Traitement médical des sarcomes des tissus mous métastatiques: Y'a-t-il des standards ?

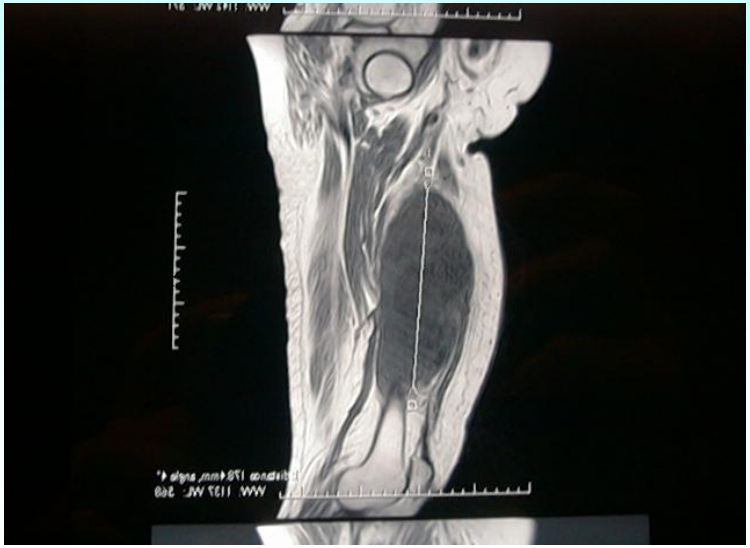
Antoine Italiano
Department d'Oncologie Médicale
Institut Bergonié, Bordeaux

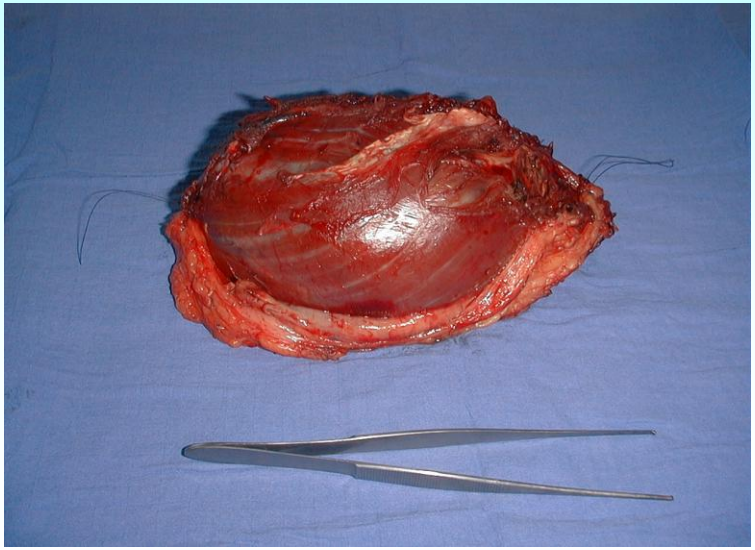
VIIèmes journées SFPO

Sarcome des tissus mous localisé: Etat des lieux en 2009

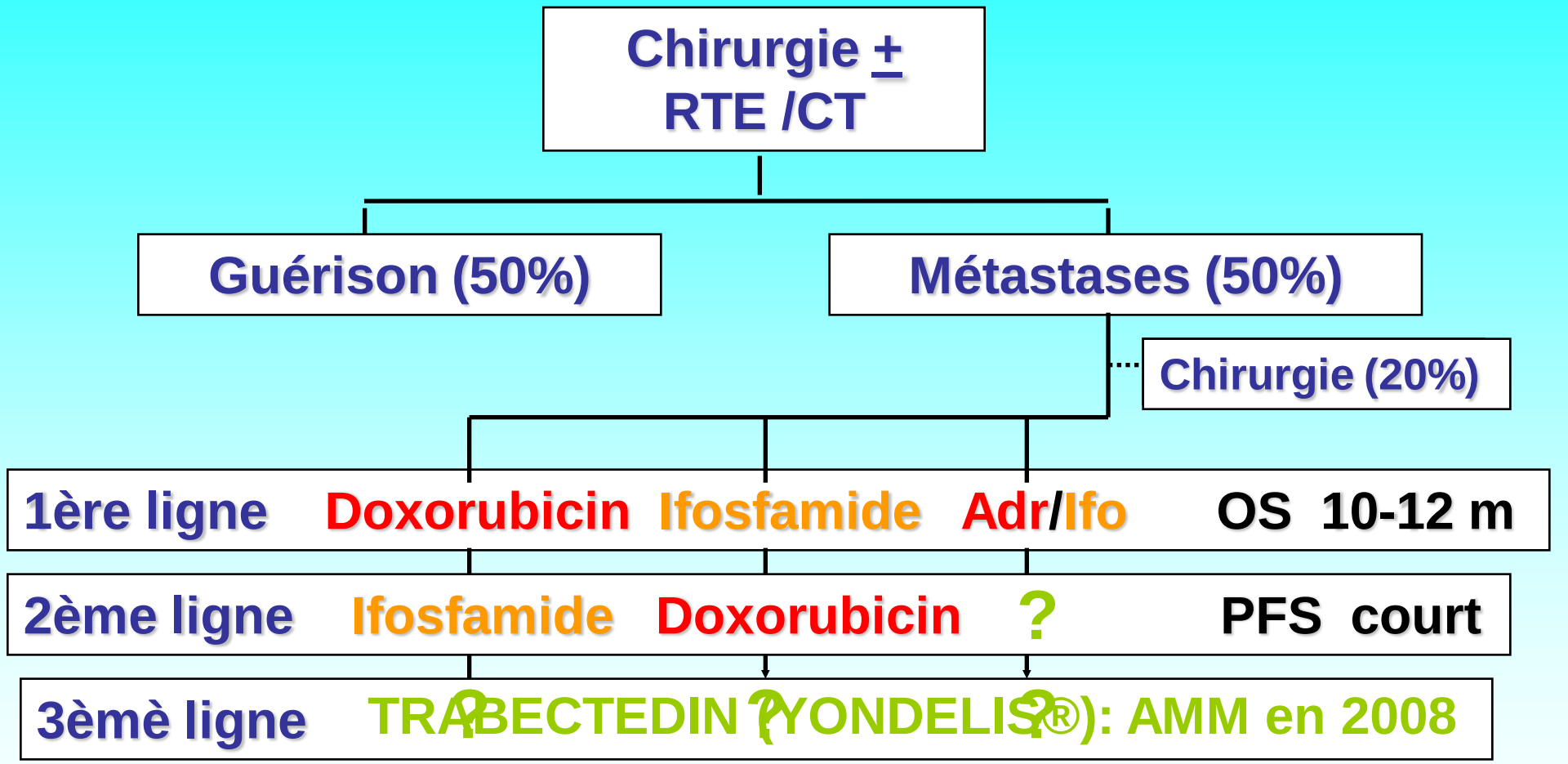
Chirurgie ± Radiotherapie

Guérison (50%)





Sarcome des tissus mous localisé: Etat des lieux en 2008



Sarcome des tissus mous avancés: 3 drogues enregistrées en 2009

- **Doxorubicin (75 mg/m²)** **RR 8 - 30%**
- Comment améliorer ces résultats ?

Survie médiane médiocre: 10-12 mois

« Standard chemotherapy is based on anthracyclines as first line treatment [I, A] ».
ESMO recommendations 2009

OPTIMISATION DU TRAITEMENT MEDICAL DES SARCOMES: APPROCHES CLASSIQUES

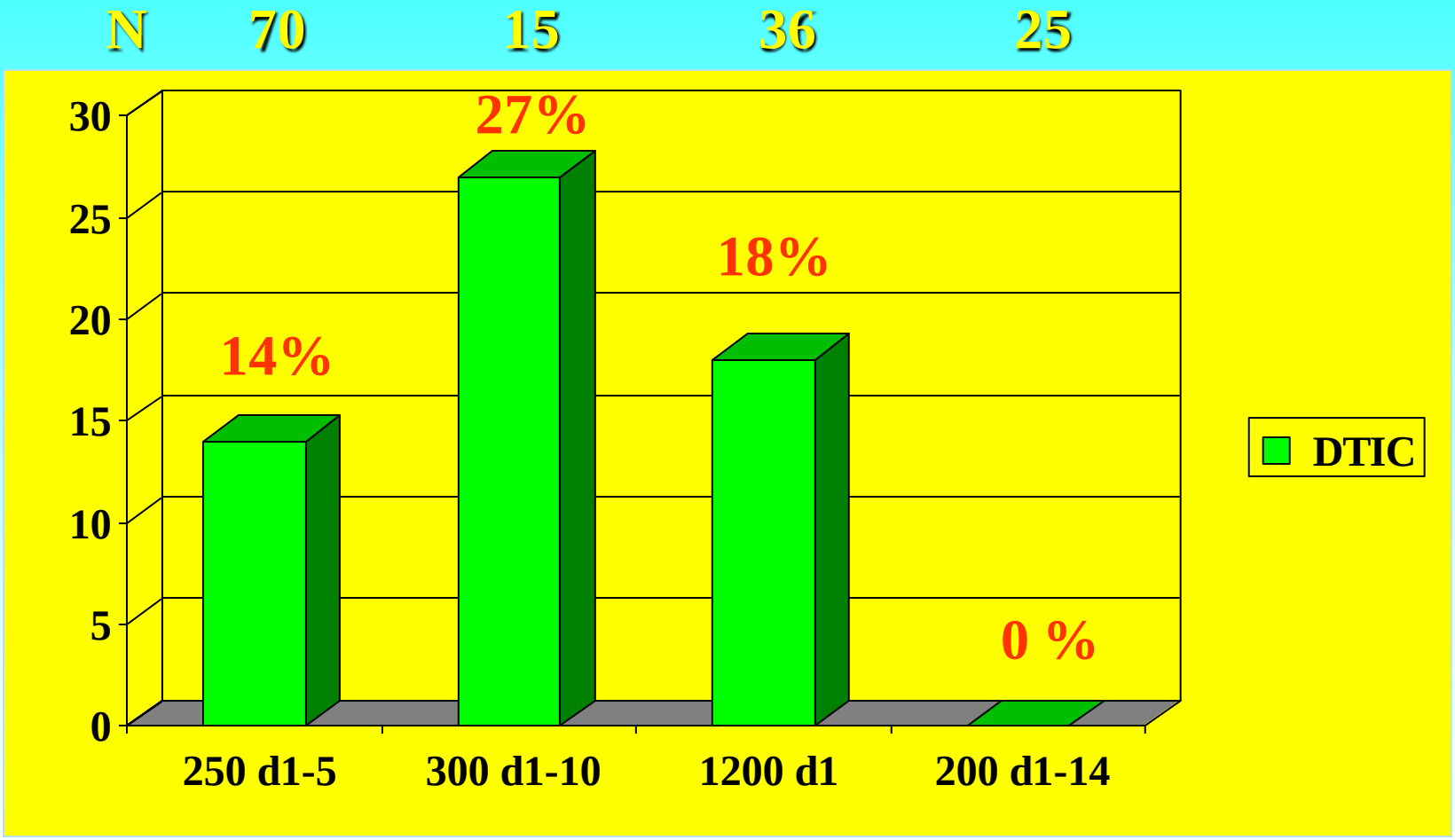
Sarcome des tissus mous (1977-2003)
Après Adriamycine et/ou Ifosfamide ?

