Sarcomes
(des tissus mous et des viscères)

JY Blay

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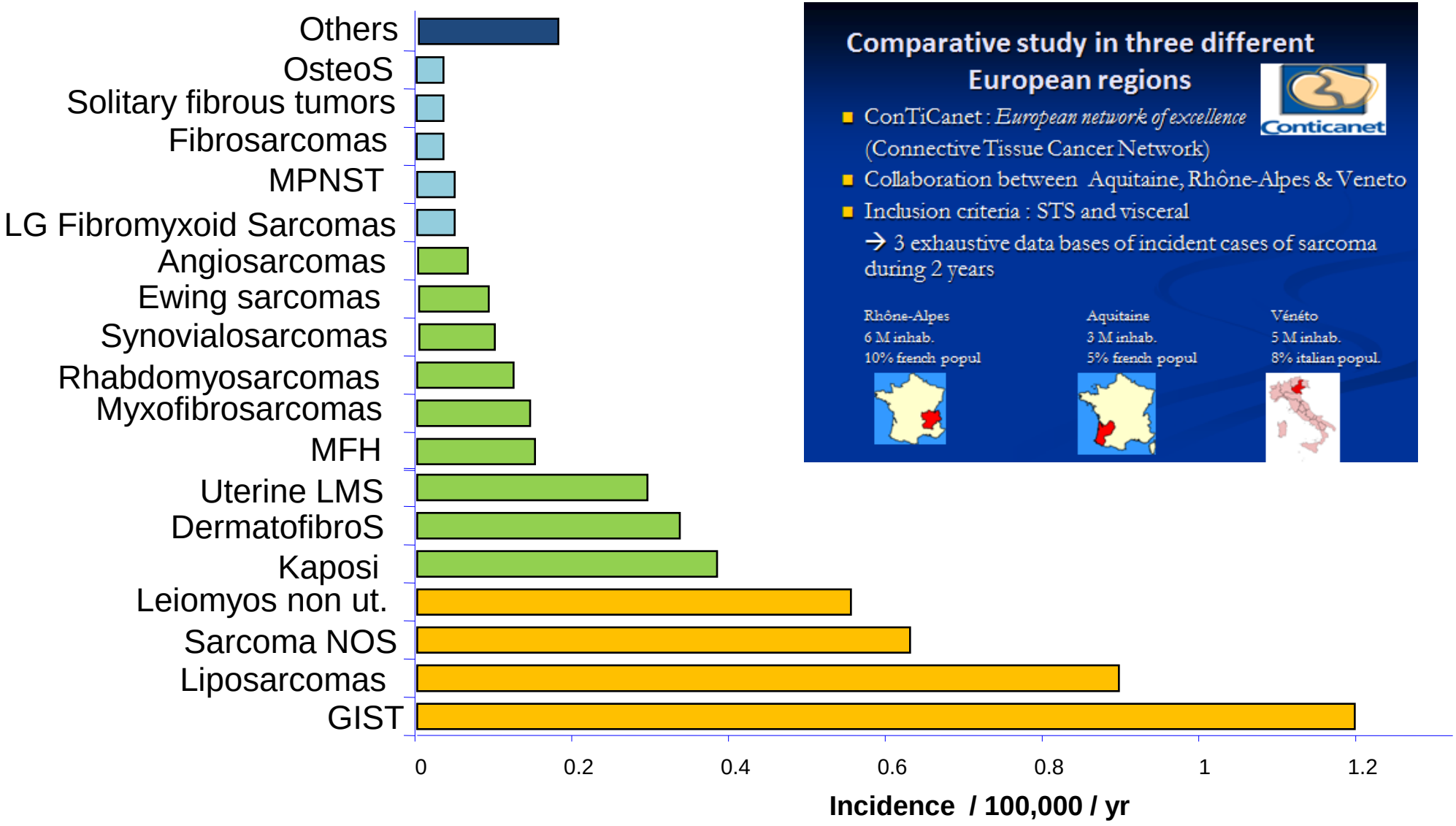
NETSARC, RREPS

Liens d’intérêt (CoI?)

- Soutiens recherche:
  - Novartis, GSK, Pharmamar, Roche, MSD, Bayer, Cytheris, Oncotherapy Science
- Conseil/ Honoraires:
  - Novartis, GSK, Pharmamar, Roche, MSD, Bayer

Over 80 histotypes of sarcomas…

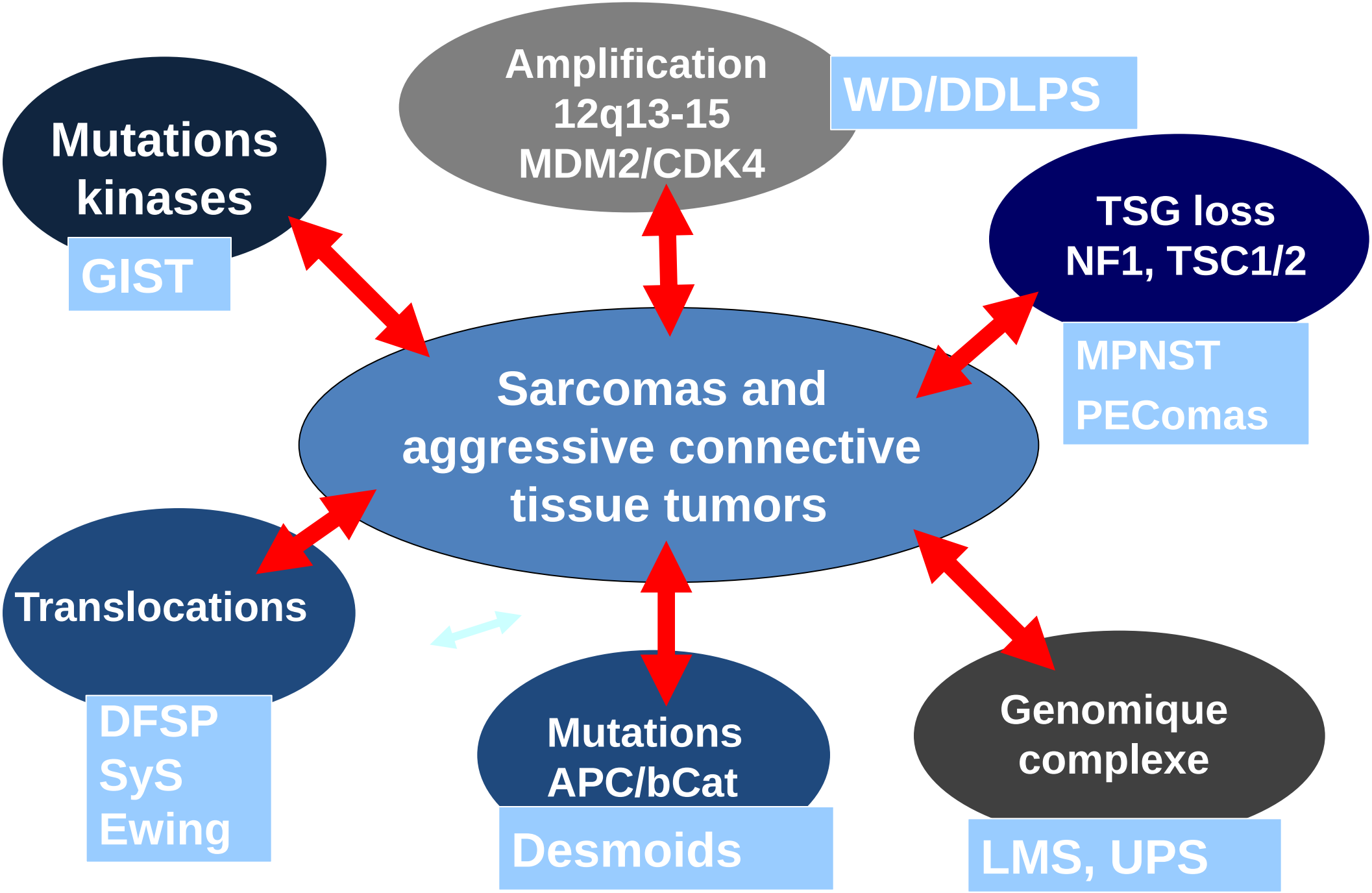


Comparative study in three different European regions

- ConTiCanet : *European network of excellence* (Connective Tissue Cancer Network)
- Collaboration between Aquitaine, Rhône-Alpes & Veneto
- Inclusion criteria : STS and visceral

→ 3 exhaustive data bases of incident cases of sarcoma during 2 years

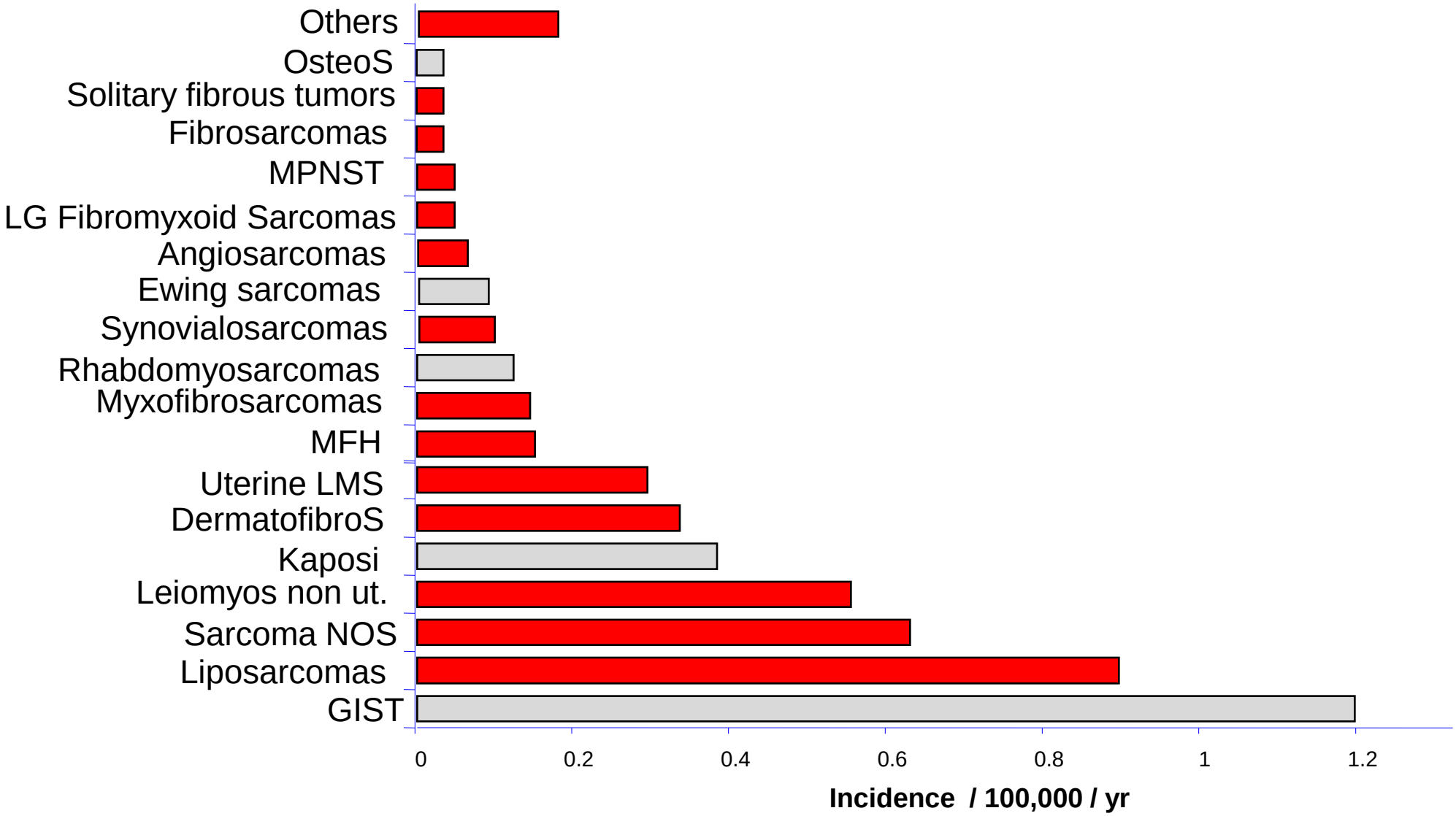
Rhône-Alpes	Aquitaine	Vénéto
6 M inhab.	3 M inhab.	5 M inhab.
10% french popul	5% french popul	8% italian popul.


