, and definitive surgery with tumor-free margins, showing a good result of skin graft reconstruction but also local tumor recurrence at the left neck (arrow). This recurrent tumor was resistant to imatinib, but sensitive to sunitinib.

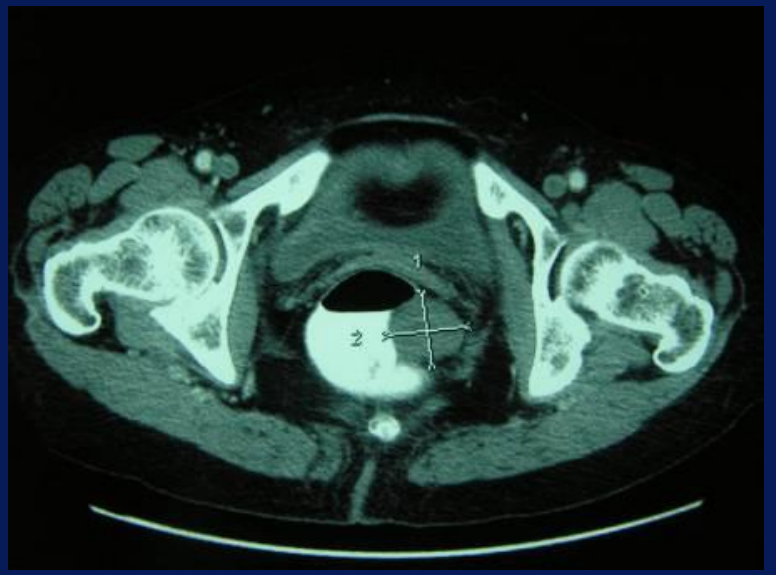
RATIONALE

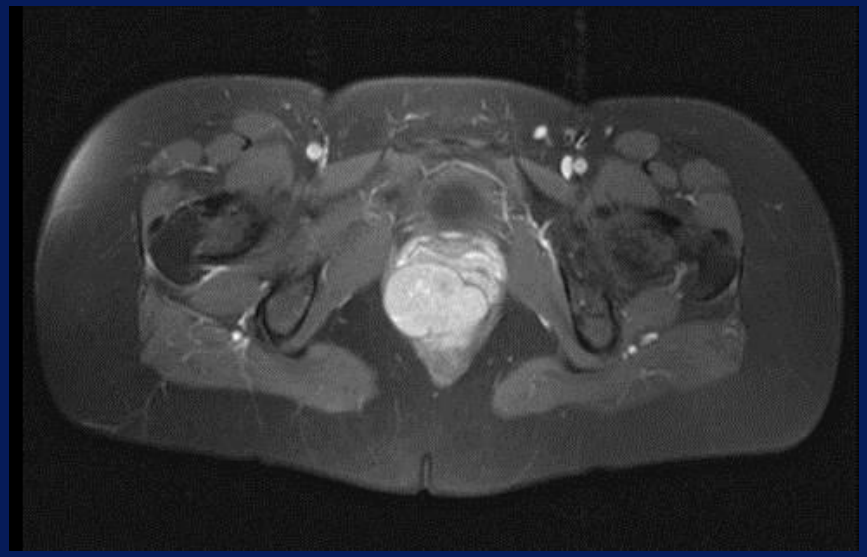
for combination of imatinib with surgery for patients with localized GISTs

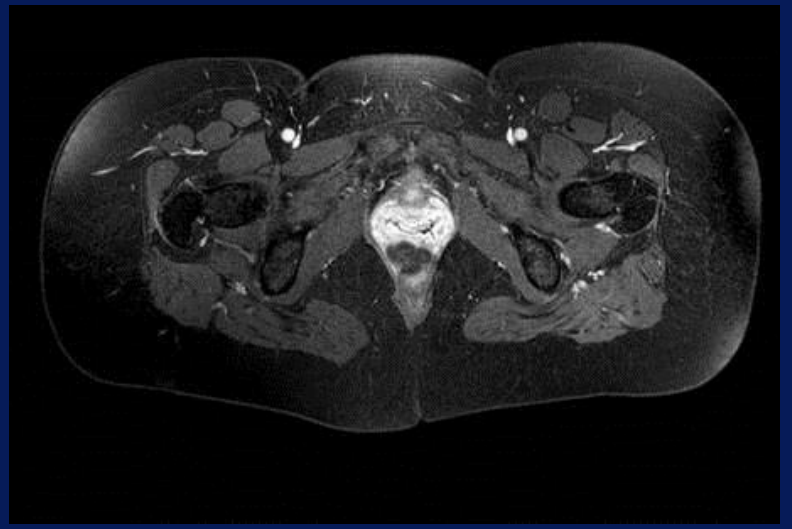
- surgery alone may not control high-risk tumors (prevention or delaying recurrences; survival prolongation?)
- TKI therapy highly efficient in advanced (inoperable/metastatic) cases (imatinib benefit > 80%)
- preoperative therapy gives possibility of avoiding mutilating surgery and devitalized tumor facilitates resection (less morbidity, less blood transfusion)