- Esorubicin
- Topotecan
- Docetaxel
- Ellipticimiu
- MZPES
- Gemcitabine
- Etoposide
- Cyclophosphamide
- Methyl-GAG
- Mitomycin C
- Trimetrexate
- Interferon-β
- 10-Edam
- CI-980
- Temozolomide
- Paclitaxel
- MDMS
- Edatrexate
- Imatinib
- Aclarubicin
- Cisplatin
- Carboplatin
- Tomudex
- Nimusitne
- Fotemustine
- Mitoxantron
- Chlorozotocin
- PALA
- Amonafide
- Piperazinedione
- Bleomycine
- Bisantrene
- Vincristine
- Actinomycin
- THP-doxorubicin
- MTPPE
- AZQ
- Fludarabine
- Mitozolomide
- Homoharringtonin
- Miltefosine
- Interferon-γ
- 5-Fluorouracil
- Etc, etc, etc……..

Drogues considérées comme inactives*

*Verweij and Van Glabbeke, 2003 ASCO Educational Book, pp 522-531

STS - DACARBAZINE



Gottlieb 1976 | Rosen 1990 | Buesa 1991 | Reichardt 2000

Rôle des polychimiothérapies

Auteurs	Schema	N	RO		Survie
Schoenfeld	A/AVC/AdVC	200	A = 27 %	(p = 0.03)	NS
Muss	A/AC	104	NS		NS
Omura	A/AD	146	NS		NS
Borden	A/AD	186	AD = 30 %	(p = 0.02)	NS
Lerner	A/AD	66	AD : 44 %	(leiomyo S)	NS
Santoro	A/AI/CYVADIC	449	NS		NS
Borden	A/AVd	295	NS		NS
Edmonson	A/AI/APM	262	AI = 34 %	(p = 0.03)	NS
Antman	AD/MAID	340	MAID : 32 %	(p = 0.002)	NS

Pas de bénéfice en survie des polychimiothérapies ?

Rôle des polychimiothérapies

EORTC STUDY 62012 : DESIGN
Study coordinator: I. Judson

Chart Title

Advanced Soft tissue sarcoma
(Histologically proven)
front line CT

Randomization

Doxorubicin
75 m/M2
q3w

Doxorubicine 25 mg/m2 d1-d3
Ifosfamide 2.5 g/m2 d1-d4
G-CSF
q 3 wks

Rôle de l'intensification thérapeutique

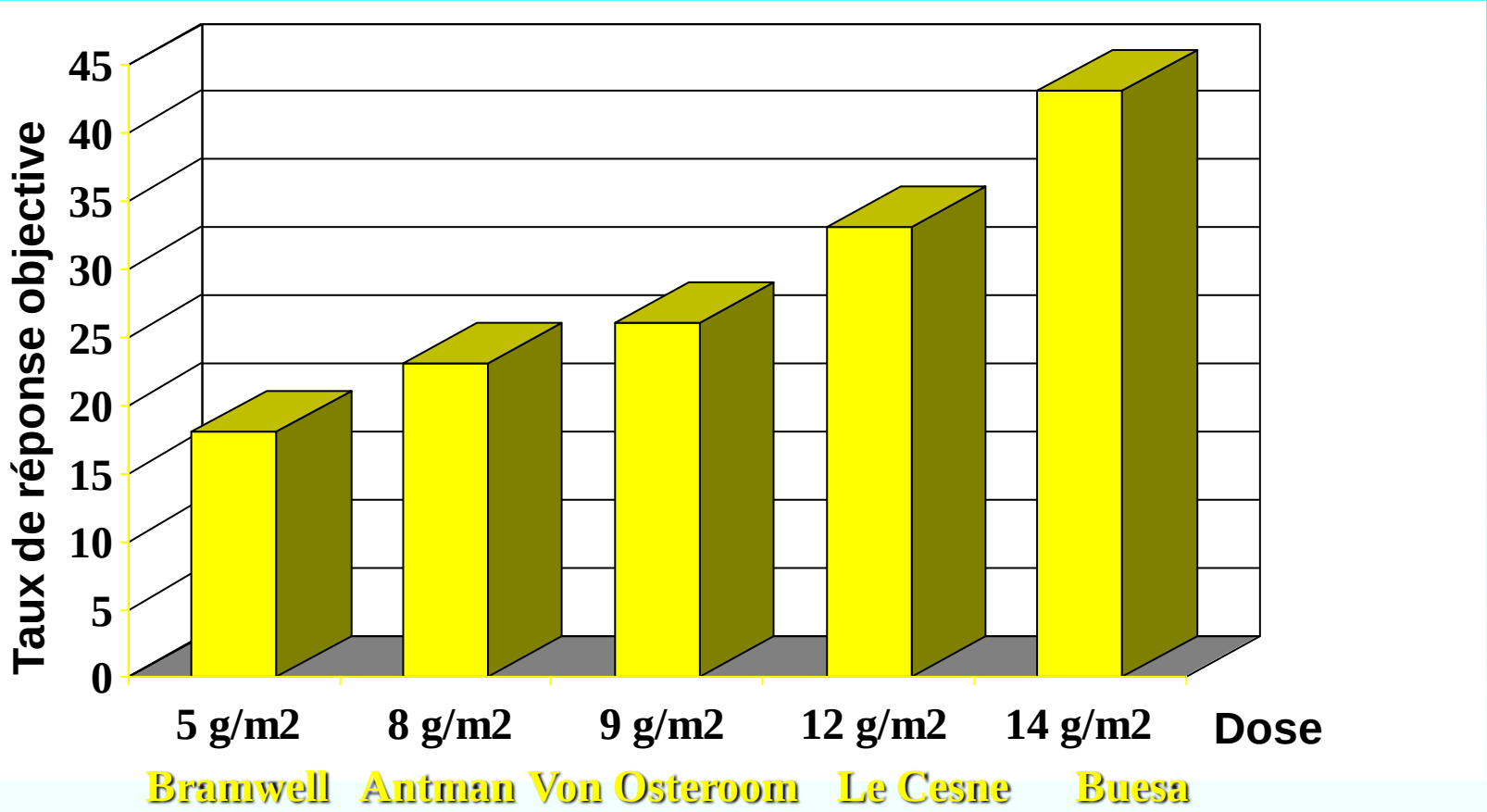
DOSE RESPONSE EVALUATION OF ADRIAMYCIN IN HUMAN NEOPLASIA *Cancer* 39:1940–1948, 1977.

TABLE 3. Remissions According to Dose Schedule and Tumor Type
(#) Remissions/(#) Patients (% Remissions)

Tumor type	Good risk			Poor risk	
	75 mg/m²	60 mg/m²	45 mg/m²	50 mg/m²	25 mg/m²
Other	7/38 (18)	2/9 (22)	2/32 (6)	1/3 (33)	3/16 (19)
TOTAL	66/263 (25.0)	26/95 (27.4)	37/191 (19.4)	21/131 (16.0)	17/138 (12.3)

	Relation dose doxorubicine/réponse objective				
Dose (mg/m²)	75	60	50	45	25
Taux RO	37	20	11	18	0

Rôle de l'intensification thérapeutique



IFOSFAMIDE: EFFET DOSE-REPONSE OBJECTIVE ?