Amplification
12q13-15
MDM2/CDK4
WD/DDLPS
Mutations
kinases
GIST
TSG loss
NF1, TSC1/2
MPNST
PEComas
Sarcomas and
aggressive connective
tissue tumors
Translocations
DFSP
SyS
Ewing
Mutations
APC/bCat
Desmoids
Genomique
complexe
LMS, UPS

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

European Society for Medical Oncology

Incidence of sarcoma



Doxorubicin alone versus intensified doxorubicin plus ifosfamide for first-line treatment of advanced or metastatic soft-tissue sarcoma: a randomised controlled phase 3 trial

Lancet Oncol 2014; 15: 415–23

*Ian Judson, Jaap Verweij, Hans Gelderblom, Jörg T Hartmann, Patrick Schöffski, Jean-Yves Blay, J Martijn Kerst, Josef Sufliarsky, Jeremy Whelan, Peter Hohenberger, Anders Krarup-Hansen, Thierry Alcindor, Sandrine Marreaud, Saskia Litière, Catherine Hermans, Cyril Fisher, Pancras C W Hogendoorn, A Paolo dei Tos, Winette T A van der Graaf, for the European Organisation and Treatment of Cancer Soft Tissue and Bone Sarcoma Group**

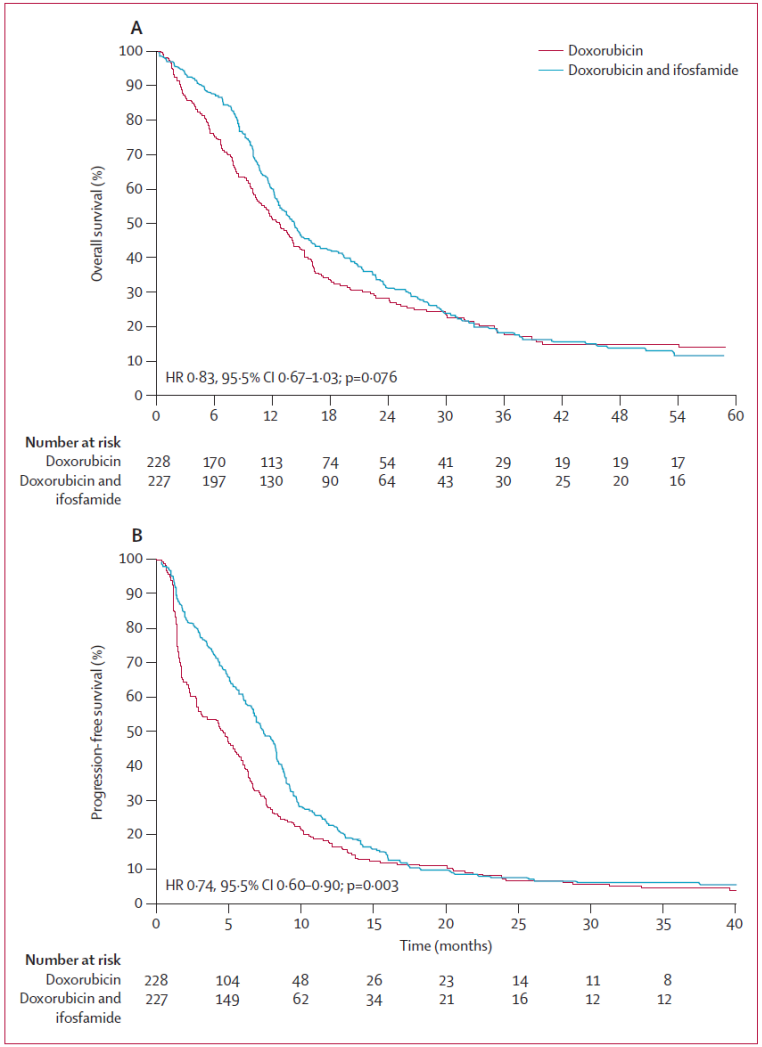


Figure 2: Kaplan-Meier curves for overall survival (A) and progression-free survival (B)
HR=hazard ratio.

	Doxorubicin group (n=228)	Doxorubicin and ifosfamide group (n=227)
Complete response	1 (<1%)	4 (2%)
Partial response	30 (13%)	56 (25%)
Stable disease	105 (46%)	114 (50%)
Progressive disease	74 (32%)	30 (13%)
Early death (progression)	4 (2%)	5 (2%)
Early death (other cause)	3 (1%)	2 (1%)
Not evaluable	11 (5%)	16 (7%)

Data are n (%).

Table 3: Responses to treatment

High doses when response or PFS is the most important enpoint (eg presurgery)

After failure of anthracyclins

Ifosfamide

Trabectedine

Pazopanib

Gemcitabine and Docetaxel

Dacarbazine and Gem

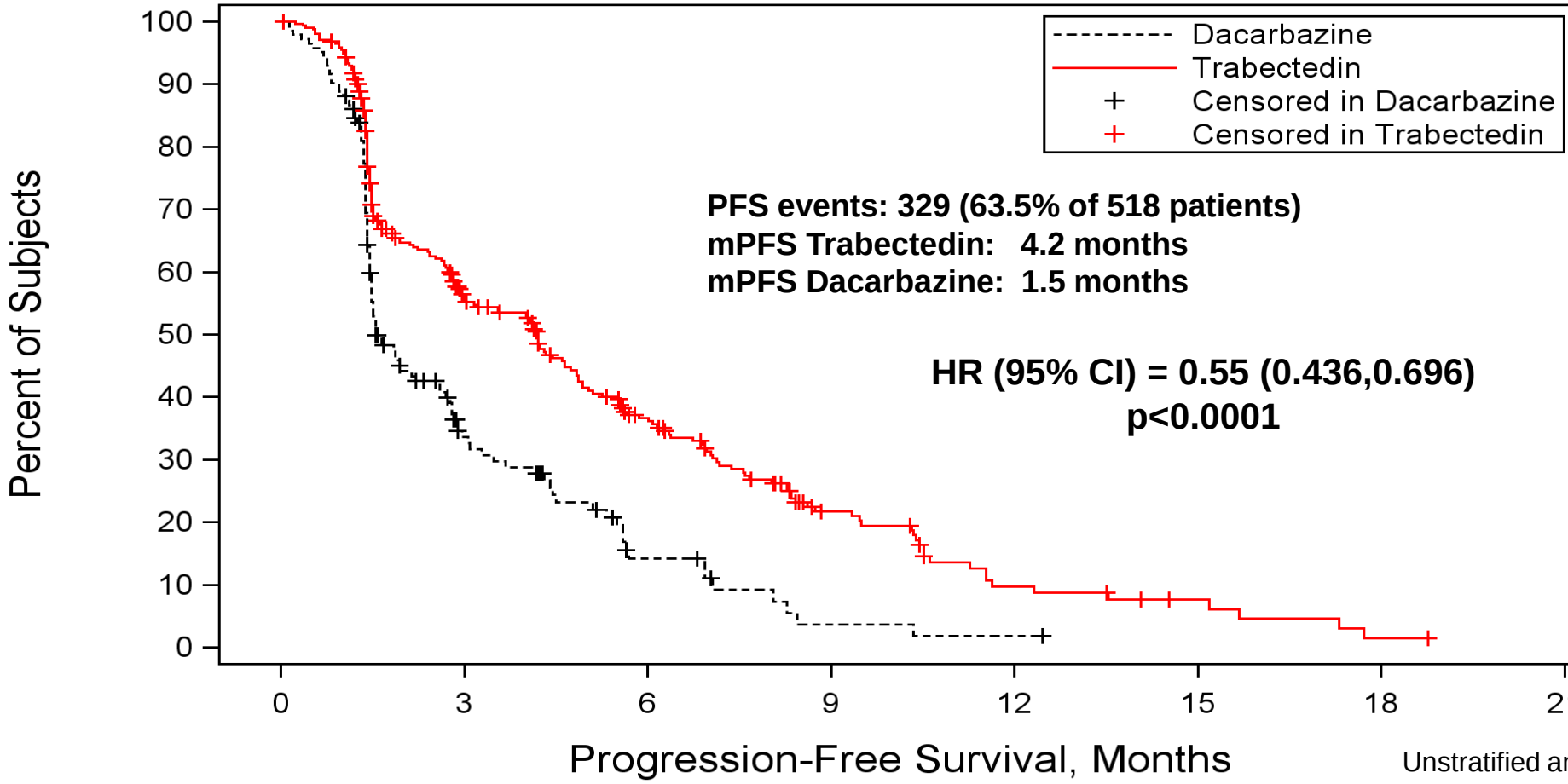
A Randomized Phase 3 Study of Trabectedin or Dacarbazine for the Treatment of Patients With Advanced Liposarcoma (LPS) or Leiomyosarcoma (LMS)

George D. Demetri, Margaret von Mehren, Robin Lewis Jones, Martee Leigh Hensley, Scott Schuetze, Arthur P. Staddon, Mohammed M. Milhem, Anthony D. Elias, Kristen N. Ganjoo, Hussein Abdul-Hassan Tawbi, Brian Andrew Van Tine, Alexander I. Spira, Andrew Peter Dean, Nushmia Z. Khokhar, Youn Choi Park, Roland E. Knoblauch, Trilok V. Parekh, Robert G. Maki, Shreyaskumar Patel

Dana-Farber Cancer Institute and Ludwig Center at Harvard Medical School, Boston, MA; Fox Chase Cancer Center, Philadelphia, PA; Seattle Cancer Care Alliance, Seattle, WA; Memorial Sloan Kettering Cancer Center, New York, NY; University of Michigan, Ann Arbor, MI; University of Pennsylvania, Philadelphia, PA; University of Iowa Hospitals and Clinics, Iowa City, IA; University of Colorado Cancer Center, Aurora, CO; Stanford Univ, Stanford, CA; University of Pittsburgh Cancer Institute, Pittsburgh, PA; Washington University in St Louis, St Louis, MO; Virginia Cancer Specialists, Fairfax, VA; St. John of God Hospital Subiaco, Subiaco, Australia; Janssen Pharmaceuticals, Raritan, NJ; Janssen Research &Development, LLC, Raritan, NJ; Mount Sinai School of Medicine, New York, NY; MD Anderson Cancer Center, Houston, TX

Final Analysis of PFS

(Investigator Assessed)

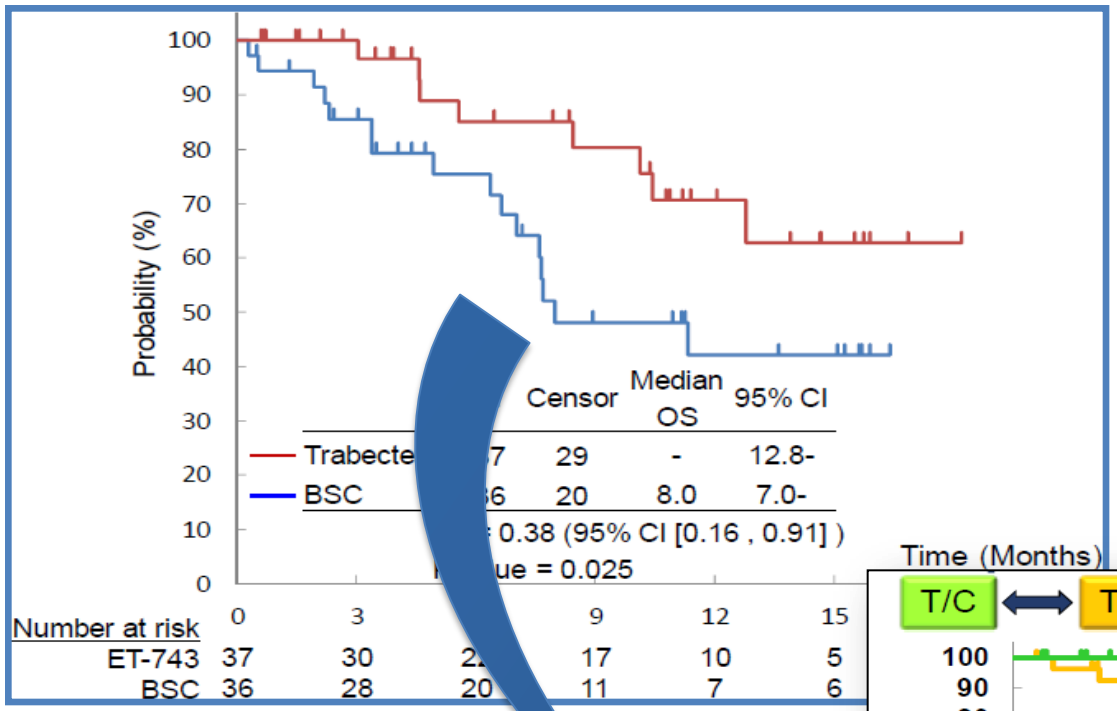


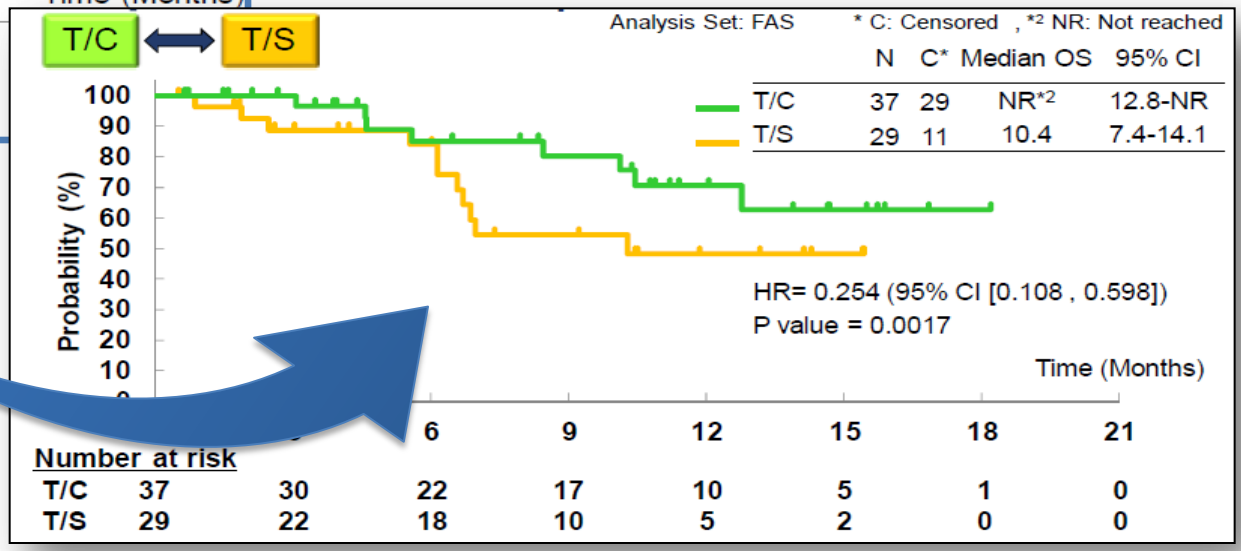
No. Subjects at Risk

Dacarbazine	173	35	10	2	1	0		
Trabectedin	345	133	71	29	10	5	1	0

Trabectedin vs BSC in Translocation-Related Sarcomas (TRS)

