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UNIVERSITÄTSMEDIZIN
MANNHEIM

Medizinische Fakultät Mannheim
der Universität Heidelberg

Universitätsklinikum Mannheim

Überblick: Medikamentöse Therapieoptionen bei Weichgewebesarkomen

WissensWert Online-Webinar Deutsche Sarkom Stiftung (DSS)

DKG
KREBSGESELLSCHAFT
Zertifiziertes Sarkomzentrum für Weichteilsarkome Knochensarkome

Prof. Dr. med. Bernd Kasper
Universität Heidelberg
Sarkom Zentrum @ Universitätsmedizin Mannheim (UMM)
German Interdisciplinary Sarcoma Group (GISG)
Chair-Elect EORTC / Soft Tissue and Bone Sarcoma Group (STBSG)

European Reference Network
for rare or low prevalence complex diseases
Network Adult Cancers (ERN EURACAN)
Member Universitätsklinikum Mannheim — Deutschland

Weichgewebesarkome - Grundlagen

- **Seltenheit:**
  - Deutschland: ca. 5-6 / 100.000 Einwohner pro Jahr*
- **Heterogenität:**
  - > 50 unterschiedliche histologische Subtypen nach WHO
  - Keine Geschlechtsunterschiede
- **Ungünstige Prognose:**
  - Mittleres Überleben 12-15 Monate (M1 Situation)

RARE CANCERS EUROPE
Joining forces for action

EURACAN

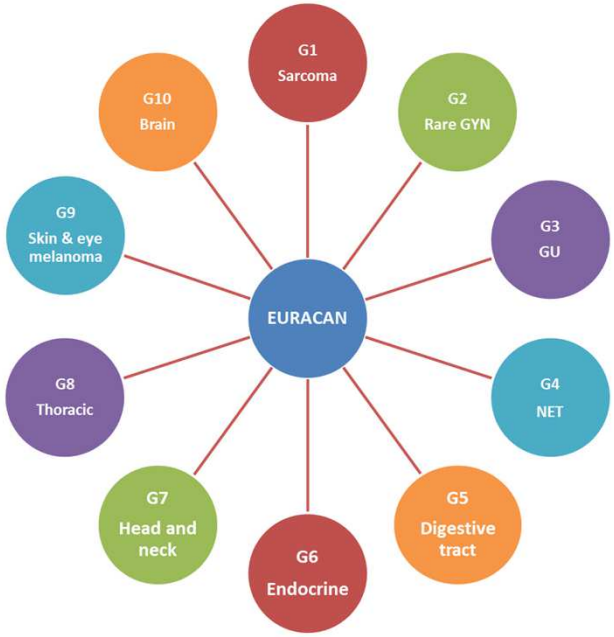
JARC
JOINT ACTION ON RARE CANCERS

*Ressing M et al. BMC Public Health 2018; 18: 235

European Reference Network
for rare or low prevalence complex diseases

Network Adult Cancers (ERN EURACAN)

EURACAN



Melanoma Patient Network Europe

Sarcoma Patients EuroNet

RARE SOLID ADULT CANCERS

DKG / OnkoZert Zertifizierung von Sarkomzentren

GISG German Interdisciplinary Sarcoma Group

DKG KREBSGESELLSCHAFT

Erhebungsbogen Sarkomzentren

Modul im Onkologischen Zentrum

der Deutschen Krebsgesellschaft

Vorsitz der Zertifizierungskommission: Prof. Dr. P. Hohenberger, Prof. Dr. V. Grünwald

Erarbeitet von der Zertifizierungskommission Sarkomzentren der DKG.
Beteiligte Fachgruppen (in alphabetischer Reihenfolge):

S3 Leitlinie „Adulte Weichgewebesarkome“

GISG
German Interdisciplinary Sarcoma Group

Leitlinienprogramm Onkologie

AWMF online
Das Portal der wissenschaftlichen Medizin

Hauptantrag

Adulte Weichgewebesarkome

vom 04.04.2016

Diese Vorgabe adressiert die wesentlichen Inhalte eines Antrags an das Leitlinienprogramm Onkologie. Soweit möglich sollte zu den Unterpunkten Stellung bezogen werden. Bitte auf der ersten Seite eine Zusammenfassung des Projektantrages einfügen. Bei Rückfragen wenden Sie sich bitte an das OL Office (Dr. Follmann: 030 322932959) bzw. leitlinienprogramm@krebsgesellschaft.de

DKG Deutsche Krebshilfe AWMF Version 1.6 vom 06.03.2014

Leitlinien-Detailansicht
Angemeldetes Leitlinienvorhaben

Registernummer 032 - 044OL

Klassifikation S3

Adulte Weichgewebesarkome

Anmeldedatum:	01.07.2016
Geplante Fertigstellung:	01.09.2020

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CANCER *January* 1974

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.

