SARCONNECT

Mejorando la Supervivencia en Pacientes con Sarcoma de Partes Blandas

INDICACIÓN DE QUIMIOTERAPIA COMBINADA EN PRIMERA LÍNEA DE ENFERMEDAD AVANZADA

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INDICACIONES DE QT COMBINACION

- SARCOMAS DE PARTES BLANDAS AVANZADOS. IMPLICACIONES DE LA HISTORIA NATURAL

- ESTUDIOS EN PRIMERA LINEA
  - DOXORRUBICINA MONOTERAPIA VS COMBINACION
  - DOXORRUBICINA + IFOSFAMIDA
  - DOXORRUBICINA + OLARATUMAB
  - ALTERNATIVAS A DOXORRUBICINA

- APLICACIÓN CLÍNICA DE LOS ESTUDIOS EN PRIMERA LINEA

- CONCLUSIONES

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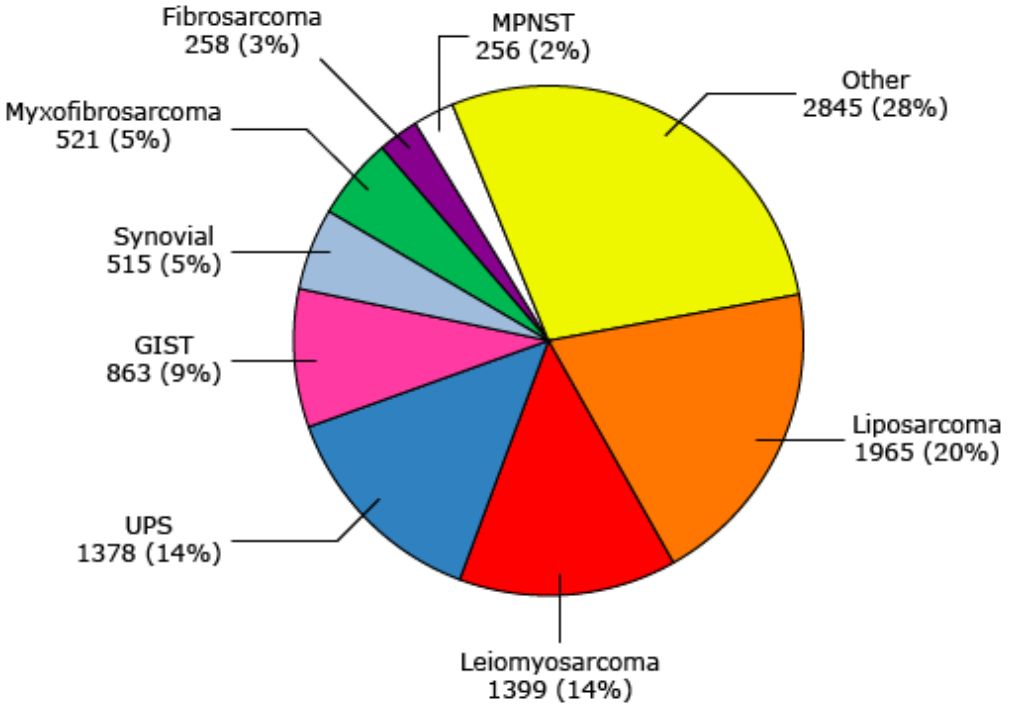
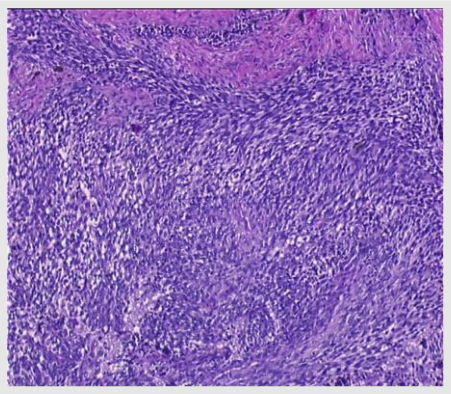
ENFERMEDAD AVANZADA

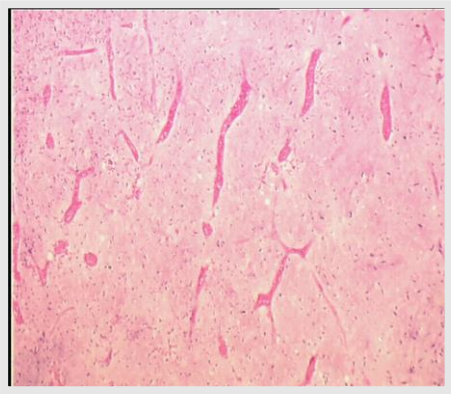


UN 10-15% SON METASTÁSICOS DE INICIO
UN 50% DE LOS LOCALIZADOS RECAERÁN

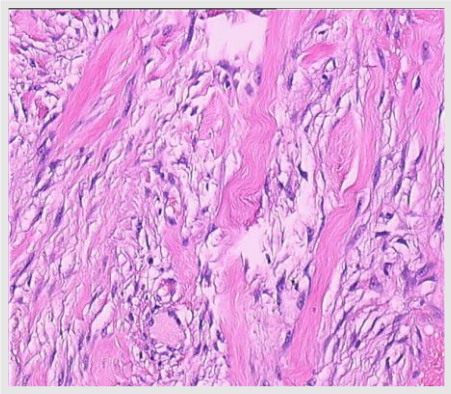
HETEROGENEIDAD



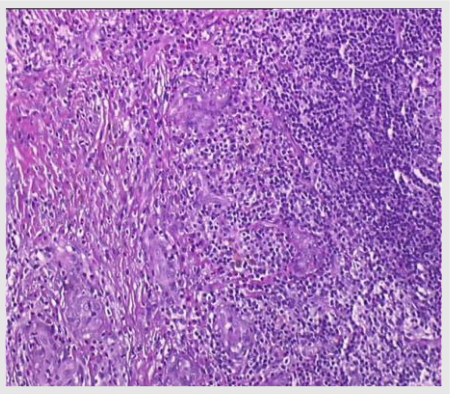
LEIOMIOSARCOMA



LIPOSARCOMA



DESMOIDE



ANGIOSARCOMA

SUBTIPOS DIANAS

GRADO HISTOLÓGICO

CLÍNICA INDOLENTE

CLINICA AGRESIVA

HETEROGENEIDAD DE PACIENTES

HISTORIA NATURAL

- GENERALMENTE INCURABLE,
  - SUPERVIVENCIA 12-19 MESES
  - 20-25% VIVOS A LOS 2-3 AÑOS
  - EXISTE UN IMPACTO DE LOS TRATAMIENTOS?
- PERO:
  - OPCIONES CURATIVAS: METASTASECTOMIA: SUPERVIVENCIA 25-40% A 5 AÑOS
  - BENEFICIO EN SUPERVIVENCIA Y PALIACION CON TRATAMIENTO SISTEMICO EN PRIMERA LINEA

HISTORIA NATURAL

- TOMA DE DECISIONES INDIVIDUALIZADA

- Histología
- Comportamiento biológico
- Estado de salud
- Preferencias del paciente

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ADRIAMYCIN CHEMOTHERAPY—EFFICACY, SAFETY, AND PHARMACOLOGIC BASIS OF AN INTERMITTENT SINGLE HIGH-DOSAGE SCHEDULE

ROBERT S. BENJAMIN, MD, PETER H. WIERNIK, MD, AND NICHOLAS R. BACHUR, MD, PHD

A study designed to correlate clinical and pharmacologic observations was undertaken in 96 patients treated with adriamycin. The basic dosage schedule was 60 mg/m² I.V. q 3 weeks. Pharmacokinetic studies showed a prolonged plasma half-life, low urinary excretion, and undetectable levels in CSF. Patients with significantly impaired liver function had marked elevation and prolongation of plasma drug levels associated with severe toxicity unless dosage was reduced by 50–75%. Of the 82 evaluable patients, 10/25 with sarcomas, 9/31 with carcinomas, and 15/26 with hematologic malignancies have achieved complete or partial remission. An additional 22/48 have improved. Six patients with solid tumors had progressive CNS disease while responding systemically. Adriamycin can be used with relative safety and high efficacy in a dosage schedule that resulted from pharmacologic studies. Dosage reduction in patients with liver disease is essential to avoid life-threatening toxicity.

ACTIVIDAD DOSIS-DEPENDIENTE

75 mg/m2 /3 sem

TR 10-25%

90% RP

TOXICIDADES:

MIELOSUPRESION,
MUCOSISTIS,
CARDIOTOXICIDAD >
450 mg/m2 acumulada

TABLE 2. Response to Adriamycin in Sarcomas

Tumor type	Patients treated	Patients evaluable	Improved‡	Partial remission†	Complete remission*	Progressive disease
Osteosarcoma	5	5	1 (19)§	1 (18)§	0	3
Rhabdomyosarcoma	5	5	0	4 (10, 15, 24+, 35)	0	1
Leiomyosarcoma	5	5	2 (9, 15)	2 (12, 30+)	0	1
Liposarcoma	4	3	2 (transient, 16)	0	0	1
Ewing's sarcoma (soft tissue)	1	1	0	0	1 (37)§	0
Mesothelioma	1	1	0	1 (28+)	0	0
Malignant fibrous histiocytoma	4	2	1 (2)	0	0	1
Giant cell tumor of bone	2	2	0	1 (12+)	0	1
Meningiosarcoma	1	1	0	0	0	1
TOTALS	28	25	6 (median 12+)	9 (median ≥ 18)	1 (median 37)	9

* Complete remission—Complete disappearance of measurable disease; symptomatic improvement; ≥4 wks' duration.
† Partial remission—>50% reduction in tumor mass; symptomatic improvement; ≥4 wks' duration.
‡ Improvement—Subjective and objective improvement not sufficient to be judged a partial remission.
§ Duration in weeks.

