

# *Comité multidisciplinar de Sarcomas de Partes Blandas*

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La Laguna, Santa Cruz de Tenerife*



**Universidad  
Europea** MADRID



# CASO CLÍNICO

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Varón de 41 años.  
HIV + en 2004. Carga indetectable desde 2011  
(Truvada/Isemtriss)

Maestro. Su pareja y él acaban de adoptar a un niño de 1 año

Derivado a Onco por BULTOMA en pierna izda desde 2010.

Ecografía (sep/2010): Hematoma organizado de 8x3,6x5,5cm



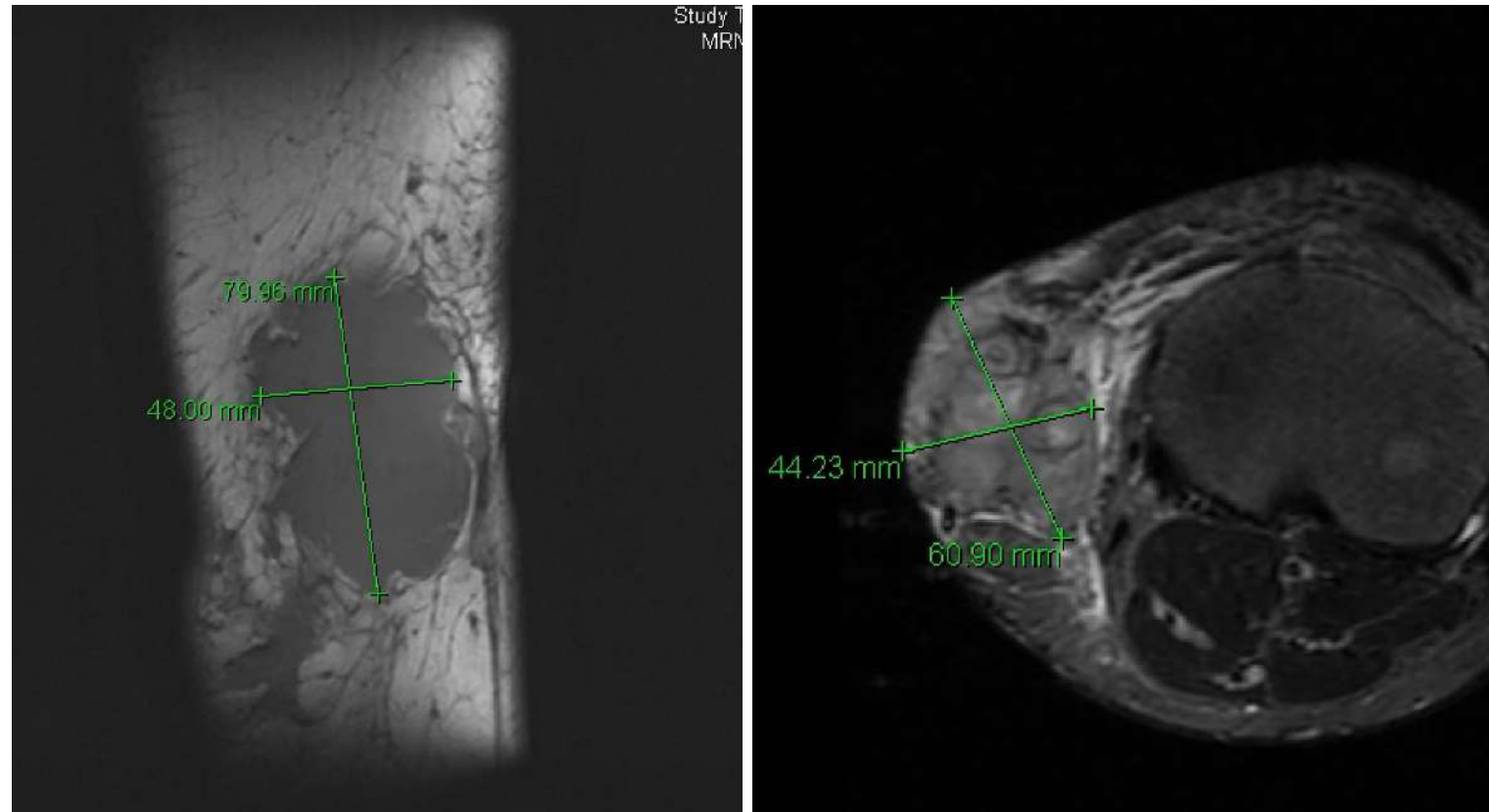
# CASO CLÍNICO

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1. Tumoración de partes blandas.
2. Dura y bien delimitada.
3. Cara interna de tibia proximal izquierda.
4. No infiltra hueso poplíteo.
5. Ha crecido.



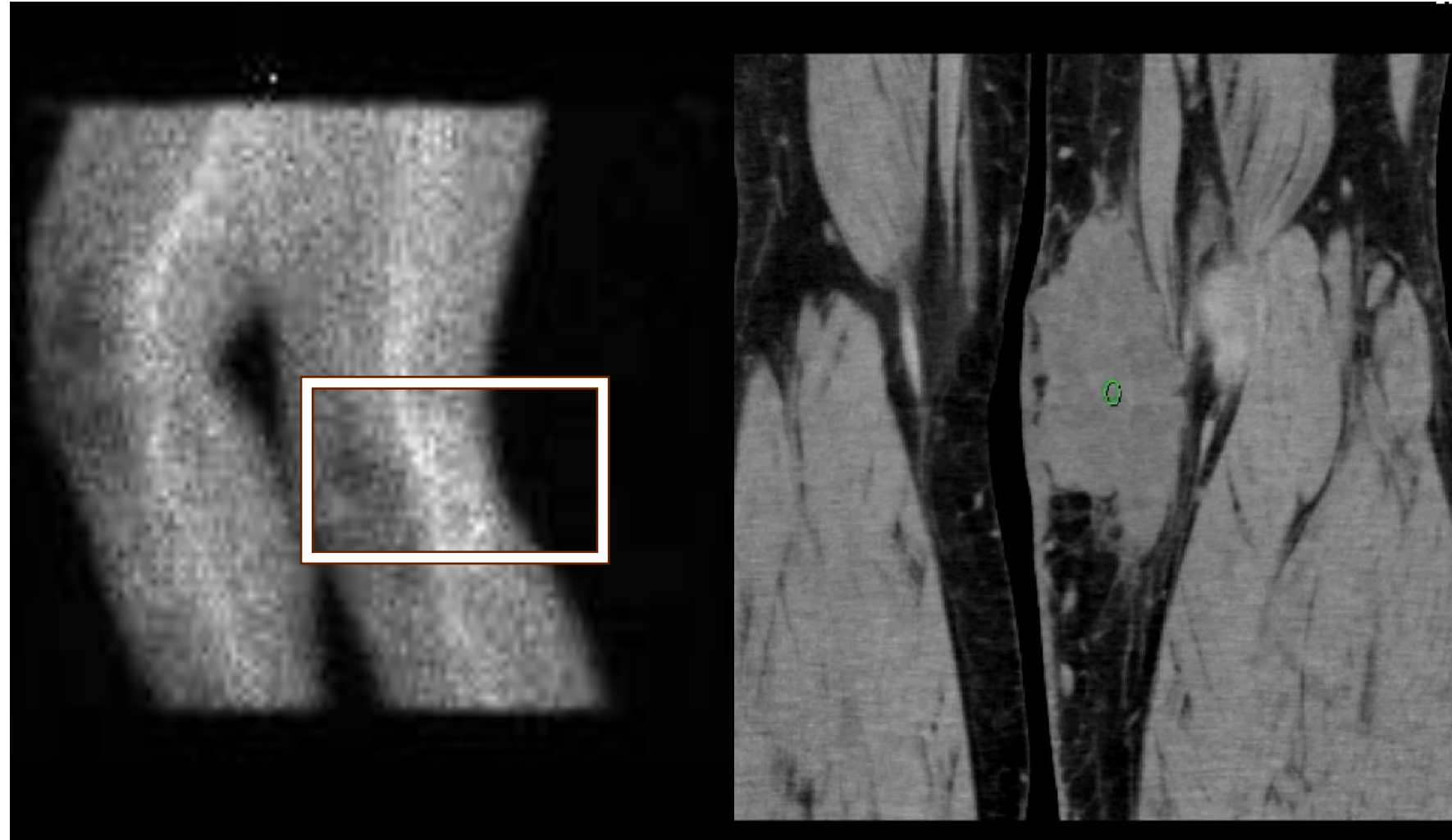
RMN  
01/11



Tras la administración de contraste intravenoso experimenta realce periférico

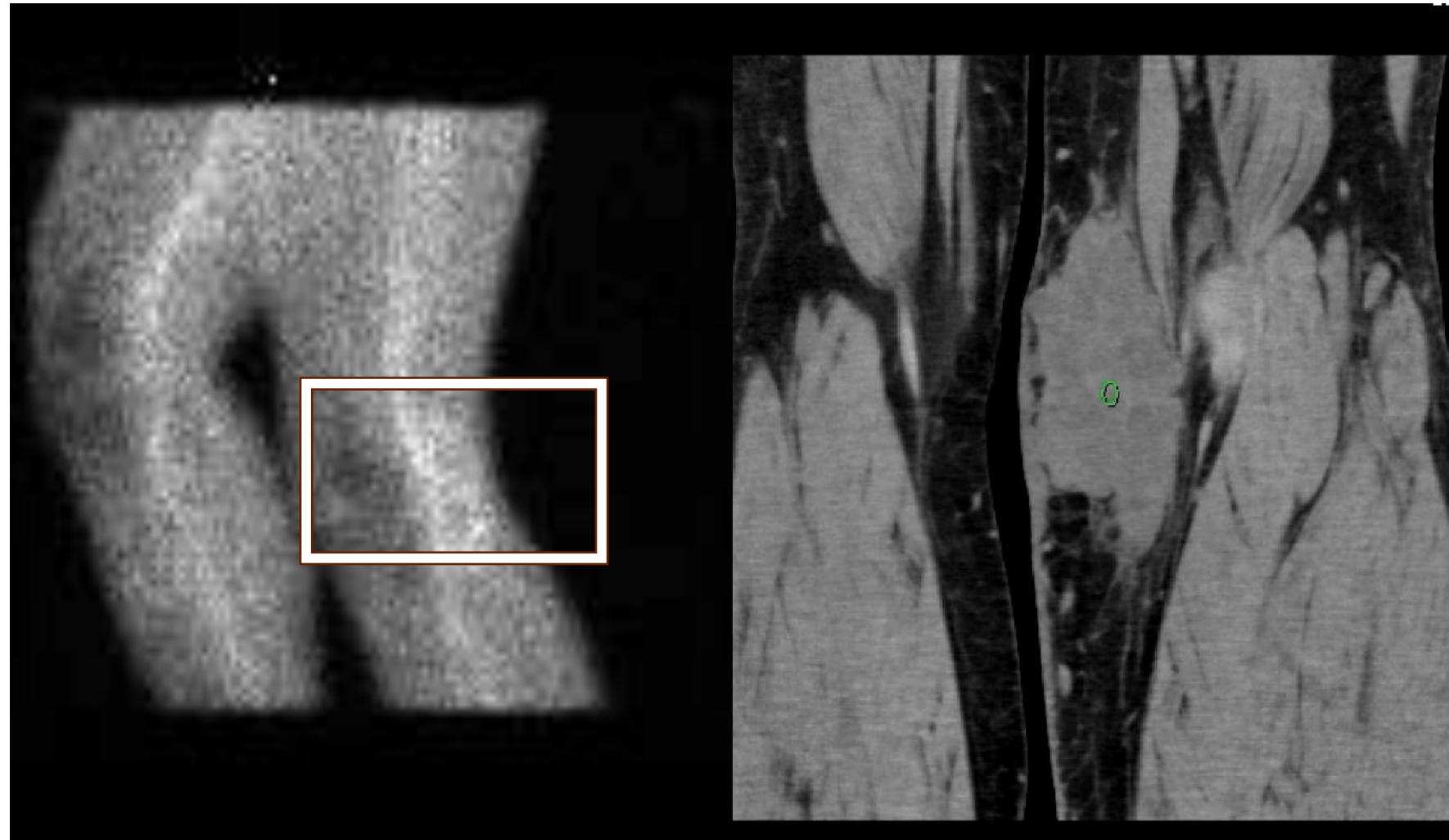
→ hematoma encapsulado Vs sarcoma

GGO  
02/11



No lesiones óseas metabólicamente activas.

TC  
03/11



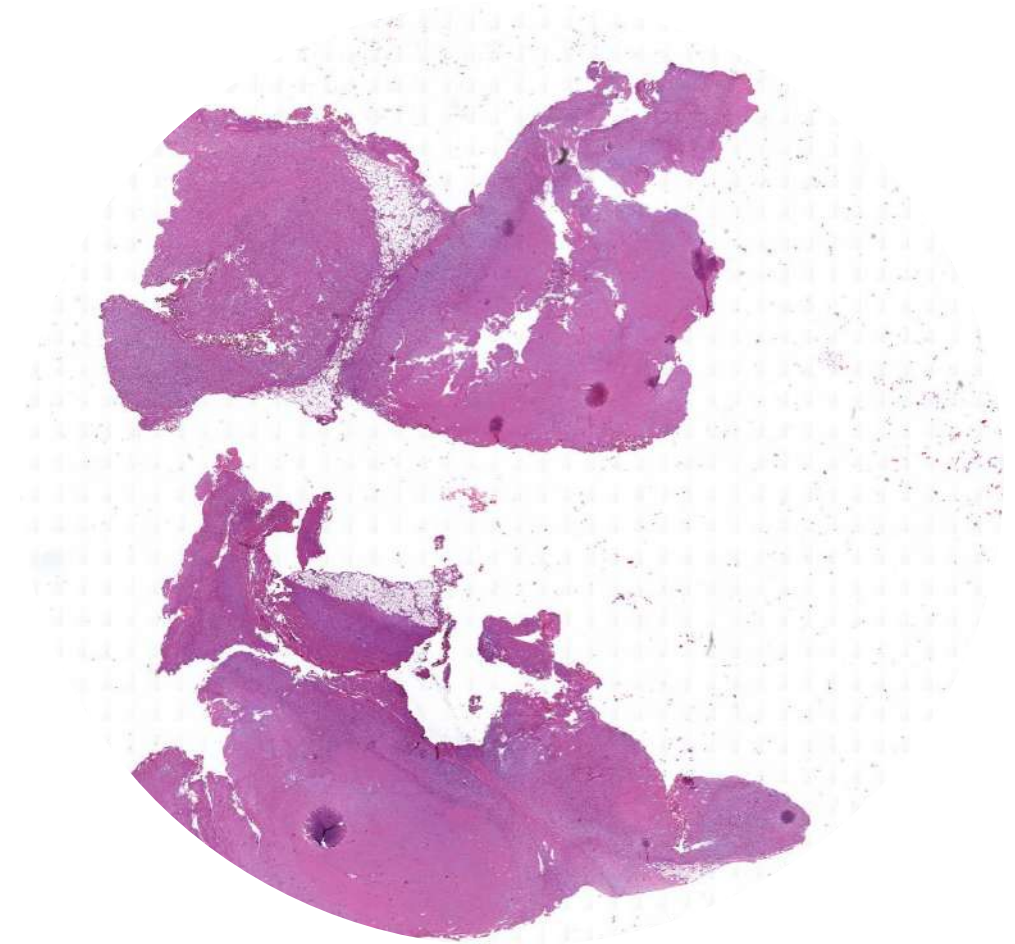
Densidad de tejidos blandos de 12,6 x 5 x 6 cm de diámetro.

Engrosamiento nodular de la piel adyacente, en íntima relación con estructuras vasculares vecinas.

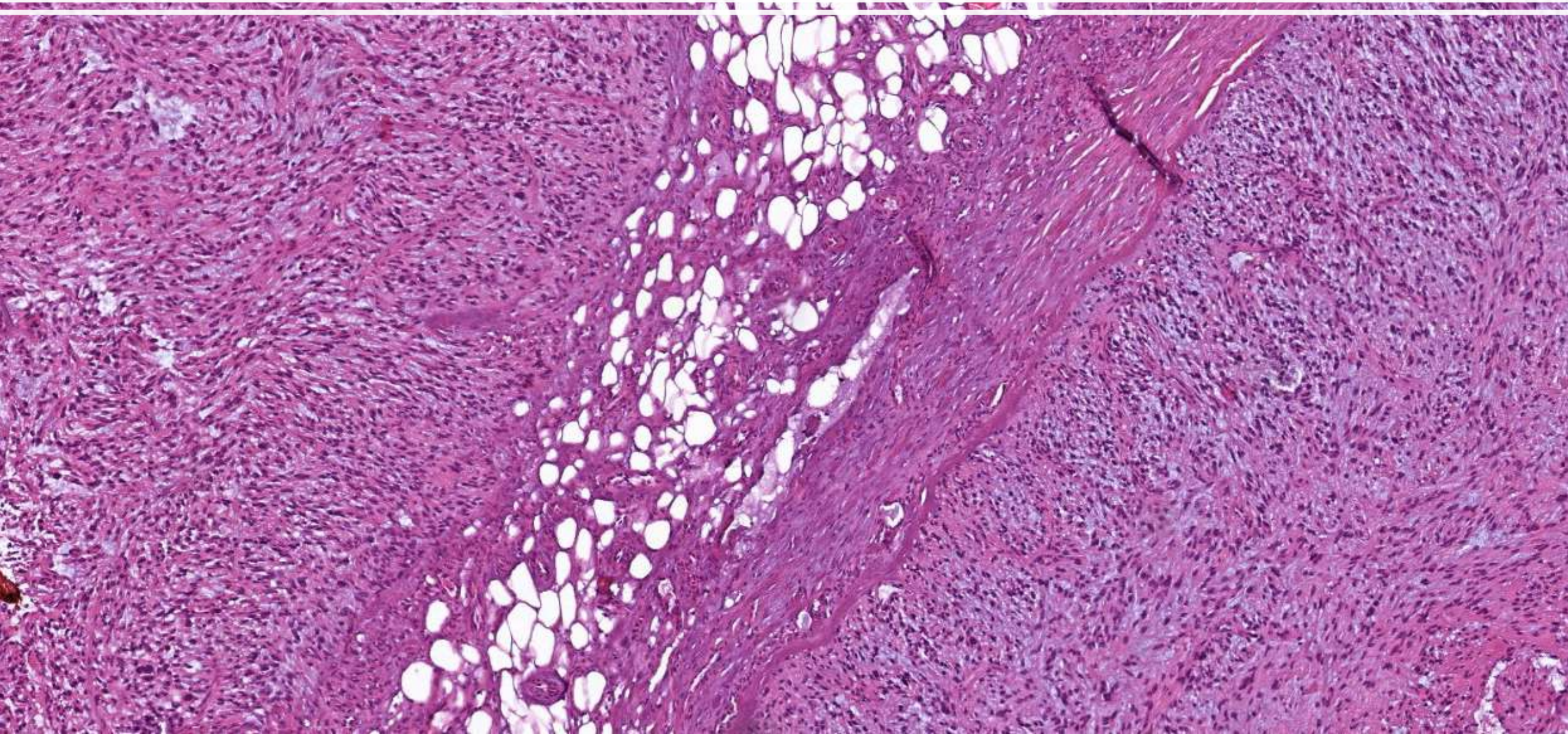
## Biopsia incisional 04.03.11

- Proliferación mesenquimal consistente con:

**Leiomioma grado 3.**

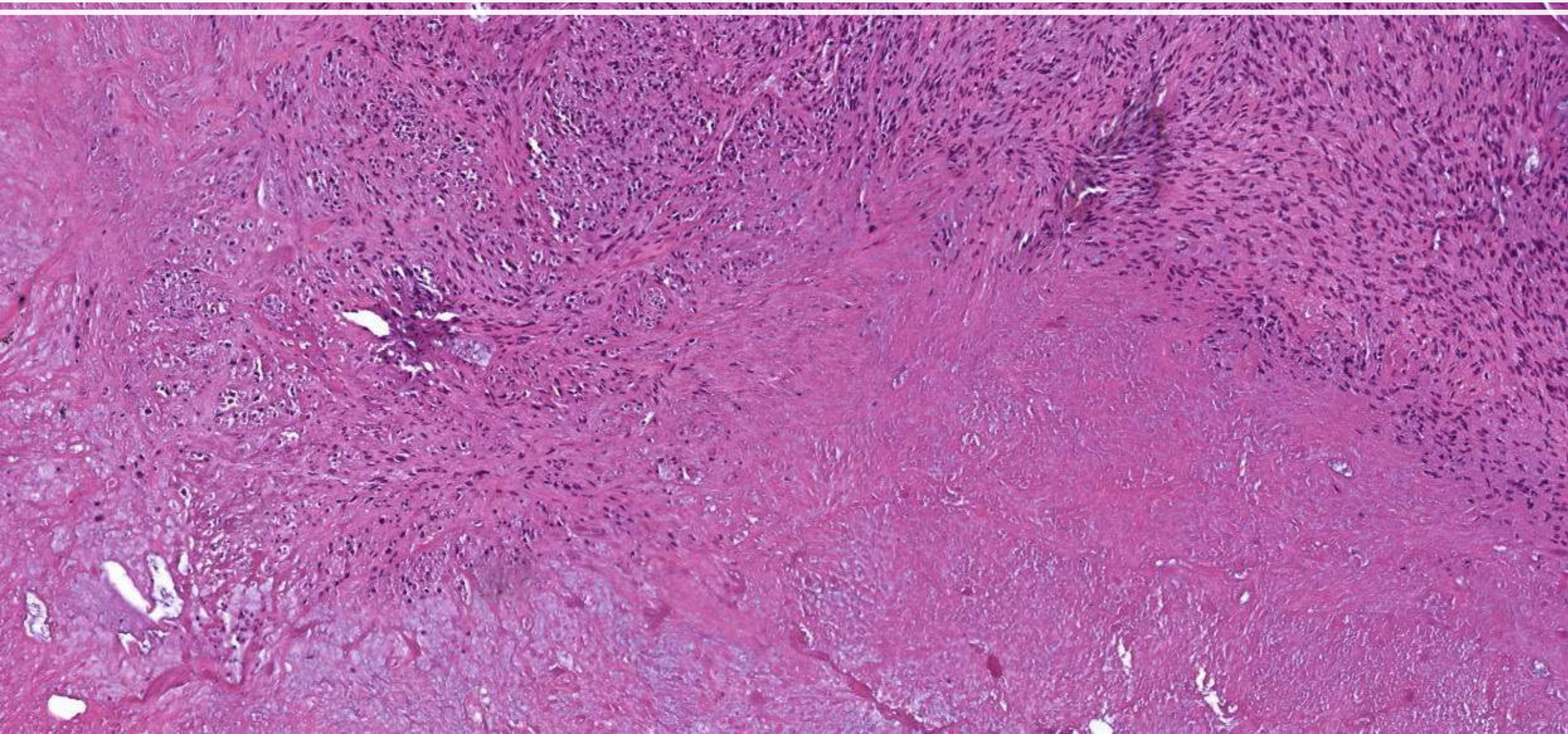


# Biopsia incisional 04.03.11

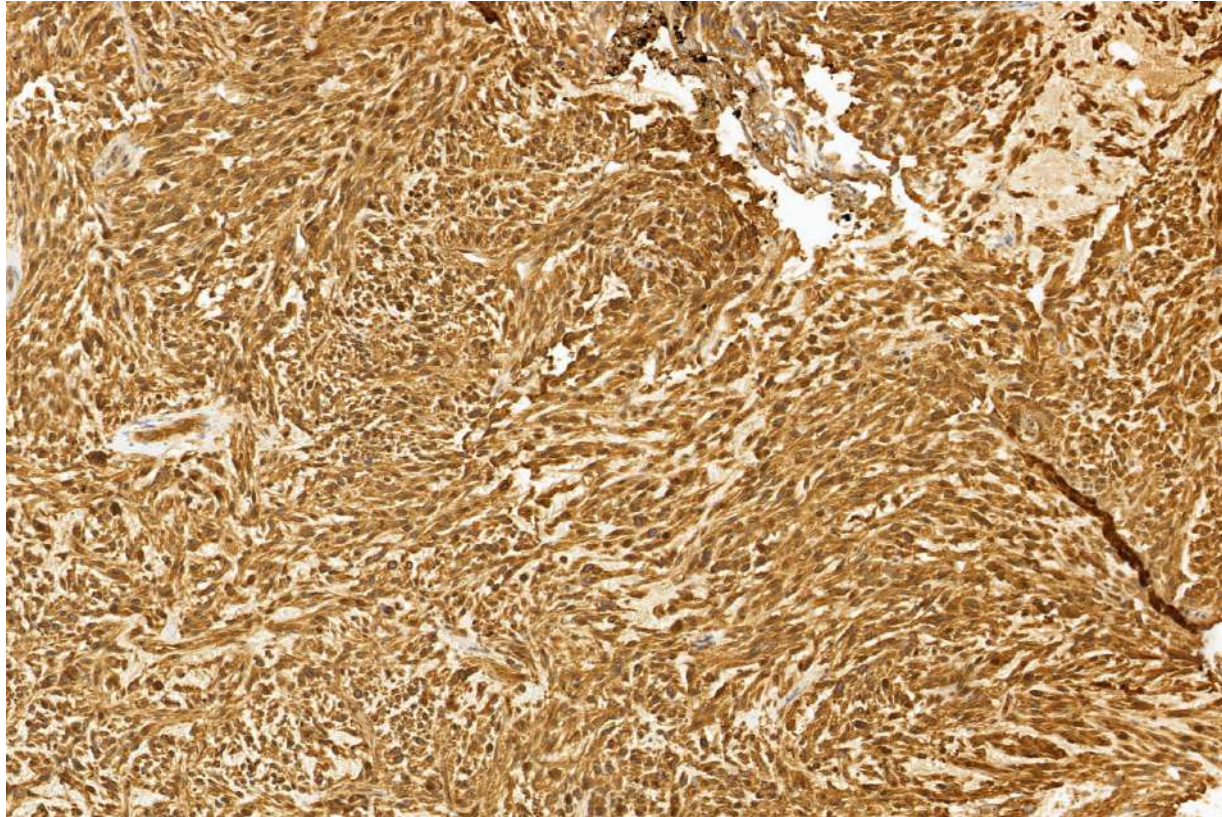


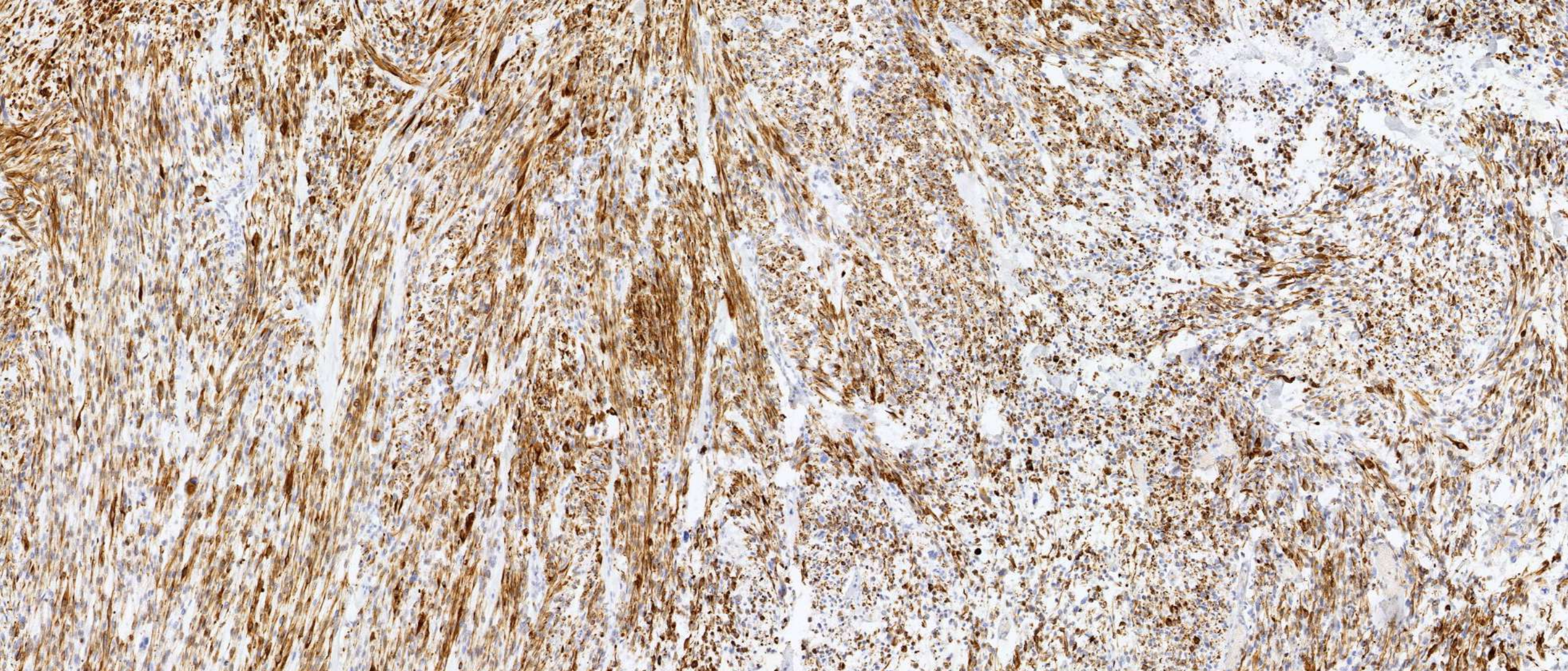


# Biopsia incisional 04.03.11

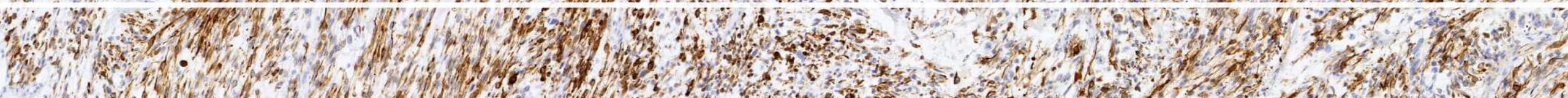


# Caldesmon +



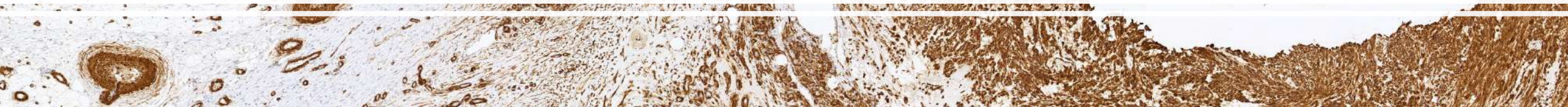


Desmina +



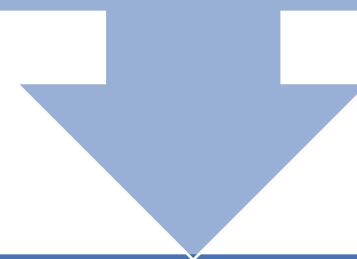


Actina +





Varón de 44 años. HIV + con carga viral indetectable.



Diagnosticado de leiomiosarcoma alto grado localmente avanzado.

Alto grado

> 5 cm.

Profundo.

T2bN0M0.

# COMITÉ MULTIDISCIPLINAR



- CIRUGÍA
- RADIOTERAPIA
- NEOADYUVANCIA

# COMITÉ MULTIDISCIPLINAR



- CIRUGÍA
- RADIOTERAPIA
- **NEOADYUVANCIA**

# SARCUATOR

5-year OS



info

10-year OS



th 10-year OS <60% anthracycline-based chemotherapy may provide statistically and clinically significant benefits [PMID 306]

info

5-year DM



info

## Primary ESTS

Age

18-100

44

Tumor Size

0-35cm

12

FNCLCC GRADE

3

Histology

LMS

Calculate



# SARCUATOR

5-year OS



info

10-year OS



info

5-year DM



info

## Primary ESTS

Age

18-100

44

Tumor Size

0-100mm

12

FNCLCC GRADE

1-3

Histology

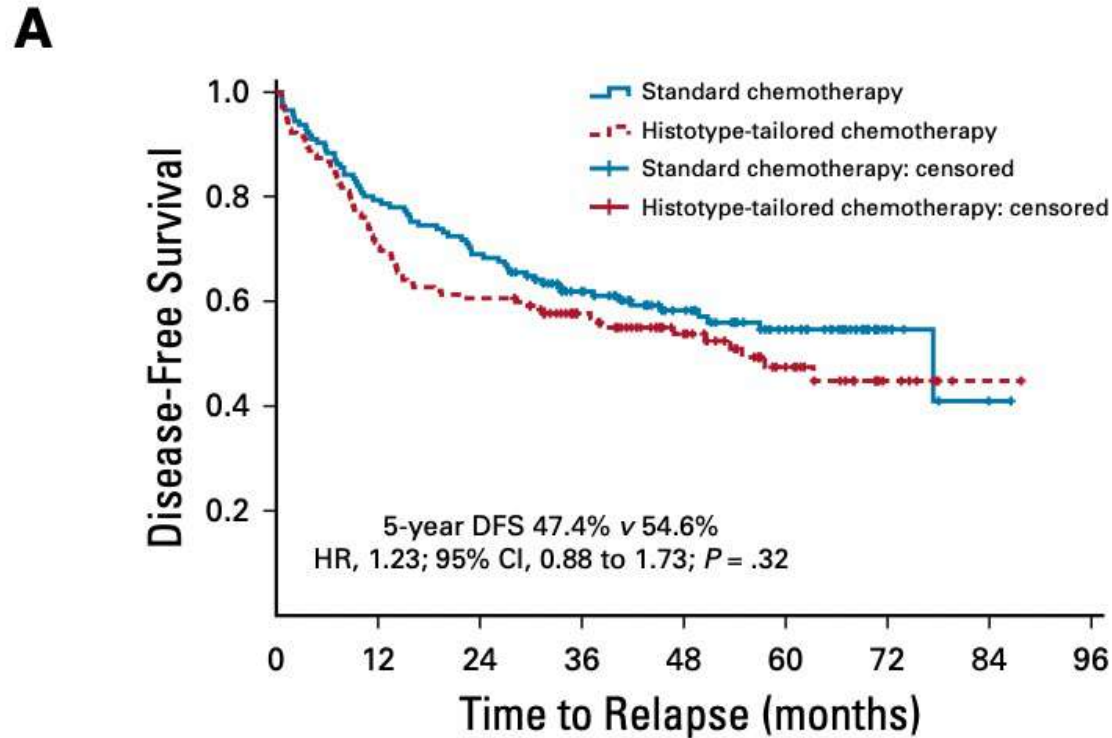
LMS

Calculate

Tratamiento dirigido??  
Antraciclinas??  
Ifosfamida??