Overall Survival



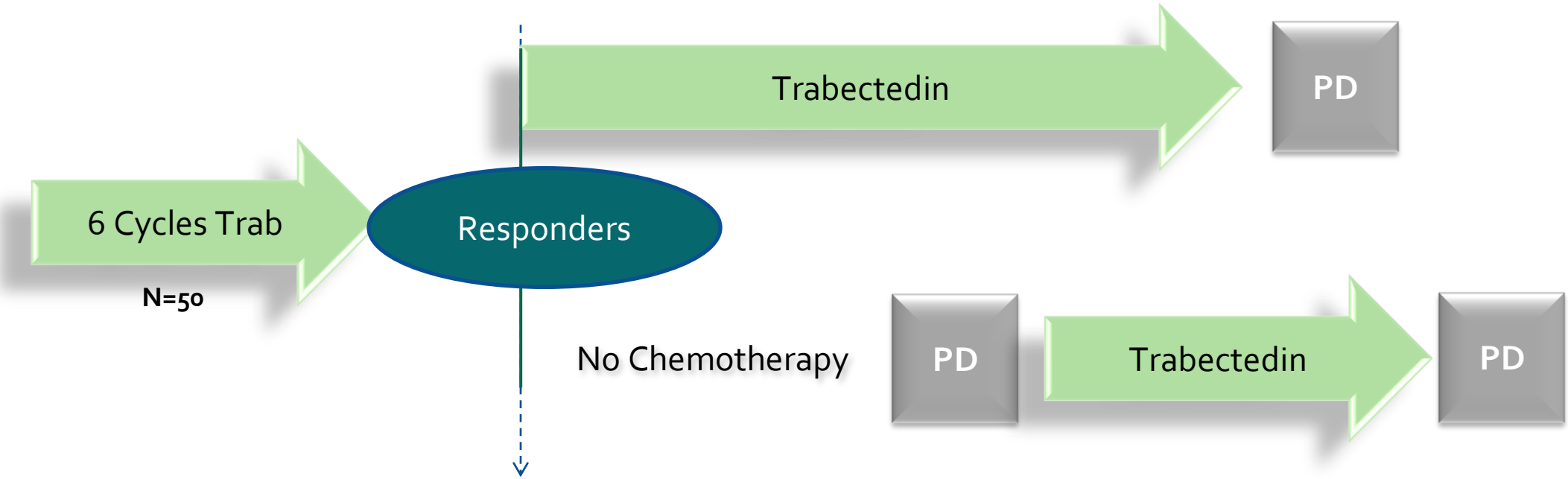


✓ **Significant prolongation of OS** HR=0,38

✓ Treatment with Trabectedin at crossover did not achieve same level of OS benefit that in the earlier line

Trabectedin : T-DIS study – Drug Holiday and Rechallenge

Interruption vs Continuation in Responding Patients After 6 Courses of Trabectedin



Primary endpoint:

- PFR 24 weeks post Randomization

Secondary endpoints:

- ORR
- PFR at 12 & 54 weeks
- Survival at 12 & 24 months

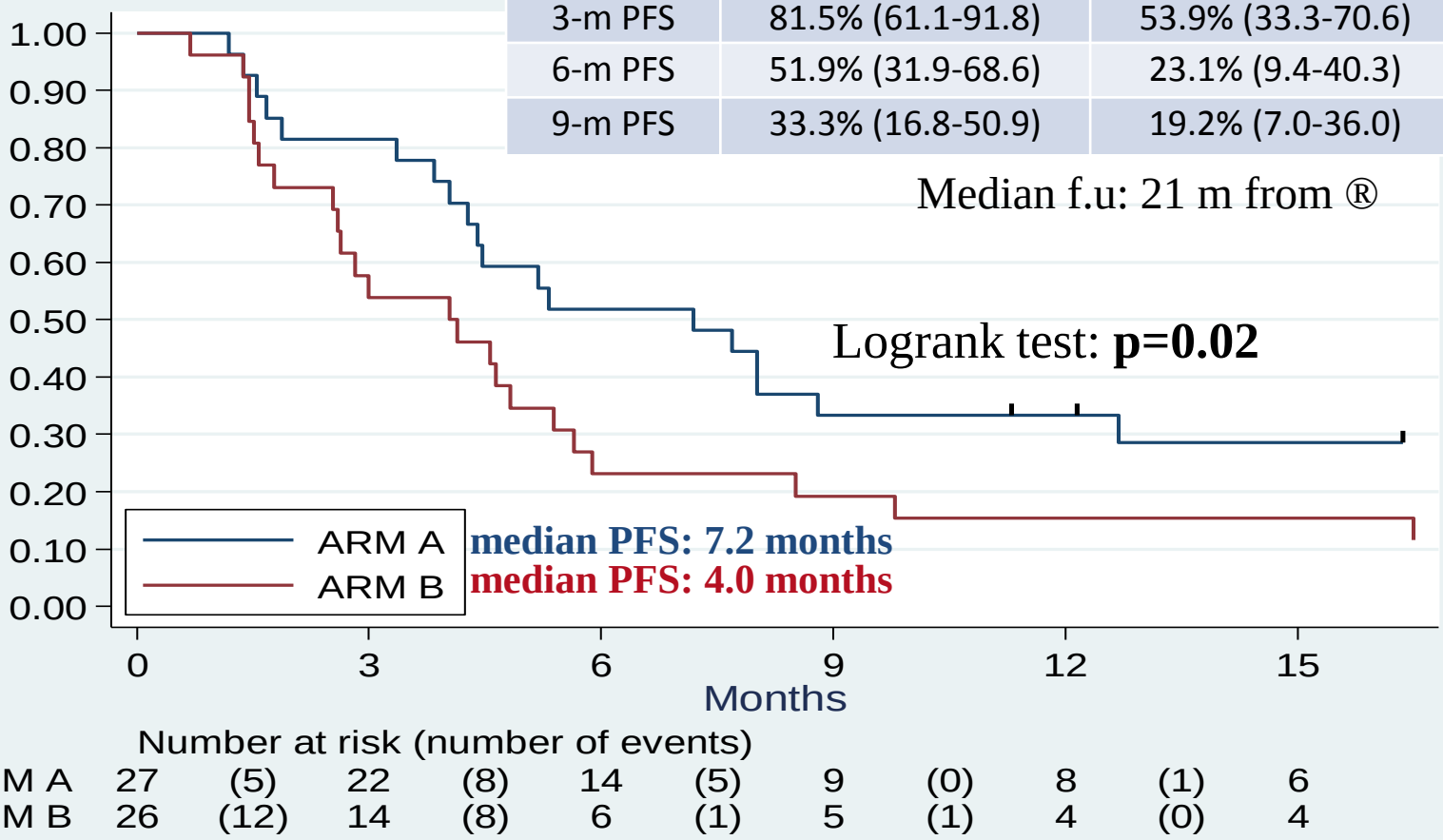
N=156 at inclusion
® = 50

Le Cesne et al, ASCO 2014 Abs Nº 10523; Le Cesne et al, ESMO 2014, Annals of Oncol 25(Supl 4): 494 Abs. Nº 1414
Le Cesne et al, Lancet Oncol 2015

T-Dis Maintenance Study

Results: Progression Free Survival (ITT)

	Arm A (cont)	Arm (discont)
3-m PFS	81.5% (61.1-91.8)	53.9% (33.3-70.6)
6-m PFS	51.9% (31.9-68.6)	23.1% (9.4-40.3)
9-m PFS	33.3% (16.8-50.9)	19.2% (7.0-36.0)

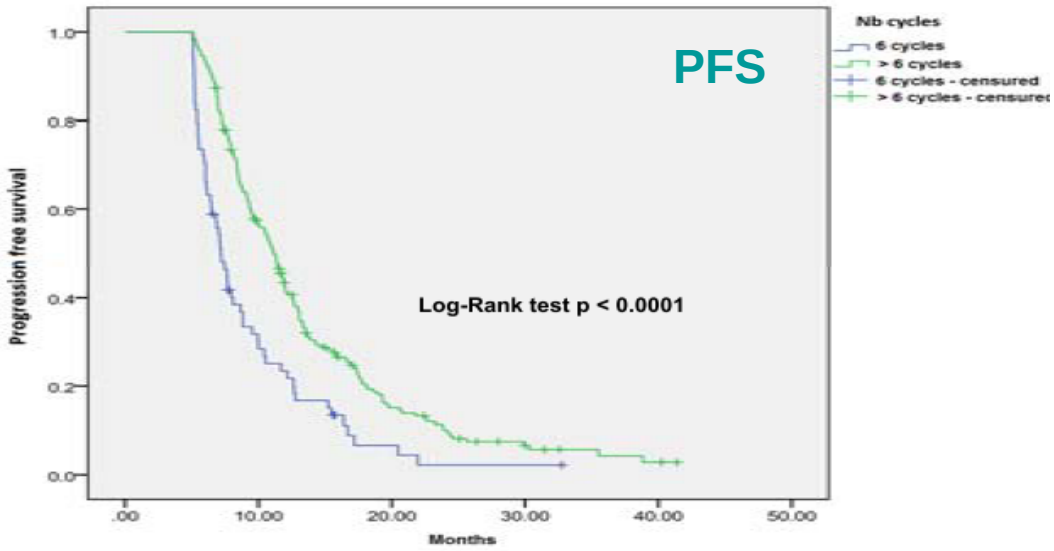


Le Cesne et al, ASCO 2014 Abs Nº 10523; Le Cesne et al, ESMO 2014, Annals of Oncol 25(Supl 4): 494 Abs. Nº 1414
Le Cesne et al, Lancet Oncol 2015

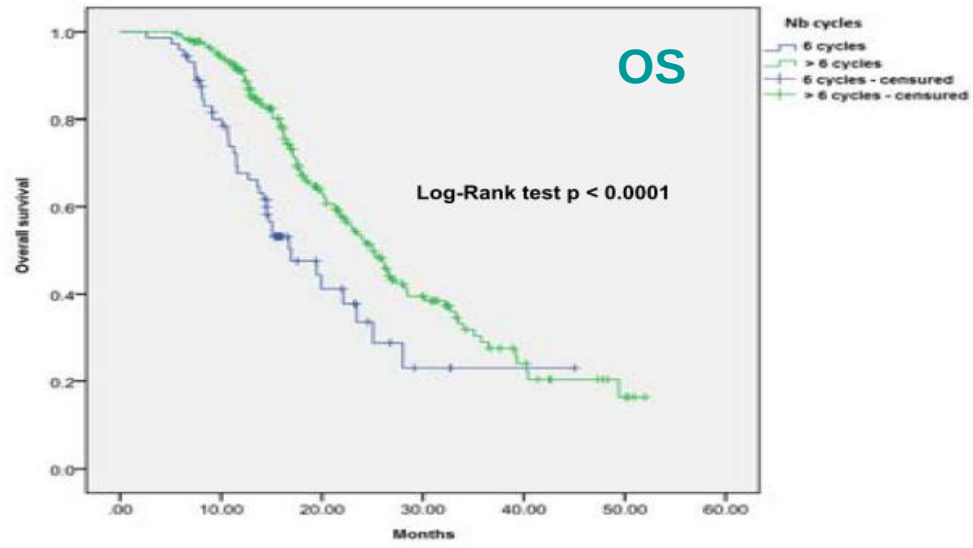
Trabectedine : Retrospectyon: Stop vs continuation >6 cycles

- After 6 cycles, 205 of the 273 patients with non-progressive disease received trabectedin as maintenance treatment and obtained a superior **PFS (median 11 vs. 7.2 months**, p=0.0001) and **OS (median 25.1 vs. 16.9 months**, p<0.0001) that those who stopped trabectedin after 6 cycles:

	Nb patients	Nb events	Median PFS	CI 95%
Interruption	68	61	7.2 months	(6.3 - 8)
Maintenance therapy	205	179	11.2 months	(10.3 - 12)



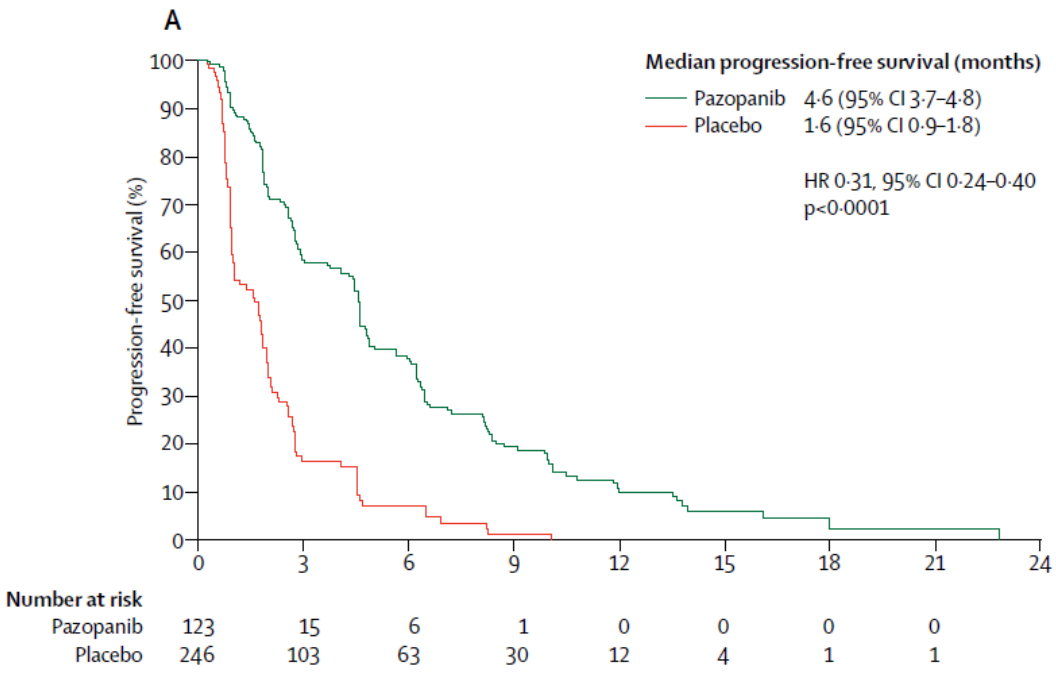
	Nb patients	Nb events	Median OS	CI 95%
Interruption	73	39	16.9 months	(11,8 - 22)
Maintenance therapy	223	113	25.1 months	(22.3 – 27.8)