MONOTERAPIA VS POLIQUIMIOTERAPIA

Authors	Chemotherapy	N	Response Rate		Survival
Muss et al. 1985	A/AC	104	NS		NS
Omura et al. 1983	A/AD	146	NS		NS
Borden et al. 1987	A/AD	186	AD = 30 %	(*p = 0.02*)	NS
Lerner et al. 1987	A/AD	66	AD = 44 %	(LMS)	NS
Santoro et al. 1995	A/AI/CYVADIC	449	NS		NS
Borden et al. 1990	A/AVd	295	NS		NS
Edmonson et al. 1993	A/AI/APM	262	AI = 34 %	(*p = 0.03*)	NS
Antman et al. 1993	AD/MAID	340	MAID = 32 %	(*p = 0.002*)	NS
Judson et al. 2014	A/AI	415	AI = 26 %	(A = 14 %)	NS
Ryan et al. 2016	A/APal	447	APal = 28 %	(A = 19 %)	NS

Muss et al.Cancer 1985
Omura et al. Cancer 1983
Borden et al. J Clin Oncol 1987

Santoro et al. J Clin Oncol 1995
Borden et al Cancer 1990
Edmonson J et al J Clin Oncol 1993

Antman K et al. J Clin Oncol 1993
Judson I et al Lancet Oncol 2014
Ryan et al J Clin Oncol 2016

MONOTERAPIA VS POLIQUIMIOTERAPIA

- TR: 16-46%, RC 5-10%, 1/3 de los que hacen RC son largos respondedores
- No diferencias significativas en SG
- Mayor toxicidad
- DOXORRUBICINA 75 mg/m2 GOLD STANDARD EN PRIMERA LINEA

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

*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**

EORTC 62012

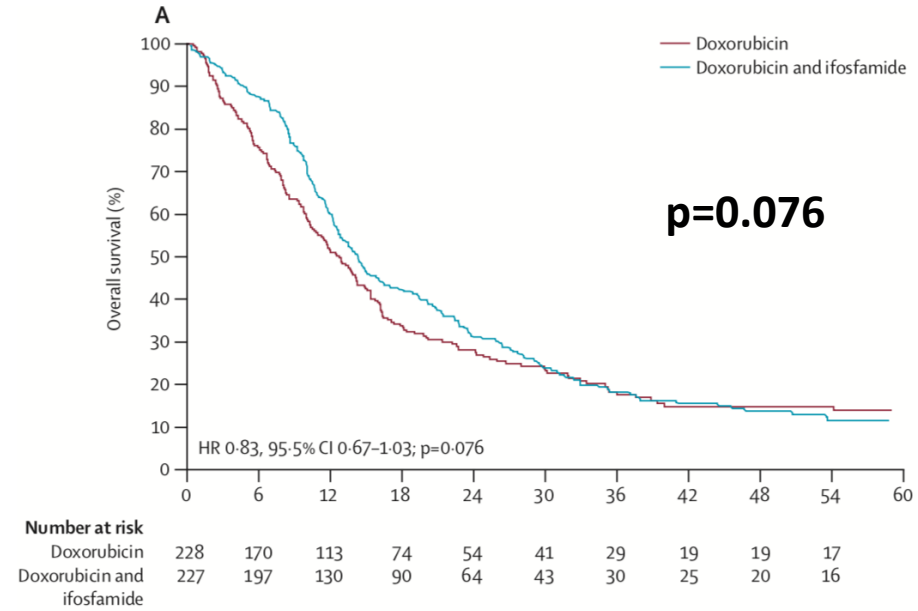
Esquema:
Doxorrubicina 75mg+ifosfamida 10g/m2+ mesna+pegfilgrastin vs doxorrubicina 75 mg/m2

Objetivo principal: supervivencia global

n : 456

SG: 12.8 vs 14.3, **P=0.076 NS**

NO ALCANZÓ EL OBJETIVO PRINCIPAL



p=0.076

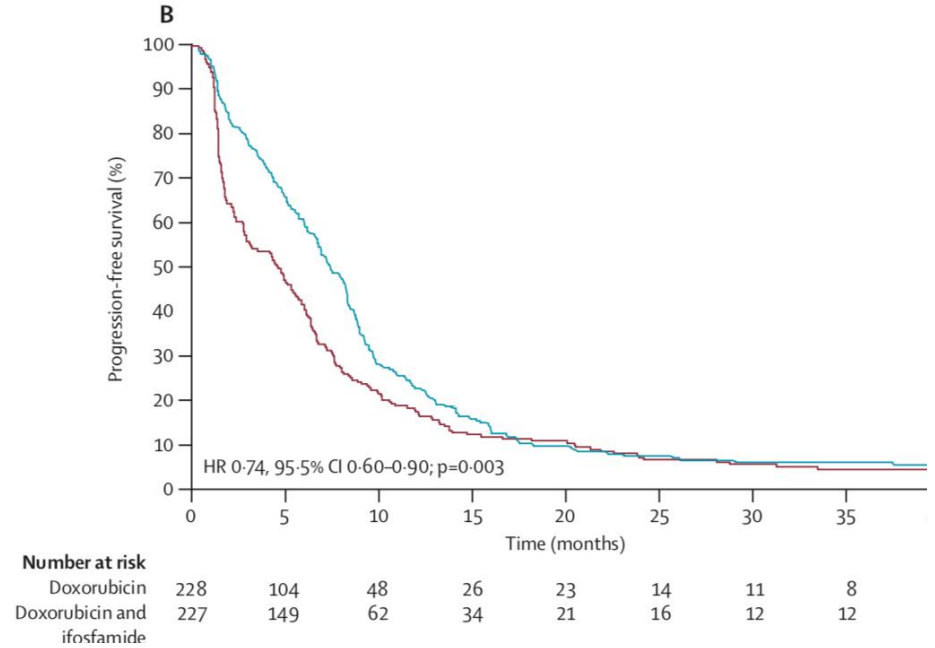
Judson I, et al. Lancet Oncol. 2014;15;415-423

EORTC 62012. RESULTADOS DE EFICACIA

	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**



TR 27 vs 14% HR 0.74, signi

SLP 7.4 vs 4.6 meses p=0.003

Judson I, et al. Lancet Oncol. 2014;15;415-423

EORTC 6012. INTERPRETACIÓN

PACIENTES SELECCIONADOS
PS 0-1
MENORES DE 60 AÑOS

30-40% DE LOS PACIENTES CON ESTADIO IV EN PRIMERA LINEA

EL OBJETIVO DEL TRATAMIENTO DEBE BASAR LA ELECCION DEL TRATAMIENTO

	Doxorubicin group (n=223)	Doxorubicin and ifosfamide group (n=224)
Neutropenia	83 (37%)	93 (42%)
Leucopenia	40 (18%)	97 (43%)
Febrile neutropenia	30 (13%)	103 (46%)
Anaemia	10 (4%)	78 (35%)
Thrombocytopenia	1 (<1%)	75 (33%)

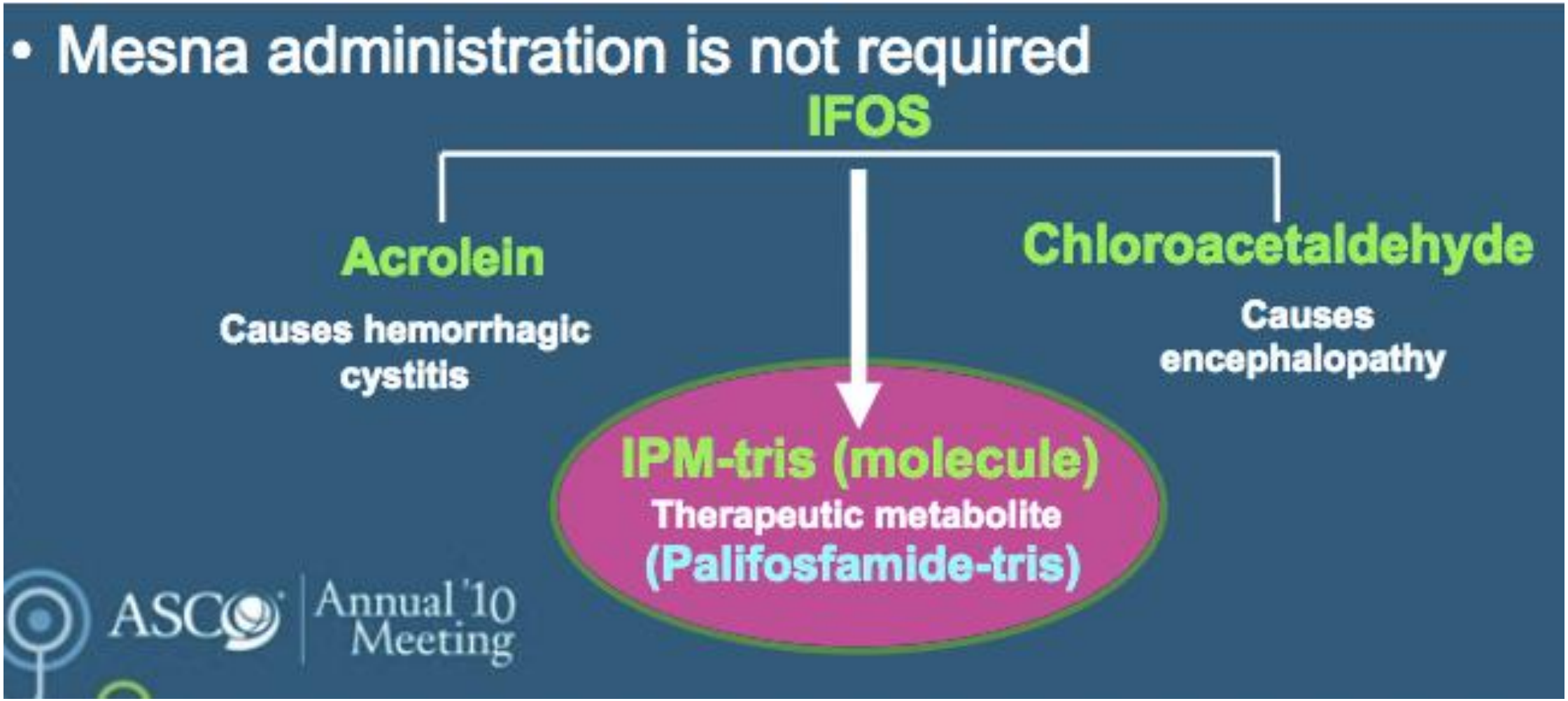
Data are n (%).

Table 5: Grade 3–4 adverse events

Interpretation Our results do not support the use of intensified doxorubicin and ifosfamide for palliation of advanced soft-tissue sarcoma unless the specific goal is tumour shrinkage. These findings should help individualise the care of patients with this disease.

Judson I, et al. Lancet Oncol. 2014;15;415-423

COMBINACIONES CON OTROS ALQUILANTES



PALIFOSFAMIDA

ESQUEMA:
DOXORRUBICINA 75 MG/M2+PLACEBO D 1-3 VS DOXORRUBICINA 75 MG/M2 + PALIFOSFAMIDA 150 MG/M2 D 1-3

OBJETIVO PRINCIPAL SLP

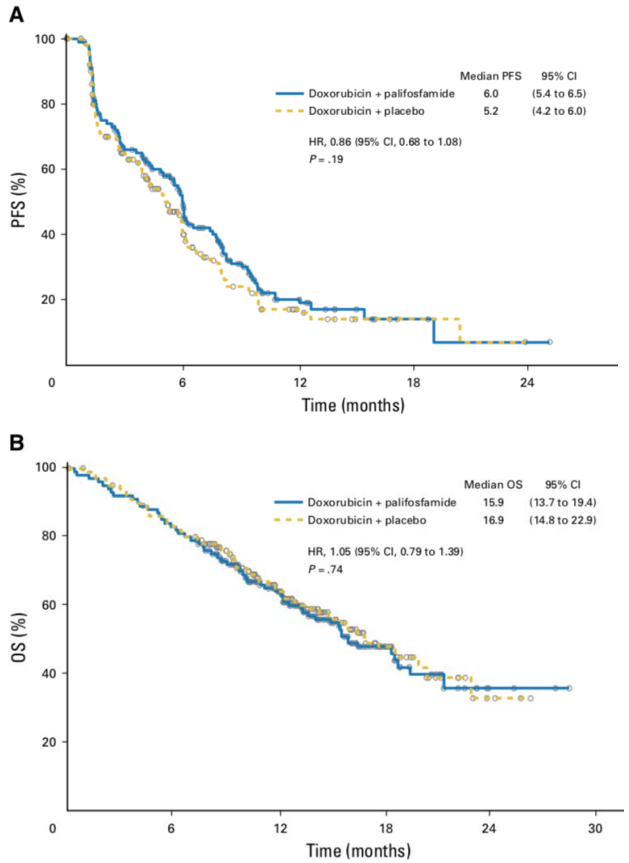
N 447

RESULTADOS:
- **TR 28.3 vs 19.9%, p:0.047**
- SLP 6 vs 5.2 m (HR 0.86)
- SG 15.9 vs 16.9 m (HR 1.05)

Table 2. Best Response to Study Treatment

Response	Doxorubicin + Palifosfamide (n = 226) No.	%	Doxorubicin + Placebo (n = 221) No.	%
CR	3	1.3	2	0.9
PR	61	27.0	42	19.0
SD (> 12 weeks)	53	23.5	47	21.3
Clinical benefit (CR + PR + SD)	117	51.8	91	41.2

Abbreviations: CR, complete response; PR, partial response; SD, stable disease.