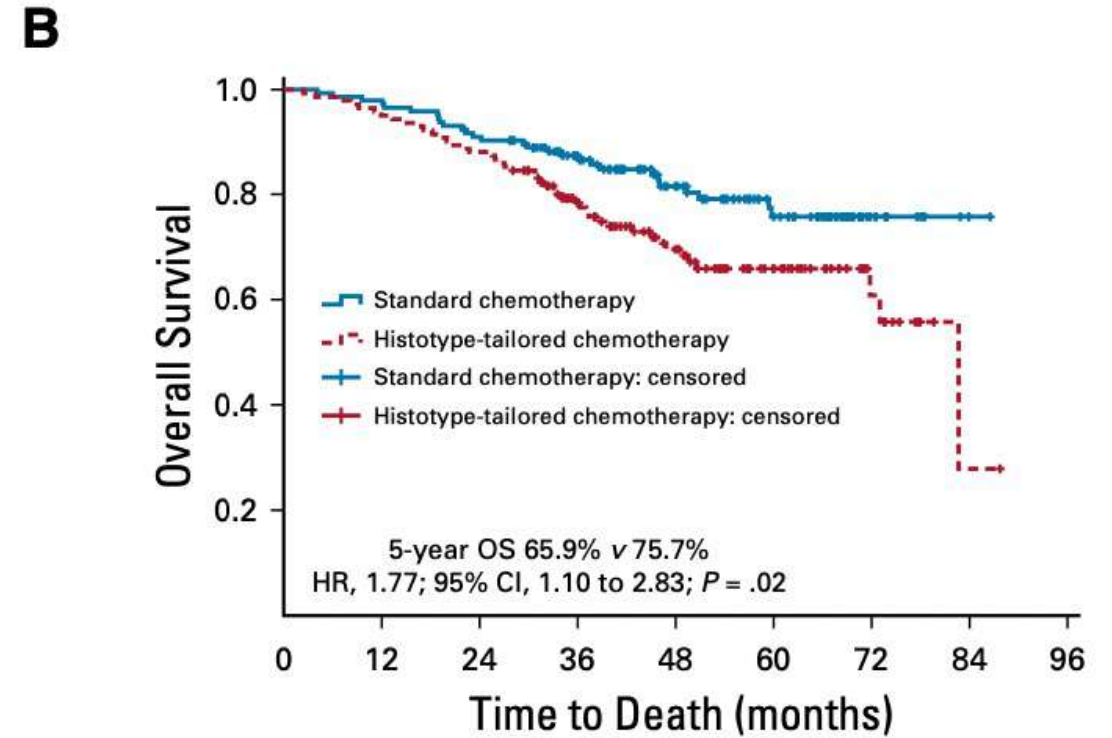
th 10-year OS <60% anthracycline-based chemotherapy may provide statistically and clinically significant benefits [PMID: 306]

# ENSAYO ISG + GEIS + FIS + PIS



No. at risk:

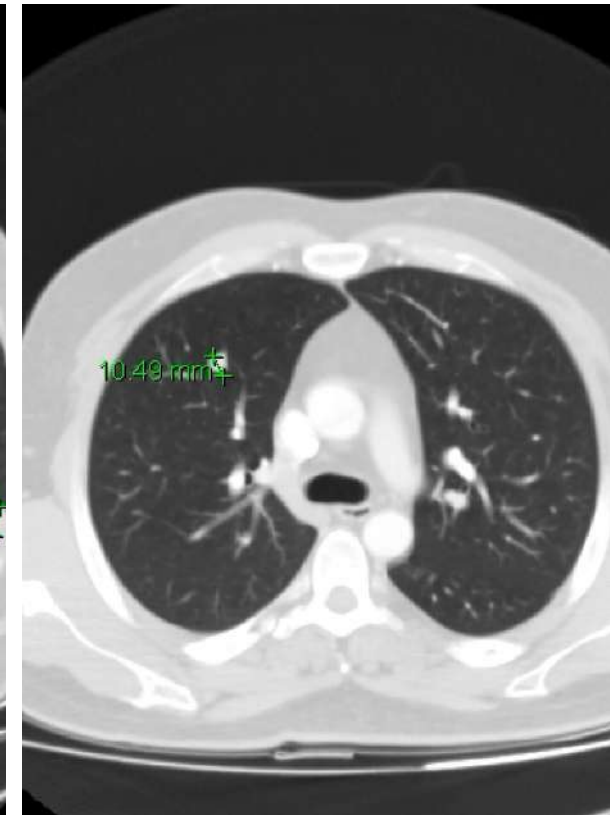
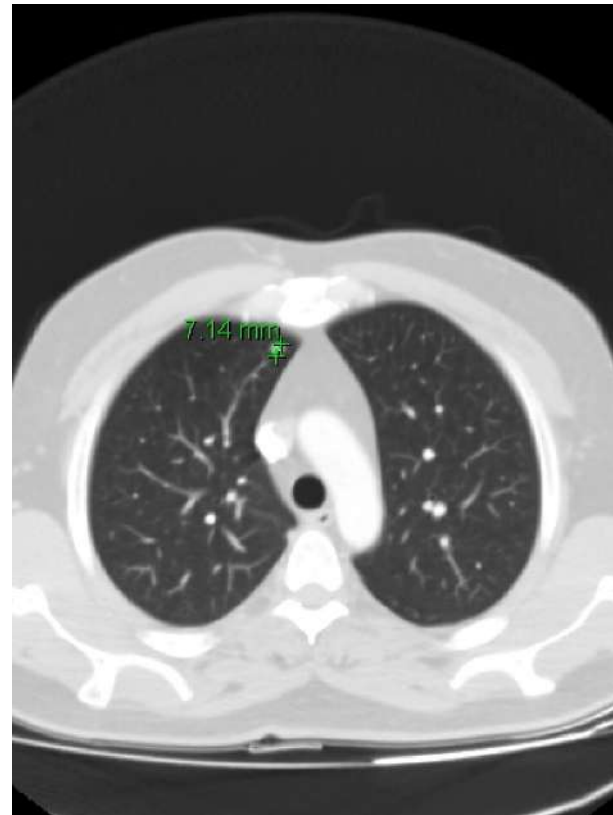
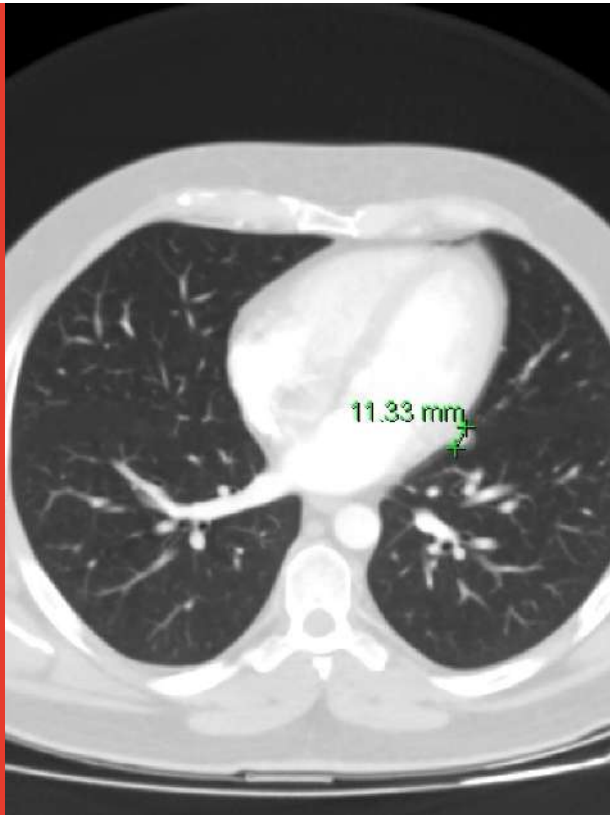
Standard CT	145	115	100	77	55	36	8	2	0
HT CT	142	101	86	65	44	23	8	1	0



No. at risk:

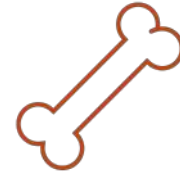
Standard CT	145	142	131	104	72	45	13	2	0
HT CT	142	135	125	92	61	35	13	1	0

Neoadjuvant Chemotherapy in High-Risk Soft Tissue Sarcomas: Final Results of a Randomized Trial From Italian (ISG), Spanish (GEIS), French (FSG), and Polish (PSG) Sarcoma Groups



# ESTUDIO DE EXTENSIÓN

Marzo de 2011 → 4 metástasis pulmonares



## ENFERMEDAD

Leiomiomasarcoma.

Alto grado.

4 Metástasis  
pulmonares.

Bilaterales.

Sincrónicas.



## PACIENTE

Joven

ECOG 0.

HIV sin carga viral.



¿Es posible  
un R0?



## ENFERMEDAD

Leiomiomasarcoma.

Alto grado.

4 Metástasis  
pulmonares.

Bilaterales.

Sincrónicas.

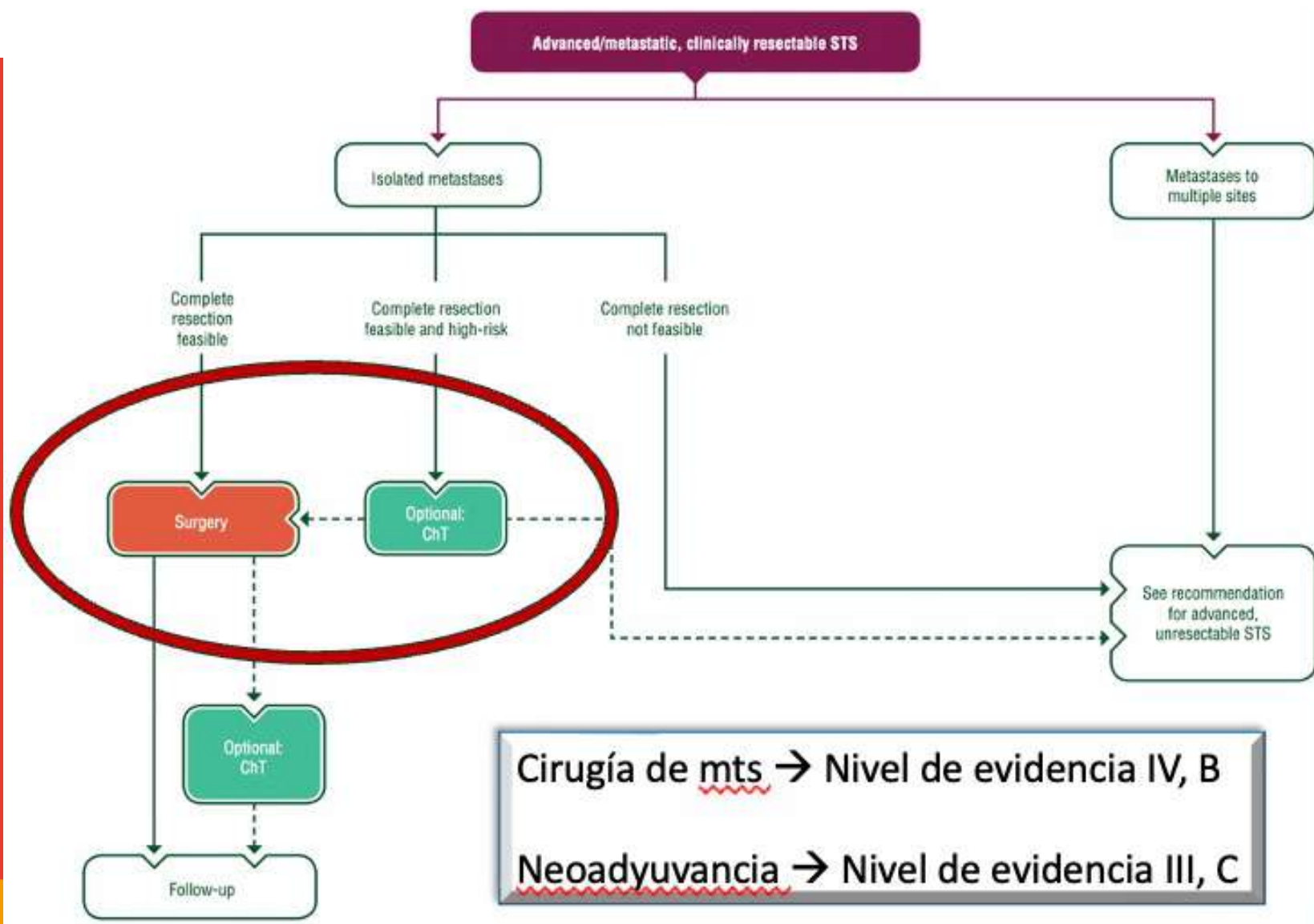


## PACIENTE

Joven

ECOG 0.

HIV sin carga viral.



Cirugía de mts → Nivel de evidencia IV, B  
Neoadyuvancia → Nivel de evidencia III, C



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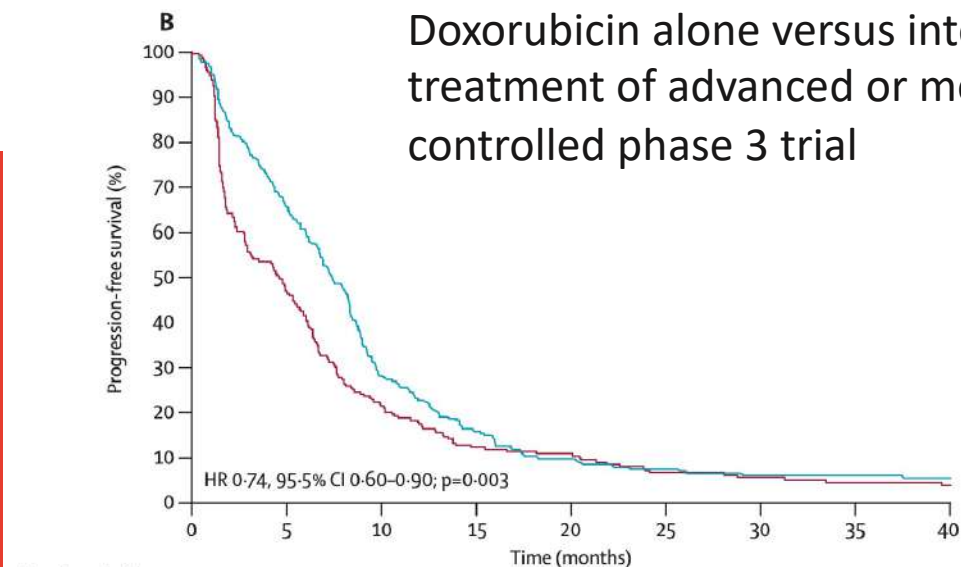
# Doxorrubicina

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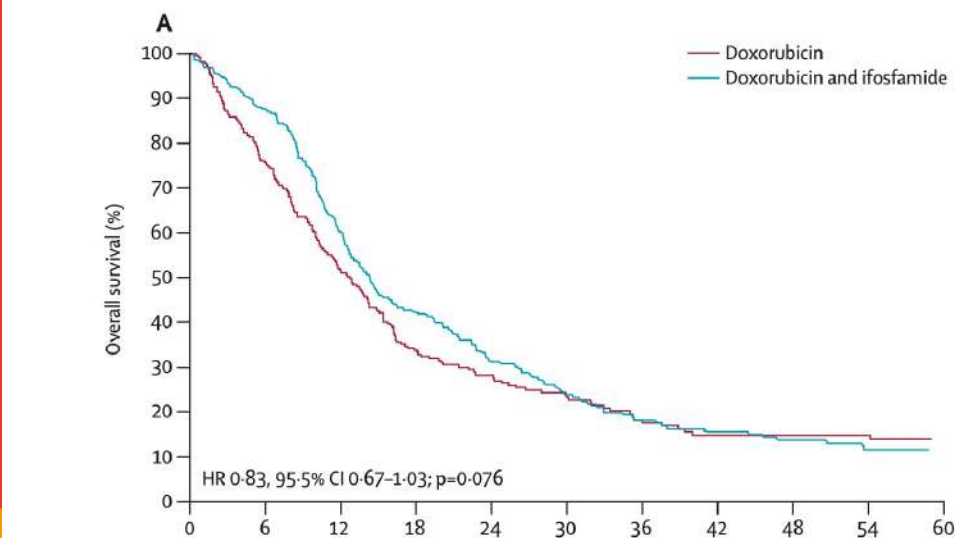
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# Doxorrubicina + Ifosfamida

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



Number at risk		0	5	10	15	20	25	30	35	40
Doxorubicin	228	104	48	26	23	14	11	8		
Doxorubicin and ifosfamide	227	149	62	34	21	16	12	12		



Number at risk		0	6	12	18	24	30	36	42	48	54	60
Doxorubicin	228	170	113	74	54	41	29	19	19	17		
Doxorubicin and ifosfamide	227	197	130	90	64	43	30	25	20	16		

	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**



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**Doxorrubicina**

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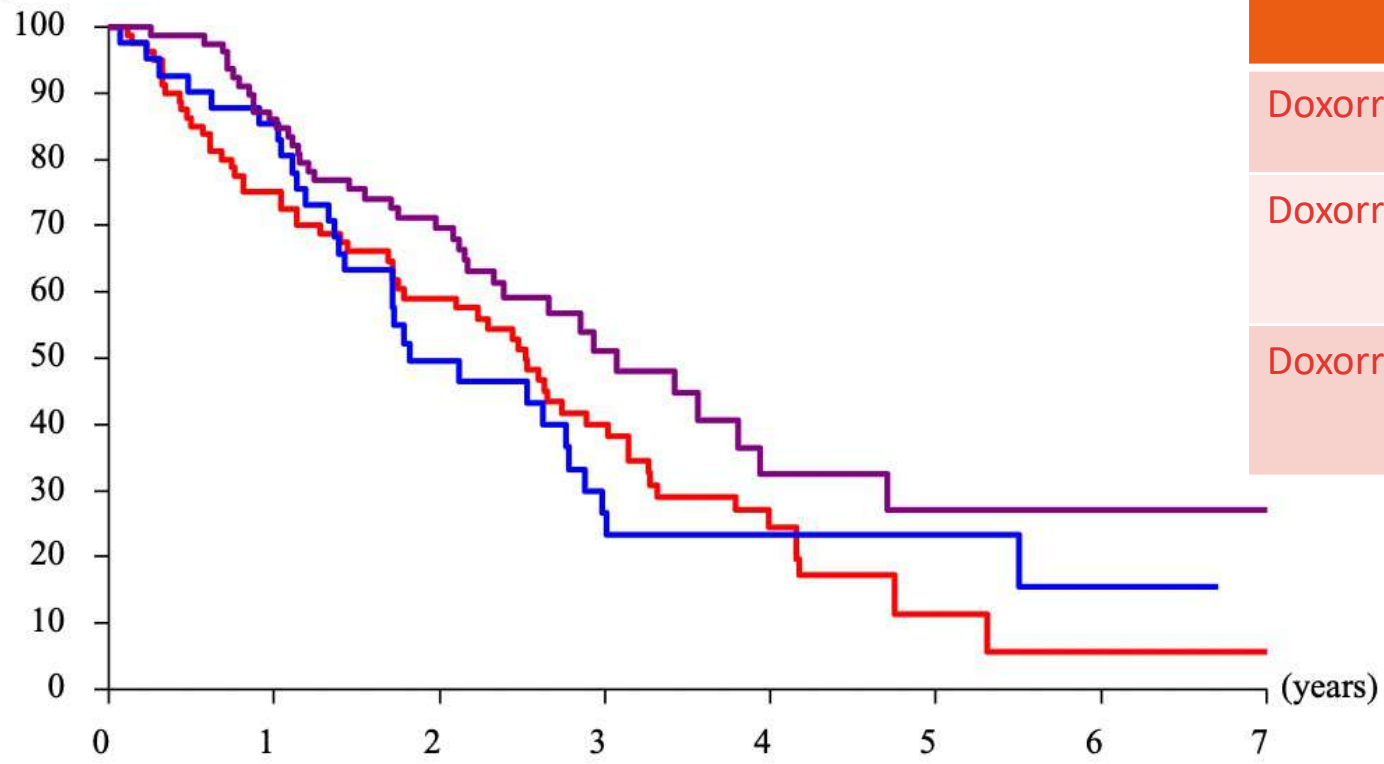
**Doxorrubicina  
+ Ifosfamida**

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**Doxorrubicina  
+ Dacarbazina**