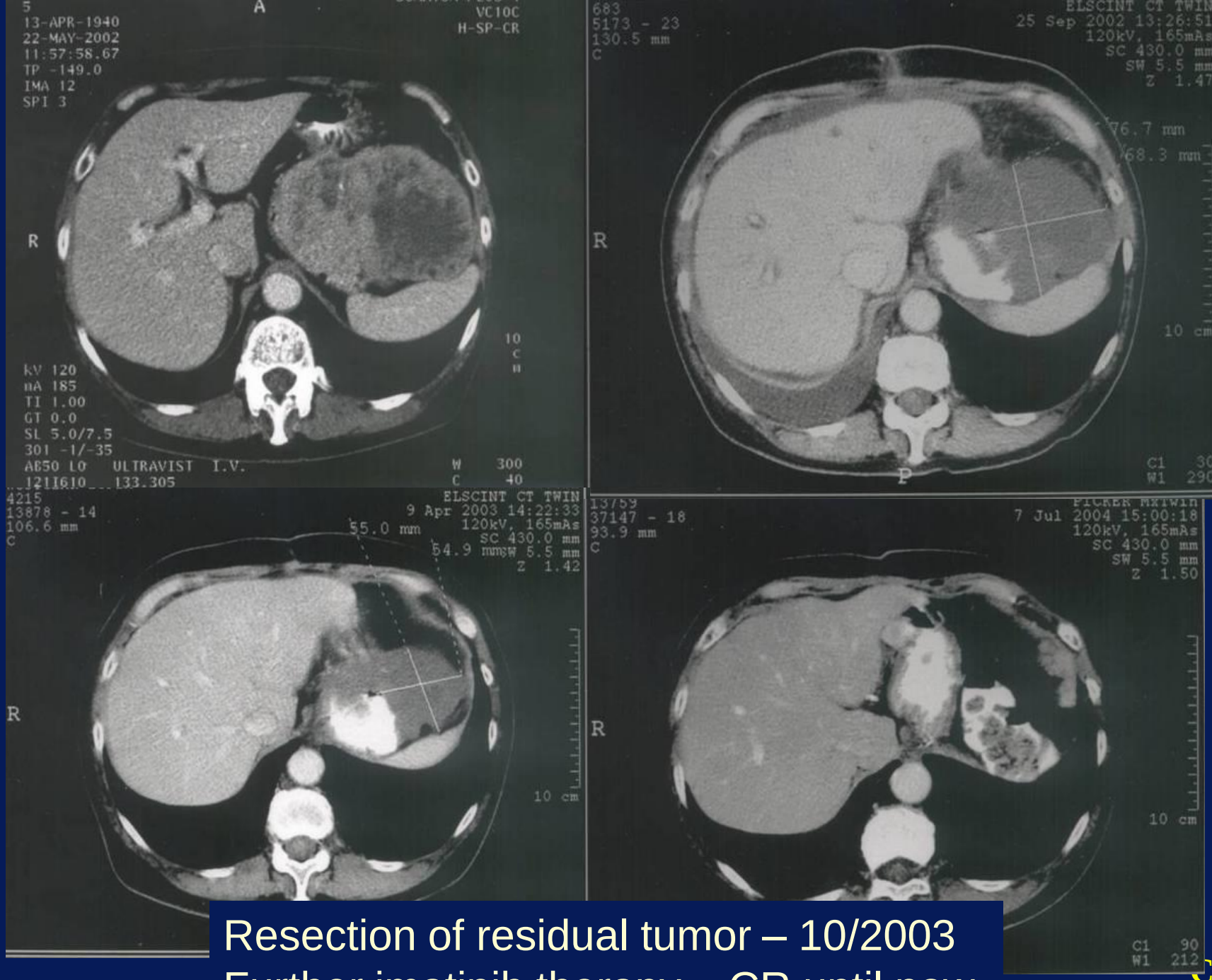
Rectal GIST


ROT
1: [-36,112] mean 54.94 area 120mm2
2: distance 44.2mm angle 78°
3: distance 38.7mm angle 9°