TOXICIDAD IMPORTANTE: ENCEFALOPATIA, FALLO RENAL

NO ALCANZA EL OBJETIVO PRIMARIO SLP NI DE SG

Ryan CW, et al. J Clin Oncol. 2016;34:3898-3905

EVOFOSFAMIDA. SARC 21

- ESQUEMA

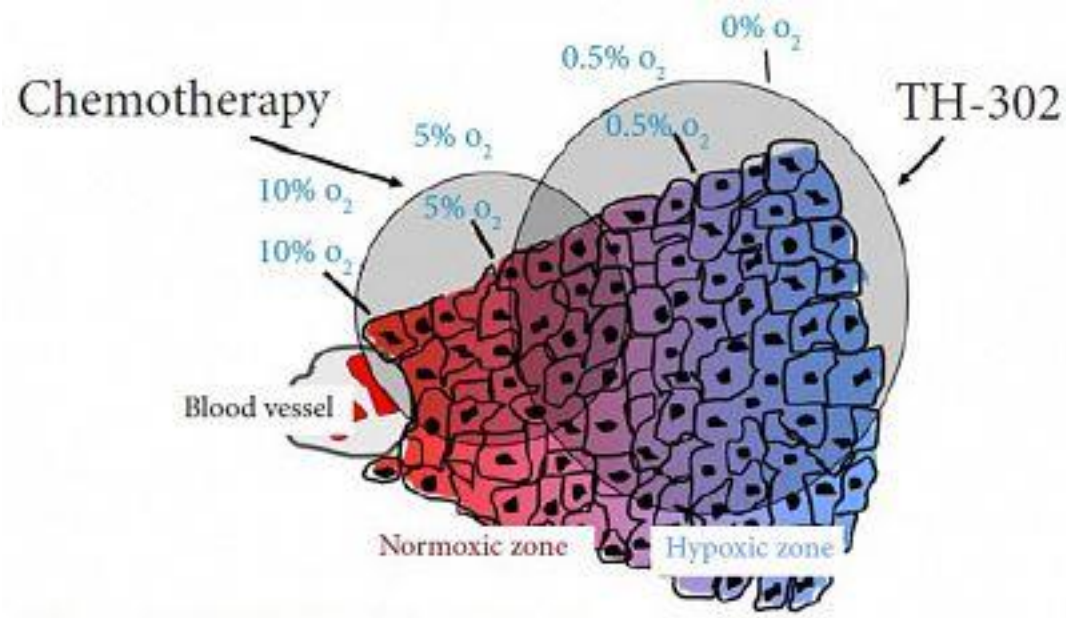
  Doxorrubicina 75mg/m2 cada 3 semanas, 6 ciclos VS
  Doxorrubiicna 75 mg/m2 + TH302300 mg iv, días 1 y 8 cada 21 d. Se permite mantenimiento con TH302

- OBJETIVO PRINCIPAL: SG (aumento en 4 m, 12 vs 16m) y seguridad

- RESULTADOS
  - **TR 28.4 vs 18.3%, p:0.0026**
  - SLP 6.3 VS 6.0 m (HR 0.85, p.099)
  - SG 18.4 vs 19.0 m (HR 1.06, p.527)

  - TOXICIDAD MAYOR (hematuria, fallo renal, encefalopatía)

- NO ALCANZA EL OBJETIVO PRINCIPAL DE SG



Tap WD, et al. Lancet Oncol. 2016;388;488-497

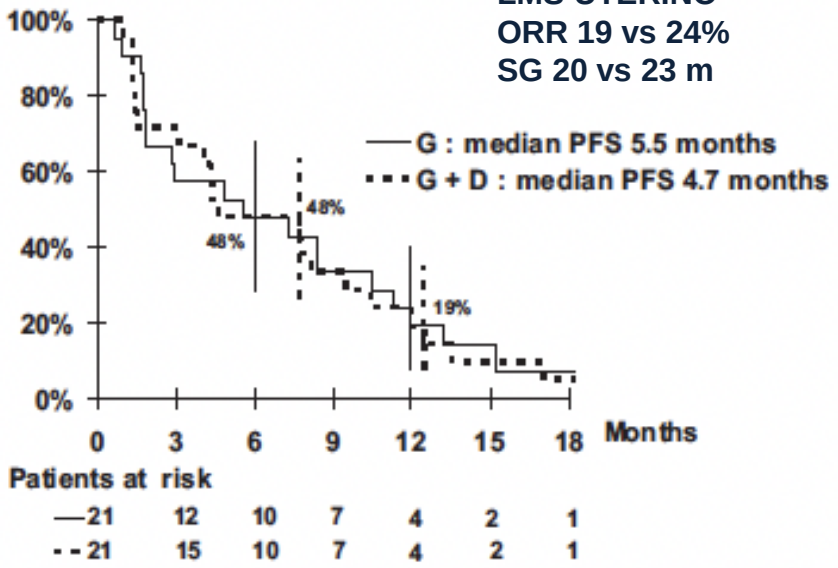
COMBINACION GEMCITABINA + DOCETAXEL

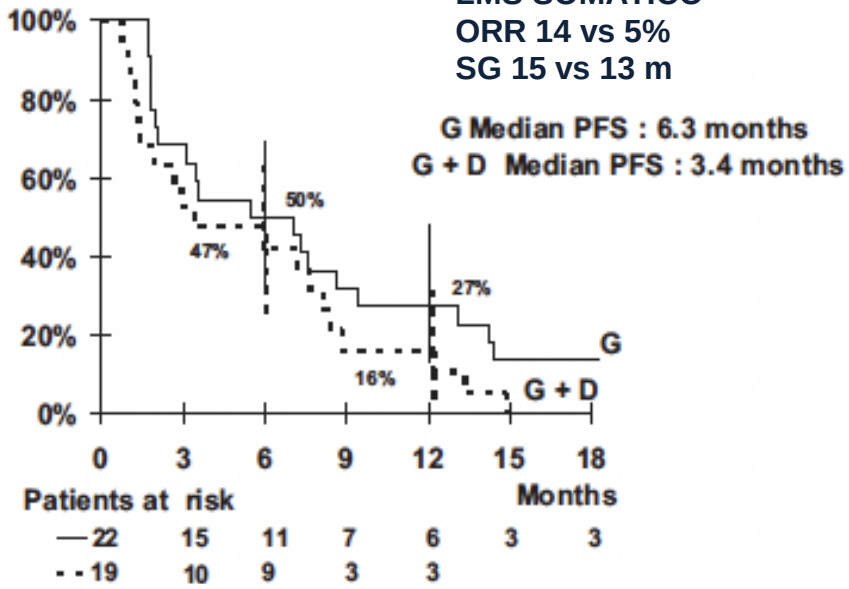
ESTUDIO FASE II CON GEMCITABINA DOCETAXEL VS GEMCITABINA

N=122
TR: 16 VS 8%
SLP 3 VS 6.2 m
SG 11.5 VS 17.9 m

ESTUDIO FASE II
TAXOGEM

N: 90
LEIOMIOSARCOMAS



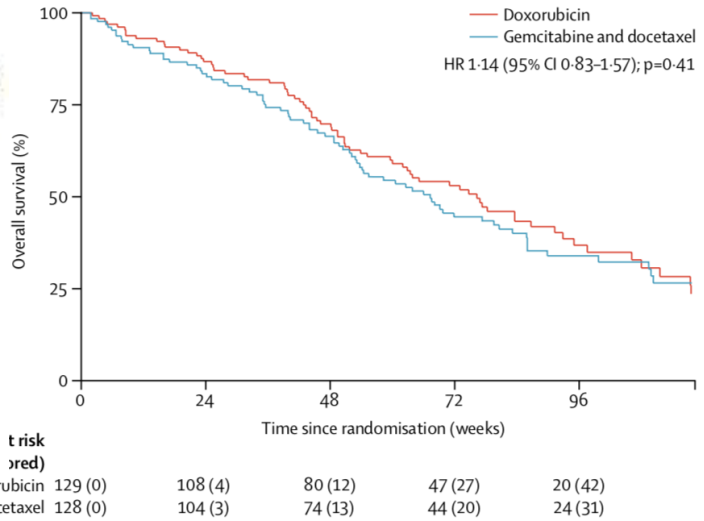


Maki et al. JCO 2007.

Pautier et al. The Oncologist 2012

Gemcitabine and docetaxel versus doxorubicin as first-line treatment in previously untreated advanced unresectable or metastatic soft-tissue sarcomas (GeDDiS): a randomised controlled phase 3 trial

Beatrice Seddon, Sandra J Strauss, Jeremy Whelan, Michael Leahy, Penella J Woll, Fiona Cowie, Christian Rothermundt, Zoe Wood, Charlotte Benson, Nasim Ali, Maria Marples, Gareth J Veal, David Jamieson, Katja Küver, Roberto Tirabosco, Sharon Forsyth, Stephen Nash, Hakim-Moulay Dehbi, Sandy Beare

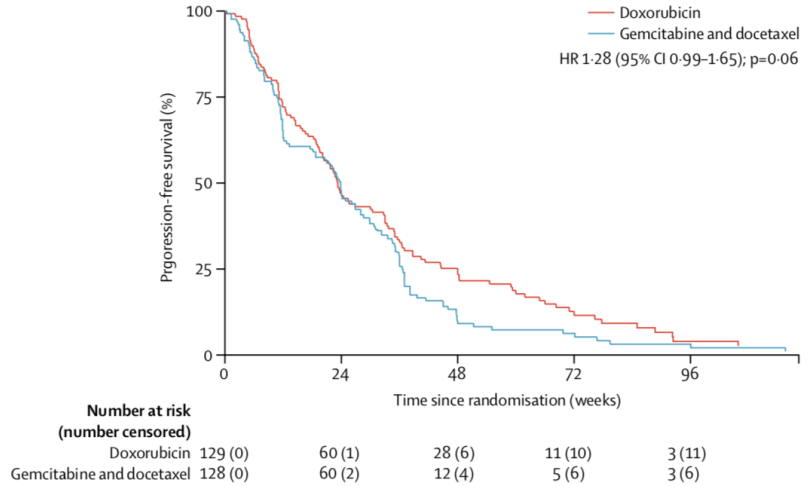


Esquema:
DOXORRUBICINA 75 mg/m2/21d vs
GEMCITABINA 675 mg/m2 d 1,8 +
DOCETAXEL 75 mg/m2 d 1/21d x 6 ciclos