# Doxo.+ DTIC Vs. Doxo. + Ifosf. Vs Doxorubicina

**B**

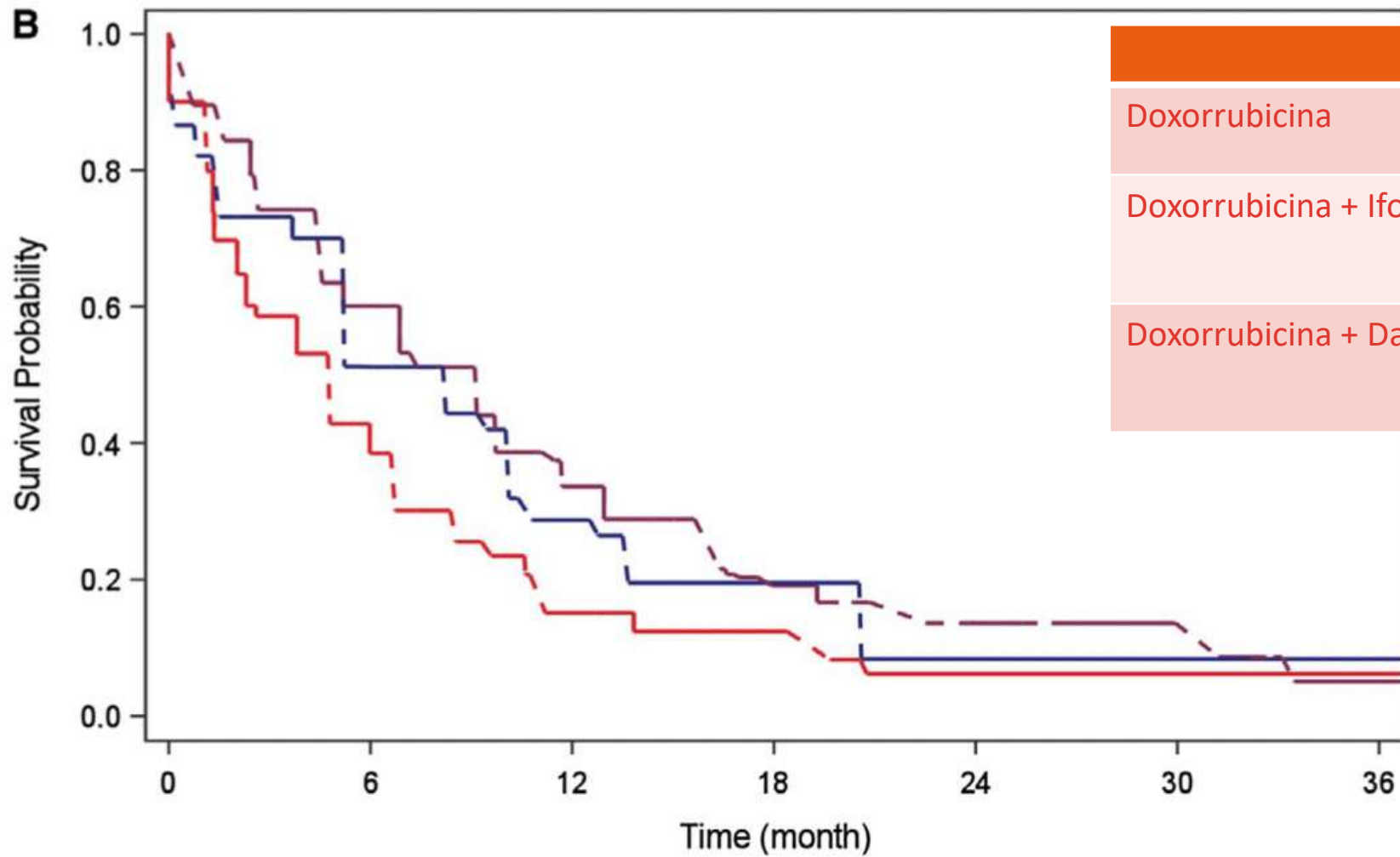


	PFS	ORR	OS
Doxorubicina	4,8 m	25,6%	30,3 m.
Doxorubicina + Ifosfamida	8,2 m.	19,5%	21,9 m.
Doxorubicina + Dacarbazina	9,2 m	30,9%	36,8 m.

O	N	Number of patients at risk :							Chemotherapy of interest
57	82	60	41	22	10	2	1	<span style="color: red;">—</span> Doxorubicin alone	
29	41	35	18	8	5	3	2	<span style="color: blue;">—</span> Doxorubicin + Ifosfamide	
38	82	67	45	18	7	4	2	<span style="color: purple;">—</span> Doxorubicin + Dacarbazine	

Doxorubicin Plus Dacarbazine, Doxorubicin Plus Ifosfamide, or Doxorubicin Alone as a First-Line Treatment for Advanced Leiomyosarcoma: A Propensity Score Matching Analysis From the European Organization for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group

# Doxo.+ DTIC Vs. Doxo. + Ifosf. Vs Doxorubicina



	PFS	ORR	OS
Doxorubicina	4,8 m	25,6%	30,3 m.
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Doxorrubicina

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Doxorrubicina  
+ Ifosfamida

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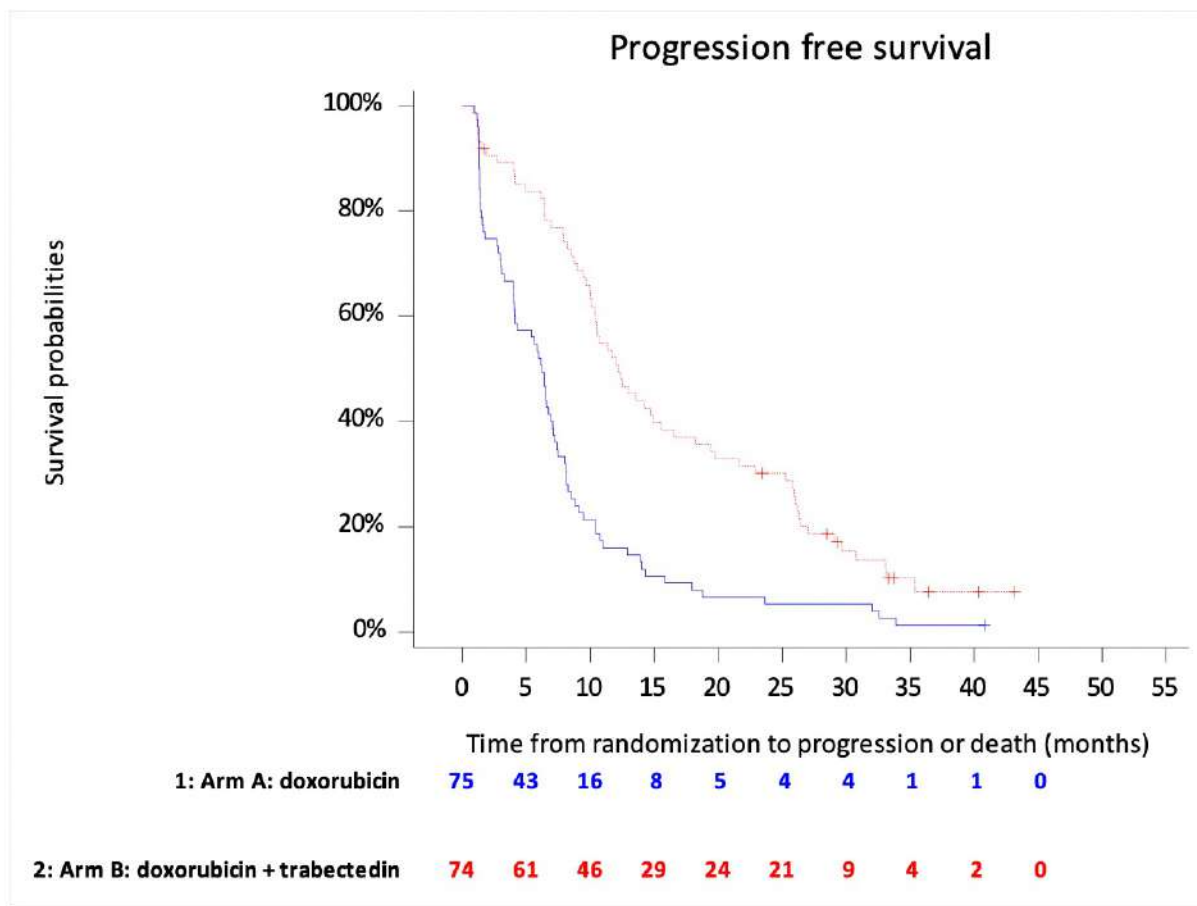
Doxorrubicina +  
Dacarbazina

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Doxorrubicina +  
Trabectedina

## LMS-04 study





Events, n (%)

Median PFS, months

	Doxo (N = 76)	Doxo + Trab (N = 74)
Events, n (%)	74 (97%)	65 (88%)
Median PFS, months	<b>6.2</b>	<b>12.2</b>
<b>HR 0.41</b>		
95% CI 0.29-0.58; P<0.0001		

Ptes de ESMO 23 para resultados de OS.

Tendencia positiva para tasa de respuestas y SG.

BICR, blinded independent central review; ITT: intent to treat; CI, confidence interval; HR, hazard ratio; PFS: progression-free survival; **Median follow-up was 37 months.**

# VOLVIENDO A NUESTRO CASO



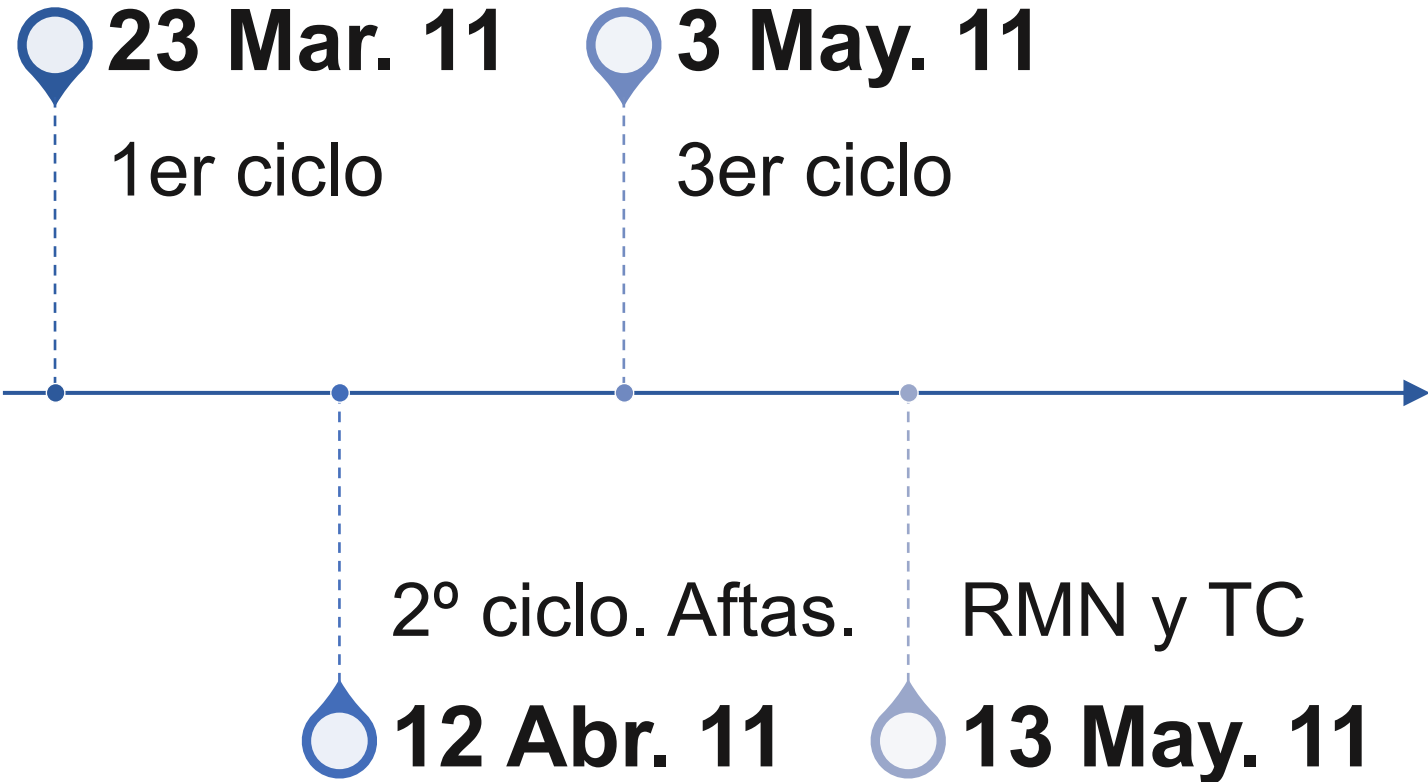
Objetivo: Intento de R0



Doxorrubicina 60 mg/m<sup>2</sup>  
Ifosfamida altas dosis 10 g/m<sup>2</sup> (escalables a 12 g/m<sup>2</sup>)  
Factores

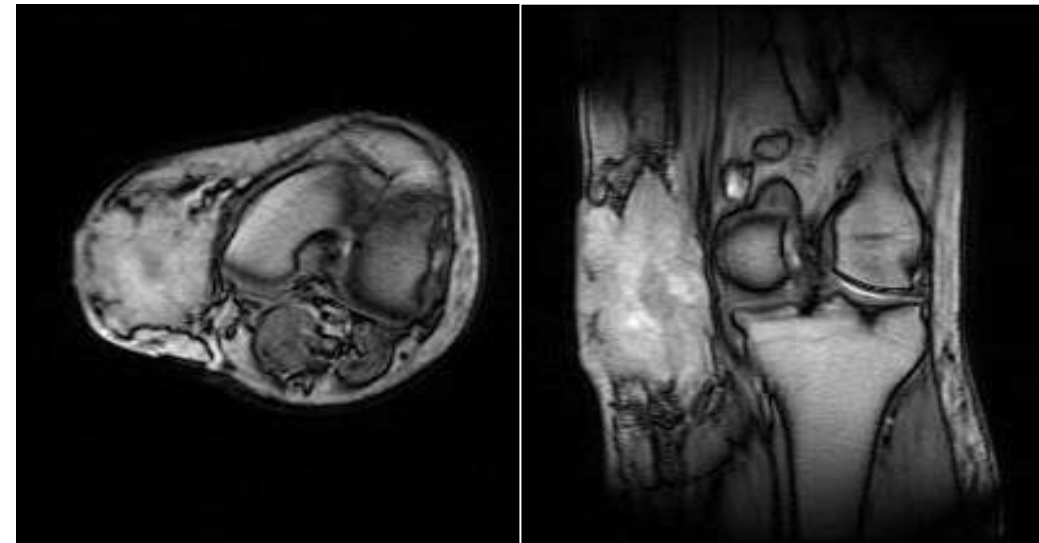


Intención de extirpación radical, según respuesta.



Comparando con exploración previa de enero del 2011 se evidencia una **progresión tumoral** (12 x 5,4 x 7,2 cm)

Nódulos pulmonares estables en tamaño y número





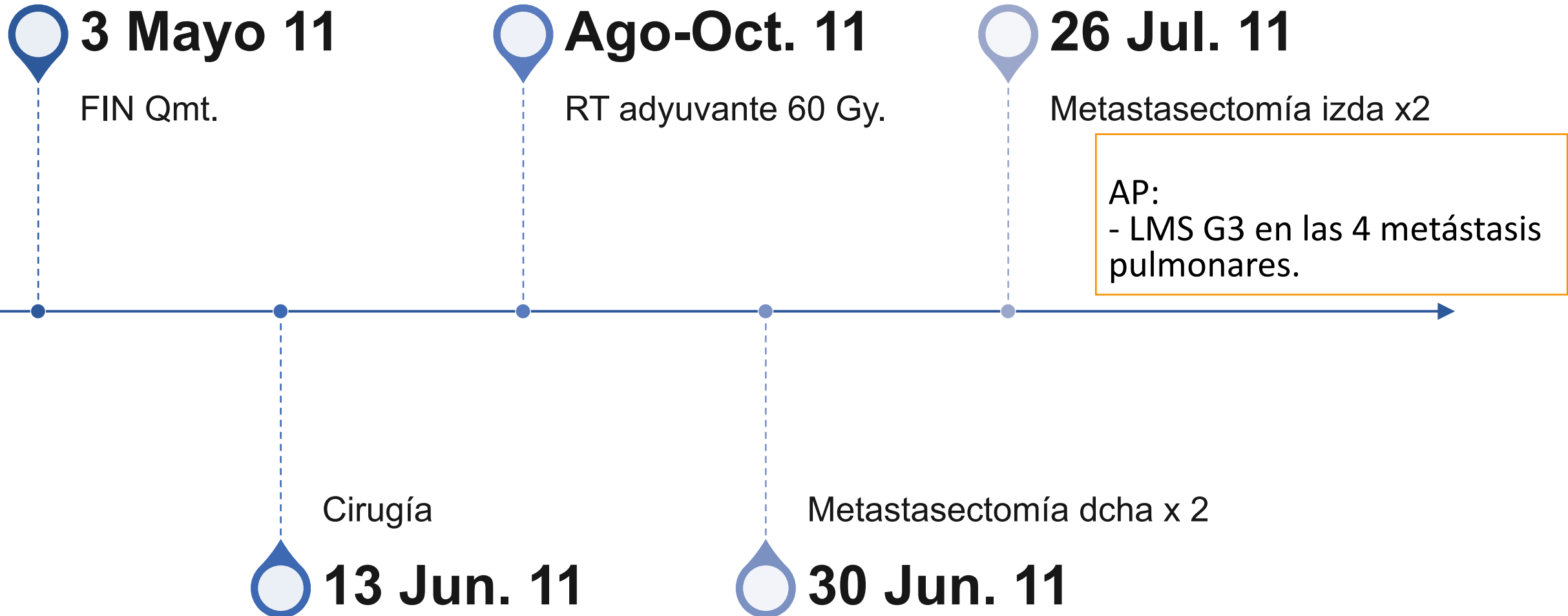


## Extirpación del tumor de la rodilla.

- Engloba el sartorio y se encuentra aislado de la cápsula de la rodilla.
- Resección amplia con margen de seguridad englobando fascia y sartorio.
- Cobertura con cirugía plástica mediante colgajos de avance locales e injerto.