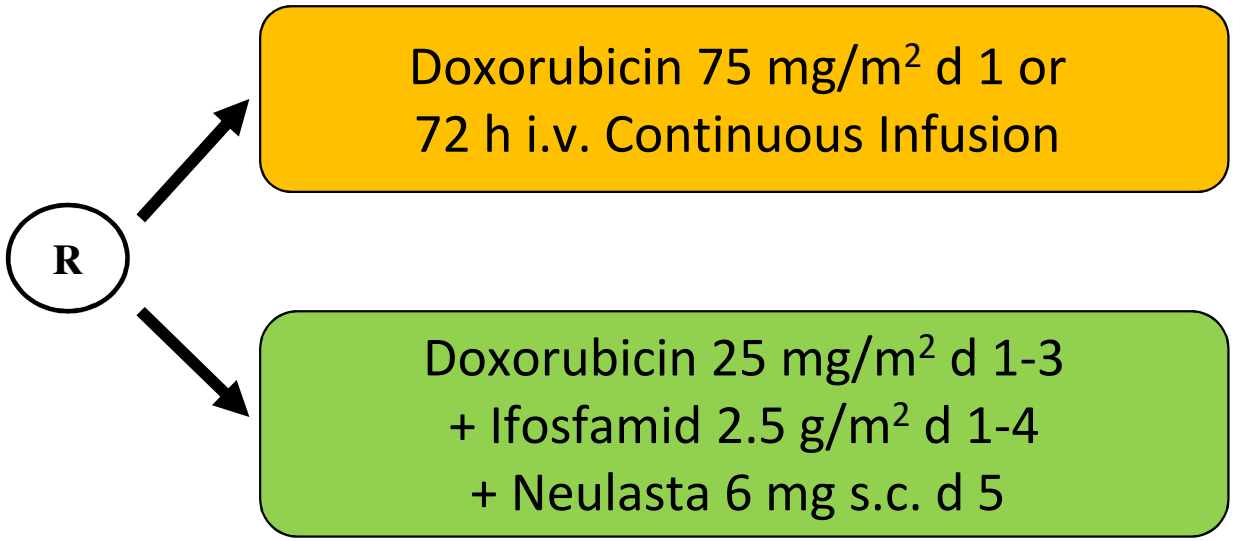
Fortgeschrittene Erkrankung - Viel (Chemotherapie) hilft viel?

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

<u>Kein</u> Überlebensvorteil: Doxorubicin (75 mg/m²) bleibt der Gold-Standard!

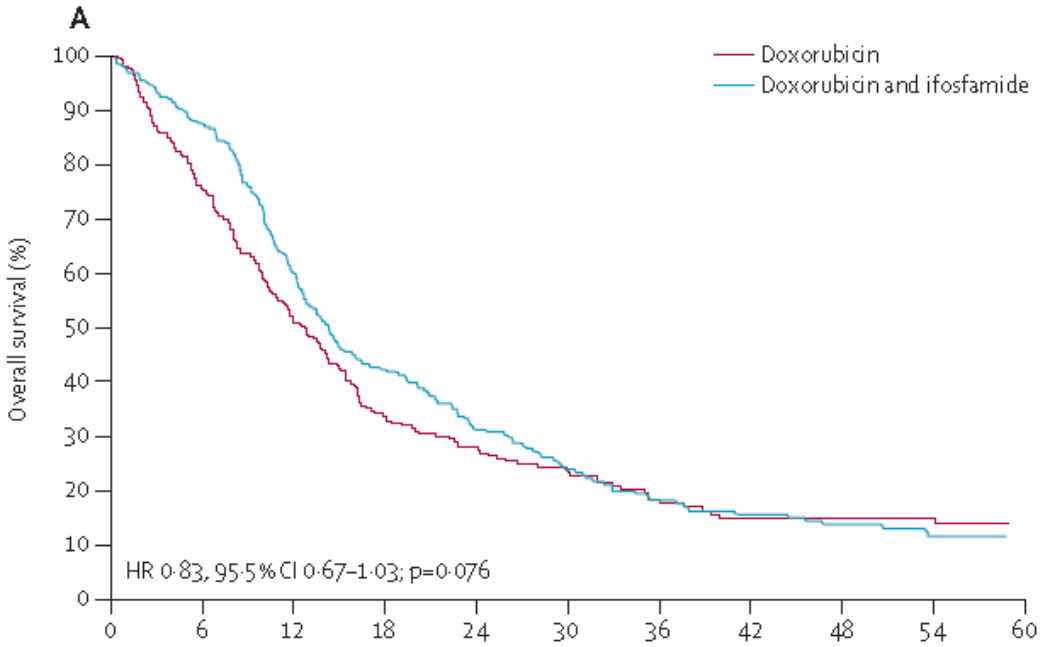
Muss H et al. Cancer 1985; 55: 1648-1653; Omura G et al. Cancer 1983; 52: 626-632; Borden E et al. J Clin Oncol 1987; 5: 840-850; Santoro A et al. J Clin Oncol 1995; 13: 1537-1545; Borden E et al. Cancer 1990; 66: 862-867; Edmonson J et al. J Clin Oncol 1993; 11: 1269-1275; Antman K et al. J Clin Oncol 1993; 11: 1276-1285; Judson I et al. Lancet Oncol 2014; 15: 415-423; Ryan CW et al. J Clin Oncol 2016; 34: 3898-3905