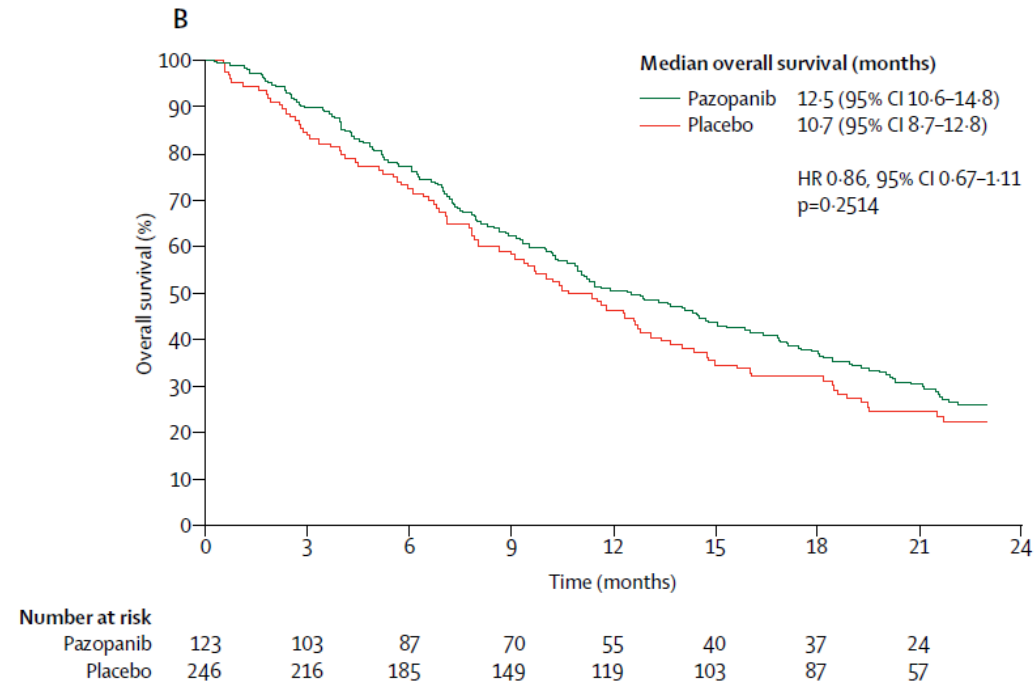


Le Cesne A, et al. J Clin Oncol. 2013;31(suppl):abstr 10563

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 P Dei Tos, Peter Hohenberger, on behalf of the EORTC Soft Tissue and Bone Sarcoma Group and the PALETTE study group





NCRI
National
Cancer
Research
Institute

SAKK

GeDDiS

A prospective randomised controlled phase III trial of gemcitabine and docetaxel compared with doxorubicin as first line treatment in previously untreated advanced unresectable or metastatic soft tissue sarcoma

Beatrice Seddon, Jeremy Whelan, Michael Leahy, Penella Woll, Fiona Cowie, Christian Rothermundt, Zoe Wood, Sharon Forsyth, Paul Patterson, Stephen Nash, Sandy Beare

CANCER RESEARCH UK

Cancer Research UK and
UCL Cancer Trials Centre

PRESENTED AT: ASCO Annual '15 Meeting

Trial Design

Eligible patients (n=250)

***Stratification factors:**

- age (≤18 years, >18 years)
- histological subtype:
  - Uterine leiomyosarcoma
  - Synovial sarcoma
  - Pleomorphic
  - Other types of eligible STS

1:1 randomisation*

Control Arm:
Doxorubicin 75 mg/m^2 day 1
every 21 days x 6 cycles

Investigational Arm:
Gemcitabine 675 mg/m^2 days 1, 8
Docetaxel 75 mg/m^2 day 8
every 21 days x 6 cycles

Disease assessments (RECIST 1.1) at:

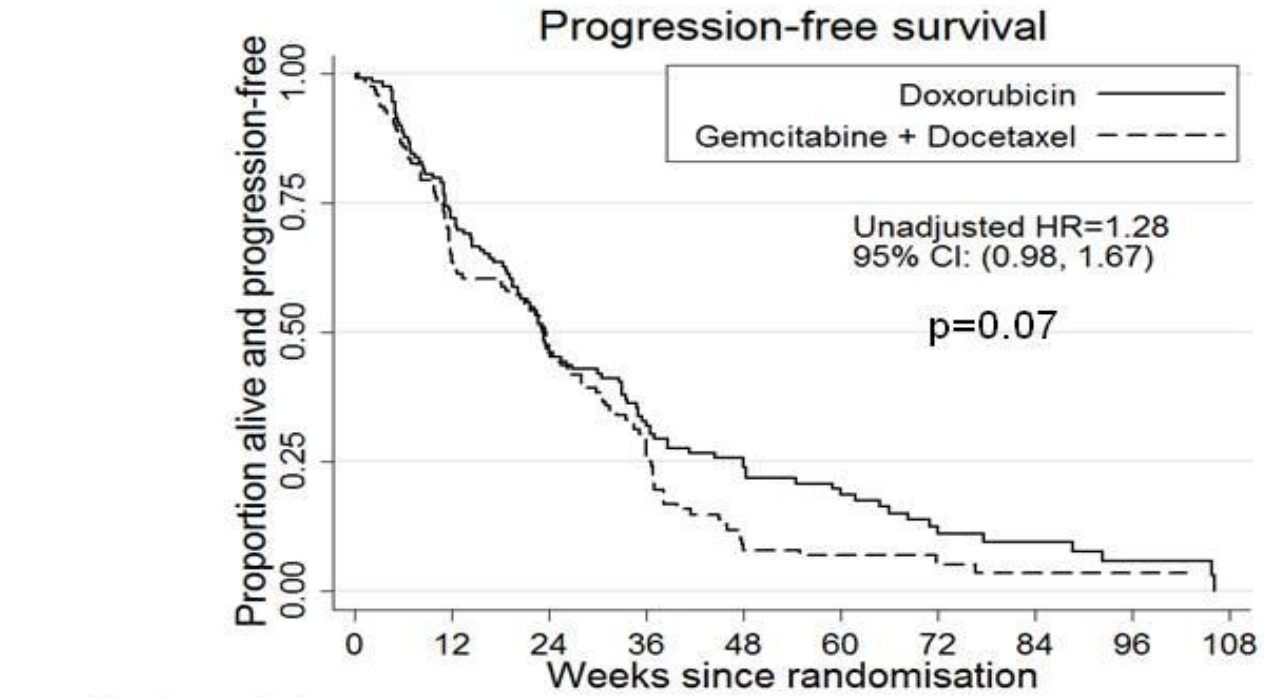
- Baseline
- 12 weeks post randomisation
- 24 weeks post randomisation
- 12 weekly thereafter

Quality of life assessments at:

- Baseline
- 12 weeks post randomisation
- 18 weeks post randomisation
- 24 weeks post-randomisation

PRESENTED AT: ASCO Annual '15 Meeting

Progression-free survival



	Median PFS (months)	24 week PFS
Dox	5.4	46.1%
GemDoc	5.5	46.0%

PRESENTED AT: ASCO Annual '15 Meeting

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] FRANÇOISE COLLIN,[f] JEAN-YVES BLAY,[k] MARTA JIMENEZ,[l] FLORENCE DUFFAUD[m]

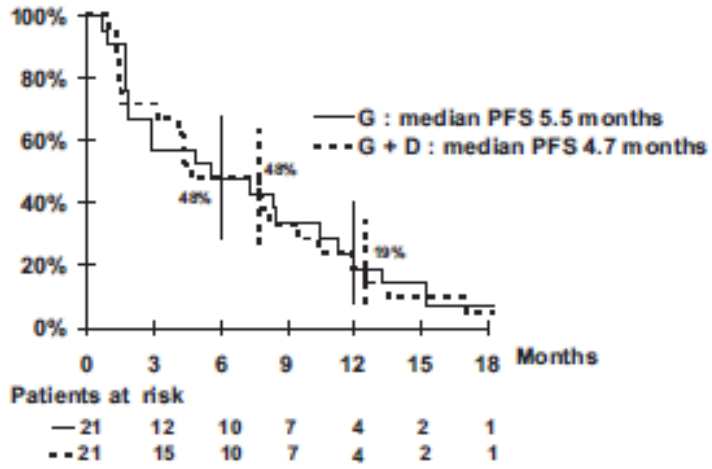


Figure 1. Kaplan–Meier curve of progression-free survival for the uterine leiomyosarcoma group.

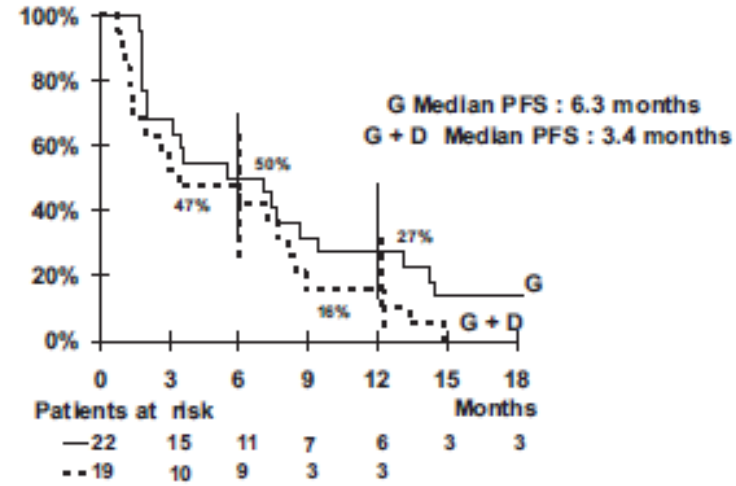
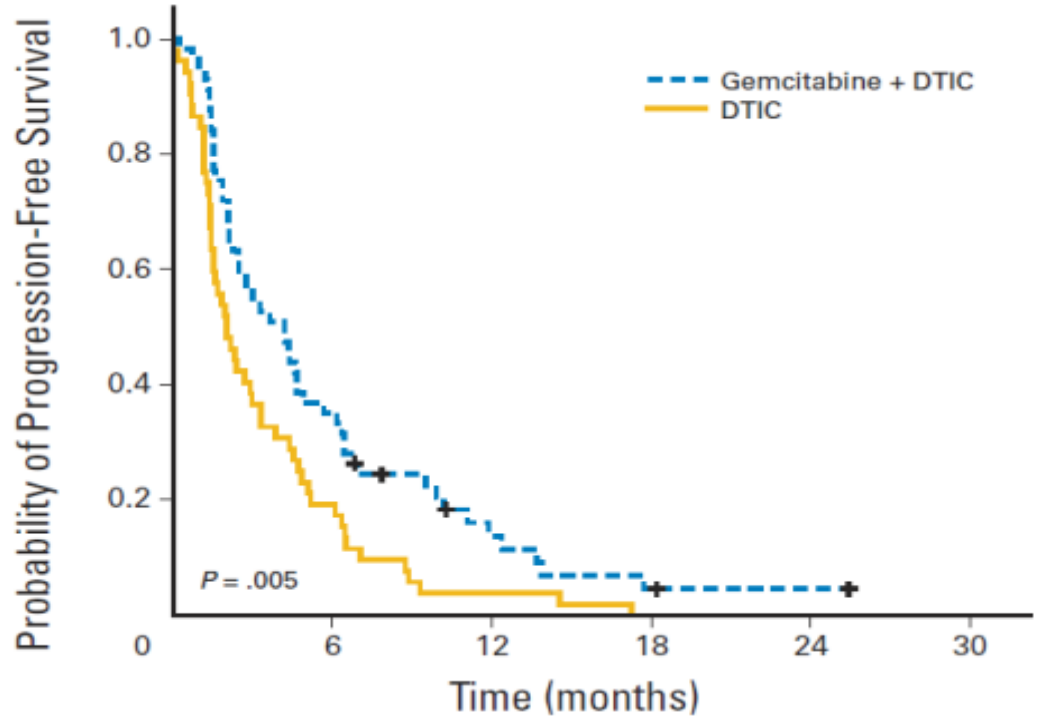


Figure 2. Kaplan–Meier curve of progression-free survival for the nonuterine leiomyosarcoma group.

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

- 113 pts with STS (2 previous lines of CT; adria & ifosfamide)
- Gem 1800mg/m² fixed + DTIC 500 mg/m² q2 weeks or DTIC 1200 mg/m² q3 weeks
- Primary endpoint, PFR @ 3 months (40% to 60%)



García-del-Muro et al. J Clin Oncol 29:2528-2533

Novel agents for all sarcomas?

Randomized, open-label, multicenter, phase 3 study of eribulin versus dacarbazine in patients (pts) with leiomyosarcoma (LMS) and adipocytic sarcoma (ADI)

Professor Dr. Patrick Schöffski

Department of General Medical Oncology

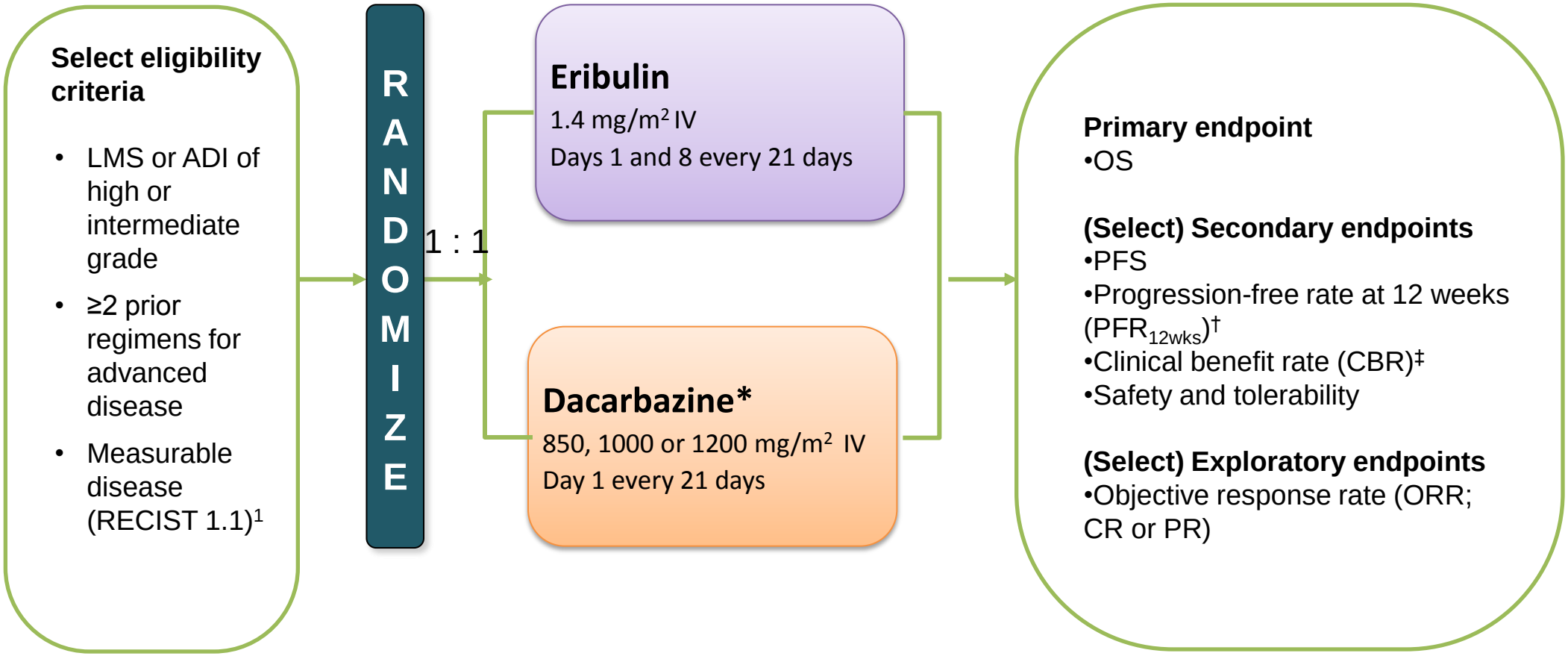
University Hospitals Leuven, Leuven Cancer Institute

KU Leuven, Leuven

Abstract # LBA10502 submitted by **P Schöffski**, R Maki, A Italiano, H Gelderblom, E Choy, G Grignani, V Camargo, S Bauer, SY Rha, S Chawla, JY Blay, P Hohenberger, DR D'Adamo, B Wang, B Chmielowski, AL Cesne, GD Demetri and S Patel.