## AP:

- LMS G3 con necrosis 40-60%.
- Respeta bordes.
- Infiltra dermis.
- >20 mits x 20 cga
- Ki67 60-70%

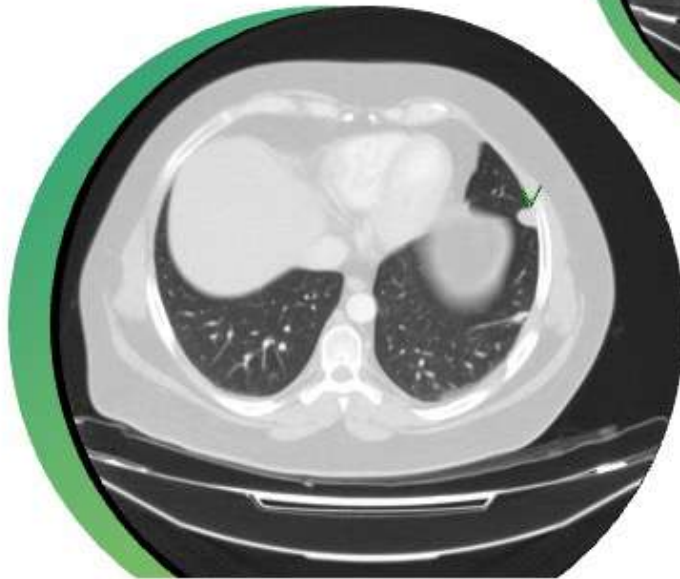
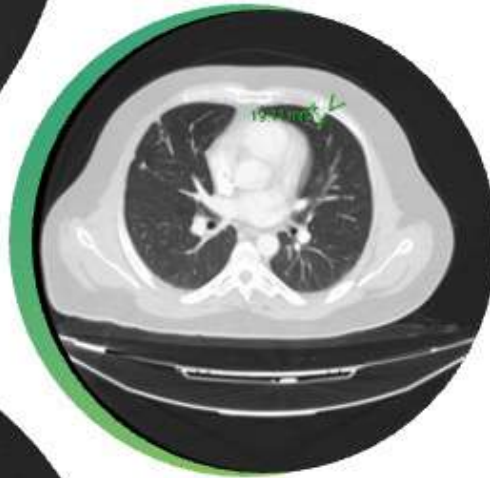


Sin evidencia de  
enfermedad



# 1ª RECIDIVA

## 7 Dic 2011



- 5 meses PLP.
- RM sin recaída local
- TC: hasta 8 lesiones nodulares de nueva aparición en ambos hemitórax la mayor de 19 mm en lóbulo superior izquierdo

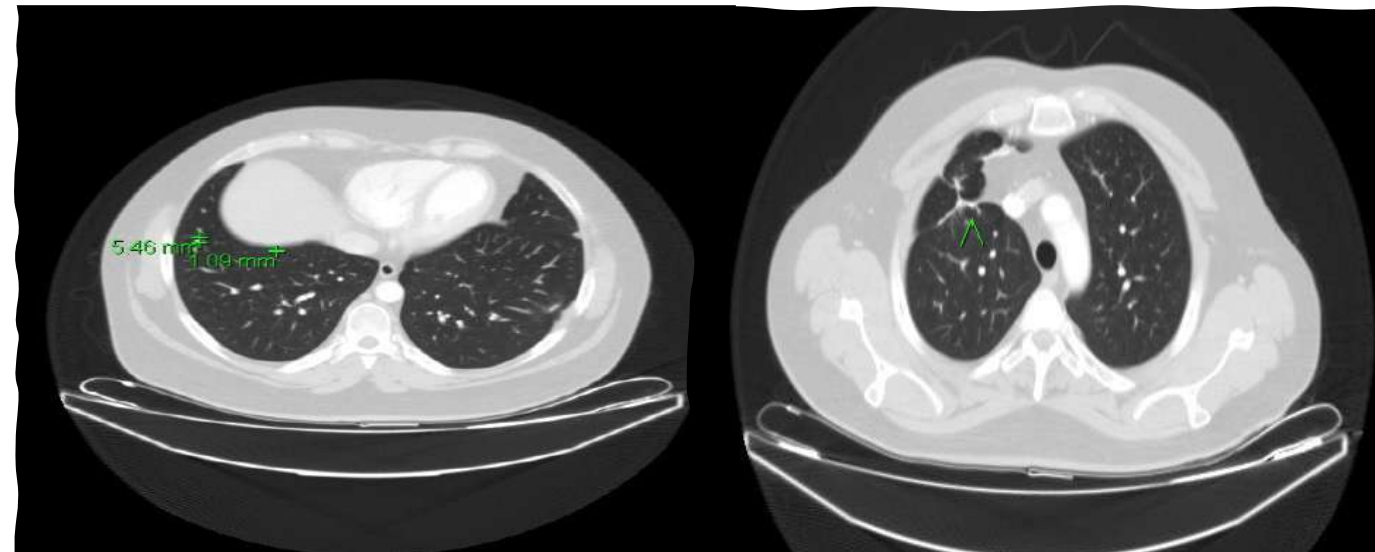
## Respuesta Parcial

- LID 7,6 mm (12,7 mm en previo).
- LSI 7,6 mm (19,1 mm en previo).
- No visualizamos algunos nódulos milimétricos que estaban presentes en el estudio previo

**Ene´12**  
Inicia Qmt

TC.  
x 6 ciclos

**Mar´12**



## JOURNAL OF CLINICAL ONCOLOGY

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

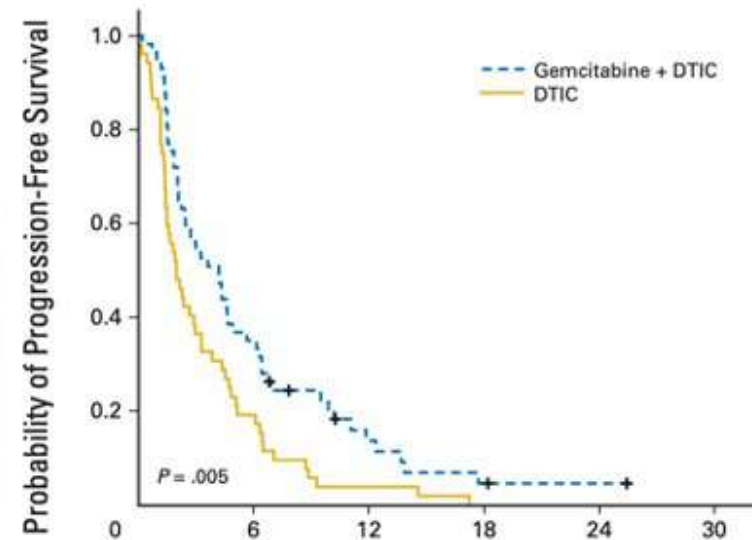
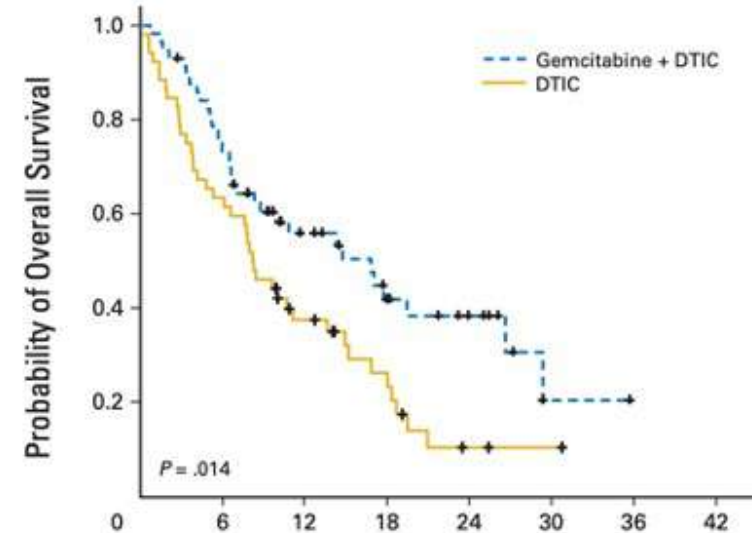
### FII randomizado GEIS.

N= 113 pacientes.  
Múltiples histologías

### RESULTADOS

RR 12 Vs 4  
SLP 4,2m Vs 2m  
SG 16,8m Vs 8,2m

**Mayor actividad en  
LMS.**





- **4 Metástasis pulmonares izdas.**
- **Enfermedad extrapulmonar controlada.**

**Ene. 12**

Inicia Qmt

**¿RE-  
OPERAMOS?**

finaliza 6 cic

**Mar. 12**



**ástasis pulmonares**  
**nedad extrapulmonar**  
**olada.**



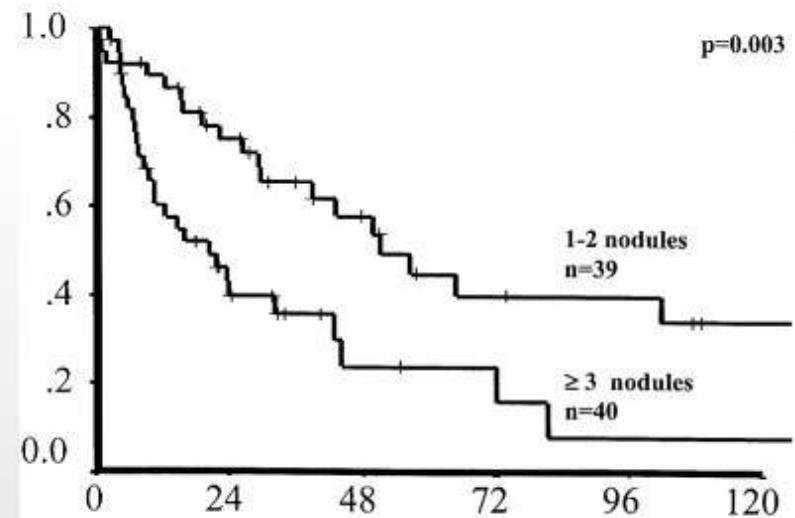
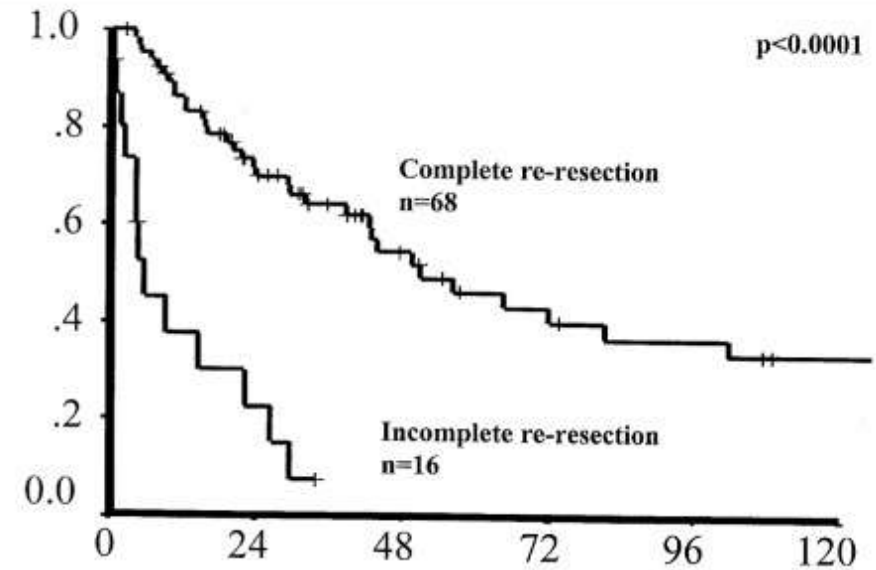
# Repeat Resection of Pulmonary Metastases in Patients with Soft-Tissue Sarcoma.

Martín R Weiser et al.

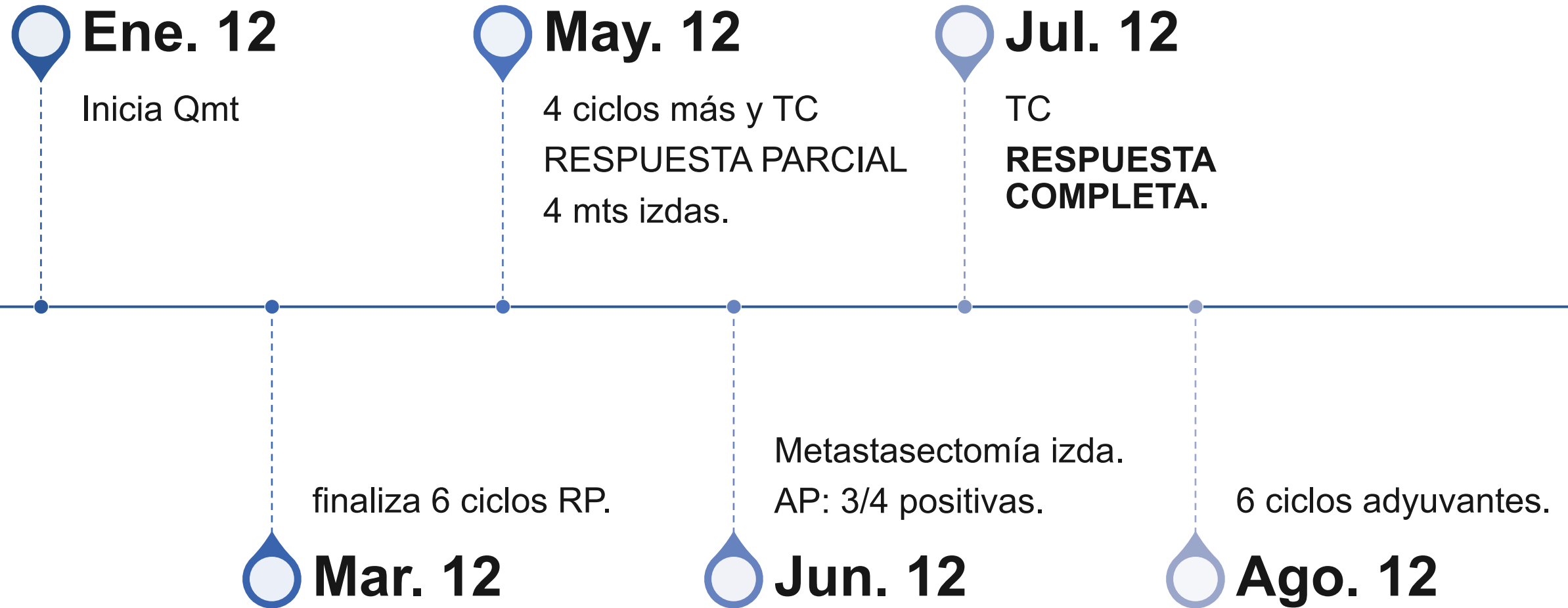
- Número de lesiones.
- Grado histológico.
- Tiempo libre de enfermedad.

¿Re-cirugía?  
**SÍ**, enfermedad extratorácica controlada.

EL factor pronóstico más importante.  
**Lograr el R0.**



# 2ª NEOADYUVANCIA → DTIC - Gemcitabina

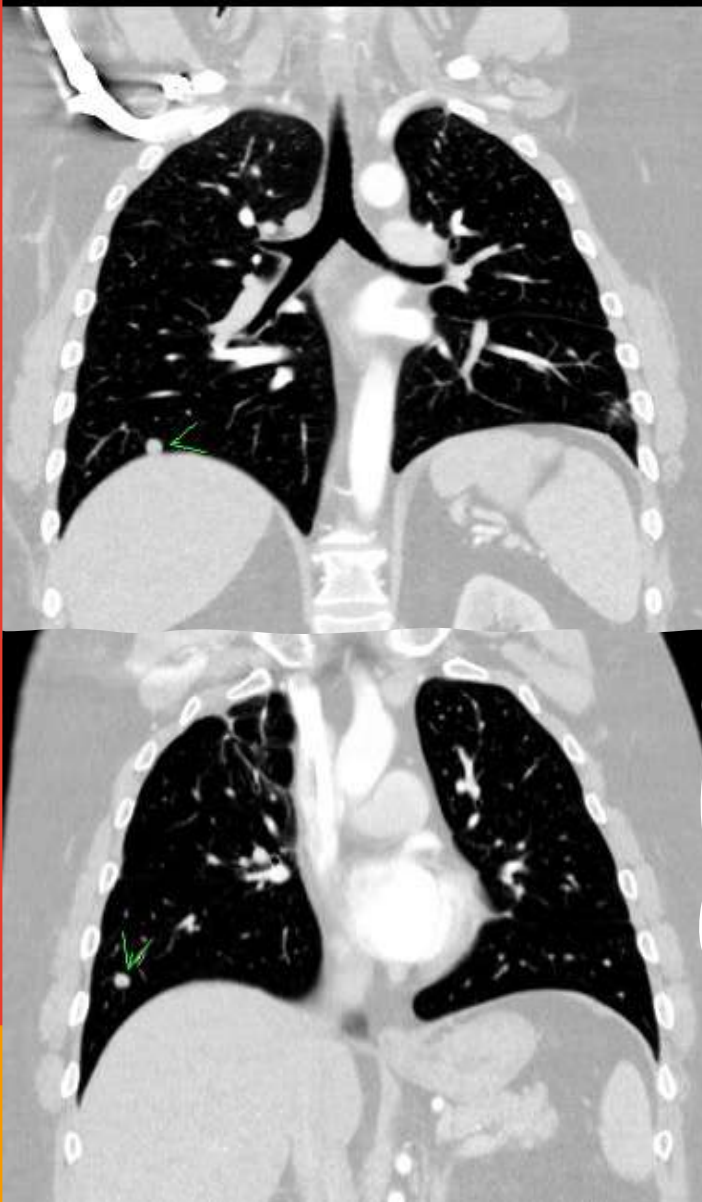


## 2ª RECIDIVA.

- TC ENERO 13. **Recidiva pulmonar.**
  - ILE: 9 MESES.
  - ILQ: 5 meses

TC:

- Nódulos de 9, 10 y 11mm en LID
- 2 nuevos en LSD y LD (ambos mm)



## 2<sup>a</sup> RECIDIVA.

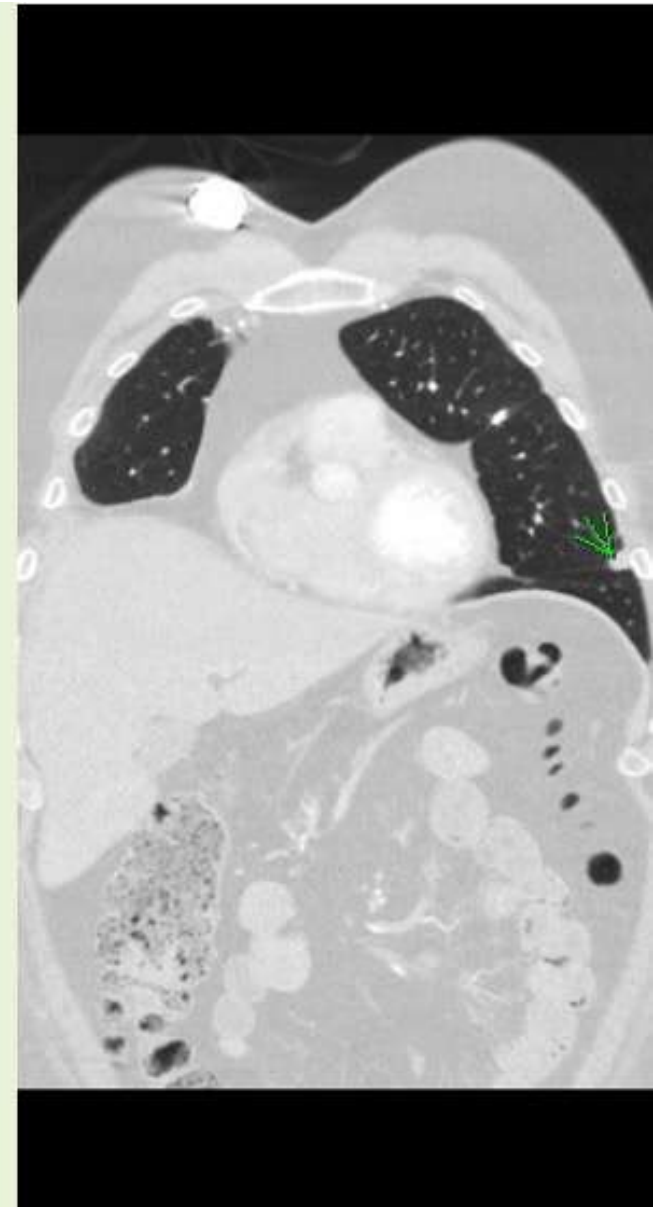
- Febrero 13: Minitoracotomía derecha videoasistida sobre incisiones previas
  - 4 nódulos LID + 1 nódulo LM
- AP: LMS en los 4 nódulos
  - mayor pleomorfismo e indiferenciación





## 3ª RECIDIVA. Mayo'13

- RM sin recurrencia local.
- TC:
  - Derrame pleural dcho.
  - Nódulos en língula y LID.