Rôle de l'intensification thérapeutique

Phase III trial of standard versus dose-intensified doxorubicin, ifosfamide and dacarbazine (MAID) in the first-line treatment of metastatic and locally advanced soft tissue sarcoma

Invest New Drugs Published online: 16 January 2009

ETUDE PALSAR I (GSF)

	MAID	MAID-I
	Per cycle	Per cycle
	Planed	Planed
Doxorubicin	60	75
Ifosfamide	7,500	9,000
Dacarbazine	900	1,200

Augmentation des doses de 25%:

- adriamycine
- ifosfamide
-dacarbazine

Rôle de l'intensification thérapeutique

Response to treatment according to RECIST criteria

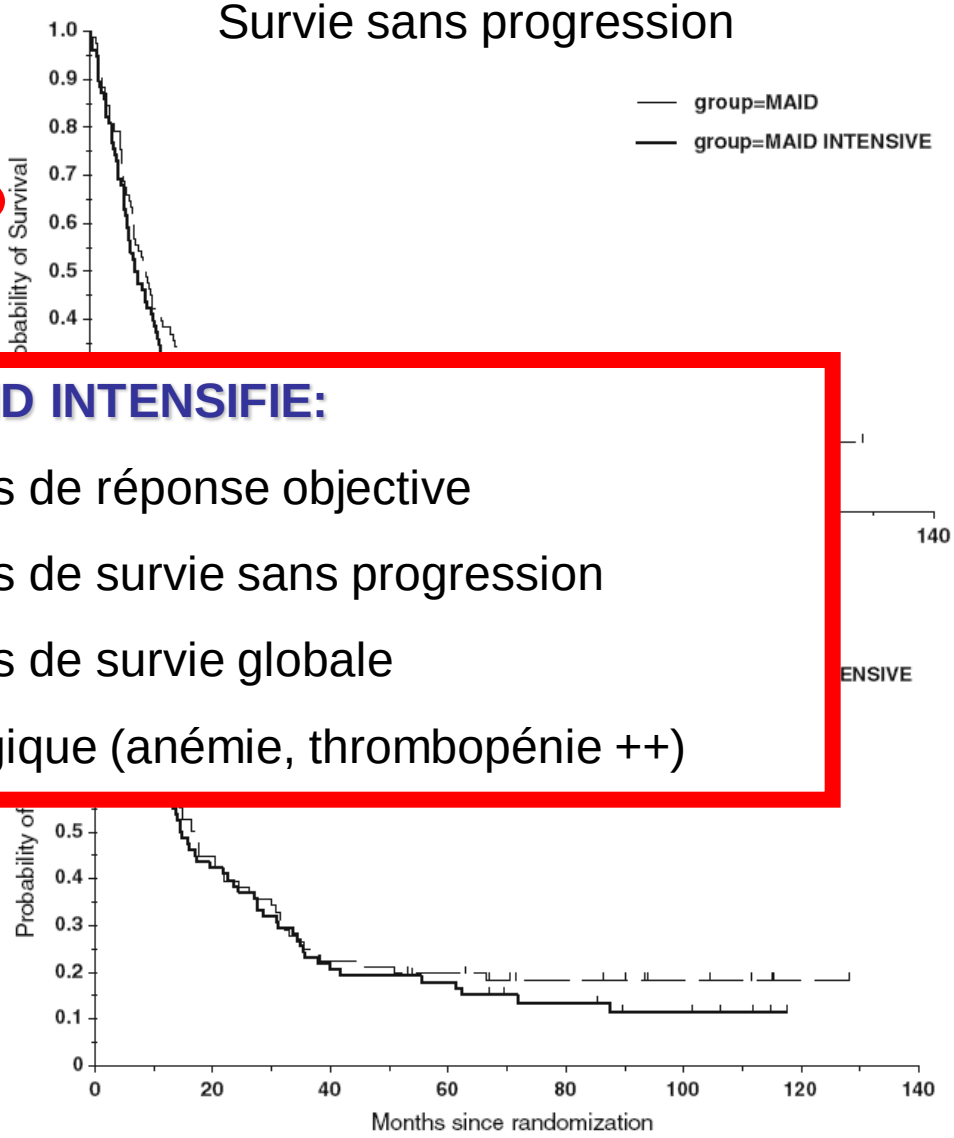
	MAID		MAID-I	
	N=74	%	*N*=71	%
Overall response*	26	35	27	38
Complete response	4	5	0	0
Partial response	22	30	27	38
Stabilization	29	39	34	48
Progression	19	26	10	14

Percentages are ir
*p=0.72

Table 3 Grade
greater

Neutropenia					
Thrombocytope					
Anemia	48	60	63	77	0.02
Infection	7	9	13	16	0.17
Hemorrhage	1	1	4	5	0.4*
Asthenia	7	9	12	15	0.24
Stomatitis	5	6	12	15	0.08
Nausea/vomiting	16	20	21	26	0.4

Survie sans progression



MAID INTENSIFIE:

-Pas de bénéfice en termes de réponse objective

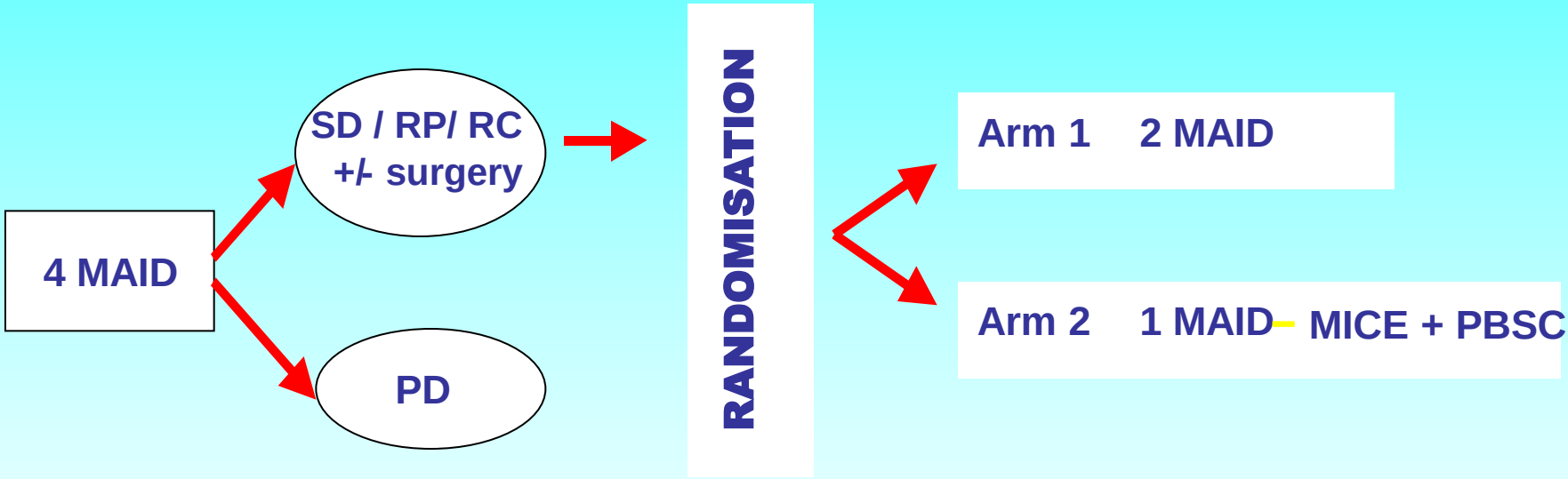
-Pas de bénéfice en termes de survie sans progression

-Pas de bénéfice en termes de survie globale

-Plus de toxicité hématologique (anémie, thrombopénie ++)

Rôle de l'intensification thérapeutique

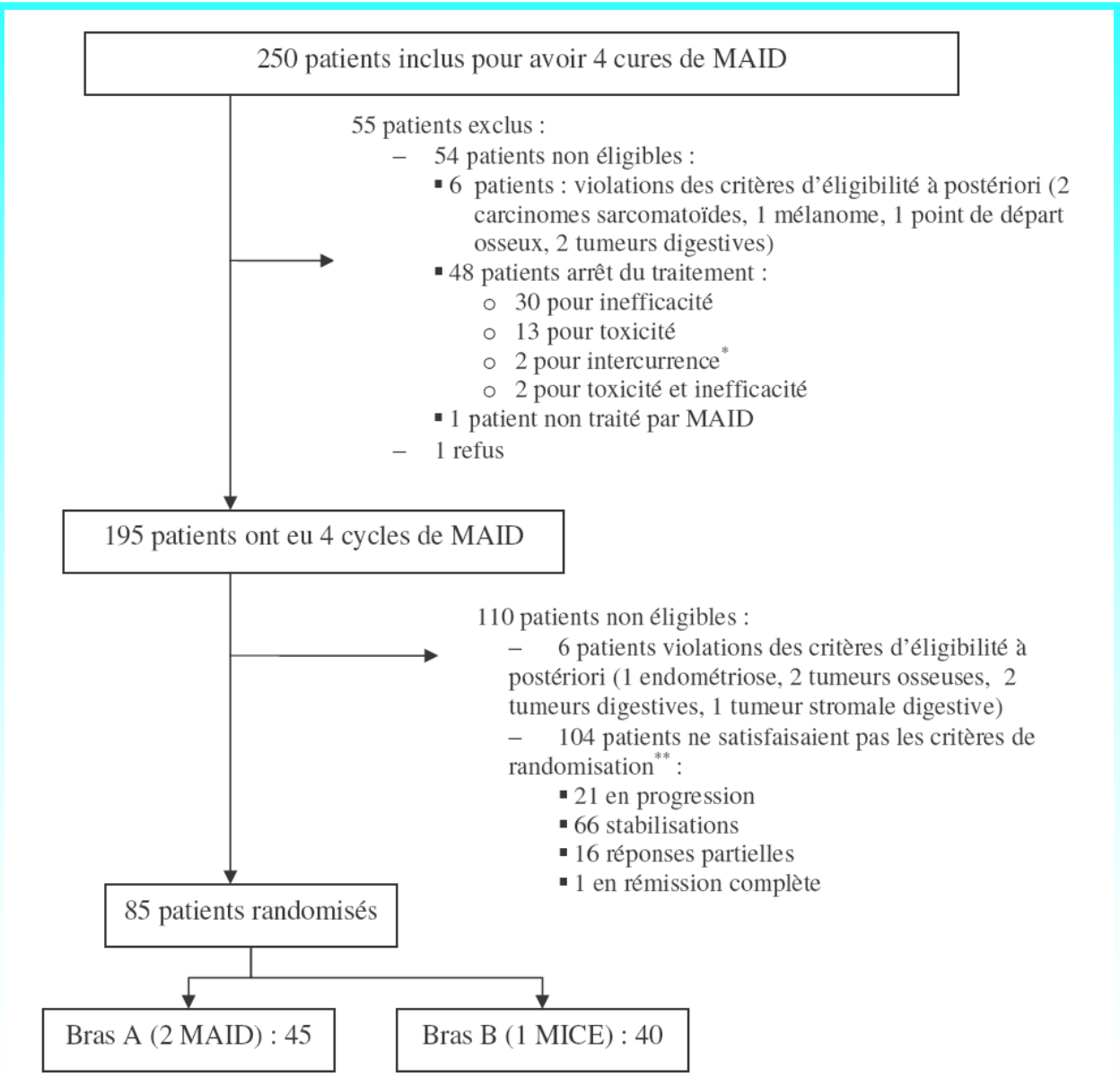
Sarcome 02 PALSAR II



Main end-point: overall survival
Statistical hypothesis: 3-yr OS: 40% vs 15% (N per arm: 50)