OBJETIVO PRINCIPAL : SLP a 24 sem

RESULTADOS:
- TR: 20% VS 20% p = 0.06
- **SLP 24 sem: 46.3 vs 46.4% p= 0.06**
- SG: 76.3 VS 67.3 m, p=0.41
- MAYOR TOXICIDAD, PEOR QOL, MAYOR COSTE

NO DIFERENCIAS AL
ANALIZAR POR SUBTIPOS
NI LMS
NI LMS UTERINOS



Seddon B. Lancet Oncol. 2017 Oct;18(10):1397-1410

COMBINACION DOXORRUBICINA OLARATUMAB

ESQUEMA: DOXORRUBICINA 75 MG/M2 CADA 21+ OLARATUMAB 15 MG/KG D 1,8/21

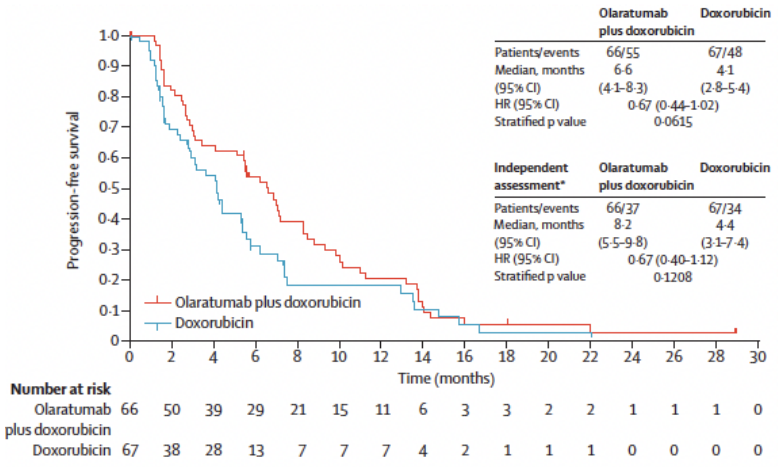
OBJETIVO PRINCIPAL: AUMENTO DE SLP (61%, 2.5 m)

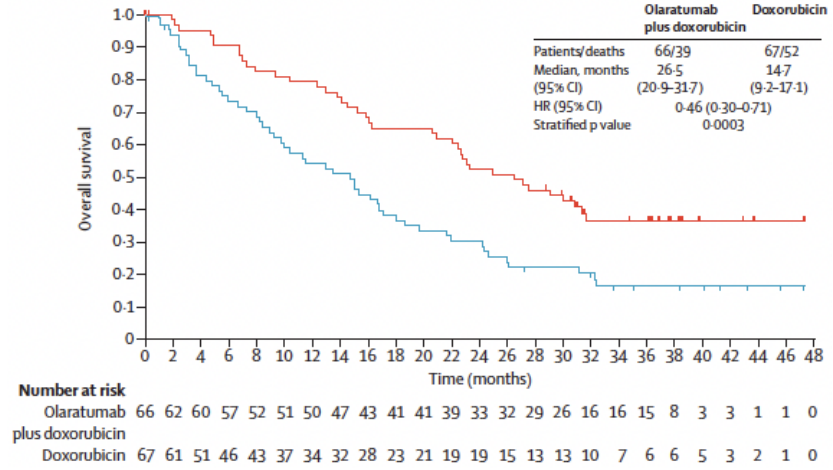
PS 0-2, TODOS LOS SUBTIPOS

RESULTADOS:
SG: 26.5 VS 14.7 meses p=0.0003

EVENTOS ADVERSOS: DISCRETAMENTE SUPERIOR EN LA COMBINACIÓN

POR PRIMERA VEZ AUMENTO EN LA SUPERVIVENCIA, Independiente de la expresión de PDGFR





Tap WD, et al. Lancet Oncol. 2017;18;1089-1103

Resumen de ensayos seleccionados en 1.ª línea

Esquema de tratamiento	Tasa de respuesta	Tasa de estabilidad	Mediana de SLP	Mediana de SG
Doxorrubicina 75 mg/m^2 + ifosfamida 10 g/m^2 Doxorrubicina 75 mg/m^2 Ciclos de 21 días (2)	26 *vs.* 14 %*	50 *vs.* 46 %	7,4 *vs.* 4,6* meses	14,3 *vs.* 12,8 meses
Doxorrubicina 75 mg/m^2 (día 1) + olaratumab 15 mg/kg (días 1 y 8) Doxorrubicina 75 mg/m^2 Ciclos de 21 días (3)	18 *vs.* 12 %	59 *vs.* 50,7 %	6,6 *vs.* 4,1 meses	26,5 *vs.* 14,7* meses
Doxorrubicina 75 mg/m^2 Gemcitabina 675 mg/m^2 (días 1 y 8) + docetaxel 75 mg/m^2 (día 8) Ciclos de 21 días (5)	Respuestas objetivas + estabilización 65 *vs.* 58 %		23 *vs.* 24 semanas	71 *vs.* 63 semanas

**Diferencia estadísticamente significativa.*

SLP: supervivencia libre de progresión; SG: supervivencia global.

Efecto adverso	Doxorrubicina	Doxorrubicina-olaratumab	Doxorrubina + ifosfamida	Gemcitabina-dacarbazina	Gemcitabina-docetaxel
Diarrea	25 (2)	34 (3)	27 (3)	18 (0)	13 (0)
Estreñimiento	32 (< 1)	34 (0)	42 (1)	NR	NR
Náuseas y/o vómitos	50 (3-5)	70 (2)	78 (10)	75 (2)	22 (0)
Mucositis	35 (4)	53 (3)	28 (6)	18 (2)	10 (0)
Anemia	40 (4-8)	41 (13)	80 (35)	82 (4)	84 (10)
Trombopenia	10 (< 1)	NR	55 (34)	40 (6)	44 (18)
Leucopenia	43 (18)	41 (36)	58 (44)	76 (26)	52 (9)
Neutropenia	54 (35)	58 (50)	51 (42)	76 (48)	31 (10-15)
Neutropenia febril	13	13	46	9	5%
Disfunción miocárdica	9 (< 1)	12 (2)	NR	NR	NR

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ANALISIS RETROSPECTIVOS TRATAMIENTO 1L

RESULTS. In all, 488 patients (242 male, 246 female) fulfilled the study criteria. The median age was 49 years and the majority (83%) received chemotherapy for metastatic disease. The most common histologic subtypes were leiomyosarcoma (35%) synovial sarcoma (13%), liposarcoma (10%), and malignant fibrous histiocytoma (10%). In all, 61% received single-agent chemotherapy, usually doxorubicin. An objective response was reported in 33% of patients (53% in those with synovial sarcoma); 22% had stable disease and 45% derived 'clinical benefit' (objective responses + stable disease for ≥6 months). Median duration of response was 9 months and median posttreatment overall survival (OS) was 12 months. In multivariate analysis, age <40 years, liposarcoma, and synovial histology were found to be positive, and bone involvement to be negative, independent prognostic factors. Patients treated with combination chemotherapy experienced longer OS than those treated with a single agent.

CONCLUSIONS. Palliative chemotherapy may be beneficial in approximately half of patients with advanced STS. Synovial sarcoma and liposarcoma subtypes have a better prognosis. However, the overall poor outcome of these patients indicates the need to continue the search for more effective agents. ***Cancer* 2008;112:1585–91.** © *2008 American Cancer Society.*

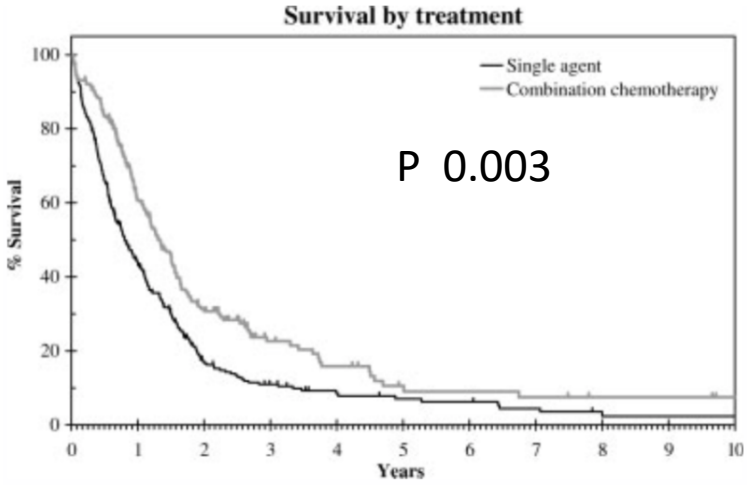


FIGURE 2. Overall survival according to treatment group (single-agent 11 months vs combination treatment 16 months, $P = .003$).

Karavasilis V, et al. Cancer 2008;112: 1585–1591

EVOLUCIÓN DE LA SUPERVIVENCIA GLOBAL

Original Article

Trends in Survival for Patients With Metastatic Soft-Tissue Sarcoma

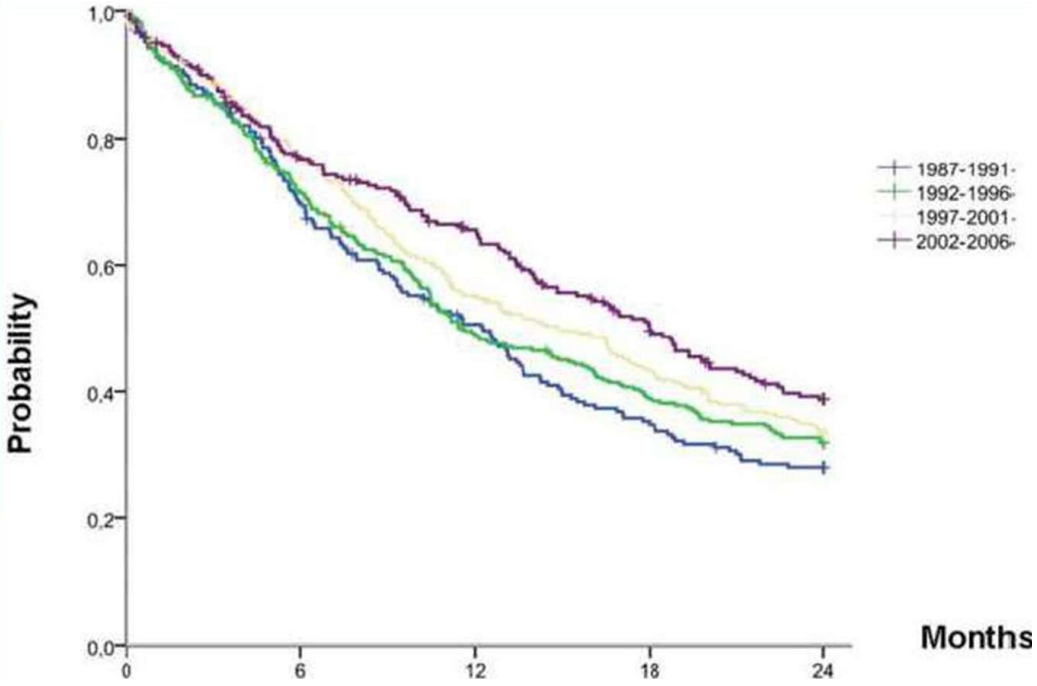
Antoine Italiano, MD, PhD[1]; Simone Mathoulin-Pelissier, MD, PhD[2,3]; Axel Le Cesne, MD[4]; Philippe Terrier
Sylvie Bonvalot, MD[6]; Françoise Collin, MD[7]; Jean-Jacques Michels, MD[8]; Jean-Yves Blay, MD, PhD[9];
Jean-Michel Coindre, MD[10]; and Binh Bui, MD[1]