Neoadyuvancia. **Adriamicina + Ifosfamida HD** → EE.

Qx + RT + Metastasectomía.

- 5 meses SLP.

2ª Neoadyuvancia. **Gemcitabina – DTIC** → RP

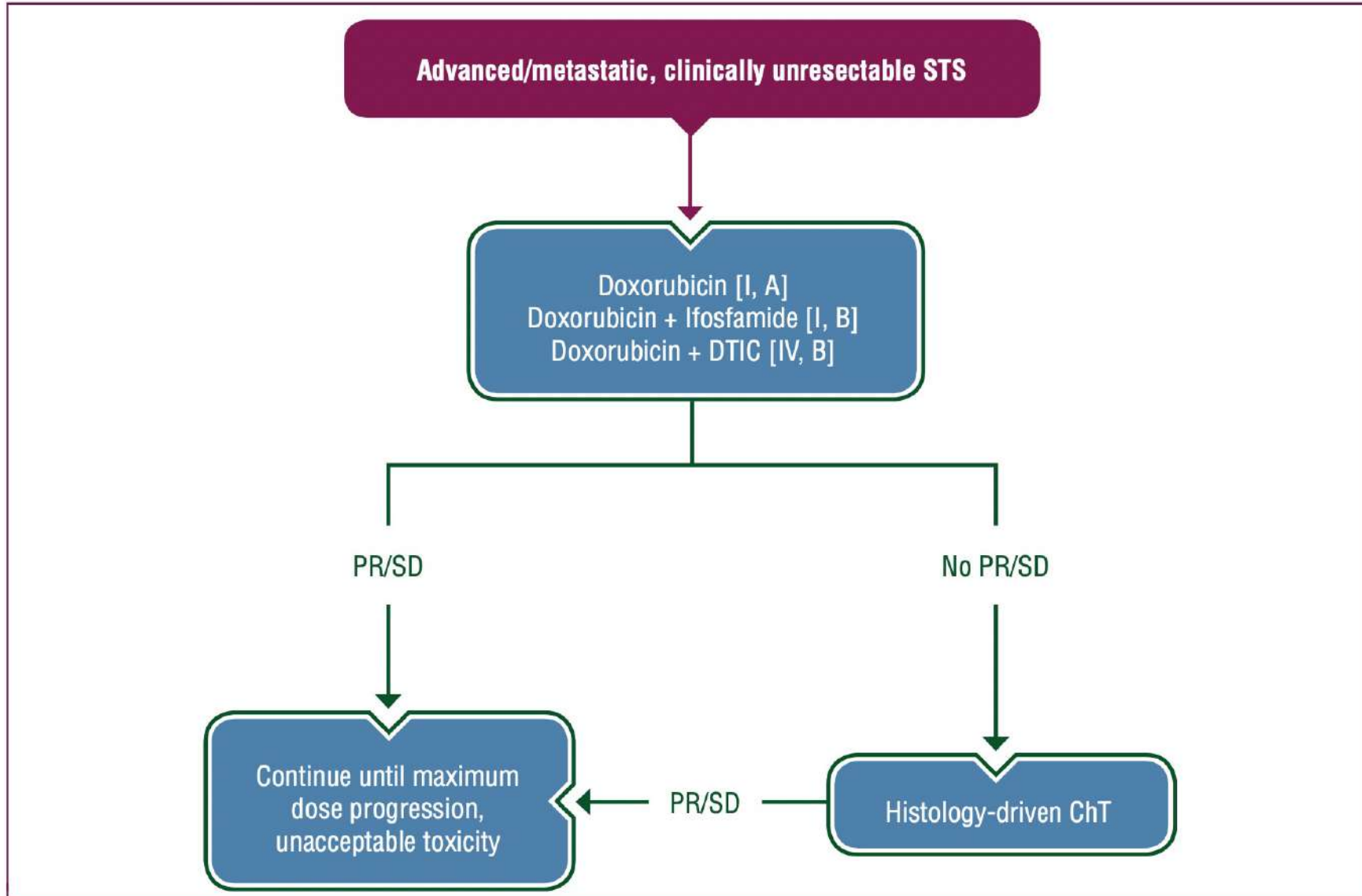
Metastasectomía

- 5 meses SLP

2 ciclos más **Gemcitabina – DTIC**

Metastasectomía

- 3 meses SLP



NO  
TRATAR

- TRO en torno a un 30%.
- Toxicidad.

Ifosfamida HD



- L-Sarcomas.
- Superv. 10,3 meses.
- Premedicación.

Trabectidina



- Excepto el Liposarcomas.

Pazopanib



- L-Sarcomas.
- Especialmente el Liposarcoma.

Eribulina



- LMS uterino y sarcoma pleomorfo indiferenciado.

Gemcitabina-  
docetaxel



Metro





# 1ª LÍNEA PALIATIVA TRABECTIDINA (1,3 mg/m<sup>2</sup>)

## EVALUACIÓN TRAS 3 CICLOS.

- Nódulo 6 mm en LID de **nueva aparición.**
- Nódulo en LID de 11 mm (9,7 mm en previo)
- Nódulo en LII de 7 mm (estable)
- Nódulo en línigula de 22 mm (12 mm en el estudio previo)
- **Desaparición** del derrame pleural derecho



# 1ª LÍNEA PALIATIVA TRABECTIDINA (1,3 mg/m<sup>2</sup>)

→ Continuamos con TRABECTEDINA



# 1ª LÍNEA PALIATIVA TRABECTIDINA (1,3 mg/m<sup>2</sup>)

→ Continuamos con TRABECTEDINA

## ESTABILIZACIÓN DE 16 MESES

- Recibe 18 ciclos
- EE hasta Septiembre de 2014



**SAR-3007**

**L-SARCOMAS**

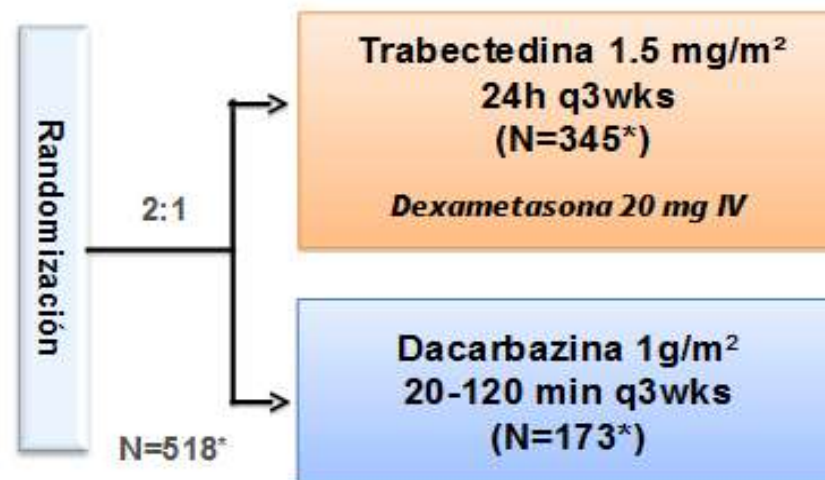
Efficacy and Safety of Trabectedin or Dacarbazine for Metastatic Liposarcoma or Leiomyosarcoma After Failure of Conventional Chemotherapy: Results of a Phase III Randomized Multicenter Clinical Trial

George D. Demetri, Margaret von Mehren, Robin L. Jones, Martee L. Hensley, Scott M. Schuetz

- LIPOSARCOMA Ó LEIOMIOSARCOMA
- PROGRESIÓN A QT (Antraciclina y  $\geq 1$  QT adicional)

Estratificación:

- Líneas de QT (1 vs 2+)
- ECOG (0 vs 1)
- Histología (LPS vs LMS)

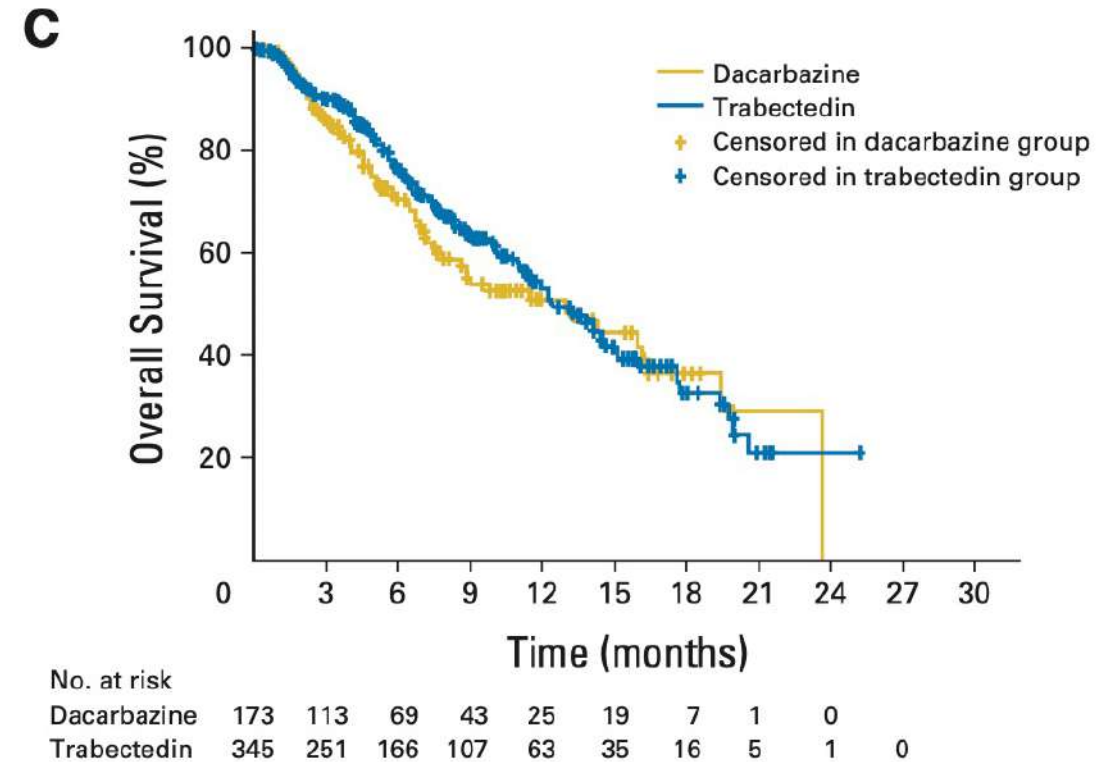
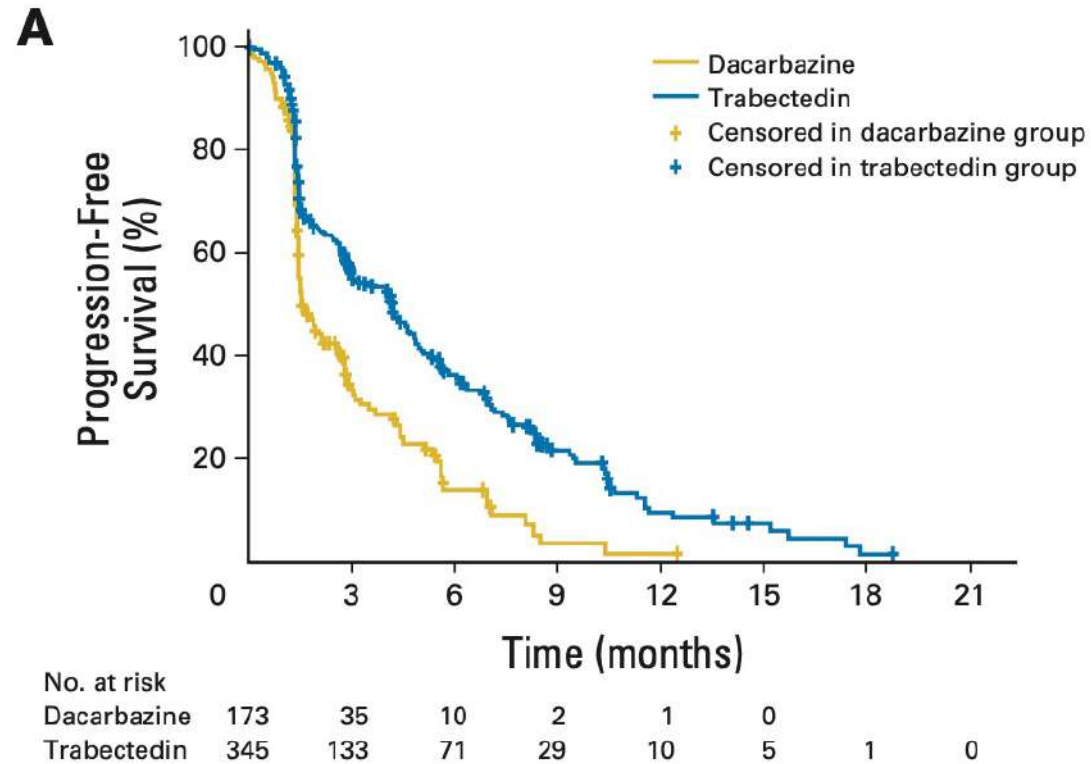


**OBJETIVO PPAL**

**SUPERVIVENCIA GLOBAL (OS)**

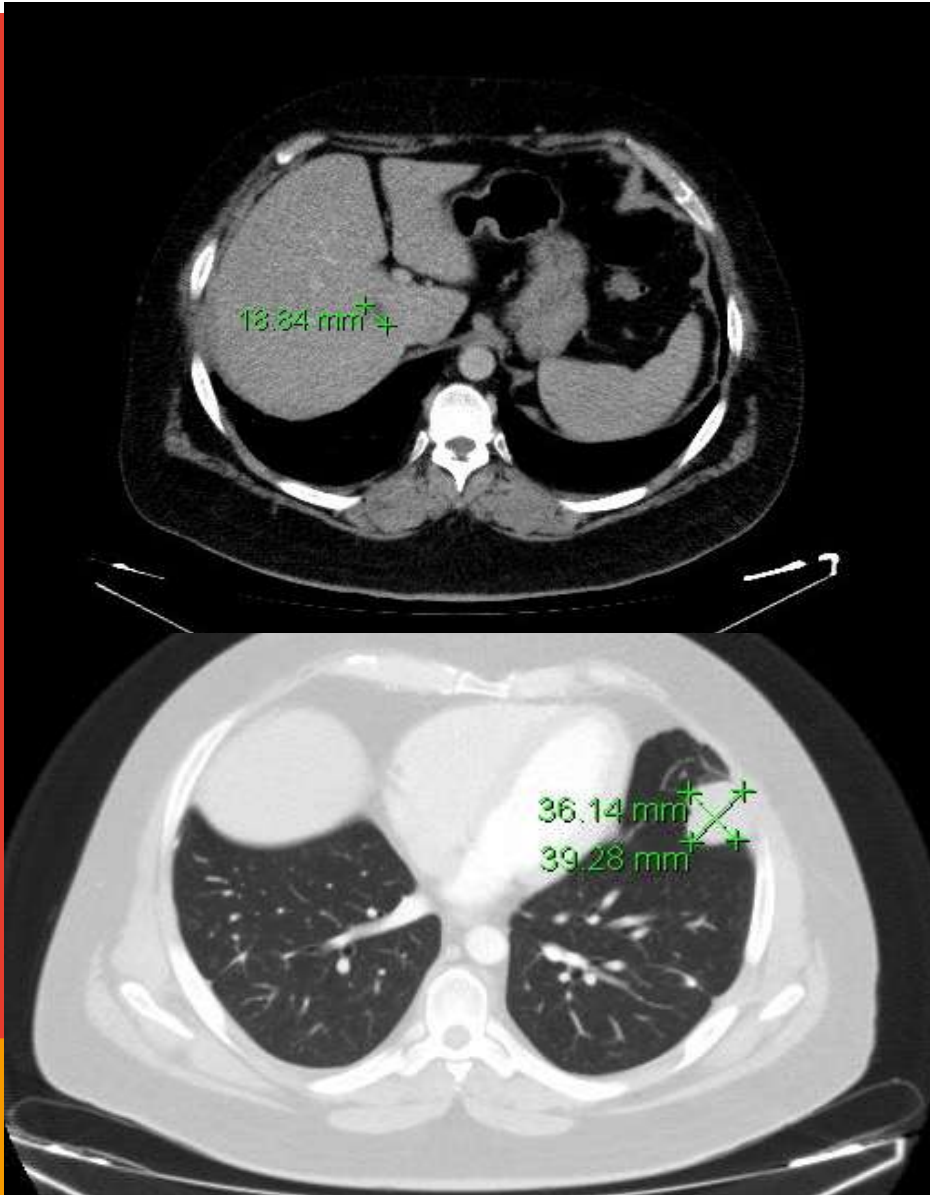
**OBJETIVOS 2ºS**

**SUPERVIVENCIA LIBRE PROGRESIÓN (PFS), TASA RESPUESTAS (ORR), DURACIÓN RSP (DOR), SEGURIDAD**



**Table 3.** End Points That Reflect Disease Control

End Point	Trabectedin (n = 345)	Dacarbazine (n = 173)	HR/OR (95% CI)*	P
PFS, months	4.2	1.5	0.55 (0.44 to 0.70)	< .001
TTP, months	4.2	1.5	0.52 (0.41 to 0.66)	< .001
No. (%) of ORR	34 (9.9)	12 (6.9)	1.47 (0.72 to 3.2)	.33
DOR, months	6.5	4.2	0.47 (0.17 to 1.32)	.14
No. (%) with SD as best response	177 (51)	60 (35)	—	—
Duration of SD, months	6.01	4.17	0.45 (0.30 to 0.67)	< .001
% of CBR	34	19	2.3 (1.45 to 3.7)	< .001