Bui et al. ASCO 2009

Rôle de l'intensification thérapeutique



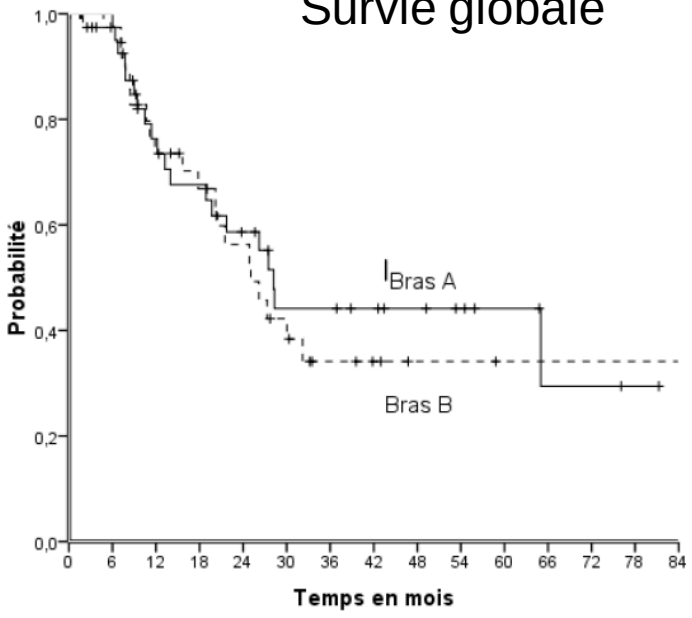
Bui et al. ASCO 2009

Rôle de l'intensification thérapeutique

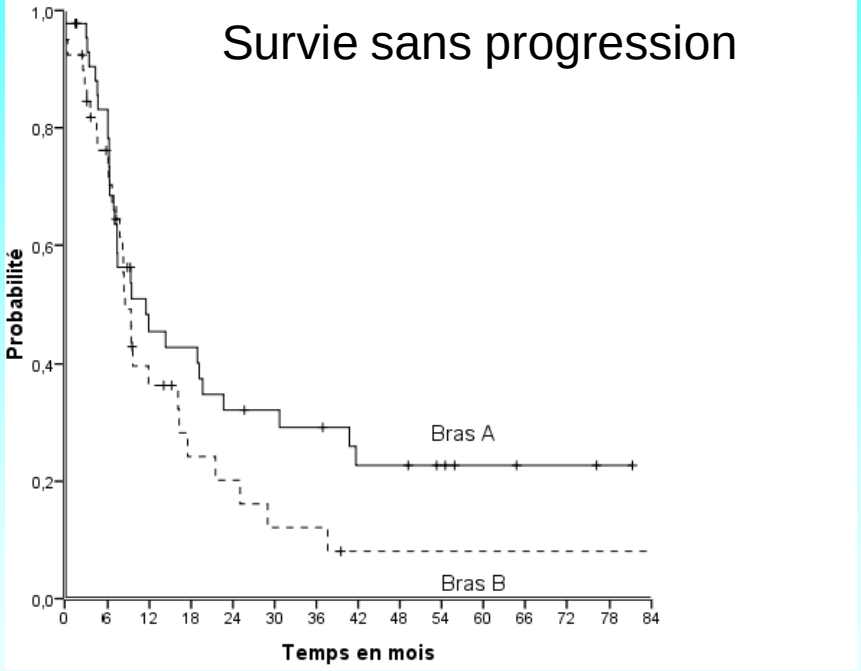
ETUDE PALSAR II

- **BRAS A: MAID**
- **BRAS B: MAID + AUTOGREFFE**

Survie globale



Survie sans progression

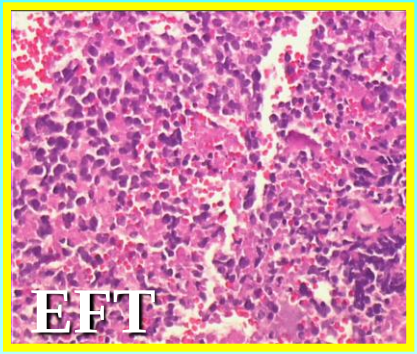


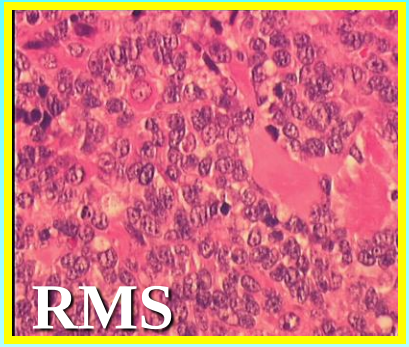
Absence de bénéfice de l'intensification thérapeutique

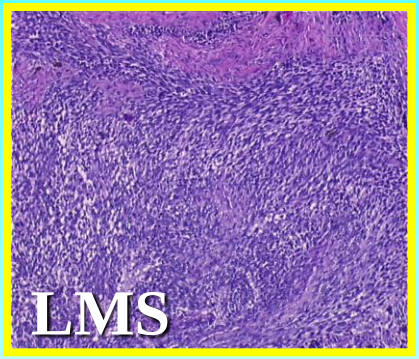
Bui et al. ASCO 2009

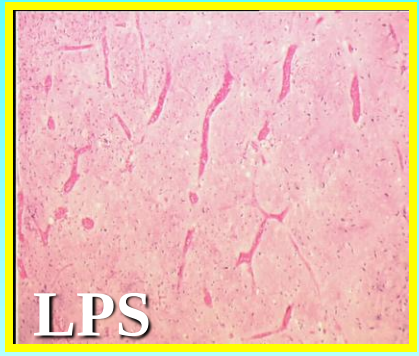
OPTIMISATION DU TRAITEMENT MEDICAL DES SARCOMES: APPROCHES INNOVANTES

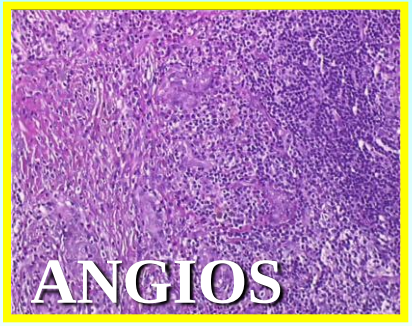
Sarcome des tissus mous métastatiques :
Un sarcome ? Des sarcomes ?

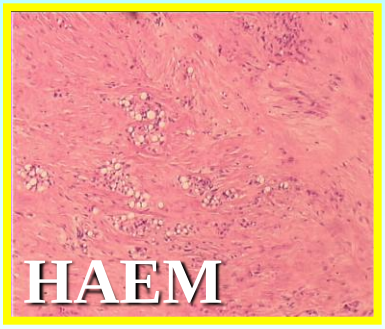


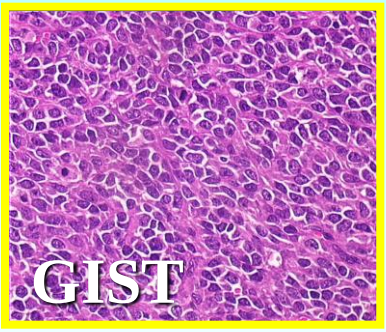












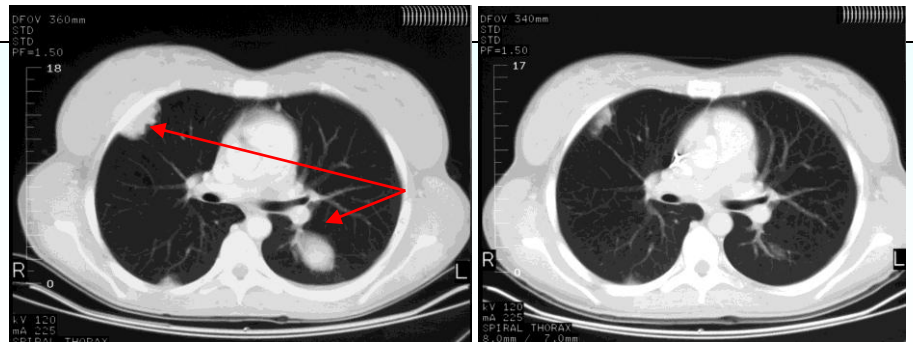
> 50 types histologiques différents !

Sarcomes des tissus mous métastatiques : Chimiosensibilité variable d'un type à l'autre ?

Auteurs	Schéma	LeiomyoS OR (%)	SynovialoS OR (%)
Bramwell	SDI (5 g/m2)	0	29
Benjamin	SDI (6-10 g/m2)	10	16
Nielsen	HDI (12 g/m2)	5	44
TOTAL		7%	45%

Synovialosarcome : sensibilité particulière à l'ifosfamide

Léiomyosarcome: résistance à l'ifosfamide ?