EN TODOS SPB M1

1987-2006

INCREMENTO SUPERVIVENCIA GLOBAL 50%
(12.3 m - 18 m)

p = 0.029



Italiano A et al. Cancer 2011 Mar 1;117(5):1049-54
Van Glabbeke M, et al, J Clin Oncol 1999;17:150–157

EVOLUCIÓN DE LA SUPERVIVENCIA GLOBAL

Sarcomas

The Oncologist®

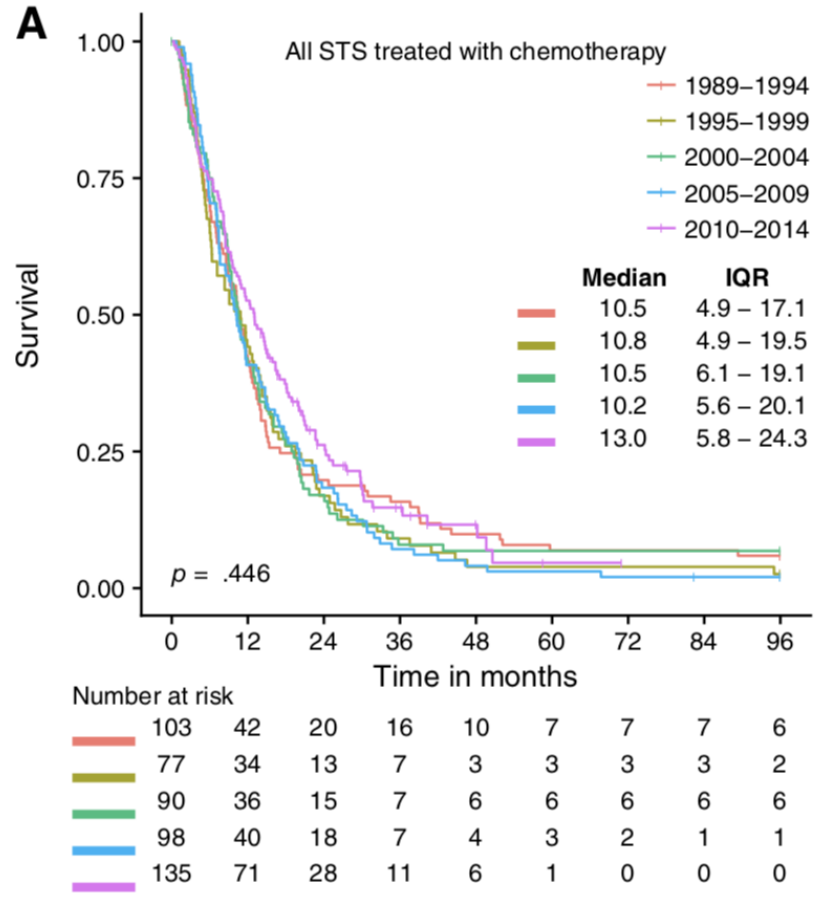
Minimal Increase in Survival Throughout the Years in Patients with Soft Tissue Sarcoma with Synchronous Metastases: Results of a Population-Based Study

Melissa Vos [a,b], Vincent K. Y. Ho,[c] Astrid W. Oosten,[a] Cornelis Verhoef,[b] Stefan Sleijfer[a]

Departments of [a]Medical Oncology and [b]Surgical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; [c]Netherlands Comprehensive Cancer Organisation, Utrecht, The Netherlands

SPB CON M1 SINCRÓNICAS
1989-2014
MEJORA SG DE 5.8 A 3.1 MESES
p = 0.15

P SIGN EN TODOS LOS PACIENTES QUE SE TRATAN, INDEPENDIENTEMENTE DE SI CIRUGIA, RADIO O QUIMIOTERAPIA



Vos, M et al. The Oncologist 2018;23:1–10

IMPACTO DE LA METASTASECTOMIA EN LA SUPERVIVENCIA GLOBAL

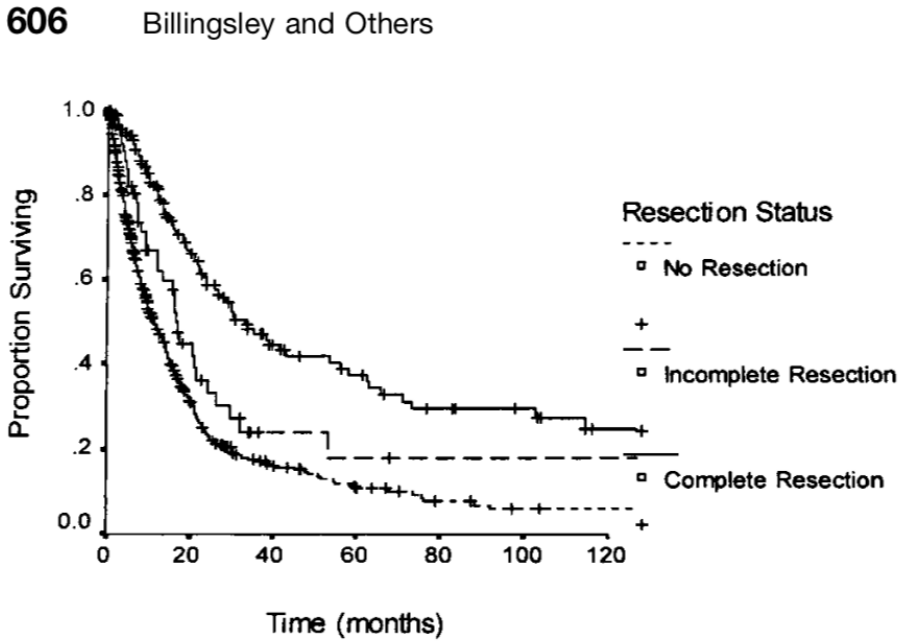


Figure 2. Kaplan-Meier plot of disease-specific survival for patients with pulmonary metastases, by treatment. Patients treated with complete resection (n = 161) had a median survival of 33 months. For patients who did not undergo resection (n = 473), the median survival was 11 months. For patients who underwent incomplete resection (n = 52), the median survival was 16 months ($p < 0.001$, complete resection *vs.* no resection or incomplete resection.)

INDICACIONES DE CIRUGIA EN SARCOMA METASTÁSICO

- Resección completa factible
- Enfermedad extratorácica limitada y completamente resecable
- Ausencia de metástasis multiviscerales
- Tumor primario controlado/controlable
- Estado general adecuado para resección pulmonar
- Paciente operable
- Información preoperatoria por CT y/o PET

INDICACION DE CIRUGIA: METASTASECTOMIA

LIMITE DE LA INDICACION :3 CICLOS DE QT BUSCANDO RR

NO POSIBLE CIRUGIA: QT PALIATIVA, SIN BUSCAR RR

Billingsley KG et al. Ann Surg. 1999;229:602-610
Juneko E et al.2018 ASCO EDUCATIONAL BOOK | asco.org/edbook

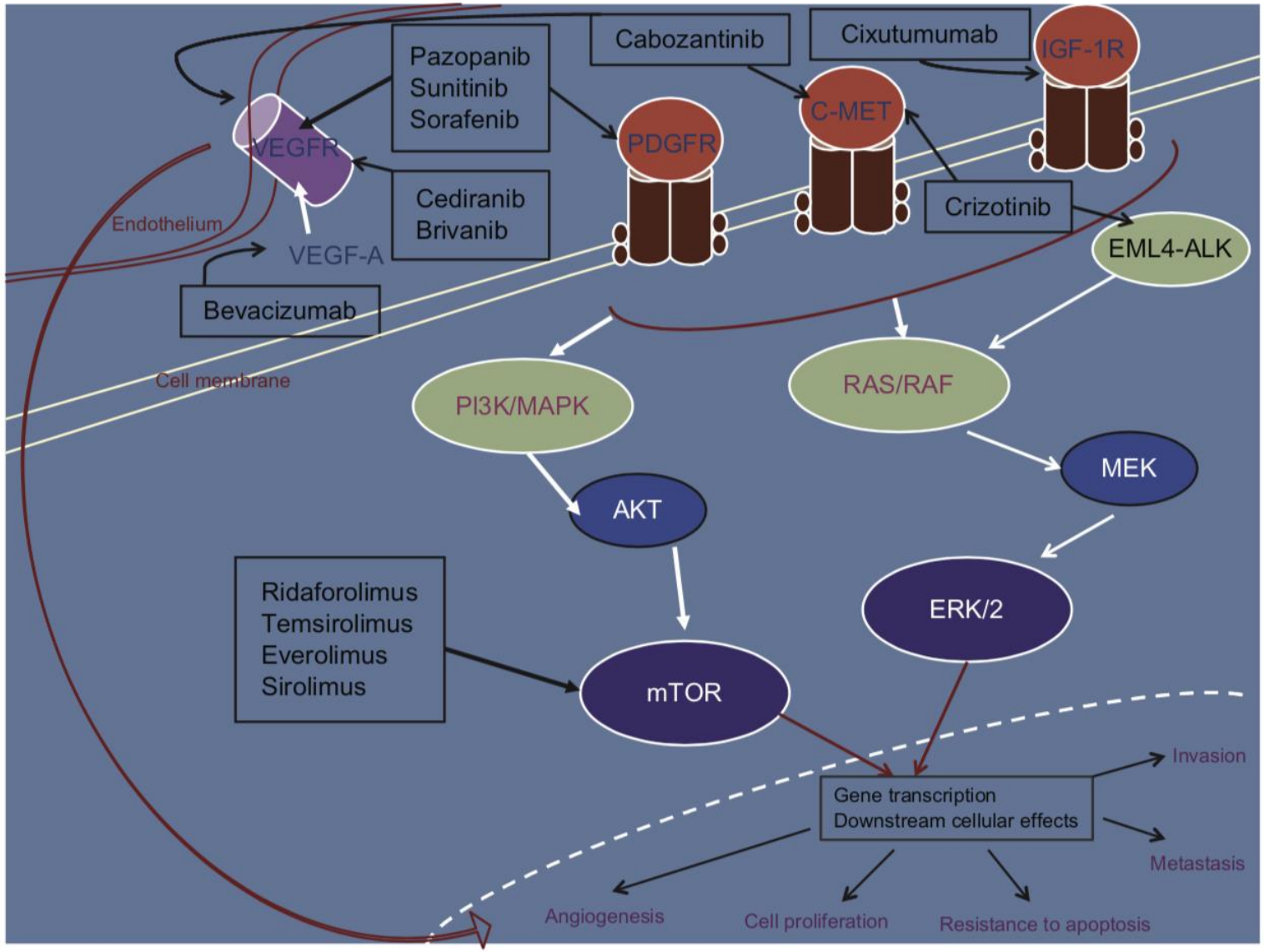


Figure 1 Molecular-targeted therapy with activity in soft-tissue sarcoma. Only the major target(s) for each of the inhibitors have been depicted.
Abbreviations: VEGFR, vascular endothelial growth-factor receptor; STS, soft-tissue sarcoma; PDGFR, platelet-derived growth-factor receptor; IGF-1R, insulin-like growth factor-1 receptor; PI3K, phosphatidylinositol 3-kinase; MAPK, mitogen-activated protein kinase; EML4, echinoderm microtubule-associated protein-like 4; ALK, anaplastic lymphoma kinase; MEK, mitogen-activated protein kinase; ERK, extracellular signal-regulated kinases; AKT, protein kinase B; mTOR, mammalian target of rapamycin.