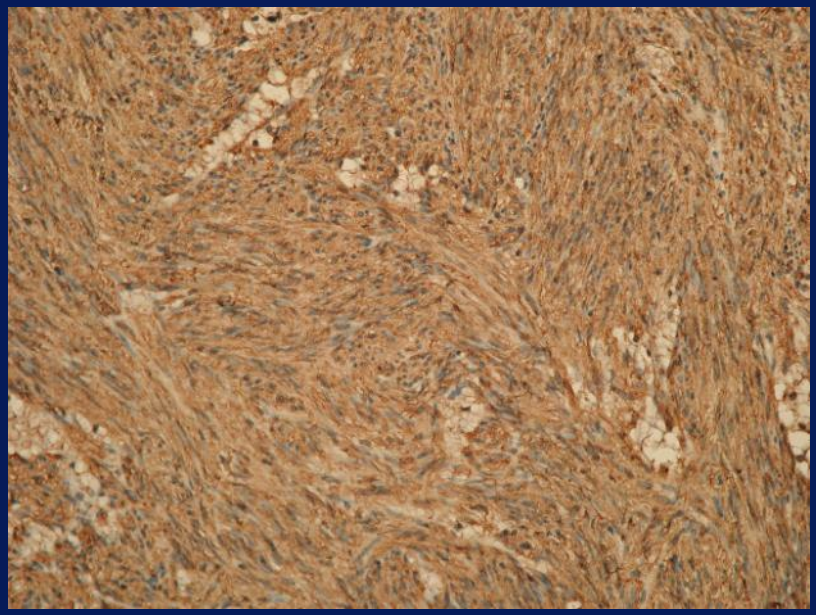


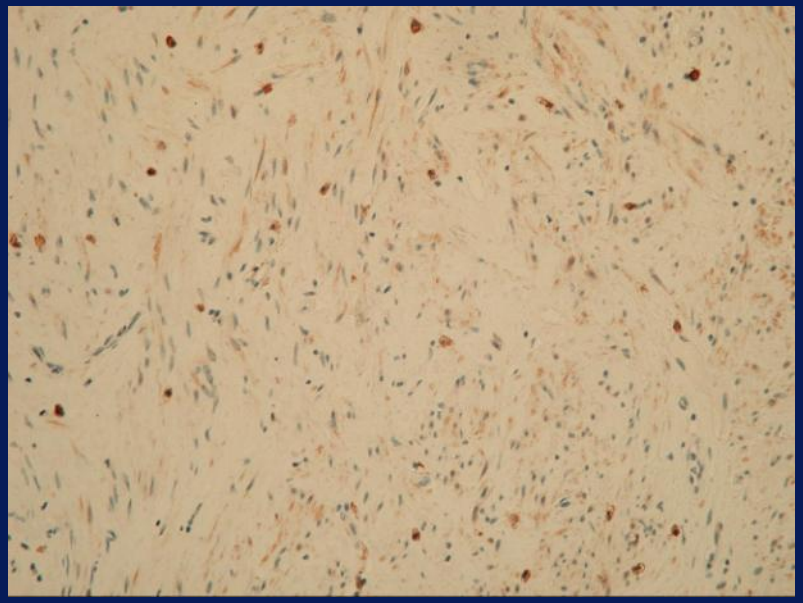






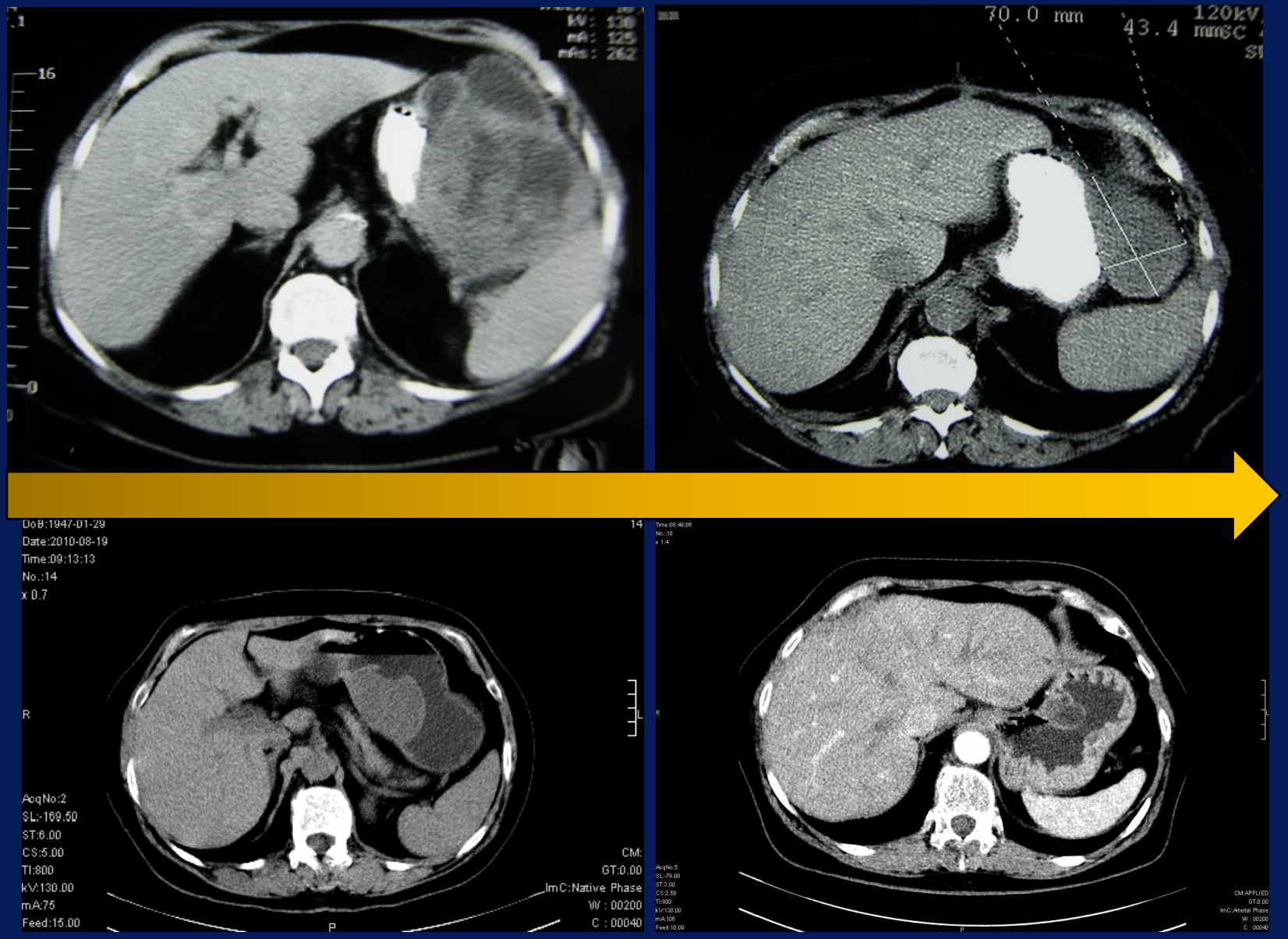
Resection of residual tumor – 10/2003
Further imatinib therapy – CR until now





Immunohistochemistry positive staining for CD 117 of gastric GIST before imatinib treatment (diffuse staining) and of the specimen after partial gastrectomy after imatinib therapy (single cells)