Chimiosensibilité variable d'un type de STM à l'autre ?

RÔLE DU PACLITAXEL

Schéma	ligne de tt	N	RO	Institution
200 mg/m2	2e ligne	13	0%	Florida
250 mg/m	SENSIBLITE PARTICULIERE DES ANGIOSARCOMES ?			WOG
250 mg/m2 3h q3s	1/2e ligne	28	7%	MSKCC
	Réponses dans les angiosarcomes			
100 mg/m2 q2s	1/2e ligne (Kaposi)	56	59%	Gill (LA)

Chimiosensibilité variable d'un type de STM à l'autre ?

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

Efficacité du paclitaxel hebdomadaire dans les formes cutanées d'angiosarcomes

Table 3. Response Rates

Assessable patients	27*	22	21
Progressive disease	7	12	16
Complete response	0	1	3†
Partial response	5	3	1
Stable disease	15	6	1
Overall response rate			
%	18	18	19
95% CI	4 to 33	2 to 34	3 to 35
Nonprogression rate			
%	74	45	24
95% CI	57 to 90	25 to 66	6 to 42

*Three patients of the 30 enrolled patients were not assessable because of the following reasons: death by unrelated stroke (one patient), severe toxicities with treatment cessation (two patients).

†Complete responses were obtained by surgery (Table 4).

Chimiosensibilité variable d'un type de STM à l'autre ?

GEMCITABINE et LEIOMYOSARCOMES

Schéma	N	RO	Auteurs	non LMS	LMS
1250 mg/m² d1, 8 q3s	29	3%	Svancarova 2002	0/19	1/12
1250 mg/m² d1, 8, 15 q4s	26	3%	Okuno 2002	0/18	1/11
200 mg/m² 6h d1, 8, 15 q4s	18	10 %	Spath 2000	1/12	2/6
1000 mg/m² s 7s/8	18	5 %	Merimsky 2000	1/16	1/2
1000 mg/m² s 7s/8	39	10 %	Patel 2001	3/29	4/10
			Réponse objective	5%	22%

Chimiosensibilité variable d'un type de STM à l'autre ?

YONDELIS (ET-743)

- Liaison au brin – de la double hélice d'ADN
- Interaction avec facteurs de transcription et protéines de liaison à l'ADN
- Perturbation cycle cellulaire: ralentissement phase S et blocage en G2
- Interaction avec les mécanismes de réparation de l'ADN

Réponse	N= 189	(%)
CR	1	0.5%
PR	13	7%
MR	11	6 %
SD	75	40%
SD > 6 mois	32	17%

Toutes histologies confondues:

Bénéfice clinique durable: 30%

PFS médiane: 7~8 mois

YONDELIS: essais de Phase II

VOLUME 23 · NUMBER 3 · JANUARY 20 2005

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Phase II Study of ET-743 in Advanced Sarcomas: A European Organisation fo and Treatment of Cancer (EORTC) So Bone Sarcoma Group Trial

A. Le Cesne, J.Y. Blay, I. Judson, A. Van Oosterom, J. Verweij, J. Radfor I. Ray-Coquard, S. Bonvalot, F. Collin, J. Piperno, E. Di Paola, M. Vite

ABSTRACT

Purpose
This nonrandomized multicenter phase II study was performe safety of Ecteinascidin (ET-743) administered at a dose of 1.5 m infusion every 3 weeks in patients with pretreated advanced

Patients and Methods
Patients with documented progressive advanced soft tissue second- or third-line chemotherapy. Antitumor activity was e progression, excessive toxicity, or patient refusal.

Results
One hundred four patients from eight European institutions (March 1999 to November 2000). A total of 410 cycles were a patients. Toxicity mainly involved reversible grade 3 to 4 transaminases in 40% of patients, and grade 3 to 4 neutrope patients. There were eight partial responses (PR; objective change (NC; > 6 months in 26% of patients), and 39 progre arrest rate (PR + NC) of 56% was observed in leiomyosarco coma. The median duration of the time to progression was progression-free survival was 29%. The median duration of s

Conclusion
ET-743 seems to be a promising active agent in advanced cumulative toxicities. The 6-months progression-free surviva tissue sarcoma compares favorably with those obtained with second-line chemotherapy in previous European Organisation ment of Cancer trials. The median overall survival was un pretreated patients mainly due to the high number of patients terms of tumor control.

J Clin Oncol 23:576-584. © 2005 by American Society of Clin

INTRODUCTION

Results of first-line chemotherapy in adult advanced soft tissue sarcoma remain disappointing. Only two drugs, doxorubicin and ifosfamide, have demonstrated a relatively consistent single-agent activity yielding re- sponse rates o despite highe some studies therapy, multi onstrated any survival when doxorubicin g

576

From the Institut Gustave Roussy, Villejuif; Centre Leon Berard, Lyon; Centre Leclerc, Dijon, France; Royal Marsden Hospital, London; Christie Hospital, Manchester; Weston Park Hospital, Sheffield, UK; U.Z. Gasthuisberg, Leuven; EORTC Data Center, Brussels, Belgium; Rotterdam Cancer Institute, Rotterdam; Antoni van Leeuwenhoekhuis, Amsterdam, the Netherlands; Pharma-Mar, Tres Cantos, Spain; Aarhus University Hospital, Aarhus, Denmark.

Submitted January 29, 2002; accepted October 12, 2004.

Authors' disclosures of potential conflicts of interest are found at the end of this article.

Address reprint requests to Axel Le Cesne, MD, Department of Medicine, Institut Gustave Roussy, 94805 Villejuif Cedex, France; e-mail: lecesne@igr.fr.

© 2005 by American Society of Clinical Oncology

0732-183X/05/2303-576/$20.00

DOI: 10.1200/JCO.2005.01.180

VOLUME 22 · NUMBER 8 · APRIL 15 2004

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Phase II and Pharmacokinetic Study of Ecteinascidin 743 in Patients With Progressive Sarcomas of Soft Tissues Refractory to Chemotherapy

R. Garcia-Carbonero, J.G. Supko, J. Manola, M.V. Seiden, D. Harmon, D.P. Ryan, M.T. Quigley, P. Merriam, J. Carneiro, G. Goss, U. Matulonis, R.G. Maki, T. Lopez, T.A. Puckalski, M.A. Sancho, J. Gomez, C. Guzman, J. Jimeno, and G.D. Demetri

ABSTRACT

Purpose
To assess the efficacy of the marine-derived alkaloid ecteinascidin 743 (ET-743) in patients with soft tissue sarcomas that progressed despite prior conventional chemotherapy and to characterize the pharmacokinetic profiles of ET-743 in this patient population.

Patients and Methods
Thirty-six previously treated soft tissue sarcoma patients from three institutions received ET-743 as a 24-hour continuous intravenous (IV) infusion at a dose of 1,500 μg/m² every 3 weeks. Pharmacokinetic studies were also performed. Patients were restaged every two cycles for response by objective criteria.

Results
Objective responses were observed in three patients, with one complete response and two partial responses, for an overall response rate of 8% (95% CI, 2% to 23%). Responses were durable for up to 20 months. Two minor responses (43% and 47% tumor reduction) were observed, for an overall clinical benefit rate of 14%. The predominant toxicities were neutropenia and self-limited transaminitis of grade 3 to 4 severity in 34% and 26% of patients, respectively. The estimated 1-year time to progression and overall survival rates were 9% (95% CI, 3% to 27%) and 53% (95% CI, 39% to 73%), respectively. The maximum observed plasma concentration and total plasma clearance of ET-743 (mean ± standard deviation), 1.04 ± 0.48 ng/mL and 35.6 ± 16.2 L/h/m², respectively, were consistent with previously reported values from phase I studies of the drug given as a 24-hour IV infusion.

Conclusion
ET-743 is a promising new option for the management of several histologic subtypes of sarcoma. Durable objective responses were obtained in a subset of sarcoma patients with disease progression despite prior chemotherapy. Additionally, the relatively high survival rate in this series of previously treated patients further justifies development of this agent.

J Clin Oncol 22:1480-1490. © 2004 by American Society of Clinical Oncology

INTRODUCTION

Sarcomas of soft tissue represent a heterogeneous family of malignancies of mesenchymal origin that account for approximately 1% of adult neoplastic diseases diagnosed annually in the United States.[1] Although the majority of patients present with a clinically localized tumor, 30% to 60% will eventually develop local recurrence or metastatic disease.[2,3] Once the tumor has progressed beyond surgical resectability, the disease is nearly always incurable.[2,3] The median survival of patients with unresectable sarcomas of soft tissues is approximately [illegible]. Patients with unresectable sarcoma have [illegible]ting needs for new effective therapeutic options.

Doxorubicin and ifosfamide represent the two most active conventional agents in the treatment of advanced soft tissue sarcomas. Prospective studies of these drugs administered as single agents to sarcoma patients with no prior chemotherapy have demonstrated response rates ranging from 11% to 30%.[4-6] Other less active drugs in-

968

From the Dana-Farber Cancer Institute and Massachusetts General Hospital, Harvard Medical School, Boston, MA; Memorial Sloan-Kettering Cancer Center, New York, NY; and Clinical Research and Development, PharmaMar, Madrid, Spain.

Submitted February 21, 2002; accepted February 2, 2004.

Supported in part by a grant of the Ministerio de Educacion y Cultura, Spain (R.G.-C.), and by research support from PharmaMar, Madrid, Spain.

Preliminary results of the study were presented at the 37th Annual Meeting of the American Society of Clinical Oncology, San Francisco, CA, May 12-15, 2001.

Both R.G.-C. and J.G.S. contributed equally to this work.

Authors' disclosures of potential conflicts of interest are found at the end of this article.