TRATAMIENTOS HISTOTIPO-DIRIGIDOS

More Than 50 Subtypes of Soft Tissue Sarcoma: Paving the Path for Histology-Driven Treatments

Daniela Katz, MD, Emanuela Palmerini, MD, PhD, and Seth M. Pollack, MD

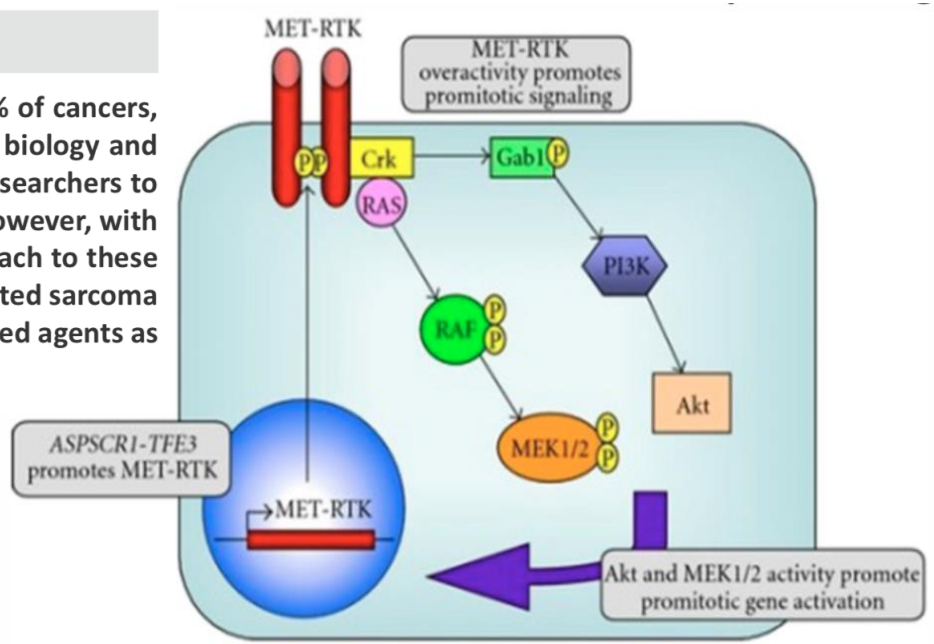
OVERVIEW

Sarcomas are a diverse group of cancers with mesenchymal origin. Although sarcomas comprise less than 1% of cancers, there are more than 50 different subtypes that are quite different from one another in terms of both their biology and clinical behavior. Historically, the need for adequate patient numbers in clinical trials has pushed sarcoma researchers to lump these very different malignancies together and treat the patients using a "one-size-fits-all" approach. However, with improvements in our scientific understanding, we are finally ready for a histology-tailored therapeutic approach to these complex diseases. In this review, we discuss key advances in our understanding of the biology underlying selected sarcoma subtypes and how targeting these subtypes is relevant therapeutically with respect to both molecularly targeted agents as well as immunotherapy.

SUBTIPOS SENSIBLES A LA QT

SUBTIPOS SENSIBLES A QT Y ANTIANGIOGÉNICOS

SUBTIPOS RESISTENTES A LA QT Y SENSIBLES A TERAPIAS DIRIGIDAS O ANTIANGIOGÉNICOS



Katz et al, ASCO EDUCACIONAL BOOK, 2018

SARCONNECT

QUIMIOTERAPIA

UPS: doxo

TMVNP: doxo

Angiosarcoma: taxanos/doxo

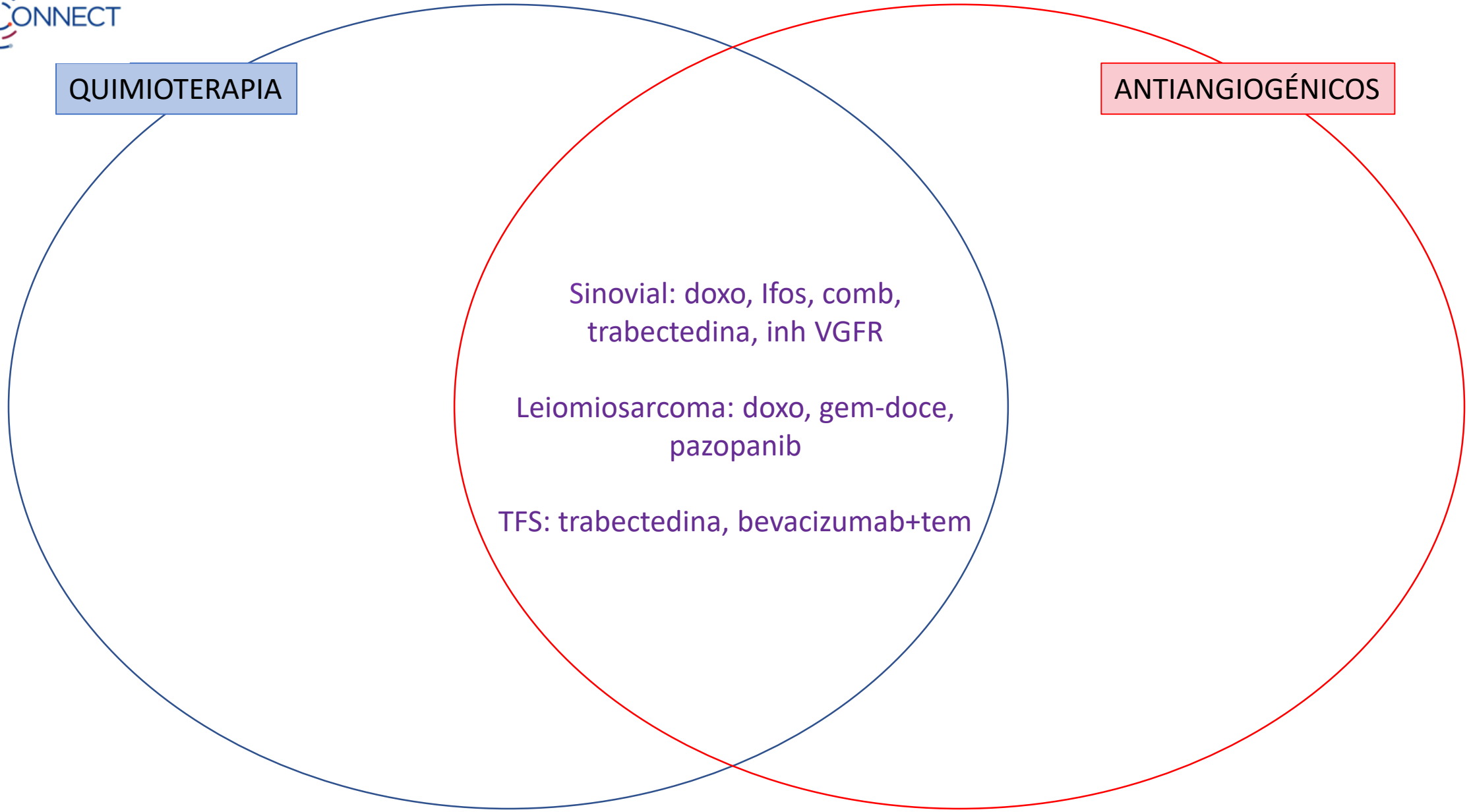
LPS DD: doxo

LPS mixoide: doxo/com trabectedina. No gem doce

Sinovial: doxo, Ifos, comb, trabectedina

Leiomiosarcoma: doxo/gem-doce

TFS: trabectedina/temodal beva

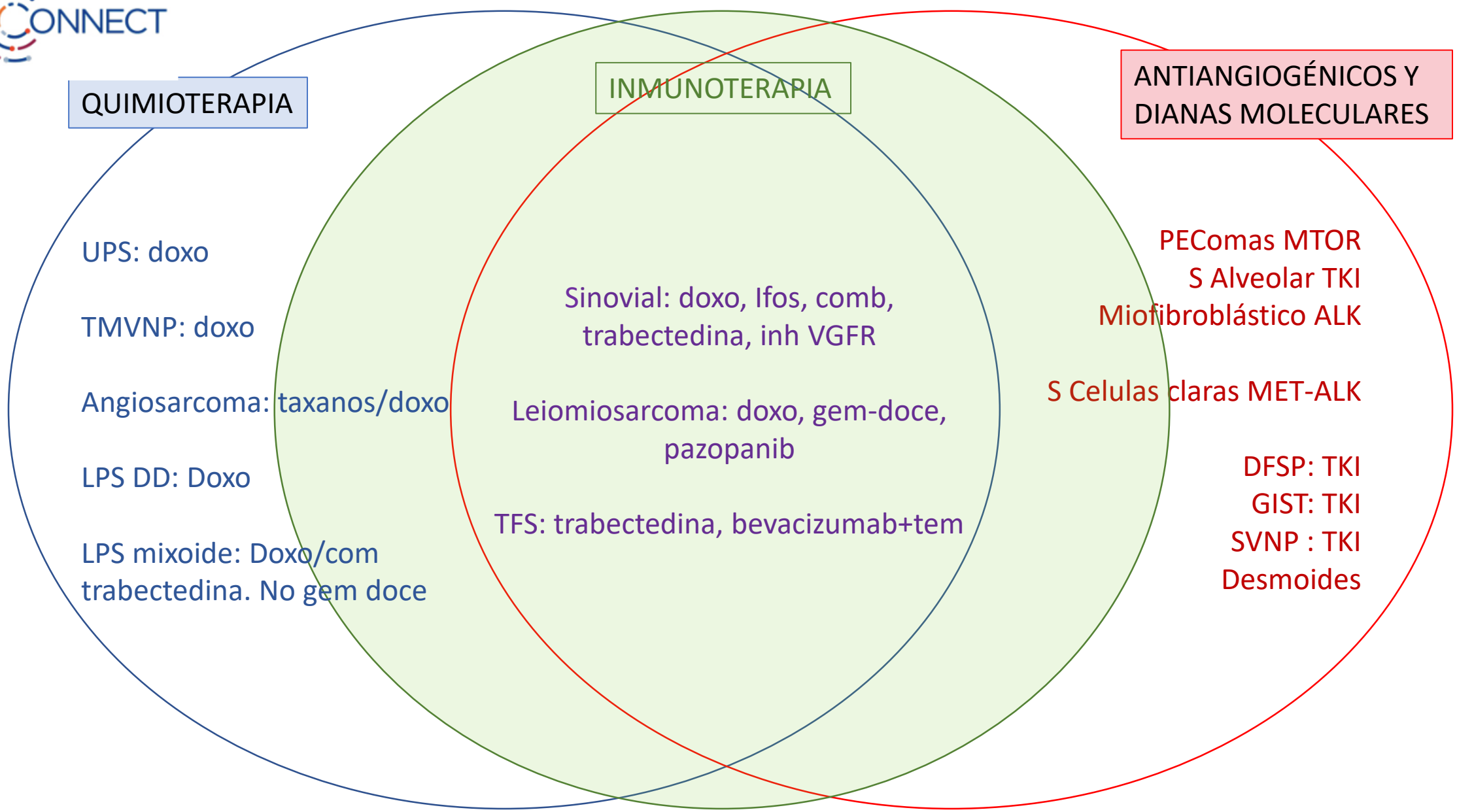

QUIMIOTERAPIA
ANTIANGIOGÉNICOS
Sinovial: doxo, Ifos, comb, trabectedina, inh VGFR
Leiomiosarcoma: doxo, gem-doce, pazopanib
TFS: trabectedina, bevacizumab+tem