Clinicaltrials.gov identifier: NCT01327885

Study design and objectives



*Starting dose selected by the Investigator at study initiation; †PFR_{12wks}, proportion of patients who are still alive without disease progression at 12 weeks from randomization; ‡CBR = CR or PR or durable SD, SD ≥11 weeks
CR, complete response; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease
1. Eisenhauer et al. *Eur J Cancer* 2009;45:228–247.

Key patient characteristics

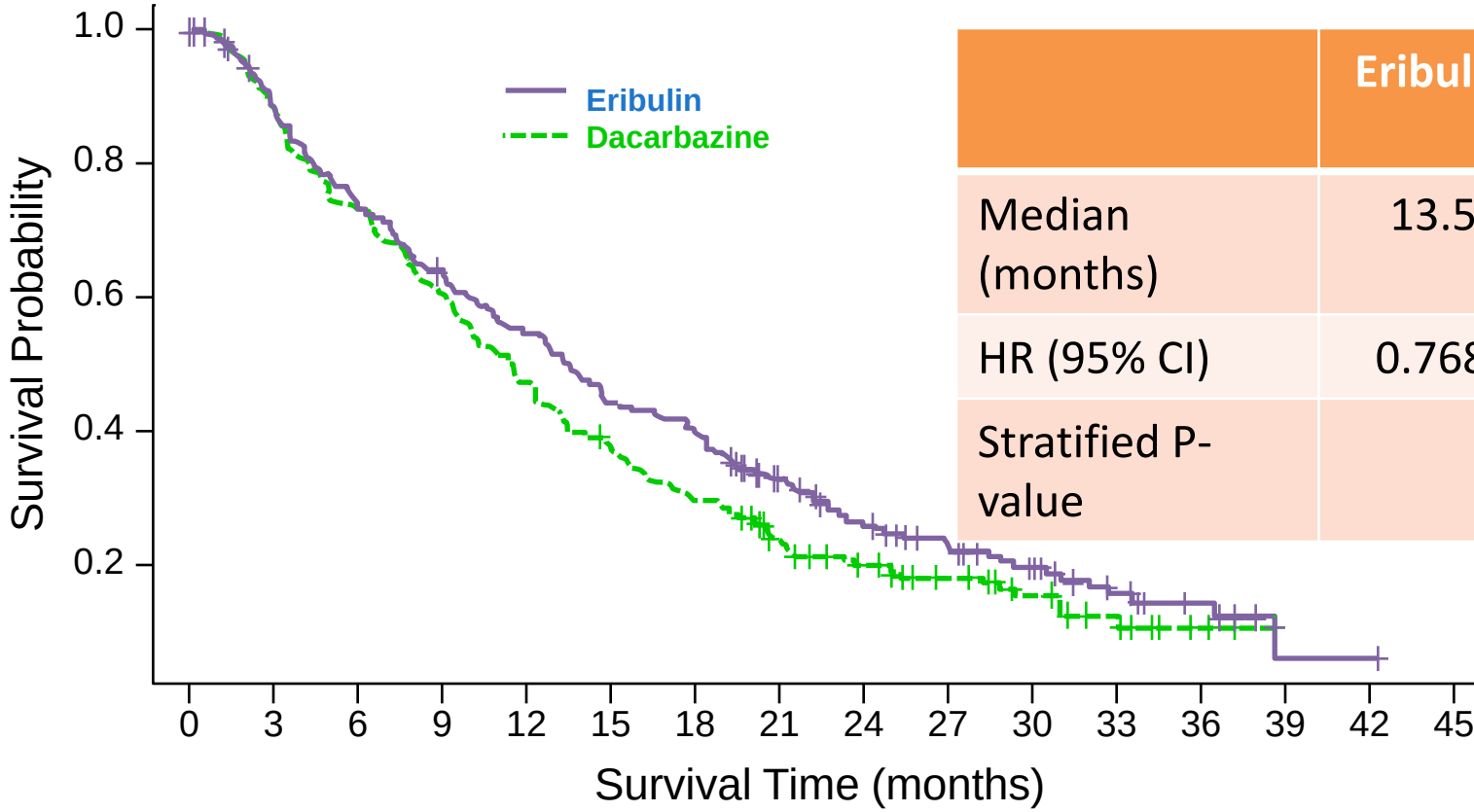
- There were no significant differences in baseline characteristics between the 2 treatment arms:

Category	Subgroup	Eribulin (n=228) n (%)	Dacarbazine (n=224) n (%)
Age	<65 years	178 (78.1)	178 (79.5)
	≥65 years	50 (21.9)	46 (20.5)
Sex	Female	161 (70.6)	142 (63.4)
Race	White	162 (71.1)	168 (75.0)
	Black or African American	6 (2.6)	6 (2.7)
	Asian*	18 (7.9)	16 (7.1)
	Other/NA	42 (18.4)	34 (15.2)
ECOG PS	0	111 (48.7)	90 (40.2)
	1	114 (50.0)	121 (54.0)
	2	3 (1.3)	13 (5.8)
Geographic region†	Region 1	87 (38.2)	86 (38.4)
	Region 2	106 (46.5)	105 (46.9)
	Region 3	35 (15.4)	33 (14.7)

Key patient characteristics (continued)

Category	Subgroup	Eribulin (n=228) n (%)	Dacarbazine (n=224) n (%)
Histology	ADI	75 (32.9)	78 (34.8)
	LMS	152 (66.7)	145 (64.7)
	Other	1 (0.4)	1 (0.4)
ADI histological subtype	Dedifferentiated	32 (14.0)	37 (16.5)
	Myxoid/Round cell	30 (13.2)	26 (11.6)
	Pleomorphic	13 (5.7)	15 (6.7)
LMS primary site	Uterine	68 (29.8)	63 (28.1)
	Nonuterine	83 (36.4)	82 (36.6)
	Unknown	1 (0.4)	0
Tumor grade	High	150 (65.8)	152 (67.9)
	Intermediate	77 (33.8)	69 (30.8)
	Not done	1 (0.4)	3 (1.3)
Number of prior regimens for advanced disease	0	1 (0.4)	1 (0.4)
	1	15 (6.6)	14 (6.3)
	2	116 (50.9)	98 (43.8)
	>2	96 (42.1)	111 (49.6)

Primary endpoint: OS



	Eribulin	Dacarbazine
Median (months)	13.5	11.5
HR (95% CI)	0.768 (0.618, 0.954)	
Stratified P-value	0.0169	

Patients at Risk:

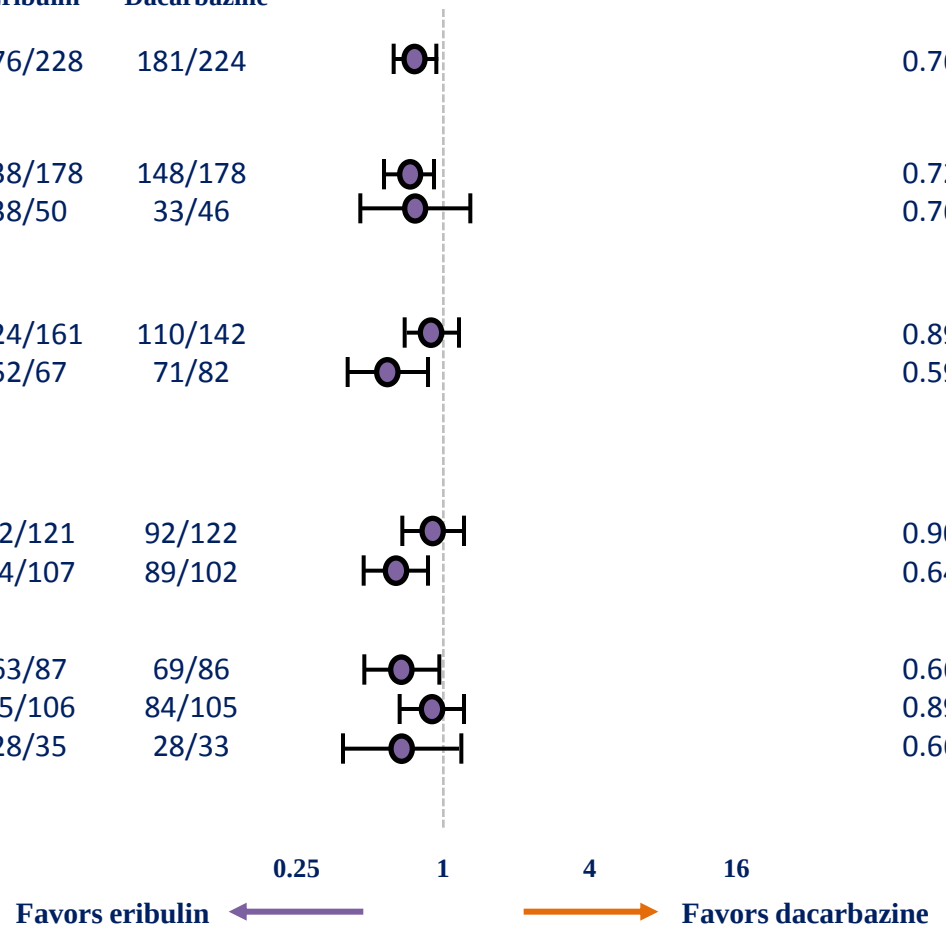
Eribulin	228	197	162	138	120	97	88	64	45	34	25	14	7	1	1	0
Dacarbazine	224	190	158	130	103	81	64	45	32	24	16	8	3	0	0	0

- The primary endpoint of OS was met, indicating a 30% improvement (based on HR)

CI, confidence interval

Preplanned OS subgroups analysis

Group/subgroup	— Events/n — Eribulin	— Events/n — Dacarbazine	HR (95% CI)	Median (months) Eribulin	Median (months) Dacarbazine
Overall	176/228	181/224	0.768 (0.618, 0.954)	13.5	11.5
Age group (years)					
<65	138/178	148/178	0.728 (0.569, 0.931)	13.5	11.3
≥65	38/50	33/46	0.766 (0.445, 1.319)	13.5	13.2
Sex					
Female	124/161	110/142	0.896 (0.682, 1.175)	13.2	12.3
Male	52/67	71/82	0.591 (0.402, 0.868)	14.7	9.6
Prior regimens for advanced STS					
2	92/121	92/122	0.902 (0.671, 1.214)	13.9	12.3
>2	84/107	89/102	0.640 (0.466, 0.879)	13.2	10.1
Stratification region*					
Region 1	63/87	69/86	0.669 (0.466, 0.958)	15.3	11.5
Region 2	85/106	84/105	0.890 (0.653, 1.214)	13.3	11.5
Region 3	28/35	28/33	0.667 (0.380, 1.171)	11.4	9.7



*Region 1: USA, Canada; Region 2: Western Europe, Australasia, Israel; Region 3: Eastern Europe, Latin America, Asia.
CI, confidence interval; HR, hazard ratio; OS, overall survival; STS, soft tissue sarcoma.

Preplanned OS subgroups analysis (continued)

Group/subgroup	Events/n — Eribulin	Events/n — Dacarbazine	HR (95% CI)	Median (months) — Eribulin	Median (months) — Dacarbazine
Histology					
ADI	52/71	63/72	0.511 (0.346, 0.753)	15.6	8.4
LMS	124/157	118/152	0.927 (0.714, 1.203)	12.7	13.0
AJCC sarcoma tumor grade score at the date of diagnosis					
High	118/150	125/152	0.796 (0.607, 1.042)	12.7	11.5
Intermediate	57/77	55/69	0.649 (0.439, 0.961)	14.8	10.1
Baseline ECOG PS					
0	76/111	72/90	0.579 (0.407, 0.823)	19.9	13.1
1	97/114	97/121	1.107 (0.826, 1.484)	9.4	10.1
2	3/3	12/13	3.000 (0.251, 35.794)	1.1	3.0
Prior anticancer therapy type					
Anthracycline	174/225	177/219	0.770 (0.619, 0.958)	13.5	11.3
Gemcitabine	101/129	111/138	0.803 (0.600, 1.074)	13.2	11.8
Ifosfamide	108/141	115/137	0.701 (0.529, 0.930)	14.7	11.0
Taxane	87/109	92/114	0.835 (0.604, 1.156)	11.3	11.6
Trabectedin	80/108	98/116	0.643 (0.469, 0.884)	13.3	10.7
Targeted therapy	23/29	19/26	1.067 (0.527, 2.161)	11.3	13.1
Other	66/83	70/90	0.902 (0.631, 1.289)	11.3	12.2

ADI, adipocytic sarcoma; AJCC, American Joint Committee on Cancer; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; LMS, leiomyosarcoma; OS, overall survival.