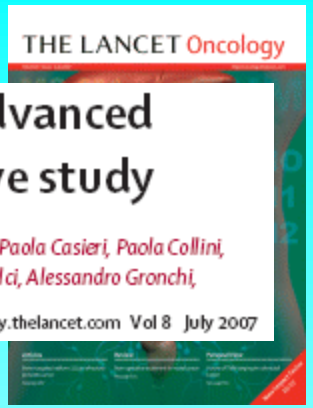
Address reprint requests to George D. Demetri, MD, Center for Sarcoma and Bone Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Shields-Warren Bldg, Room GA30, 44 Binney St, Boston, MA 02115; e-mail: gdemetri@partners.org.

© 2004 by American Society of Clinical Oncology

0732-183X/04/2208-1480/$20.00

DOI: 10.1200/JCO.2004.02.188

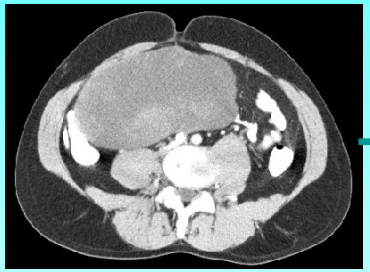
3 RO:
LIPOSARCOME MYXOIDES



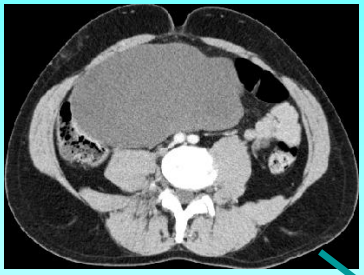
Efficacy of trabectedin (ecteinascidin-743) in advanced pretreated myxoid liposarcomas: a retrospective study

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, José Jimeno, Maurizio D'Incalci, Alessandro Gronchi, Jonathan A Fletcher, Silvana Pilotti, Paolo G Casali

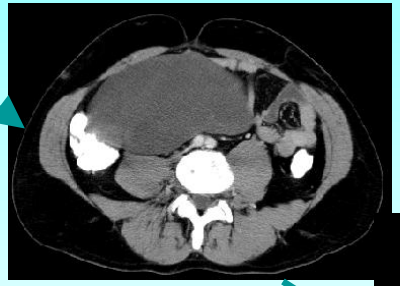
http://oncology.thelancet.com Vol 8 July 2007



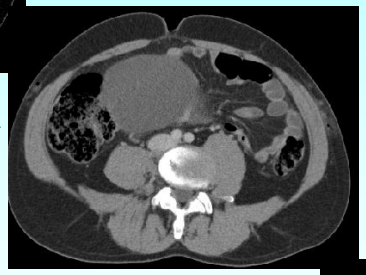
0



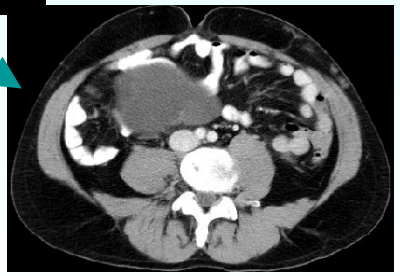
+1 c



+5 c



+8 c



+11 c

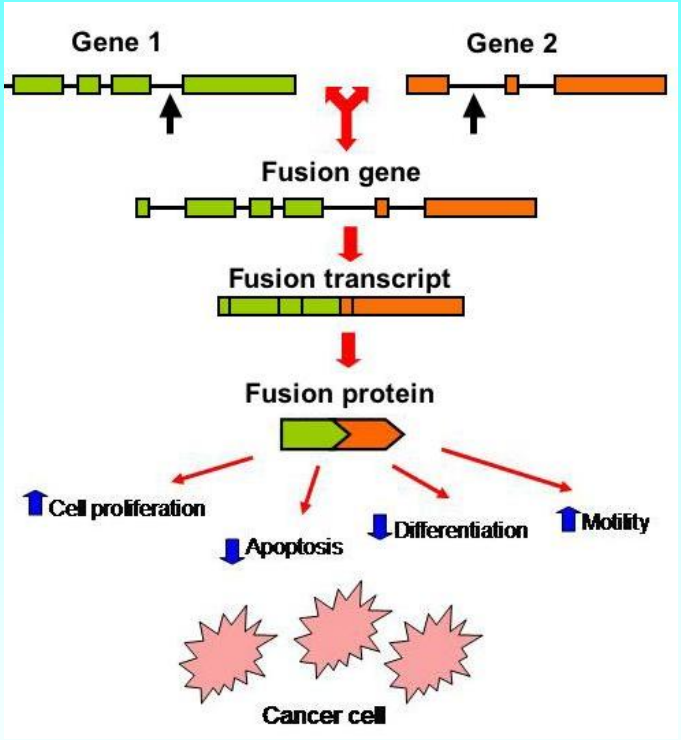
n = 51

Nb lignes antérieures > 2: 65%

Taux de réponse: 51%

PFS médiane: 14 mois

A Randomized, Multicenter ,Phase III Trial of Trabectedin (Yondelis®) versus Doxorubicin-based Chemotherapy as First-Line Therapy in Patients with Translocation -Related Sarcomas (TRS)



Translocation	Gene	Type of Fusion Gene
Ewing's sarcoma		
t(11;22) (q24;q12)	EWSR1-FLI1	Transcription factors
t(21;22) (q22;q12)	EWSR1-ERG	
t(7;22) (p22;q12)	EWSR1-ETV1	
t(17;22) (q21;q12)	EWSR1-ETV4	
t(2;22) (q33;q12)	EWSR1-FEV	
Clear cell sarcoma		
t(12;22) (q13;q12)	EWSR1-ATF1	Transcription factor
Desmoplastic small round cell tumor of the abdomen		
t(11;22) (p13;q12)	EWSR-WT1	Transcription factor
Myxoid liposarcoma		
t(12;16) (q13;p11)	FUS-DDIT3	Transcription factors
t(12;22) (q13;q12)	EWSR1-DDIT3	
Alveolar rhabdomyosarcoma		
t(2;13) (q35;q14)	PAX3-FOXO1A	Transcription factors
t(1;13) (p36;q14)	PAX7-FOXO1A	
Synovial sarcoma		
t(X;18) (p11;q11)	SYT-SSX	Transcription factor
DFSP		
t(17;22) (q22;q13)	COL1A1-PDGFB	Growth factor
Congenital fibrosarcoma		
t(12;15) (p13;q25)	ETV6-NTRK3	Transcription factor receptor
Alveolar soft-part sarcoma		
t(X;17) (p11.2;q25)	ASPL-TFE3	Transcription factor
Myxoid chondrosarcoma		
t(9;22) (q22-31;q11-12)	EWSR1-NR4A3	Transcription factor

SARCOME DES TISSUS MOUS :

QUELS FACTEURS PREDICTIFS DE REPONSE AUX AGENTS CYTOTOXIQUES ?

Sarcome des tissus mous métastatiques : Une chimiothérapie à la carte ?

AVANT 2000

ADRIAMYCINE

ADRIAMYCINE + IFOSFAMIDE

MAID

Pour tous les STM

Autres drogues inactives

APRES 2000

Traitement

à la carte:

Synovialoarcome: ifosfamide

Leiomyosarcome, MFH: gemcitabine

Liposarcomes myxoides: yondelis

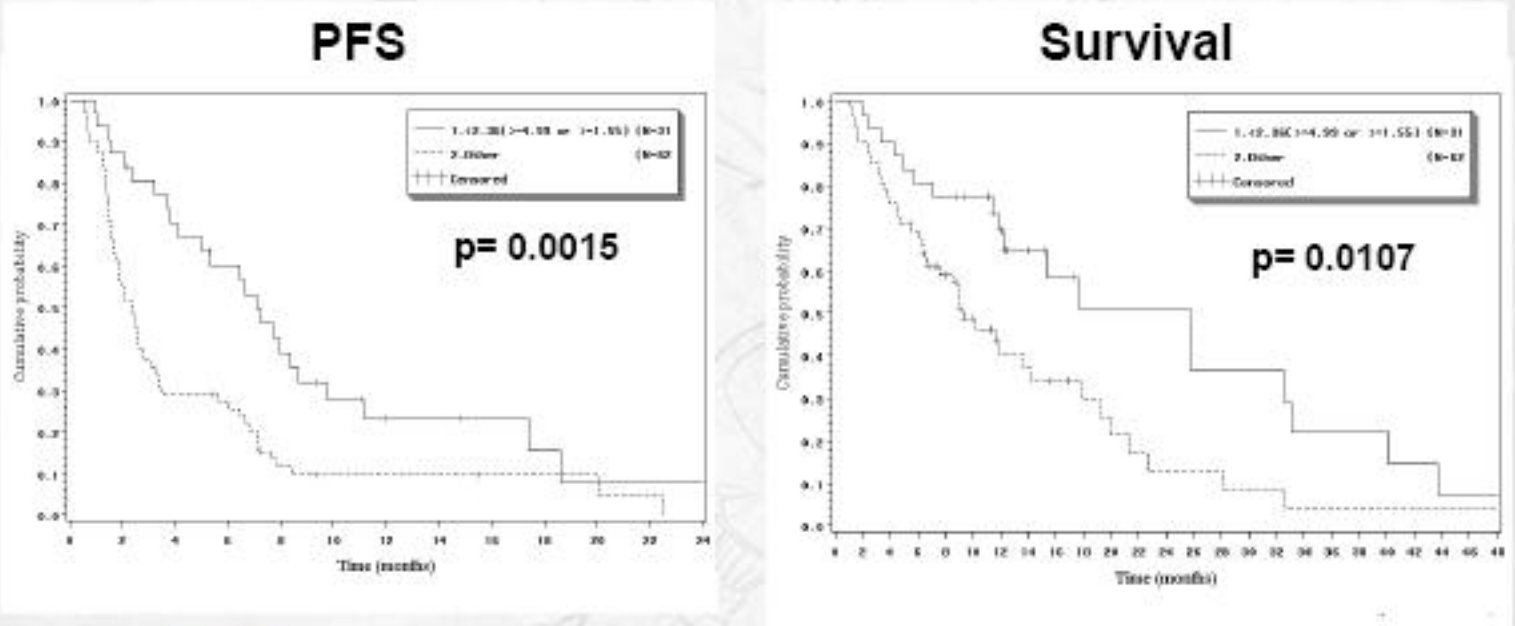
Angiosarcomes: paclitaxel

…

Nouveau concept thérapeutique

Yondelis et systèmes de réparation de l'ADN

Impact of combined Low BRCA1 + High (ERCC1 or XPG) mRNA expression in the outcome of sarcoma patients treated with trabectedin