TERAPIAS DIRIGIDAS

PEComas MTOR

Miofibroblástico ALK
S Celulas claras MET-ALK

S Alveolar TKI
DFSP: TKI
GIST: TKI
SVNP : TKI
Desmoides


QUIMIOTERAPIA
INMUNOTERAPIA
ANTIANGIOGÉNICOS Y DIANAS MOLECULARES
UPS: doxo
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Angiosarcoma: taxanos/doxo
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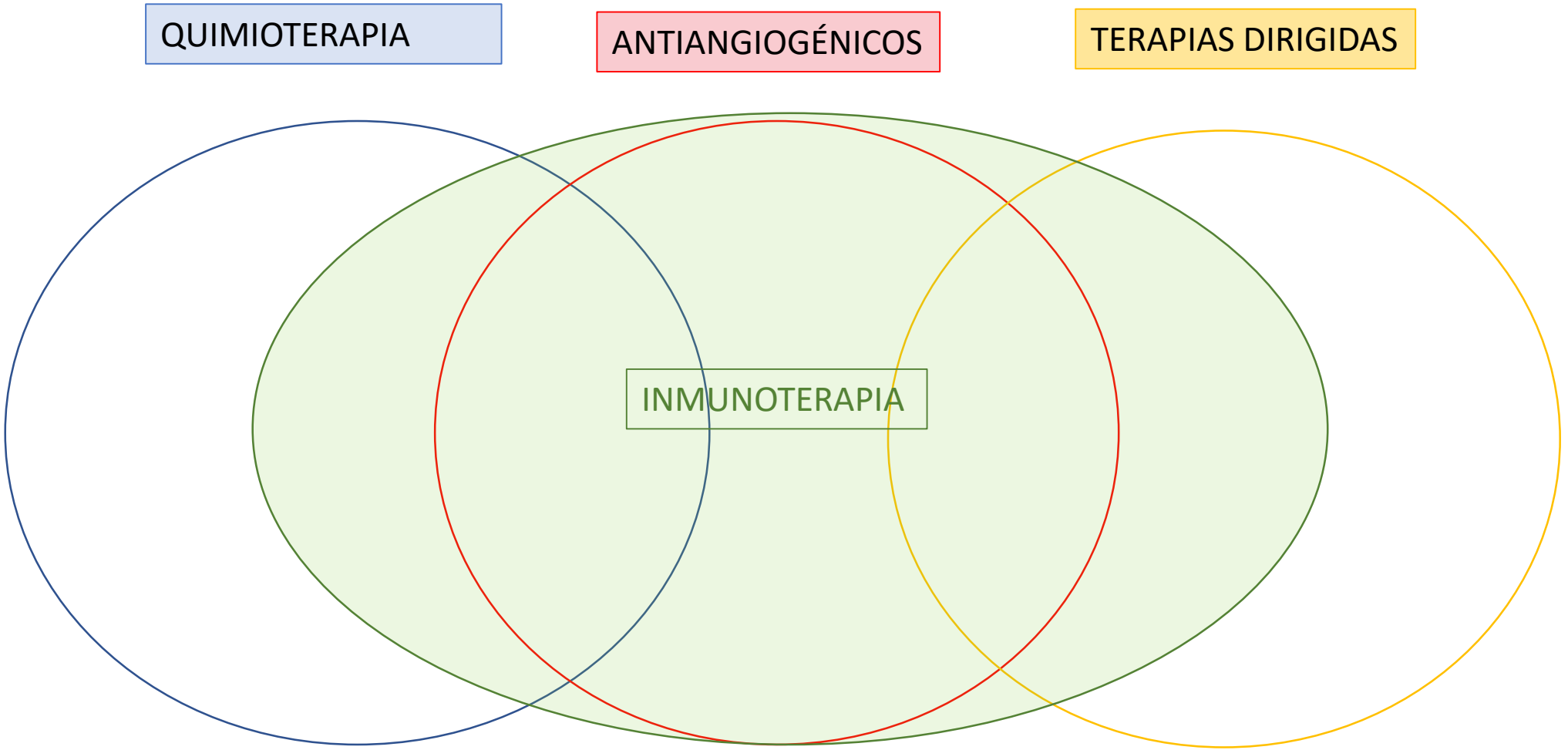
GIST: TKI
SVNP : TKI
Desmoides

MECANISMO DE ACCION DE NUEVOS FÁRMACOS. OLARATUMAB?



INDICACIONES DE QT COMBINACION

- SARCOMAS DE PARTES BLANDAS AVANZADOS. IMPLICACIONES DE LA HISTORIA NATURAL

- ESTUDIOS EN PRIMERA LINEA
  - DOXORRUBICINA MONOTERAPIA VS COMBINACION
  - DOXORRUBICINA + IFOSFAMIDA
  - DOXORRUBICINA + OLARATUMAB
  - ALTERNATIVAS A DOXORRUBICINA

- APLICACIÓN CLÍNICA DE LOS ESTUDIOS EN PRIMERA LINEA

- CONCLUSIONES

clinical practice guidelines

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

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

The ESMO/European Sarcoma Network Working Group*

Standard chemotherapy is based on anthracyclines as the first-line treatment [I, A]. As of today, there is no formal demonstration that multiagent chemotherapy is superior to single-agent chemotherapy with doxorubicin alone in terms of overall survival (OS). However, a higher response rate can be expected, in particular in a number of sensitive histological types, according to several, although not all, randomised clinical trials [18, 19]. Therefore, multiagent chemotherapy with adequate-dose anthracyclines plus ifosfamide may be the treatment of choice, particularly when a tumour response is felt to be potentially advantageous and patient performance status is good.

SARCONNECT

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 28 (Supplement 4): iv147–iv148, 2017
doi:10.1093/annonc/mdx241

CLINICAL PRACTICE GUIDELINES

Appendix 3: Soft tissue sarcoma: MCBS eUpdate published online 5 May 2017 (www.esmo.org/Guidelines/Sarcoma-and-GIST)

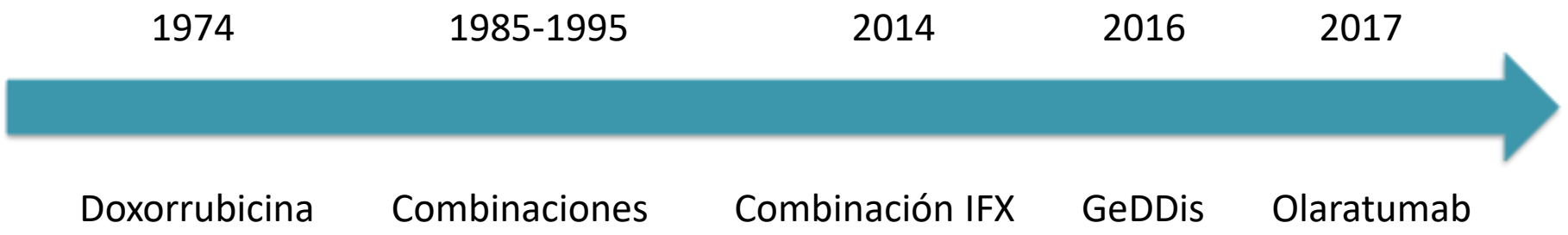
ESMO-Magnitude of Clinical Benefit Scale (MCBS) table for new therapies/indications in soft tissue and visceral sarcomas[a]

Therapy	Disease setting	Trial	Control	Absolute survival gain	HR (95% CI)	QoL/toxicity	MCBS score[b]
Olaratumab with doxorubicin	Unresectable or metastatic soft tissue sarcoma with a histologically confirmed diagnosis, PS of 0-2 and not previously treated with an anthracycline	Olaratumab and doxorubicin versus doxorubicin alone for treatment of soft-tissue sarcoma: an open-label phase 1b and randomised phase 2 trial [1] Phase Ib/II NCT01185964	Doxorubicin median OS: 14.7 months	OS gain: 11.8 months	OS HR: 0.46 (0.30–0.71)	QoL not available AEs similar (or slightly worse for leukopaenia and neutropaenia)	4 (Form 2a; secondary endpoint of OS in a small phase II randomised study)

[a]EMA approvals from January 2016 to end January 2017.
[b]ESMO-MCBS version 1.0 [2].
AE, adverse event; CI, confidence interval; EMA, European Medicines Agency; HR, hazard ratio; MCBS, Magnitude of Clinical Benefit of Scale; OS, overall survival; PS, performance status; QoL, quality of life.