Additional efficacy endpoints

	Eribulin (n=228)	Dacarbazine (n=224)
PFR_{12wks}, % (n) [95% CI*]	33.3% (76) [27.2, 39.9]	28.6% (64) [22.8, 35.0]
OR (95% CI); P-value†	1.3 (0.8, 1.9); 0.253	
ORR; % (n)	3.9 (9)	4.9 (11)

Best overall response	Eribulin (n=228) % (n)	Dacarbazine (n=224) % (n)
CR	0	0
PR	3.9 (9)	4.9 (11)
SD	52.2 (119)	47.8 (107)
PD	39.0 (89)	39.3 (88)
NE/Unknown	4.8 (11)	8.0 (18)

Tumor assessments are based on RECIST 1.1.[1]
*95% CI was calculated using exact method of binomial distribution; †*P*-value and odds ratio were calculated using the stratified Cochran-Mantel-Haenszel method.
CI, confidence interval; CR, complete response; NE, not evaluable; OR, odds ratio; ORR, objective response rate; PD, partial disease; PFR_{12wks}, proportion of patients who were still alive without disease progression at 12 weeks from randomization; PR, partial response; SD, stable disease.

1. Eisenhauer et al. *Eur J Cancer* 2009.

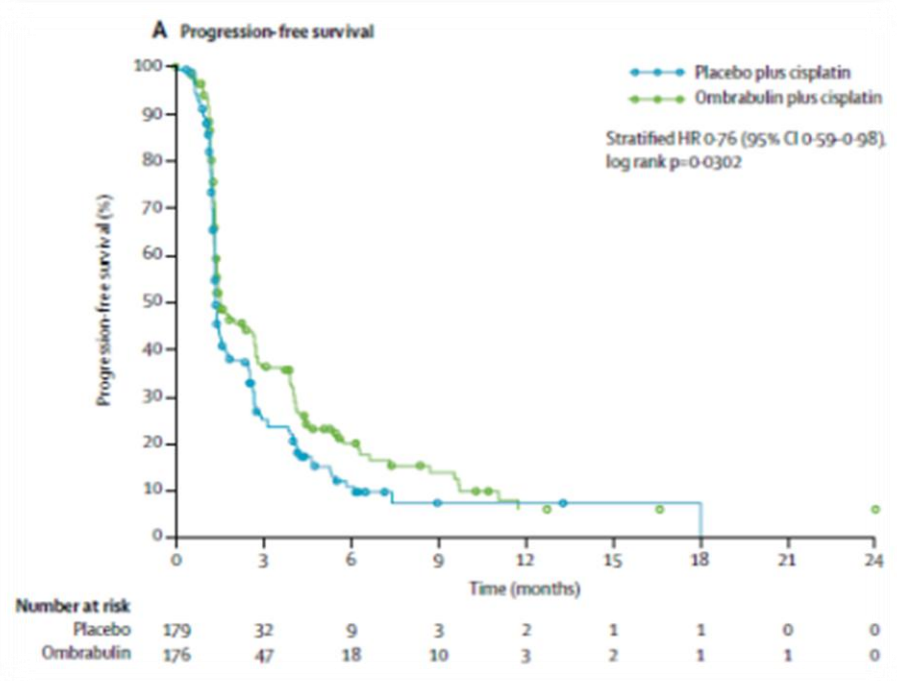
Treatments specific for histological and molecular subsets of sarcomas?

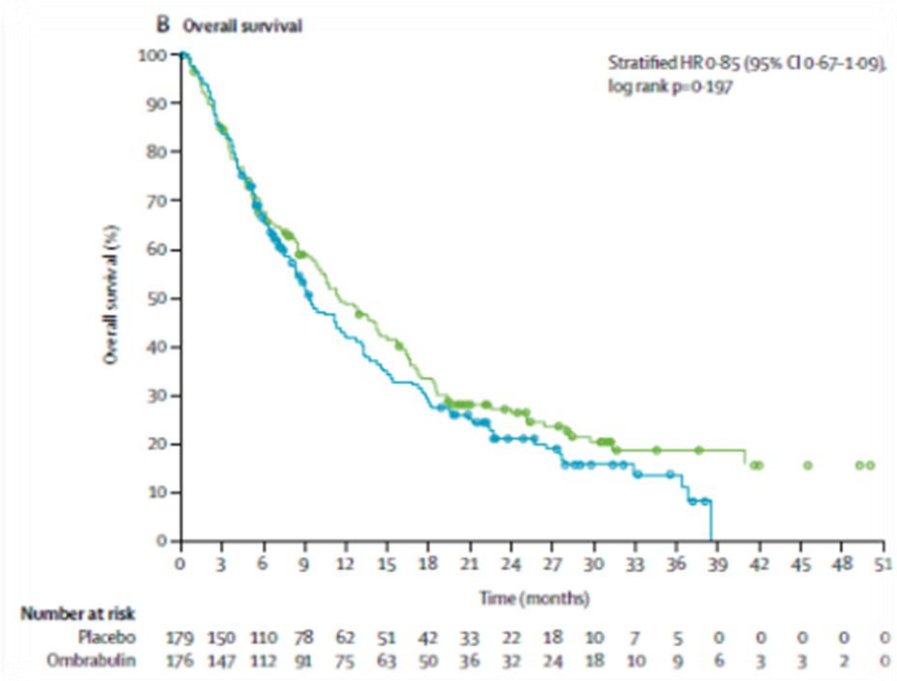
Conclusions

- Doxo, Ifo, DTIC, Trabectedine, pazopanib
- Antiangiogéniques autres
- Gemcitabine, Taxol
- Eribuline
- Traitement adapté aux altérations moléculaires
- Immunothérapie en cours d’étude

Ombrabulin plus cisplatin versus placebo plus cisplatin in patients with advanced soft-tissue sarcomas after failure of anthracycline and ifosfamide chemotherapy: a randomised, double-blind, placebo-controlled, phase 3 trial

Jean-Yves Blay, Zsuzsanna Pápai, Anthony W Tolcher, Antoine Italiano, Didier Cupissol, Antonio López-Pousa, Sant P Chawla, Emmanuelle Bompas, Nada Babovic, Nicolas Penel, Nicolas Isambert, Arthur P Staddon, Esma Saâda-Bouzid, Armando Santoro, Fabio A Franke, Patrick Cohen, Solenn Le-Guennec, George D Demetri





Activity of regorafenib (RE) in leiomyosarcomas (LMS) and other types of soft-tissue sarcomas (OTS): results of a double-blind, randomized placebo (PL) controlled phase II trial

MIR Olivier, **BRODOWICZ** Thomas, **WALLET** Jennifer , **ITALIANO** Antoine , **LE CESNE** Axel , **BLAY** Jean-Yves, **RYCKEWAERT** Thomas , **BERTUCCI** François, **PIPERNO-NEUMANN** Sophie, **PLONER** Ferdinand, **TOULMONDE** Maud , **DOMONT** Julien, **SAADA-BOUZID** Esma, **DELCAMBRE** Corinne, **ISAMBERT** Nicolas, **CLISANT** Stéphanie, **TAIEB** Sophie, **LINDNER** Elisabeth, **LIEGL-ATZAWAGER** Bernadette, **PENEL** Nicolas

On behalf of the French Sarcoma Group and Sarcoma Platform Austria

Paclitaxel Given Once Per Week With or Without Bevacizumab in Patients With Advanced Angiosarcoma: A Randomized Phase II Trial

Isabelle L. Ray-Coquard, Julien Domont, Emmanuelle Tresch-Bruneel, Emmanuelle Bompas, Philippe A. Cassier, Olivier Mir, Sophie Piperno-Neumann, Antoine Italiano, Christine Chevreau, Didier Cupissol, François Bertucci, Jacques-Olivier Bay, Olivier Collard, Esma Saada-Bouzid, Nicolas Isambert, Corinne Delcambre, Stéphanie Clisant, Axel Le Cesne, Jean-Yves Blay, and Nicolas Penel

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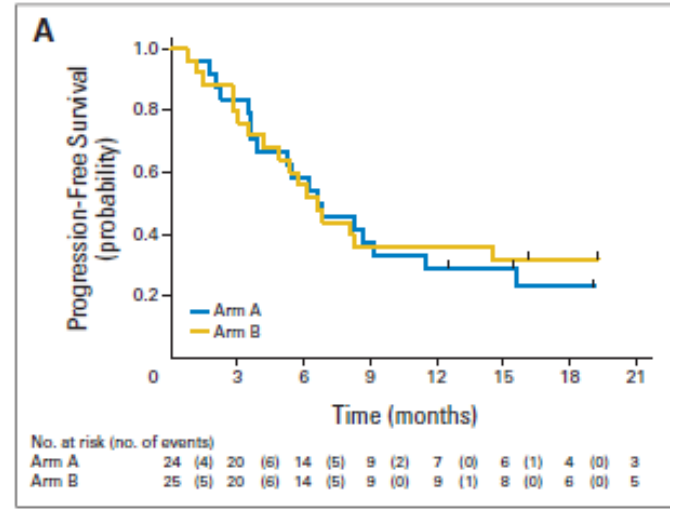
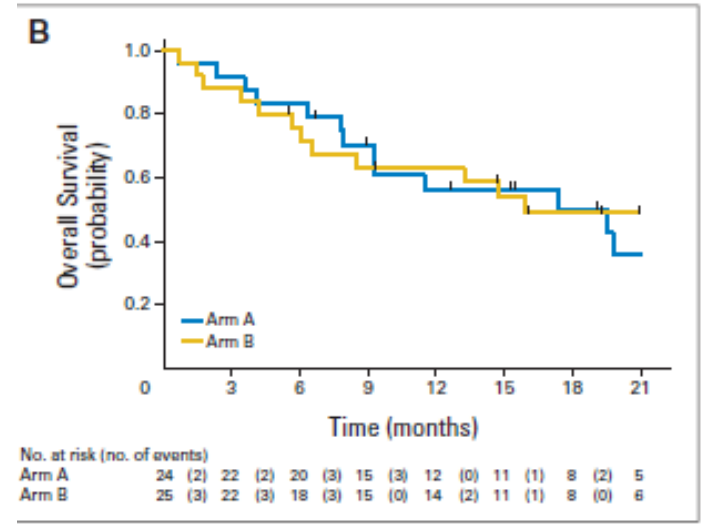
Table 1. Baseline Patient Demographics and Clinical Characteristics

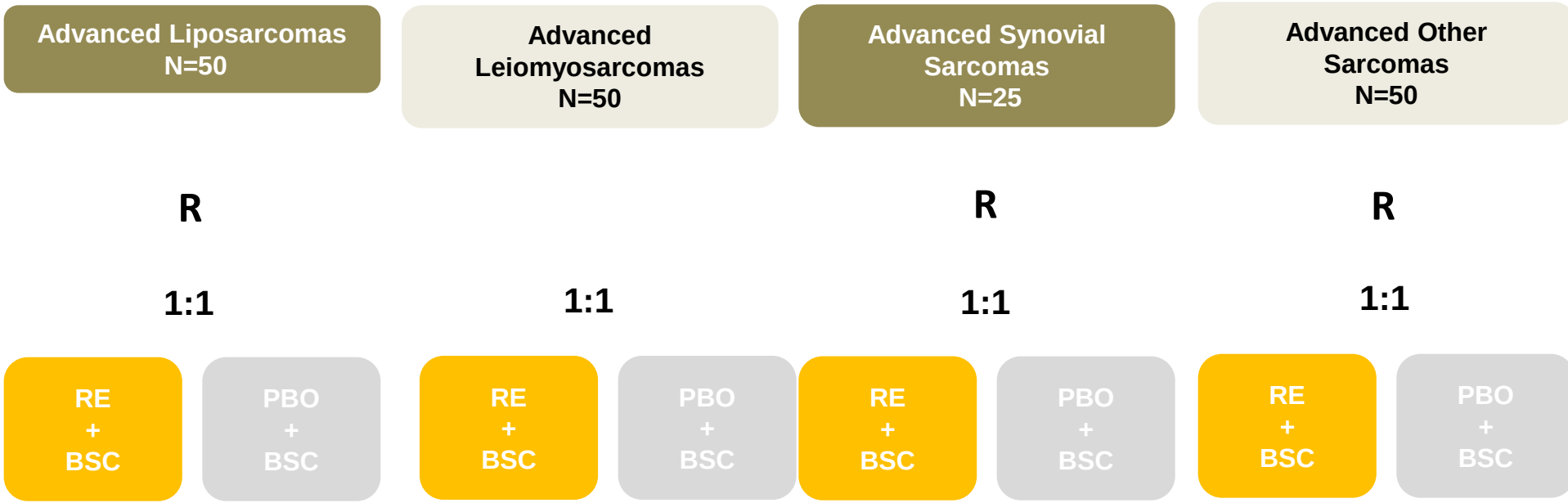
Characteristic	No. (%) of Patients	
	Arm A (n = 24)	Arm B (n = 25)
Sex		
Female	18 (75.0)	20 (80.0)
Male	6 (25.0)	5 (20.0)
Performance status*		
0	12 (50.0)	12 (48.0)
1	12 (50.0)	13 (52.0)
Stratification		
Superficial angiosarcoma	16 (66)	16 (64)
Visceral angiosarcoma	8 (34)	9 (36)
Radiation induced	12 (50.0)	12 (48.0)
De novo	12 (50.0)	13 (52.0)
Primary site of angiosarcoma		
Breast	12 (50.0)	12 (48.0)
Skin	3 (12.5)	3 (12.0)
Liver	3 (12.5)	0
Bone	2 (8.3)	1 (4.0)
Heart	0	2 (8.0)
Spleen	0	2(8.0)
Pleura	2 (8.3)	0
Mesentery	1 (4.2)	1 (4.0)
Parotid	0	1 (4.0)
Perineal wall	1 (4.2)	0
Retroperitoneum	0	1 (4.0)
Unknown	0	1 (4.0)
Grade†		
1	2 (8.3)	3 (12.0)
2	5 (20.8)	7 (28.0)
3	11 (45.8)	8 (32.0)
Unknown	6 (25.0)	7 (28.0)
Metastatic disease	13 (54.2)	16 (64.0)
Only one metastatic site	9 (37.5)	10 (40.0)
Most common metastatic site		
Lung	4 (16.7)	7 (28.0)
Liver	4 (16.7)	6 (24.0)
Bone	2 (8.3)	2 (8.0)
Soft tissue	2 (8.3)	0
Skin	5 (20.8)	3 (12.0)
Lymph nodes	1 (4.2)	1 (4.0)
Previous anthracycline	9 (37.5)	7 (28.0)

NOTE. Patients enrolled onto arm A received paclitaxel once per week alone; those in arm B, paclitaxel once per week plus bevacizumab.
*According to WHO criteria.
†According to Fédération Nationale des Centres de Lutte contre le Cancer criteria.