Favorable subpopulation: low BRCA1 + high (XPG or ERCC1)

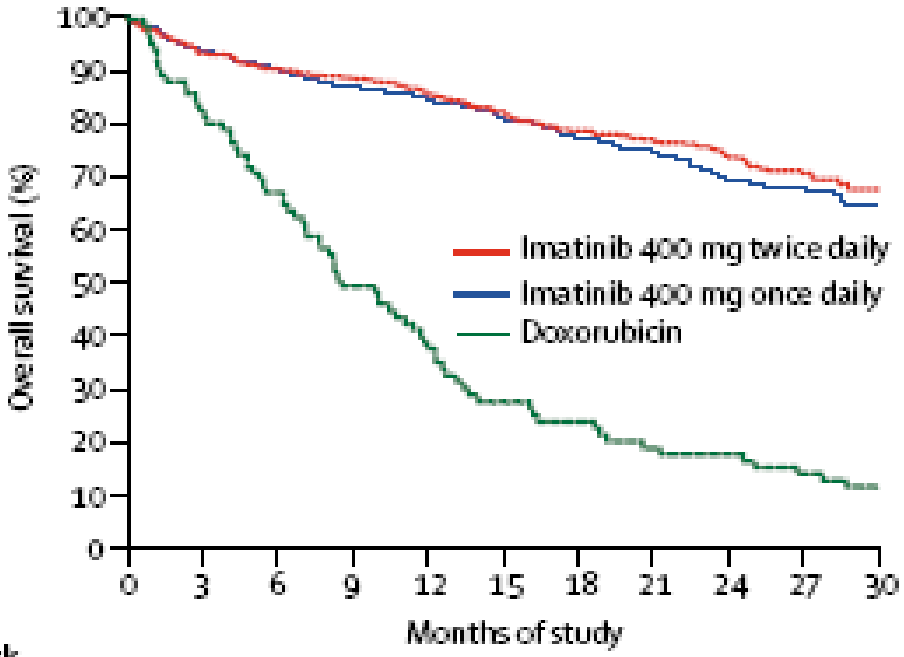
Remaining STS patients

JC Tercero, PharmaMar, data on file

Traitement médical des sarcomes des tissus mous:

Rôle des nouveaux traitements « ciblés »

L'exemple des tumeurs stromales gastro-intestinales (GIST)



Number at risk						
Imatinib 400 mg once daily	473	423	387	315	192	49
Imatinib 400 mg twice daily	473	427	399	323	201	51
Doxorubicin	86	57	31	19	14	8

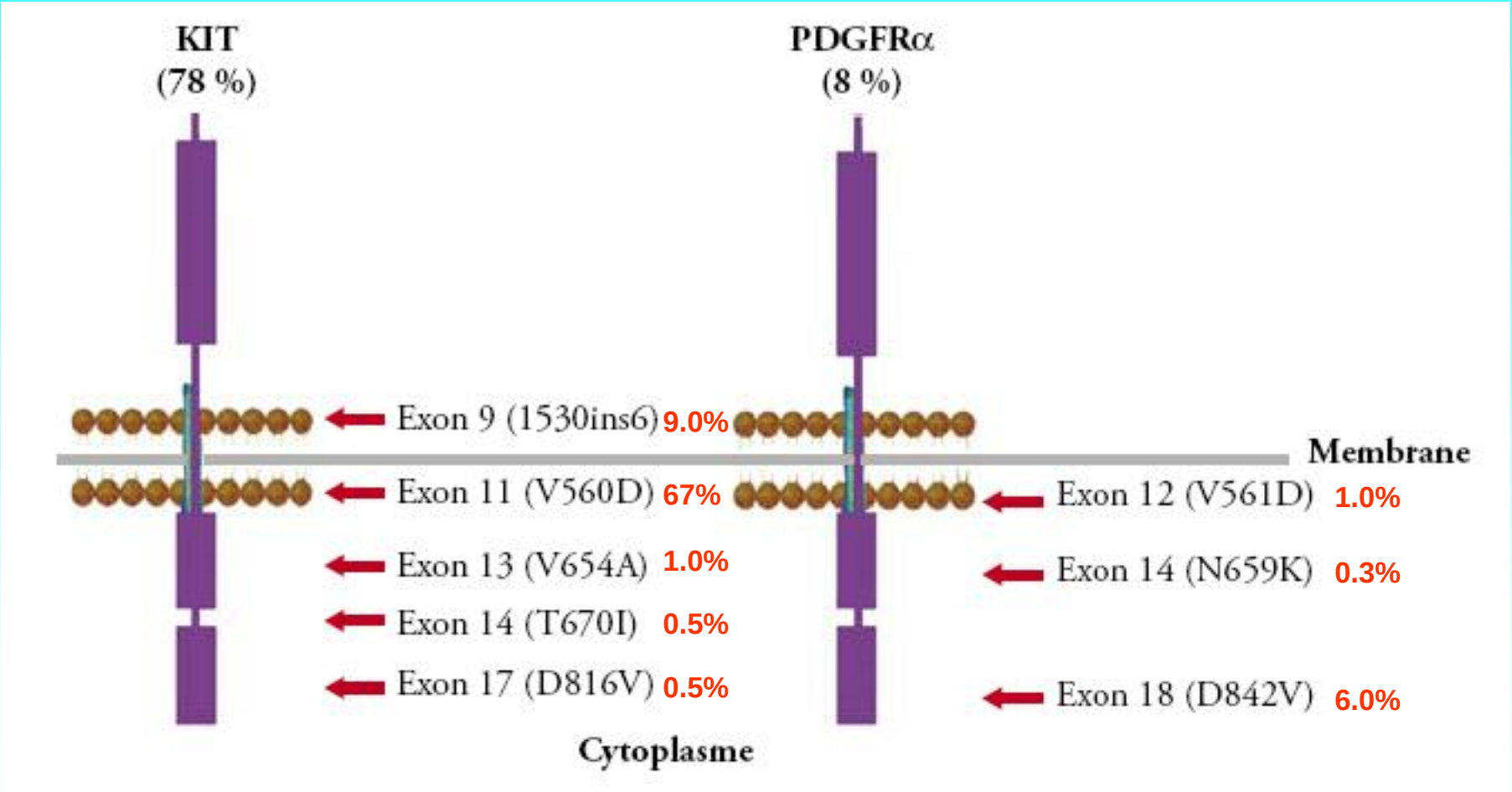
Traitement ciblé

↗ x 3 taux de survie

chimiothérapie

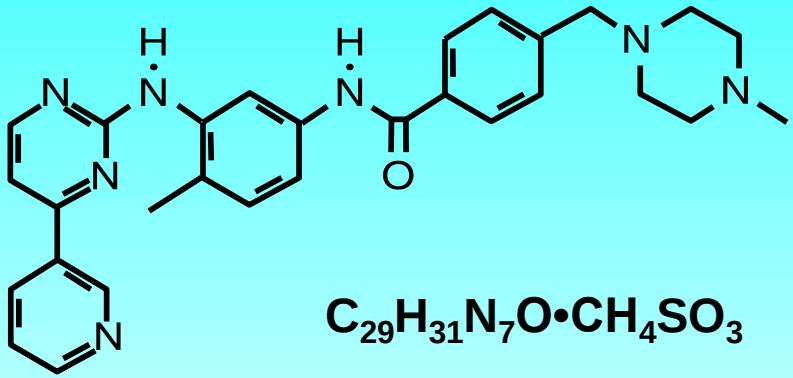
Verweij et al. Lancet 2004; 364: 1127-1134

GIST: une «définition moléculaire»

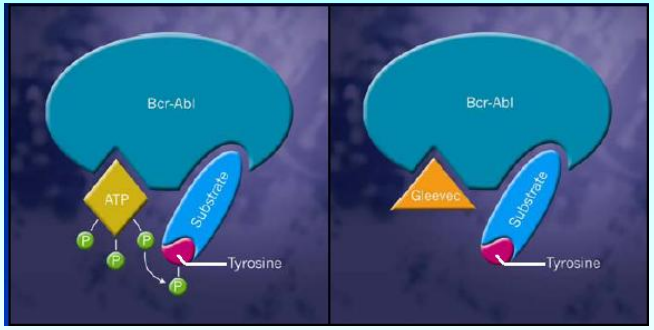


86-87% des GIST porteurs d'une mutation activatrice de *KIT* ou de *PDGFRα*

Imatinib



$C_{29}H_{31}N_7O \bullet CH_4SO_3$



Receptors	Units (IC_{50} µM)
v-ABL	0.25
p210Bcr-Abl	0.25
p185Bcr-Abl	0.25
TEL-Abl	0.35
PDGFR	0.1[a]
TEL-PDGFR	0.15
KIT	0.1[a]

IMATINIB:
Inhibiteur d'activité tyrosine kinase multi-cibles: ABL, BCR-ABL, KIT, PDGFRA, PDGFRβ, ARG et CSF1R (?)
Fixation compétitive au niveau du site de liaison à l'ATP

Druker BJ, et al. *Nat Med*. 1996;2:561; Carroll M, et al. *Blood.* 1997;90:4947.