DECISIÓN DE TRATAMIENTO

EXSITEN VARIAS OPCIONES ACTIVAS EN PRIMERA LINEA

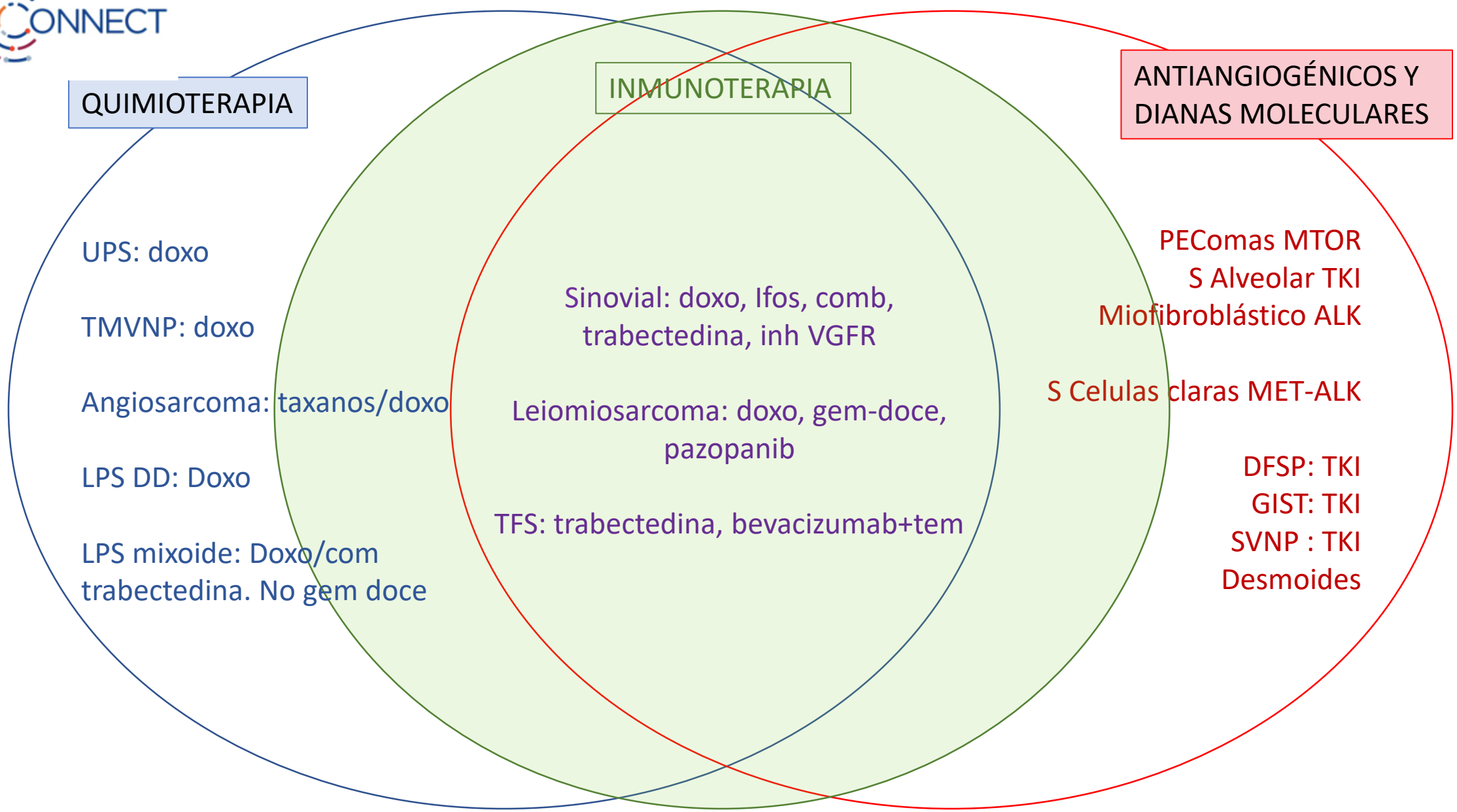


LA DECISION DEL TRATAMIENTO HA DE SER INDIVIDUALIZADA, EN FUNCIÓN DE:

TIPO HISTOLÓGICO / REFRACTARIEDAD A ANTRACICLINAS Y SENSIBILIDAD A OTROS FARMACOS
CONTRAINDICACION DE ANTRACICLINAS (ADYUVANCIA – ILE)
ECOG / COMORBILIDADES
URGENCIA POR OBTENER RESPUESTA VOLUMETRICA/POTENCIAL RESECABILIDAD

CONTRAINDICACIONES RELATIVAS DE LA DOXORRUBICINA

- FALLO CARDIACO
- DOSIS ACUMULADA EN ADYUVANCIA O NEOADYUVANCIA> 400 mg/ m^2
- ALTERNATIVAS:
  - SEGÚN SUBTIPOS HISTOLÓGICOS
  - DOXORRUBICINA LIPOSOMIAL PEGILADA
  - COMBINACIÓN GEM-DOCETAXEL
  - TRABECTEDINA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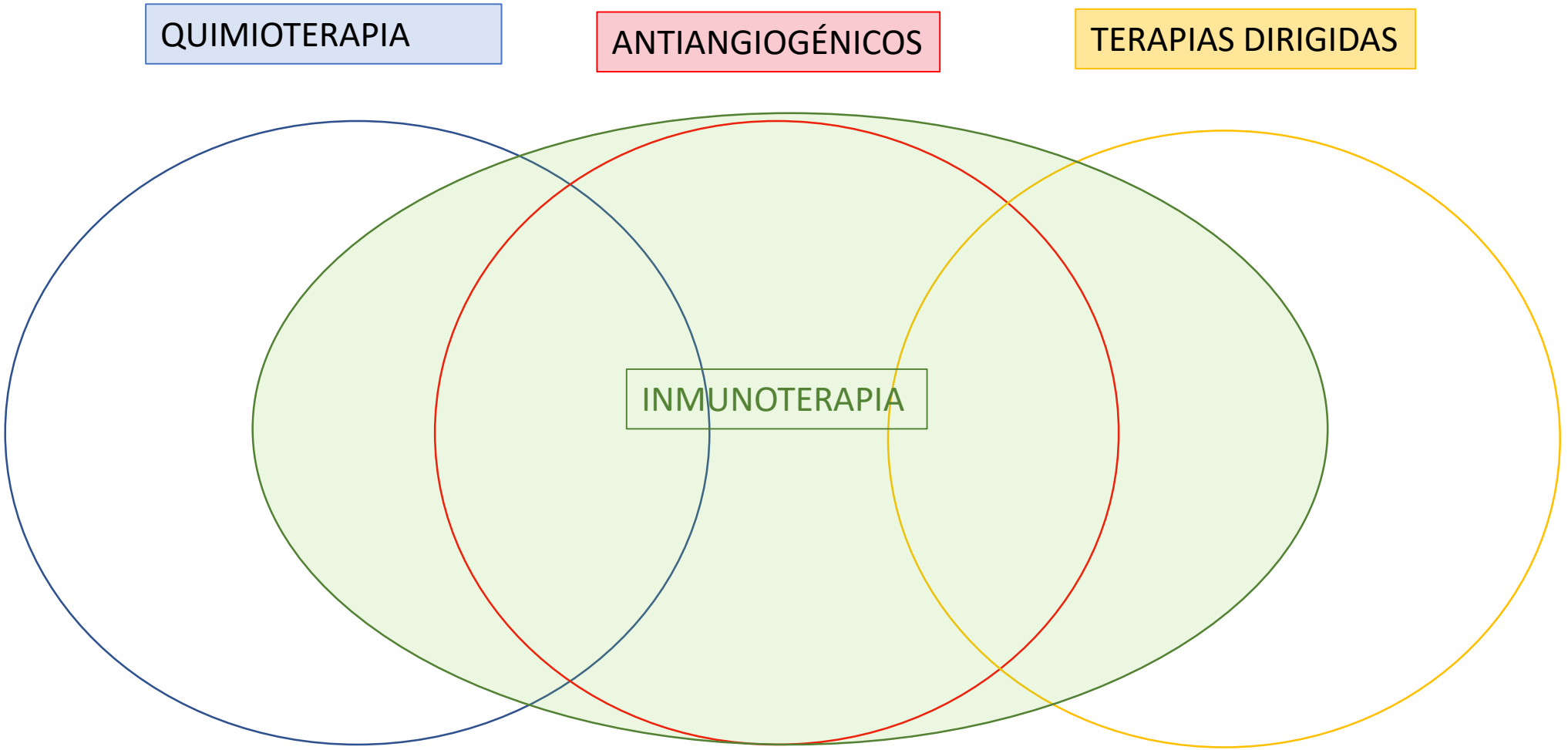
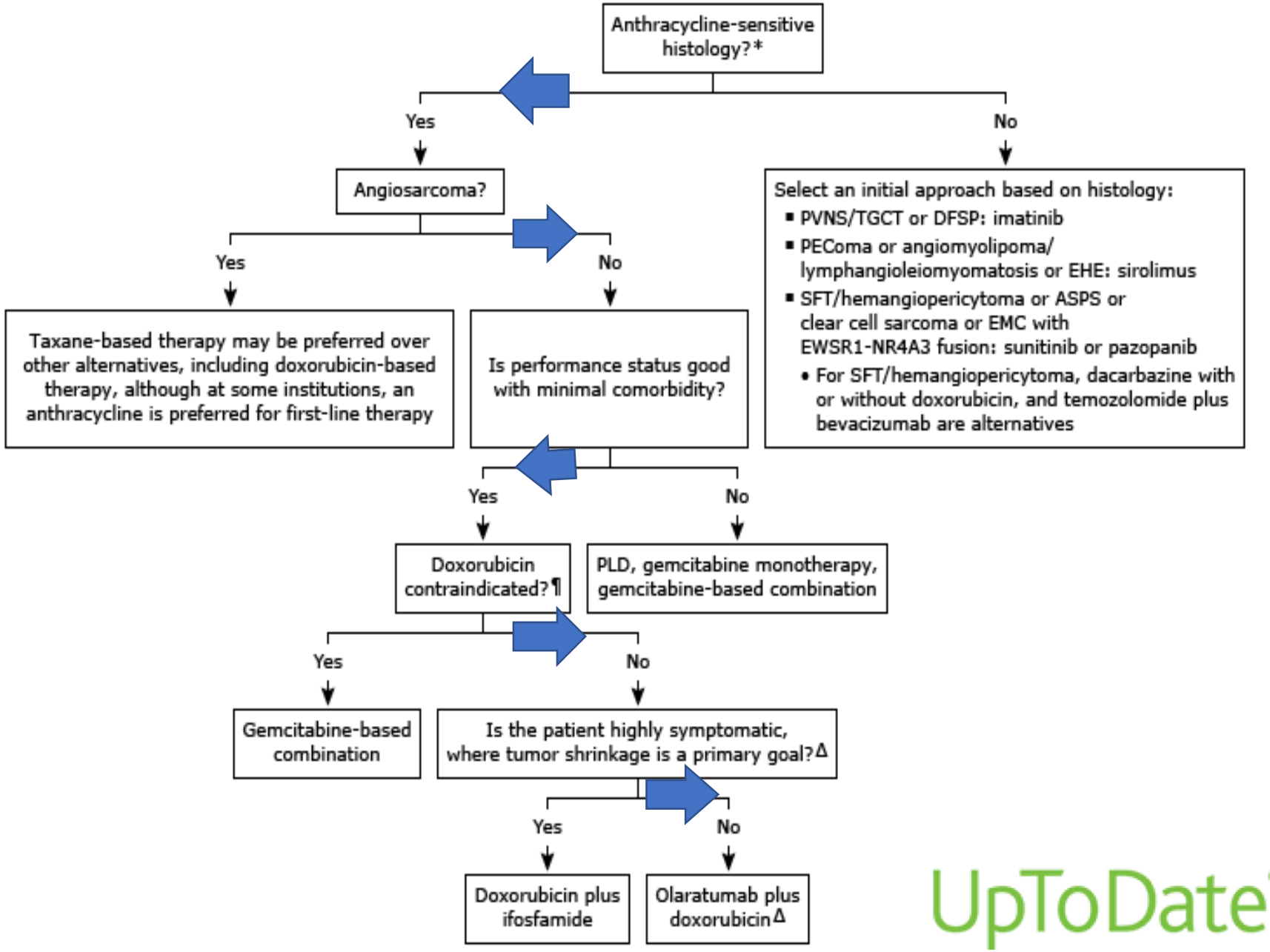


ALGORITMO



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SARCONNECT

Mejorando la Supervivencia
en Pacientes con Sarcoma
de Partes Blandas