- RM sin recaída local
- TC
  - Aumento del tamaño de mtx pulmonar
  - Progresión hepática

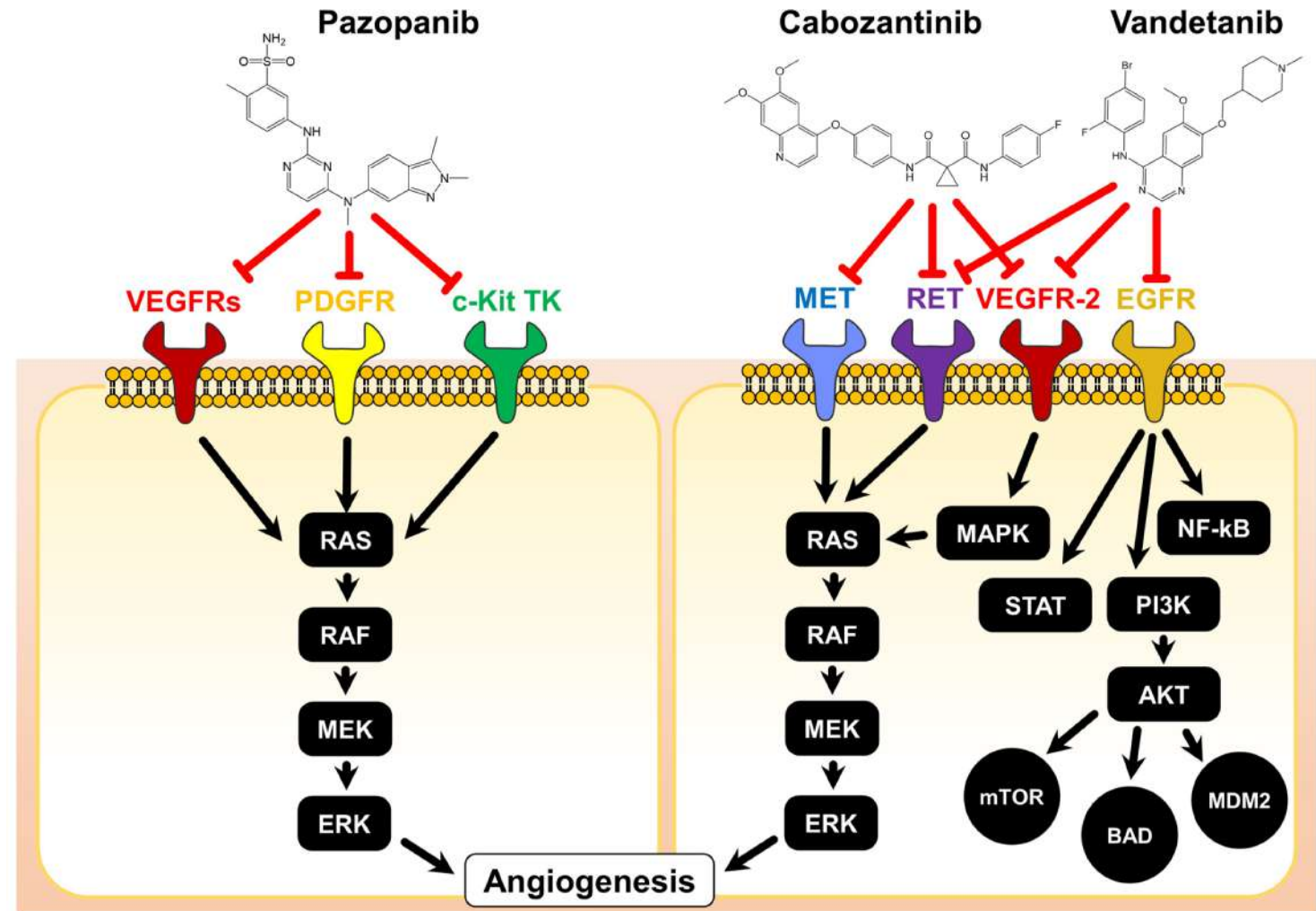
# 2ª LÍNEA PALIATIVA: PAZOPANIB

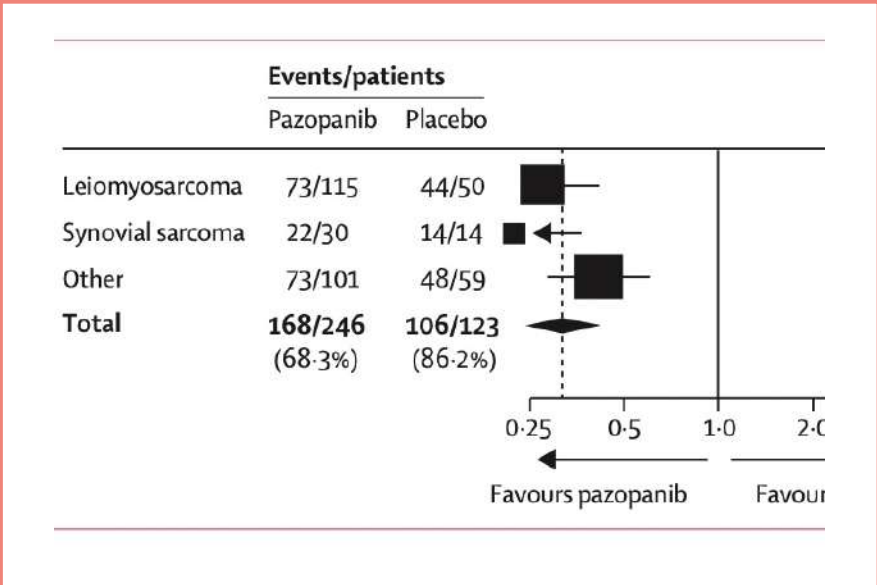
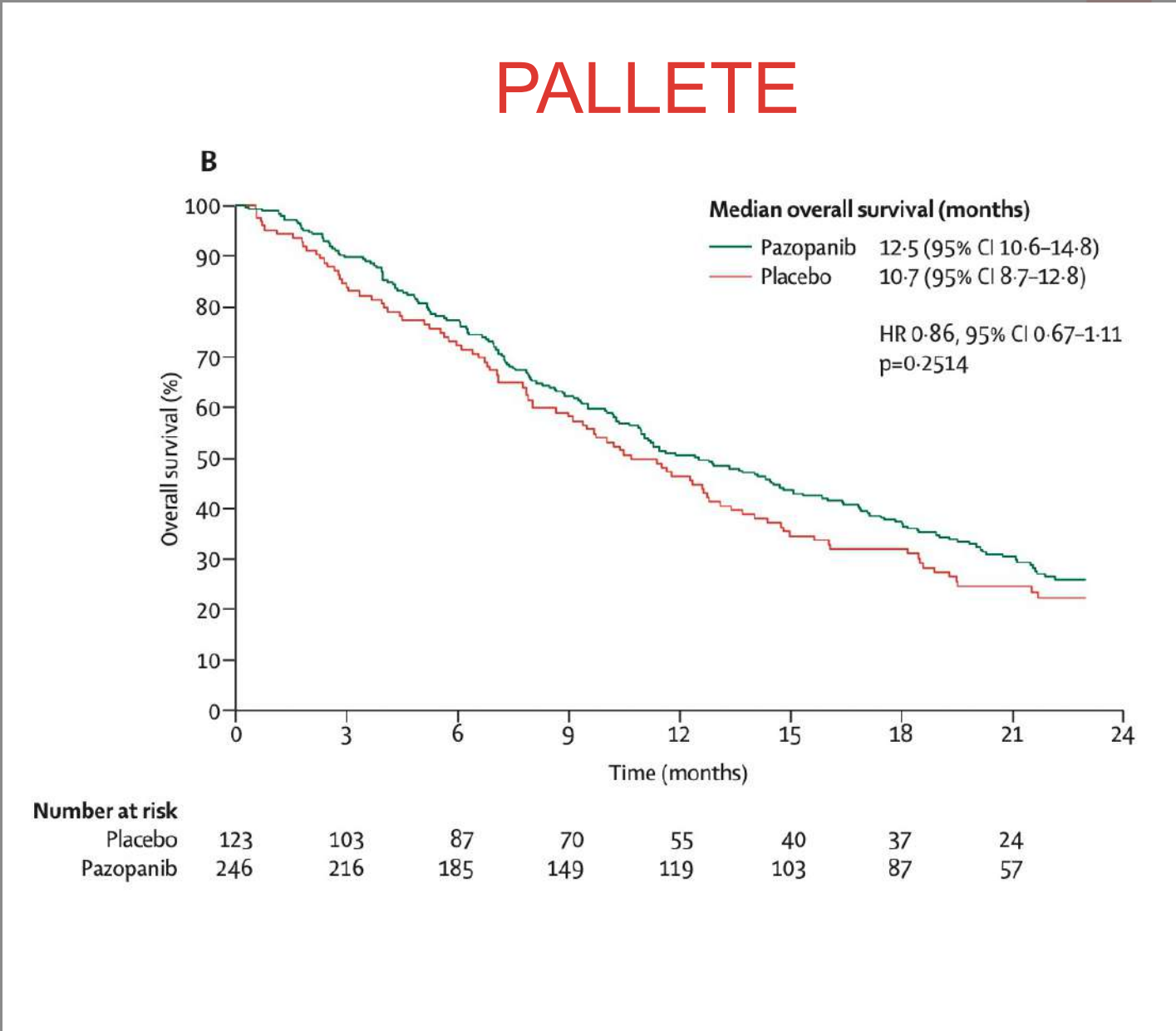
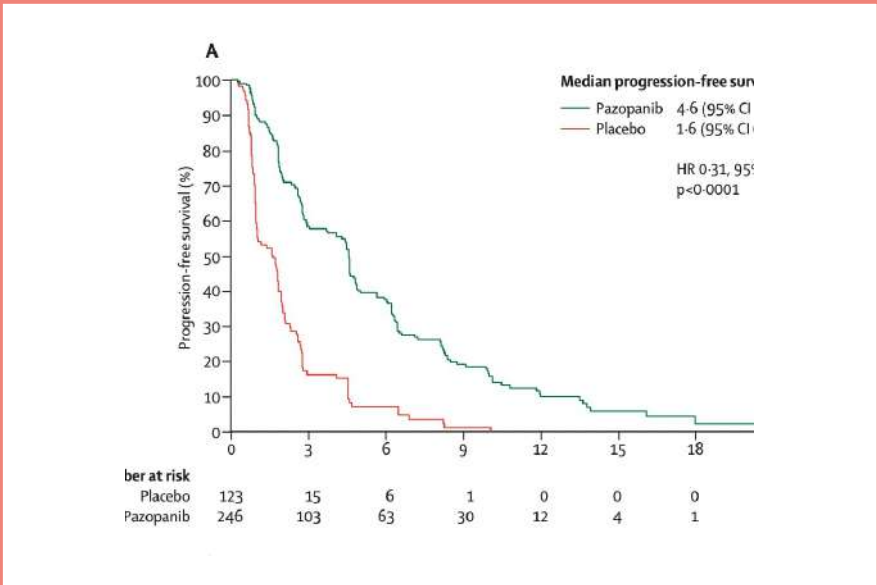
PAZOPANIB 800 mg/d

TC tras 4 meses (ene 2015)

Progresión pulmonar

Progresión hepática



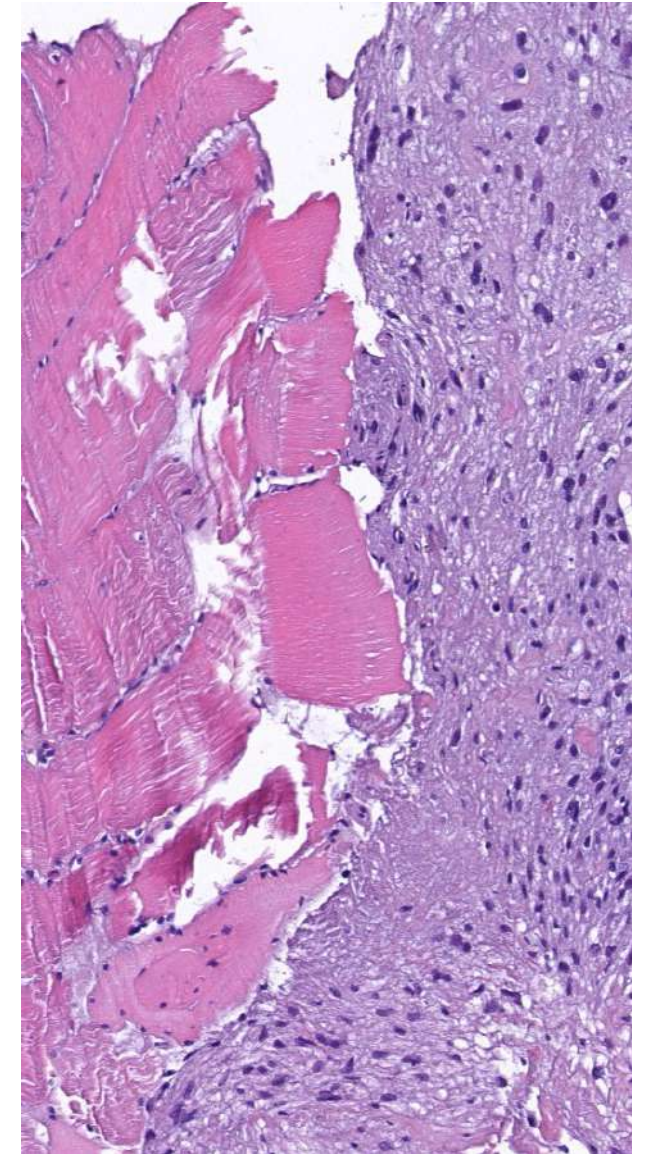




# 3ª LÍNEA PALIATIVA DOCETAXEL - GEMCITABINA



- Inicia ENERO 2015
- FEBRERO Fx tibia.
  - Cirugía AP: **LMS**
  - Estudio extensión - (GGO)
  - RT



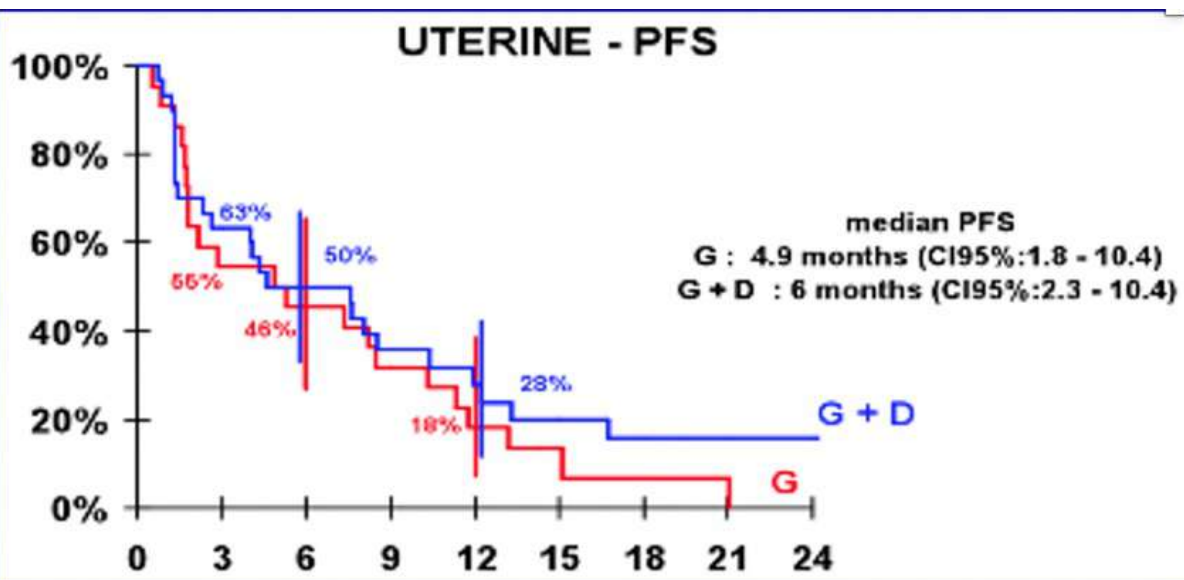
# 3ª LÍNEA PALIATIVA DOCETAXEL - GEMCITABINA