Bleeding gastric GIST

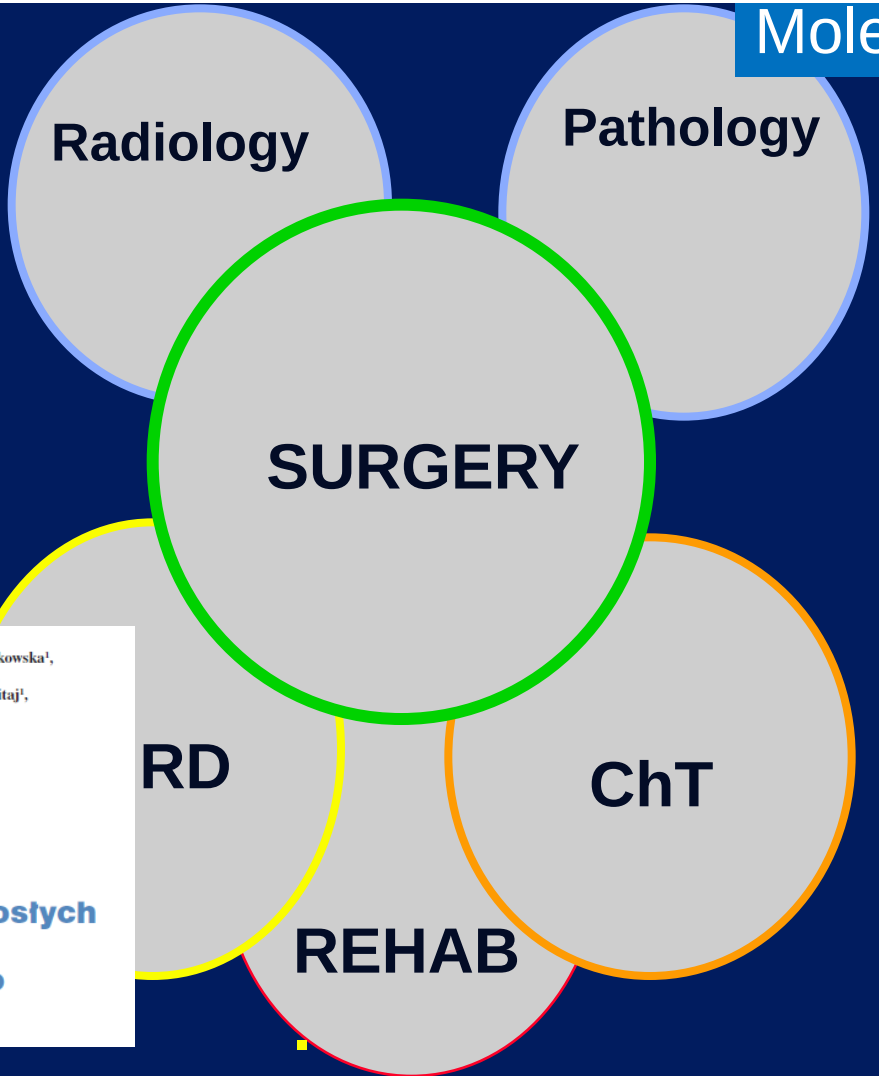


Multidisciplinary team / therapy planning

Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

The ESMO/European Sarcoma Network Working Group*

Molecular biology



Włodzimierz Ruka[1], Piotr Rutkowski[1], Maciej Krzakowski[1], Urszula Grzesiakowska[1], Konrad Ptaszyński[1], Arkadiusz Jeziorski[2], Wojciech Polkowski[3], Janusz Ryś[4], Janusz Słuszniak[5], Wirginiusz Dziewirski[1], Tadeusz Morysiński[1], Tomasz Świtaj[1], Marek Bębenek[6], Janusz A. Siedlecki[1], Janusz Limon[7], Zbigniew I. Nowecki[1]

[1]Centrum Onkologii — Instytut ul. Marii. Skłodowskiej-Curie w Warszawie
[2]Łódzki Uniwersytet Medyczny
[3]Uniwersytet Medyczny w Lublinie
[4]Centrum Onkologii — Instytut im. Marii Skłodowskiej-Curie — Oddział w Krakowie
[5]Świętokrzyskie Centrum Onkologii w Kielcach
[6]Dolnośląskie Centrum Onkologii we Wrocławiu
[7]Gdański Uniwersytet Medyczny

Mięsaki tkanek miękkich u dorosłych — zasady postępowania diagnostyczno-terapeutycznego

Soft tissue sarcoma — diagnosis and treatment

CO-I

KNTM/K i CzS

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EORTC

The future of cancer therapy