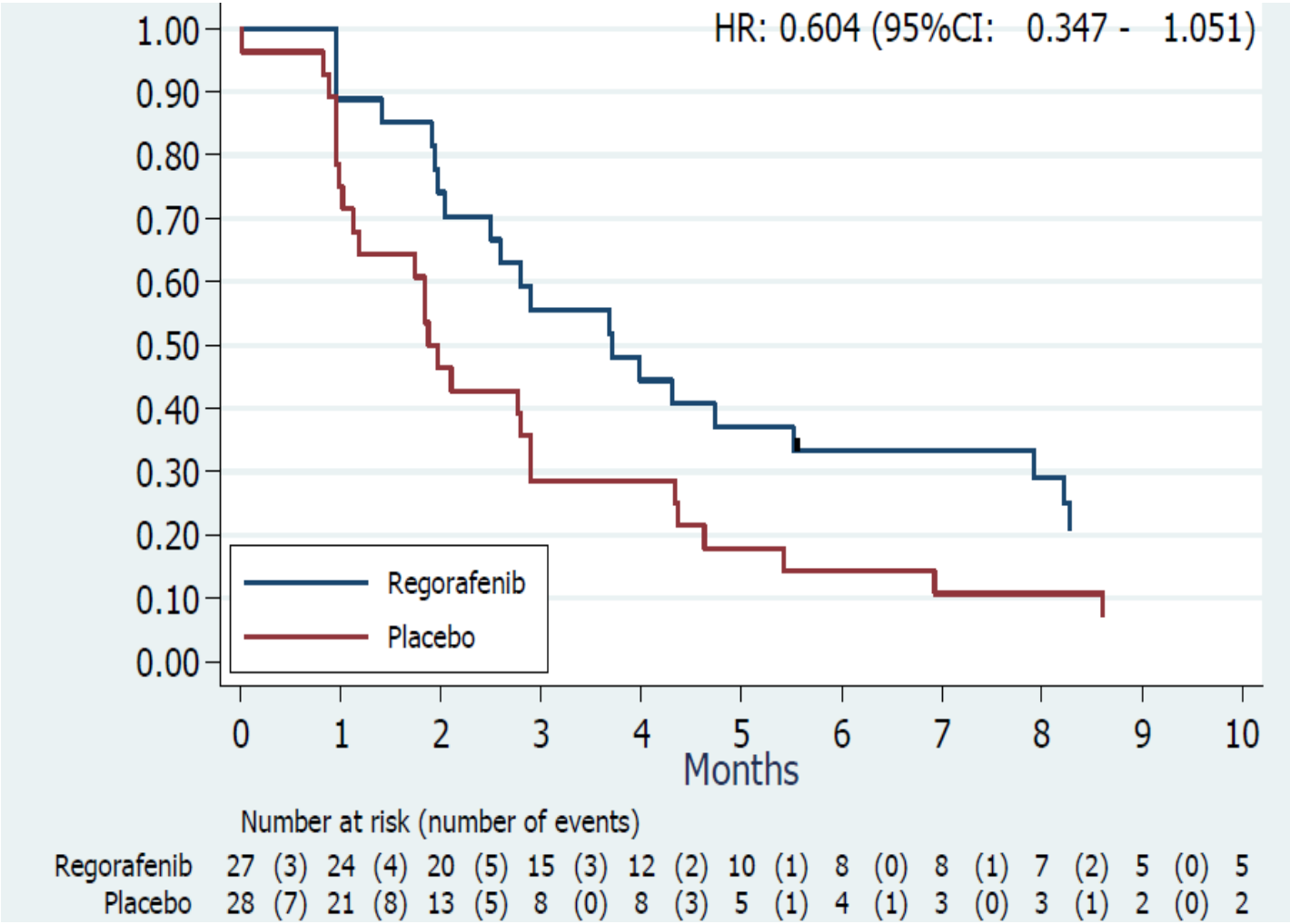


Patients and methods



- 4 parallel randomized, double-blind, placebo-controlled, multi-center phase II studies in pts with refractory STS
- Regorafenib (160 mg once daily, three weeks on/one week off) plus BSC ***versus*** placebo plus BSC
- Stratification: prior exposure to pazopanib and country

PFS - Leiomyosarcoma

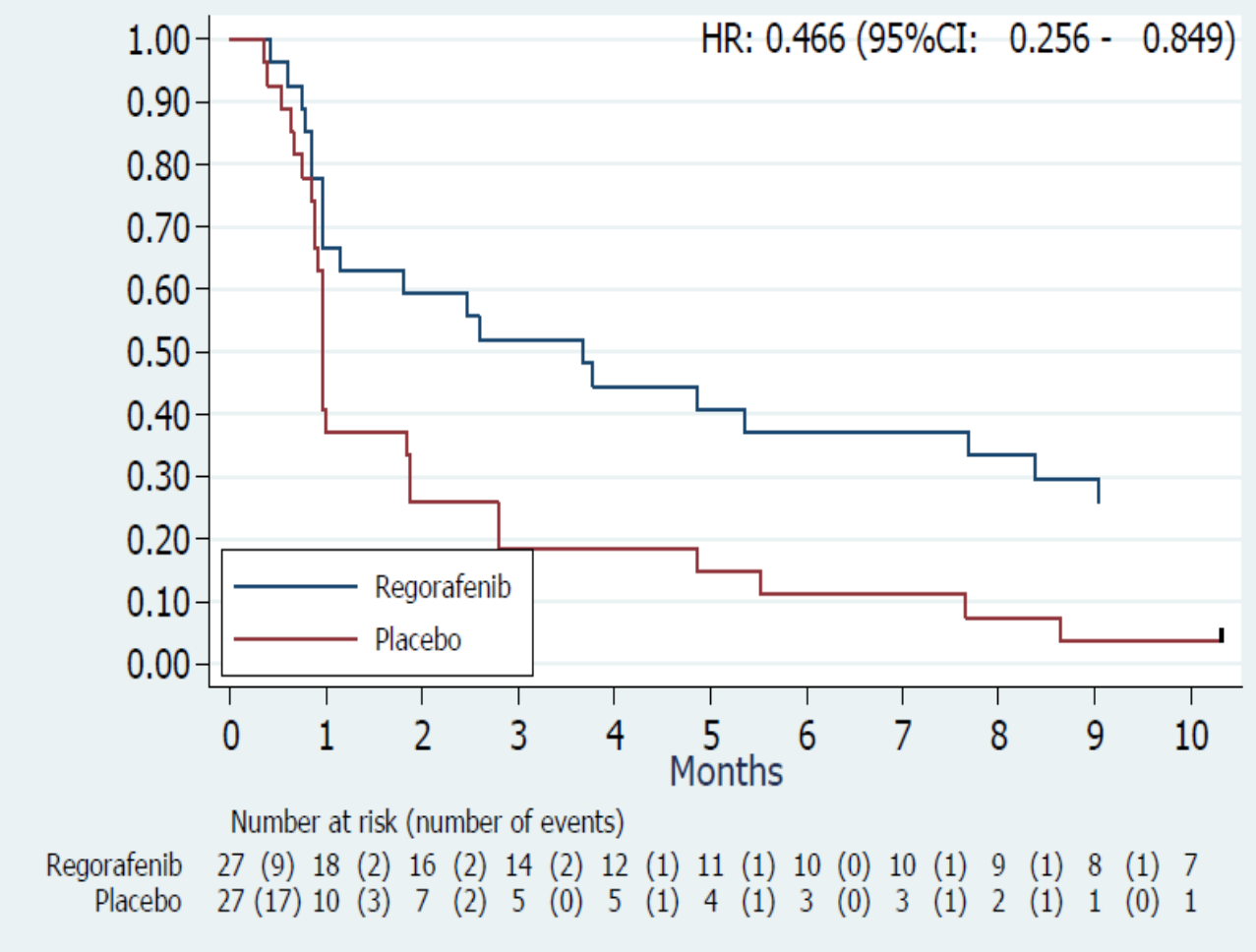


Median PFS

3.7 months (2.0 – 7.9)
vs
1.9 months (1.1 – 2.9)

P=0.07

PFS – other sarcomas



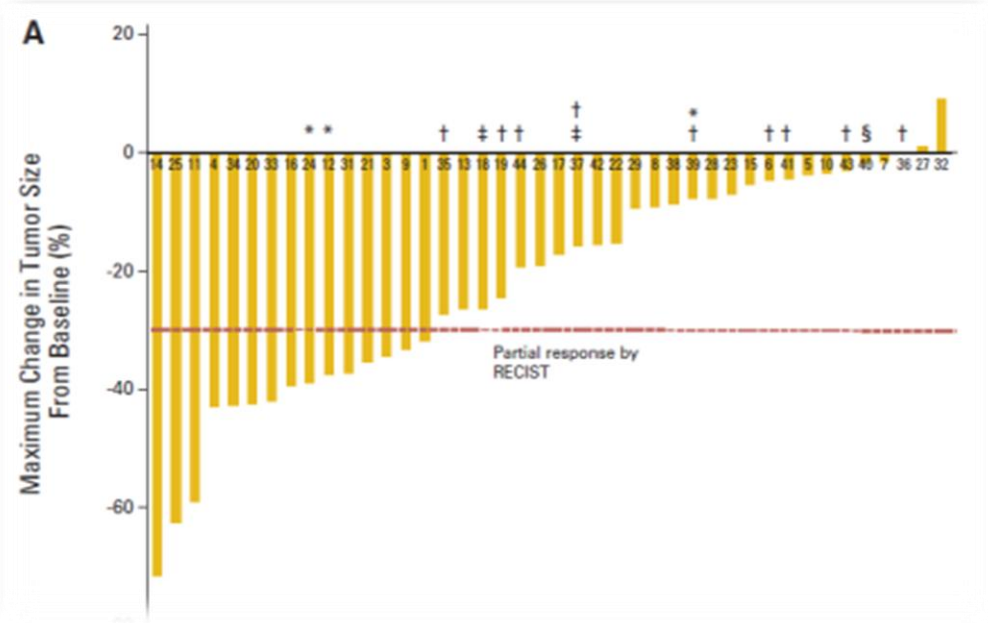
Median PFS

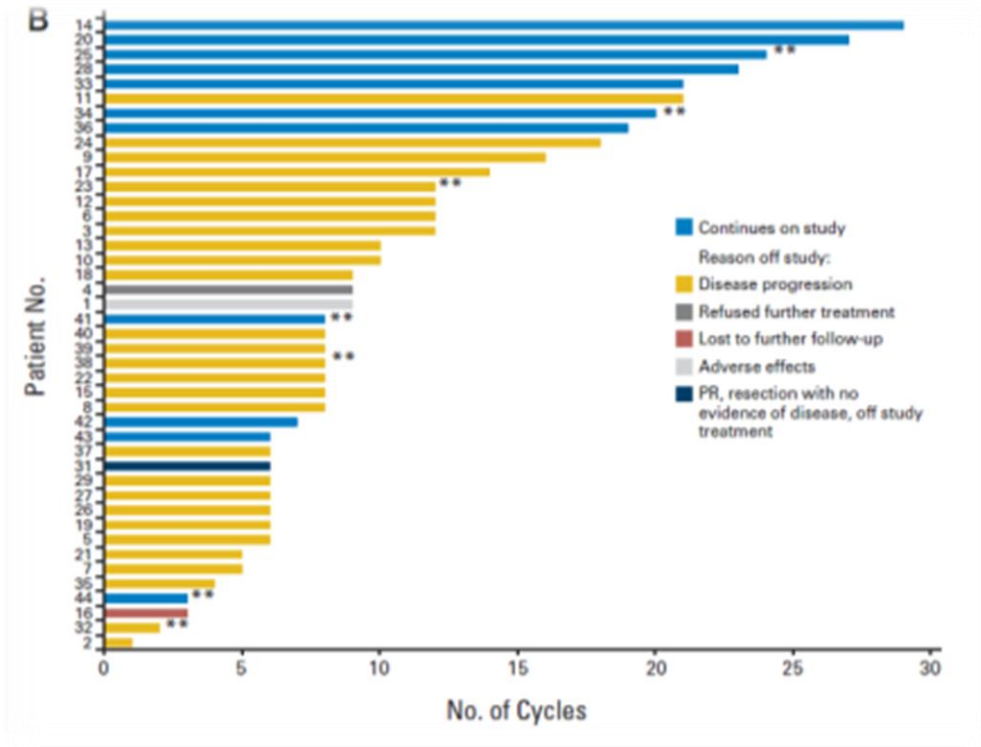
3.7 months (1.0 – 8.4**)**
vs
1.0 months (0.9 – 1.9)