x 3 ciclos  
RP pulmonar y hepática

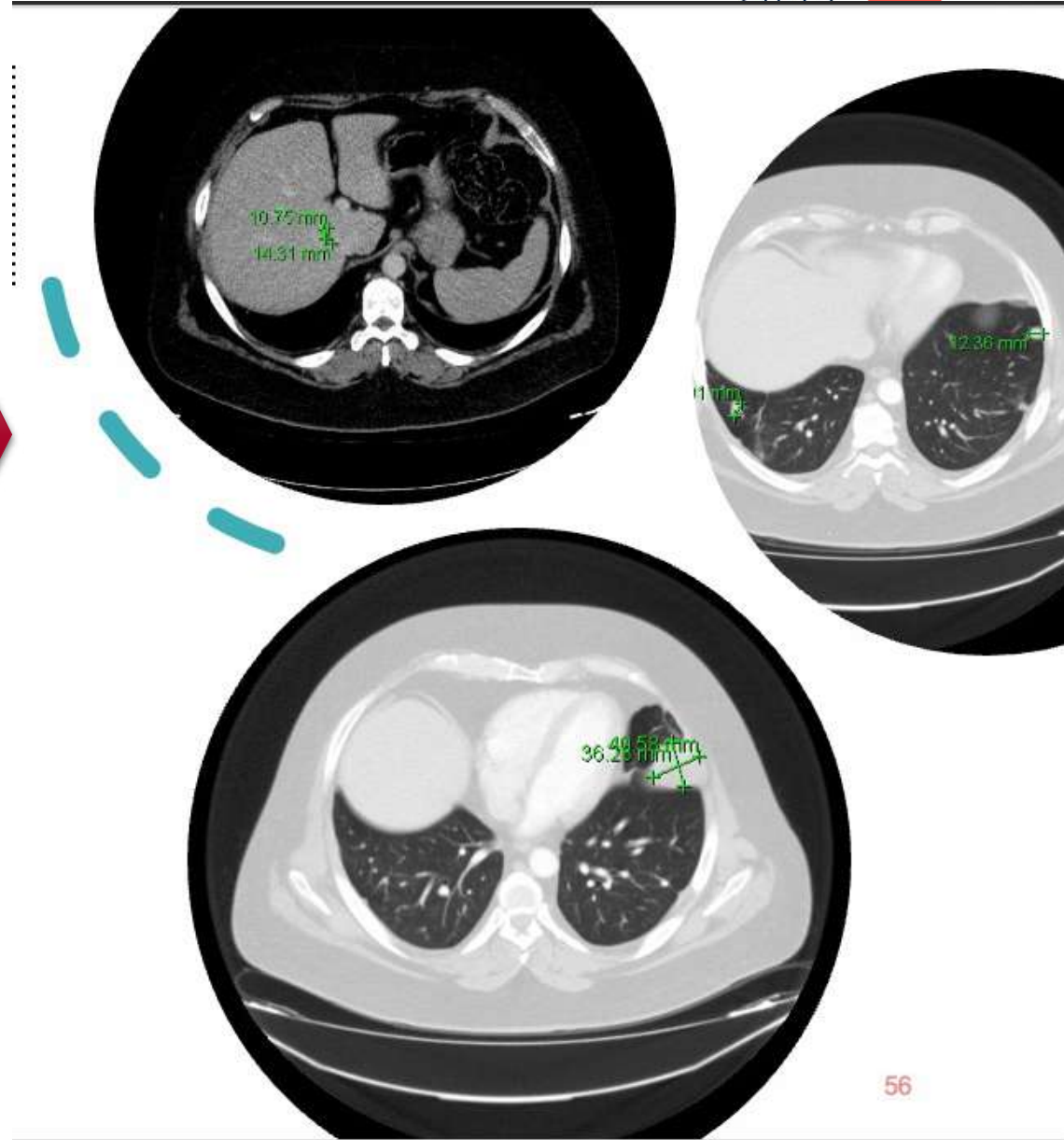
- Progresión
- Ósea.
  - Pulmonar
  - Hepática

Abr. 2015

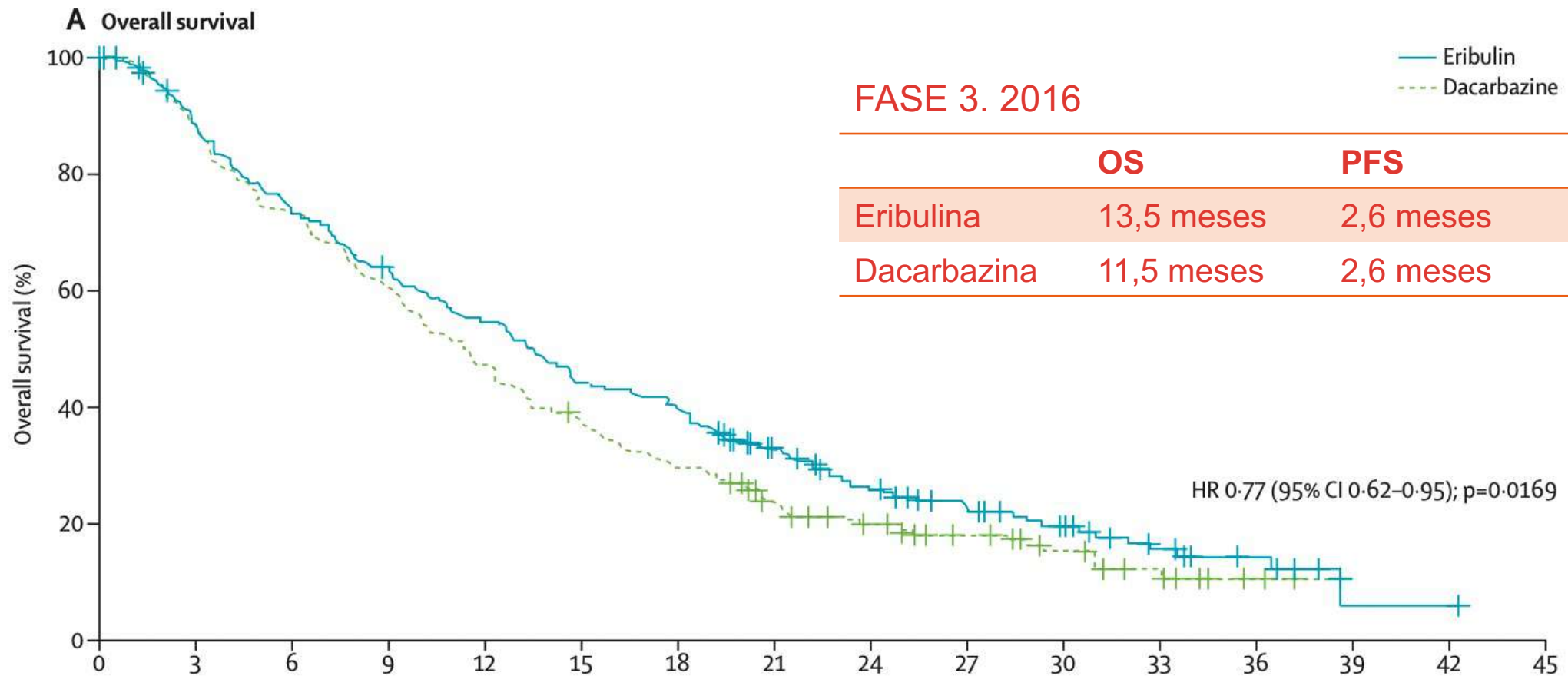
Ene. 2016



La combinación de Docetaxel y GZT vs GZT no se asocia con aumento\* RR o SLP



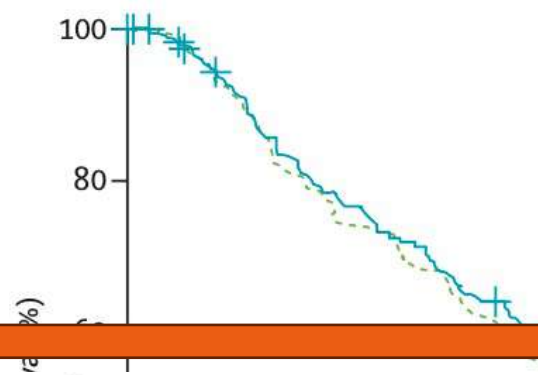
# 4ª LÍNEA PALIATIVA. ERIBULINA.



Eribulin versus dacarbazine in previously treated patients with advanced liposarcoma or leiomyosarcoma: a randomised, open-label, multicentre, phase 3 trial

# 4ª LÍNEA PALIATIVA. ERIBULINA.

**A Overall survival**



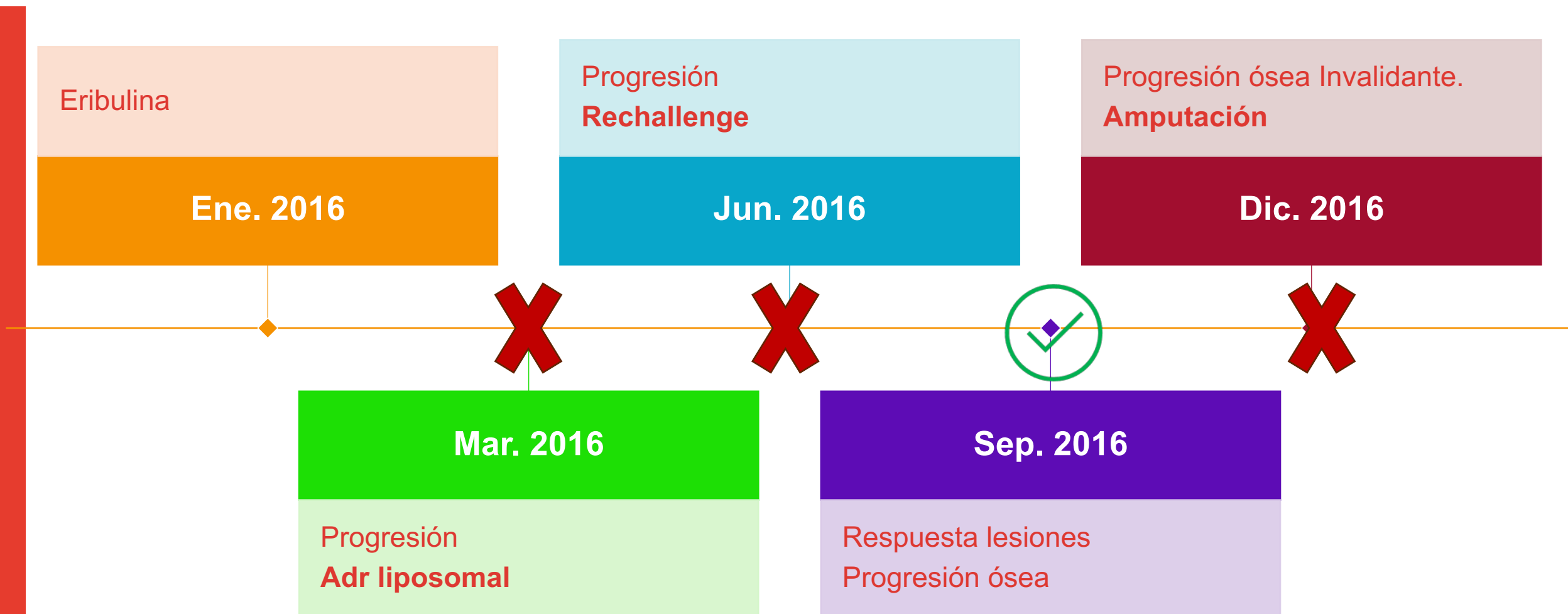
— Eribulin  
- - - Dacarbazine

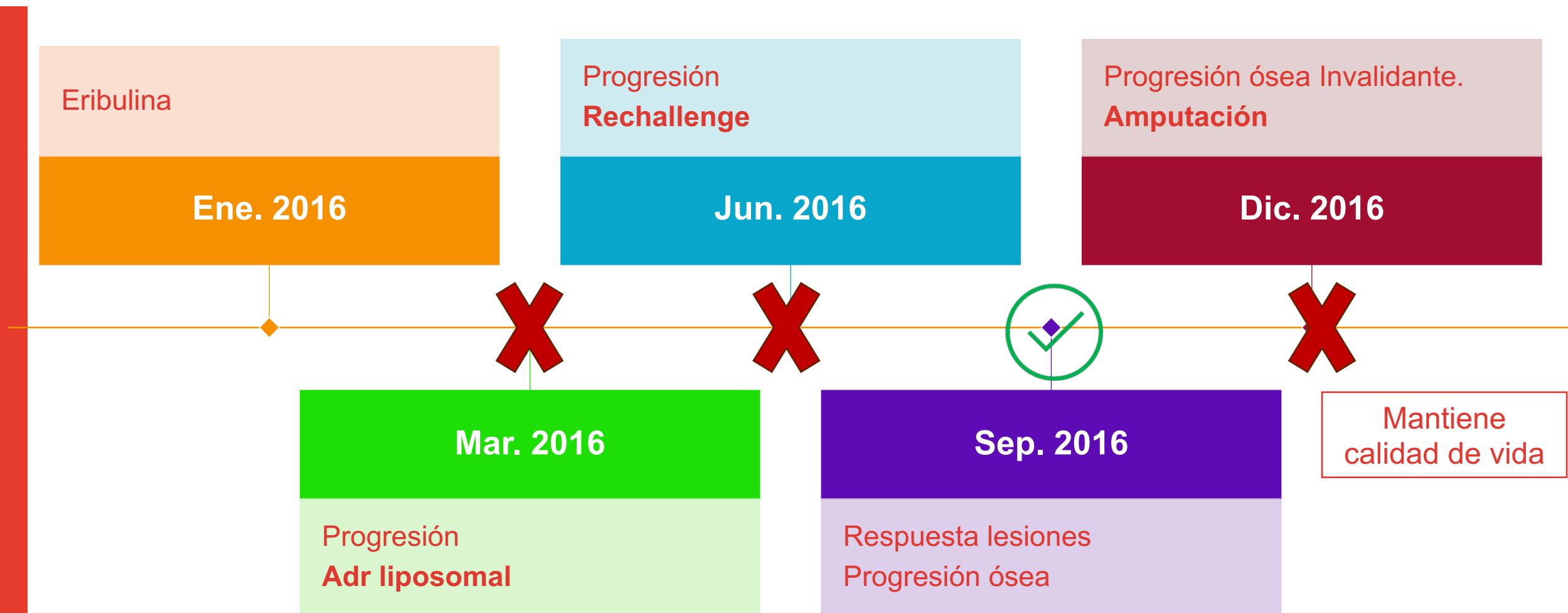
FASE 3. 2016

	OS	PFS
Eribulina	13,5 meses	2,6 meses
Dacarbazina	11,5 meses	2,6 meses

Disease type	Eribulin	Dacarbazine	Forest Plot
Liposarcoma	52/71	63/72	
Leiomyosarcoma	124/157	118/152	

AJCC sarcoma tumour grade score at diagnosis	Eribulin	Dacarbazine	Forest Plot	Hazard Ratio (95% CI)
High	118/150	125/152		0.51 (0.35-0.75)
Intermediate	57/77	55/69		0.93 (0.71-1.20)
Baseline ECOG PS	Eribulin	Dacarbazine	Forest Plot	Hazard Ratio (95% CI)
0	76/111	72/90		0.58 (0.41-0.82)
1	97/114	97/121		1.11 (0.83-1.48)
2	3/3	12/13		3.00 (0.25-35.79)





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Ifosfamida altas dosis- adriamicina x 3 ciclos : **EE**

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DTIC-Gemzar x 16 dosis y luego 2 dosis más **RP**

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Trabectedina x 18 ciclos **EE**

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Pazopanib x 3 m **PR**

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Taxotere-Gemzar x 12 **RP**

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Eribulina x 3 **PR**

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Caelyx x 2 **PR**

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DTIC –Gemzar de nuevo x 23 ciclos **RP**

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**MÁS DE 7 AÑOS DE SUPERVIVENCIA CON  
METÁSTASIS**

# Y SI PROGRESA???





Temodal 75 mg/m<sup>2</sup>

- Tolerancia excelente

Tras 3 meses  
insuficiencia hepática

Tto paliativo y exitus  
en enero de 2018

## A Phase II Trial of Temozolomide as a 6-Week, Continuous, Oral Schedule in Patients with Advanced Soft Tissue Sarcoma

*A Study by the Spanish Group for Research on Sarcomas*

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Javier Martin, M.D.<sup>3</sup>  
Jose M. Buesa, M.D., Ph.D.<sup>4</sup>  
Javier Martinez-Trufero, M.D.<sup>5</sup>  
Antonio Casado, M.D., Ph.D.<sup>6</sup>  
Andres Poveda, M.D.<sup>7</sup>  
Josefina Cruz, M.D.<sup>8</sup>  
Isabel Bover, M.D.<sup>9</sup>  
Joan Maurel, M.D., Ph.D.<sup>10</sup>  
for the Spanish Group for Research  
on Sarcomas

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<sup>2</sup> Department of Medical Oncology, Hospital Sant Pau, Barcelona, Spain.

<sup>3</sup> Department of Medical Oncology, Hospital Son Dureta, Palma de Mallorca, Spain.

<sup>4</sup> Department of Medical Oncology, Hospital Central de Asturias, Oviedo, Spain.

<sup>5</sup> Department of Medical Oncology, Hospital Miguel Servet, Zaragoza, Spain.

**BACKGROUND.** The objective of this study was to evaluate the activity and toxicity of temozolomide given as an extended schedule in patients with advanced sarcoma.

**METHODS.** Forty-nine patients with pretreated soft tissue sarcoma (the STS arm) and 18 patients with previously untreated gastrointestinal stromal tumor (the GIST arm) were enrolled onto a 2-arm, multicenter, Phase II study between November 1999 and July 2001. Temozolomide was administered on a 6-week, continuous, oral schedule at a dose of 75 mg/m<sup>2</sup> per day in 41 patients and, after an amendment, at a dose of 100 mg/m<sup>2</sup> per day in 22 patients.

**RESULTS.** Among 45 eligible patients in the STS arm, there were 7 partial responses, for an overall response rate of 15.5% (95% confidence interval [95% CI], 5–26%). Responses were seen in 5 of 11 patients who had gynecologic leiomyosarcoma. The median response duration was 12.5 months (range, 3.9–58.0 mos). In 4 patients, response lasted > 1 year, and 2 of those patients remained progression free for > 3 years. The median time to progression was 2.2 months (95% CI, 1.8–2.5 mos), and the median overall survival was 8.1 months (95% CI, 5.6–10.6 mos). Progression-free survival rates at 3 months and 6 months were 39.5% and 26%, respectively. In the GIST arm, no responses were noted. Grade 3–4 granulocytopenia, thrombocytopenia, and anemia were observed in 6 patients, 5 patients, and 7 patients, respectively. The most common nonhematologic toxicities were emesis and fatigue.

**CONCLUSIONS.** Temozolomide at the extended schedule was tolerated well and had activity in patients with pretreated soft tissue sarcomas, and especially among patients with gynecologic leiomyosarcoma. *Cancer* 2005;104:1706–12.



**GRACIAS**



**Universidad  
Europea** MADRID