Traitements ciblés des sarcomes non GIST

Enseignements tirés du traitement des GIST

Traitement ciblé possible si…

Présence d'une cible:

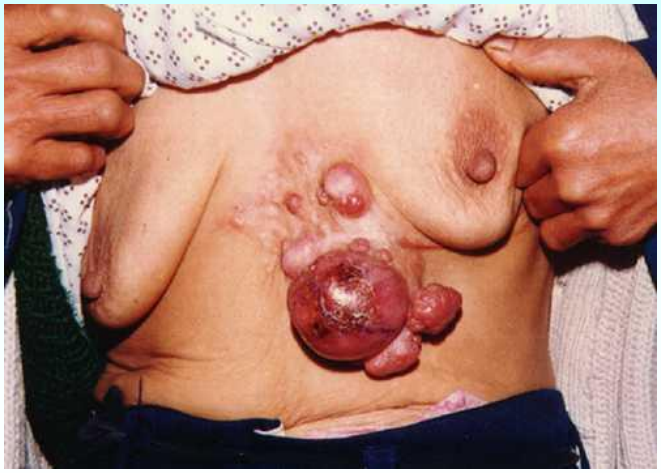
- exprimée
- activée
- jouant un rôle prépondérant dans la tumorigenèse
- pour laquelle il existe une drogue antagoniste

Dermatofibrosarcoma Protuberans

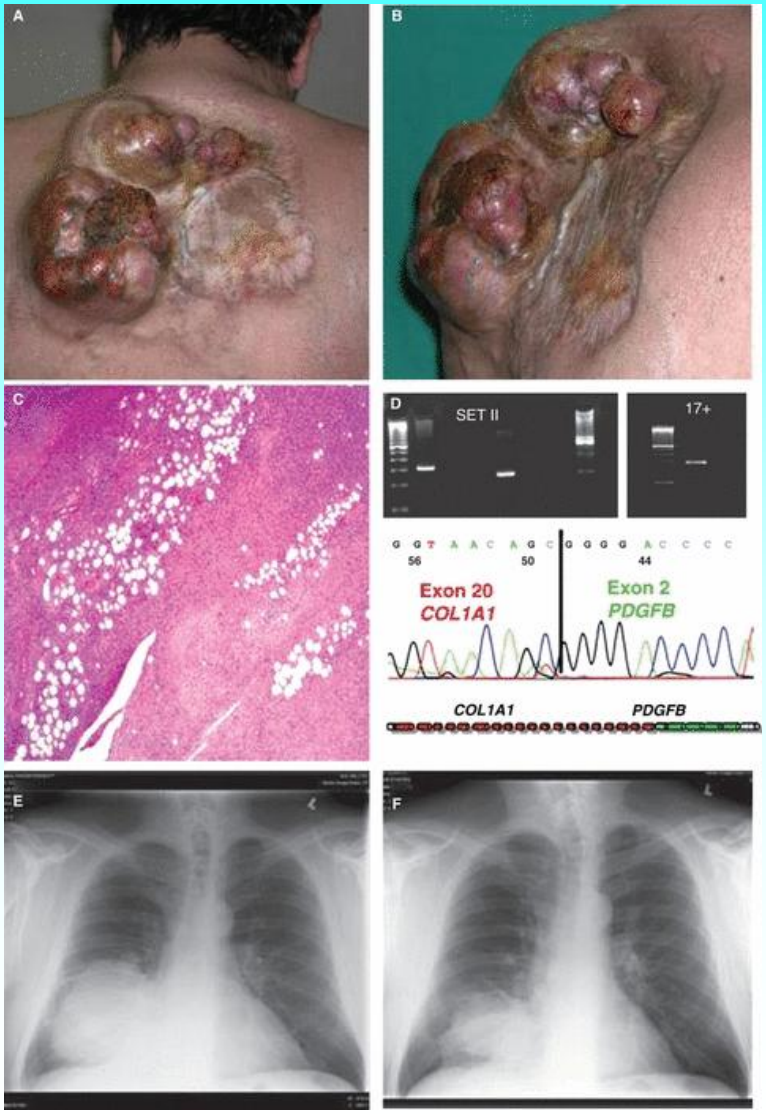
Ewing's sarcoma		
t(11;22) (q24;q12)	EWSR1-FLI1	Transcription factors
t(21;22) (q22;q12)	EWSR1-ERG	
t(7;22) (p22;q12)	EWSR1-ETV1	
t(17;22) (q21;q12)	EWSR1-ETV4	
t(2;22) (q33;q12)	EWSR1-FEV	
Clear cell sarcoma		
t(12;22) (q13;q12)	EWSR1-ATF1	Transcription factor
Desmoplastic small round cell tumor of the abdomen		
t(11;22) (p13;q12)	EWSR-WT1	Transcription factor
Myxoid liposarcoma		
t(12;16) (q13;p11)	FUS-DDIT3	Transcription factors
t(12;22) (q13;q12)	EWSR1-DDIT3	
Alveolar rhabdomyosarcoma		
t(2;13) (q35;q14)	PAX3-FOXO1A	Transcription factors
t(1;13) (p36;q14)	PAX7-FOXO1A	
Synovial sarcoma		
t(X;18) (p11;q11)	SYT-SSX	Transcription factor
DFSP		
t(17;22) (q22;q13)	COL1A1-PDGFB	Growth factor
Congenital fibrosarcoma		
t(12;15) (p13;q25)	ETV6-NTRK3	Transcription factor receptor
Alveolar soft-part sarcoma		
t(X;17) (p11.2;q25)	ASPL-TFE3	Transcription factor
Myxoid chondrosarcoma		
t(9;22) (q22-31;q11-12)	EWSR1-NR4A3	Transcription factor

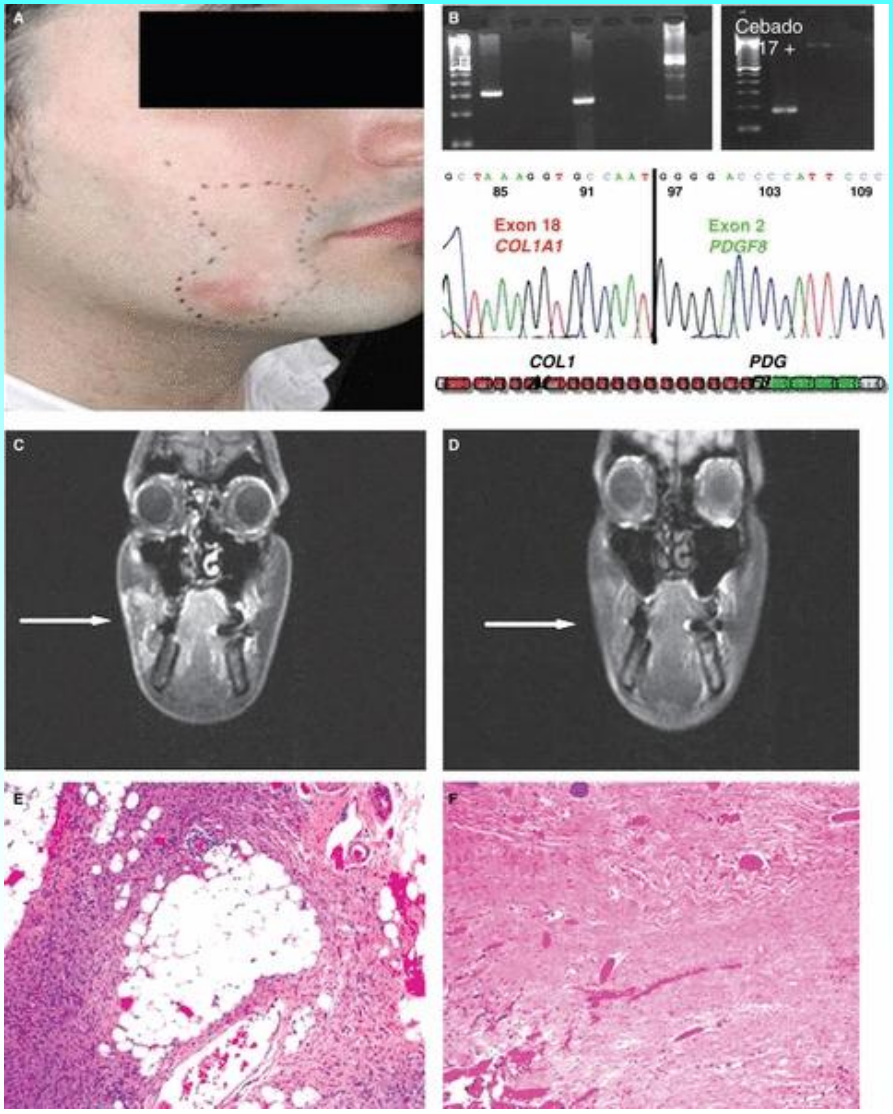
Sarcome de malignité intermédiaire

translocation t(17;22): gène collagène (*COL1A1*)/ gène platelet derived growth factor (*PDGF*)



Dermatofibrosarcome Protuberans: Imatinib





Traitement médicaux des sarcomes avancés: Perspectives

- Ne plus considérer les Sarcomes des Tissus Mous comme une seule entité
- Le meilleur standard: essai thérapeutique / recherche appliquée
- Identification de facteurs prédictifs
- Hors essai: doxorubicine en monothérapie (sauf si patient symptomatique ou potentiellement résecable: place des polychimiothérapies)
- Rôle du Yondelis en 1ère ligne : sarcomes à translocation ?
- **Refonder le schéma des essais cliniques**