P=0.008

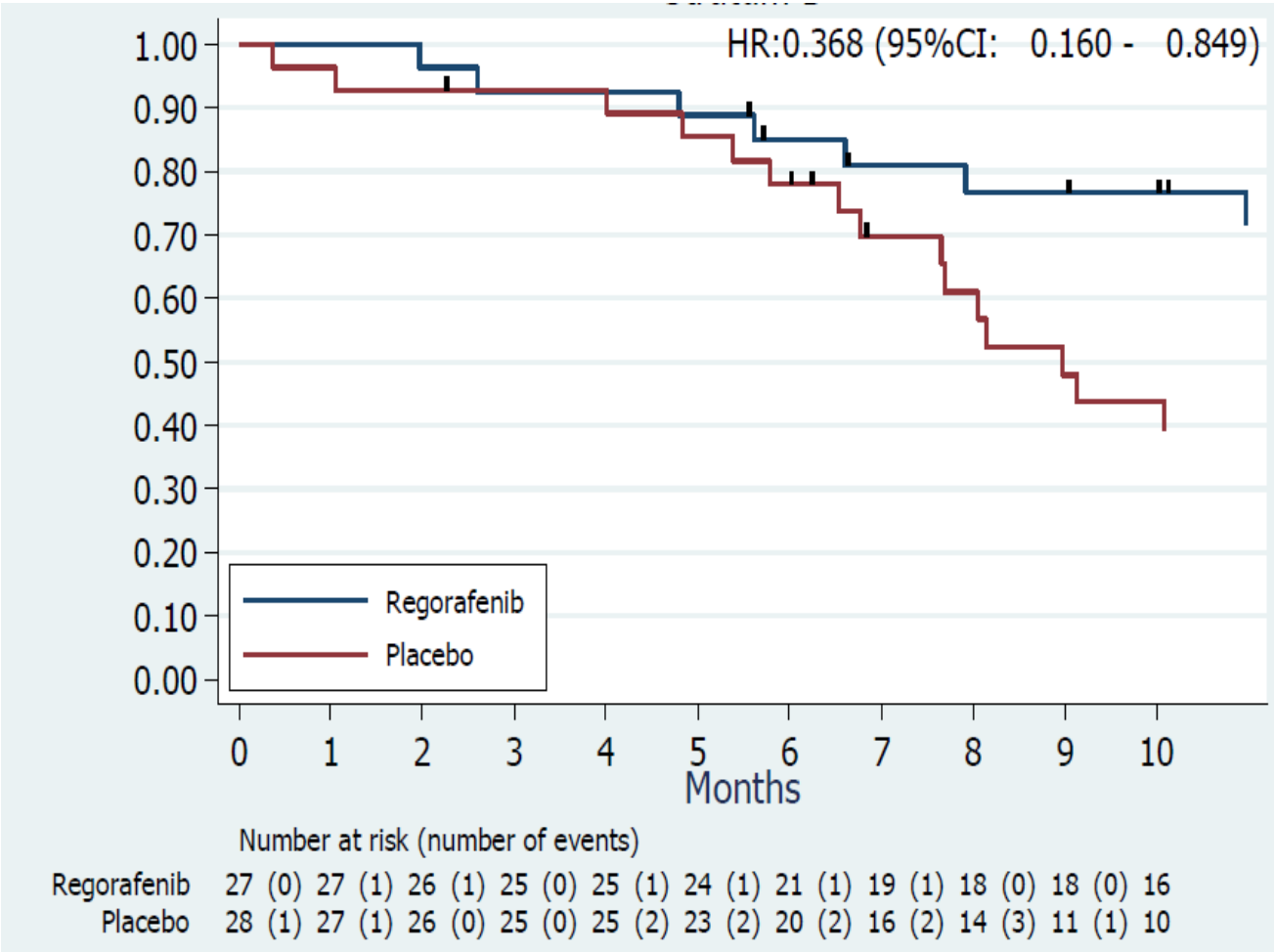
Cediranib for Metastatic Alveolar Soft Part Sarcoma

Shivaani Kummar, Deborah Allen, Anne Monks, Eric C. Polley, Curtis D. Hose, S. Percy Ivy, Ismail B. Turkbey, Scott Lawrence, Robert J. Kinders, Peter Choyke, Richard Simon, Seth M. Steinberg, James H. Doroshow, and Lee Helman





OS - Leiomyosarcoma



P=0.01

Median not reached

Cross-over in Placebo arm: 20/28

The off-label use of targeted therapies in sarcomas: the OUTC'S program

Lauriane Eberst[1,2], Claire Cropet[1], Axel Le Cesne[3], Patricia Pautier[3], Nicolas Penel[4], Antoine Adenis[4], Christine Chevreau[5], Jacques-Olivier Bay[6,7], Olivier Collard[8], Didier Cupissol[9], Florence Duffaud[10], Jean-Claude Gentet[10], Sophie Piperno-Neumann[11], Perrine Marec-Berard[1], Emmanuelle Bompas[12], Antoine Thyss[13], Loic Chaigneau[14], Philippe Cassier[1], François Bertucci[15], Jean-Yves Blay[1,2] and Isabelle Ray-Coquard[1,2*]

Table 2 Targeted therapy by histotypes

Targeted therapy	N	%	Histotype 1	n (%)	Histotype 2	n (%)	Histotype 3	n (%)	Histotype 4	n (%)	Histotype 5	n (%)
Sorafenib (1)	125	45	GIST	31 (25)	LMS	22 (18)	AS	14 (11)	Uterine LMS	8 (6)	Liposarcoma	8 (6)
Suntinib (2)	67	24	LMS	9 (13)	Ewing	8 (12)	SS	8 (12)	Unclassified S	8 (12)	Uterine LMS	4 (6)
Imatinib	23	8	Chordoma	8 (35)	AF	4 (17)	DFSP	4 (17)	Epithelioid S	2 (9)	—	—
Sirolimus-cyclophosphamide	18	6	OsteoS	8 (44)	ChondroS	5 (27)	AS/chordoma/lipoS/Ewing/SFT	1 each (6)	—	—	—	—
Everolimus (3)	10	4	GIST	3 (30)	LMS	3(30)	KS/MPNST/SS	1 each (10)	Other	1(10)	—	—
Bevacizumab (4)	9	3	Other	5 (56)	MFST	2 (22)	AS	1 (11)	Epithelioid S	1 (11)	—	—
Sirolimus alone	5	2	OsteoS	2 (40)	PEComa	1 (20)	other	1 (20)	—	—	—	—

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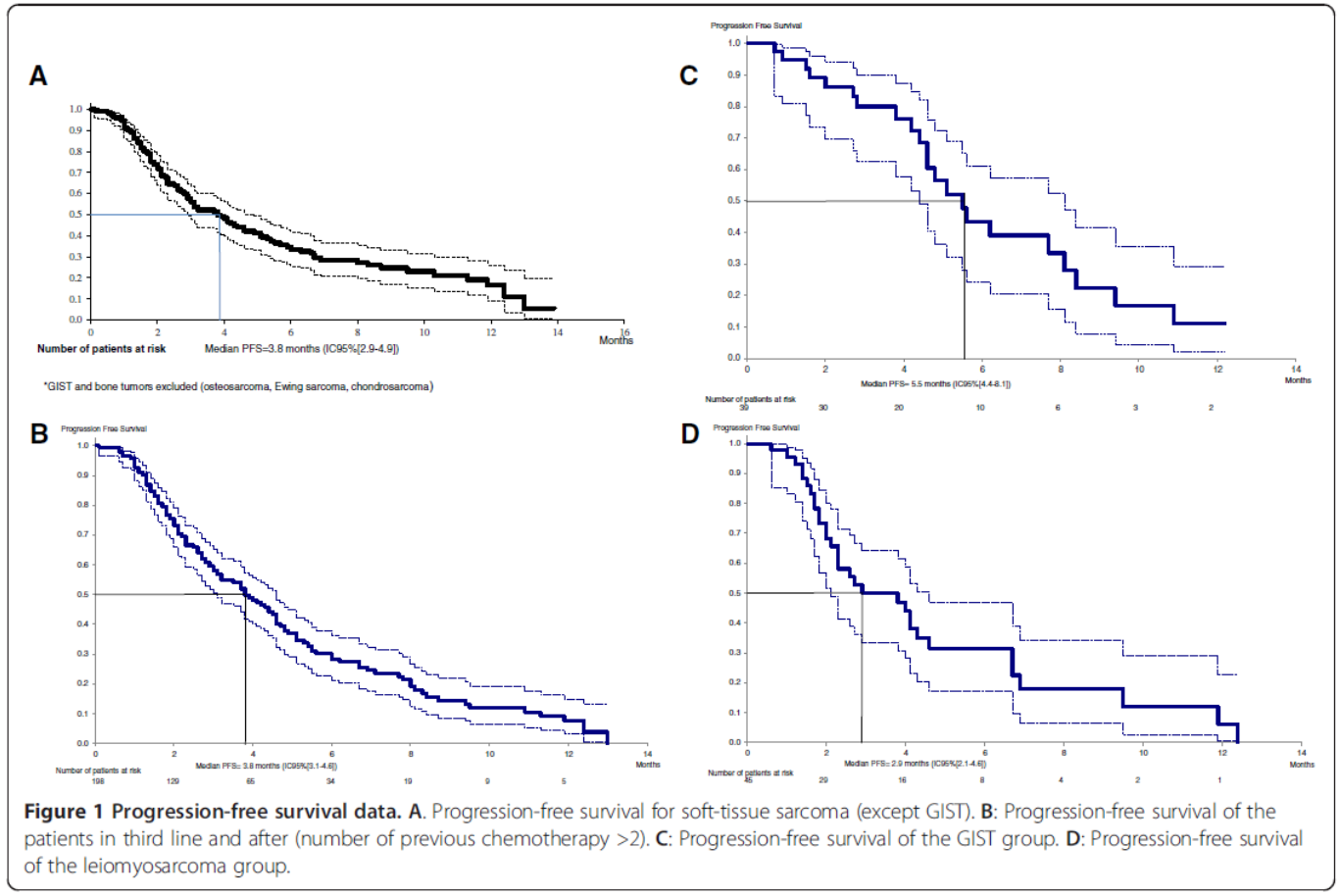


Figure 1 Progression-free survival data. A. Progression-free survival for soft-tissue sarcoma (except GIST). **B**: Progression-free survival of the patients in third line and after (number of previous chemotherapy >2). **C**: Progression-free survival of the GIST group. **D**: Progression-free survival of the leiomyosarcoma group.

Immunotherapy

An Open Label Study of MPDL3280A in Advanced Solid Tumors

ClinicalTrials.gov Identifier:
NCT02458638

ASSOCIATION DU MK3475 ET DU CYCLOPHOSPHAMIDE A POSOLOGIE METRONOMIQUE CHEZ LES PATIENTS PORTEURS D'UN SARCOME AVANCE : ESSAI MULTICENTRIQUE DE PHASE II

Résumé *PEMBROSARC*

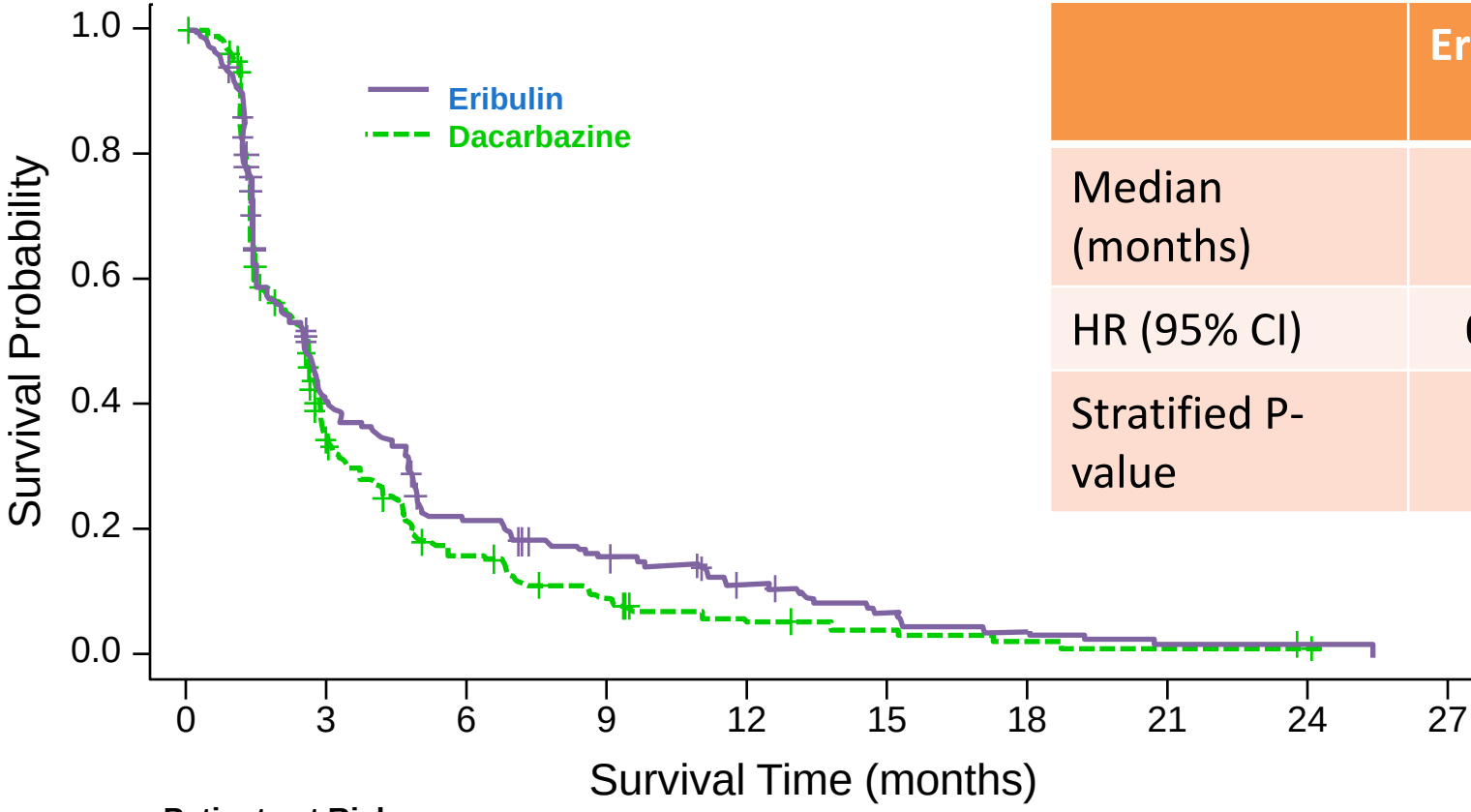
VERSION N°2.0 DU |30|04|2015|- N° : IB 2014-04

EudraCT n° 2014-004568-39

Conclusions

- Doxo, Ifo, DTIC, Trabectedine, pazopanib
- Antiangiogéniques autres
- Gemcitabine, Taxol
- Eribuline
- Traitement adapté aux altérations moléculaires
- Immunothérapie en cours d’étude

Secondary endpoint: PFS



	Eribulin	Dacarbazine
Median (months)	2.6	2.6
HR (95% CI)	0.877 (0.710, 1.085)	
Stratified P-value	0.2287	

Patients at Risk:

Eribulin	228	79	41	27	16	9	5	2	1	0
Dacarbazine	224	63	27	14	6	4	2	1	1	0