EORTC 62012 - Studiendesign



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

EORTC 62012 - Gesamtüberleben



Panel: Research in context

Systematic review

We searched PubMed for reports published in English from Jan 1, 1983, to Jan 1, 2014, for all randomised trials assessing dose intensification for treatment of soft-tissue sarcoma with the terms: "randomis(z)ed", "trial(s)", "advanced", "soft tissue", "sarcoma(s)", "ifosfamide", and "doxorubicin". We found eight randomised trials[20–27] and two meta-analyses.[28,29] Our search also returned single group and randomised phase 2 trials of higher dose treatment. Combination treatment has been shown to improve the proportion of patients who responded and progression-free survival but not overall survival in some, but not all trials.[22,25,26]

Interpretation

In our study both doxorubicin and ifosfamide doses were higher than those used in previous randomised trials. However, we did not show an improvement in overall survival. If the goal of treatment is disease control, doxorubicin alone remains an appropriate treatment but combination treatment can be justified if tumour shrinkage is desired, either to relieve symptoms or before another intervention. The lack of improvement in overall survival shows the need for better treatments for advanced soft tissue sarcoma.

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

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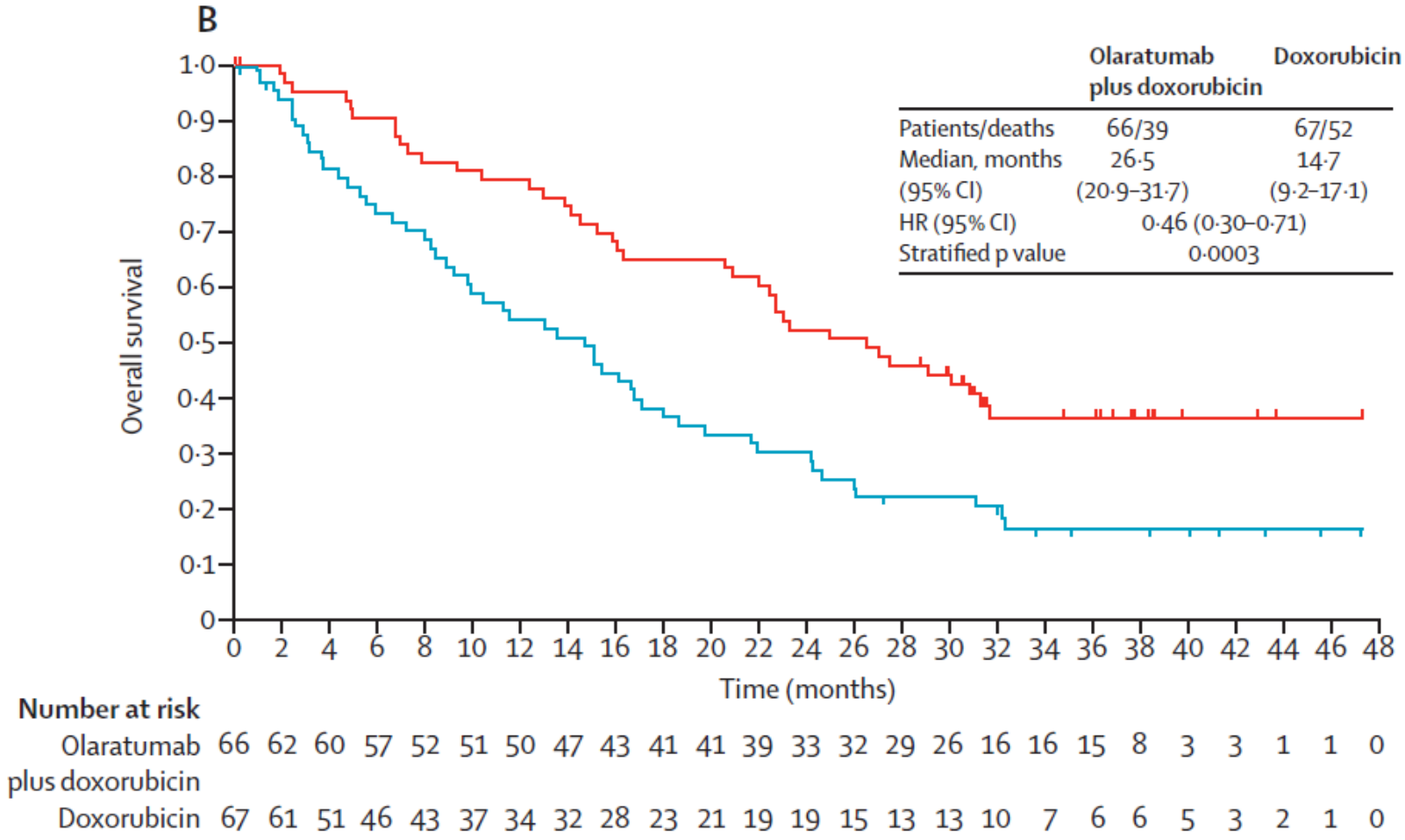
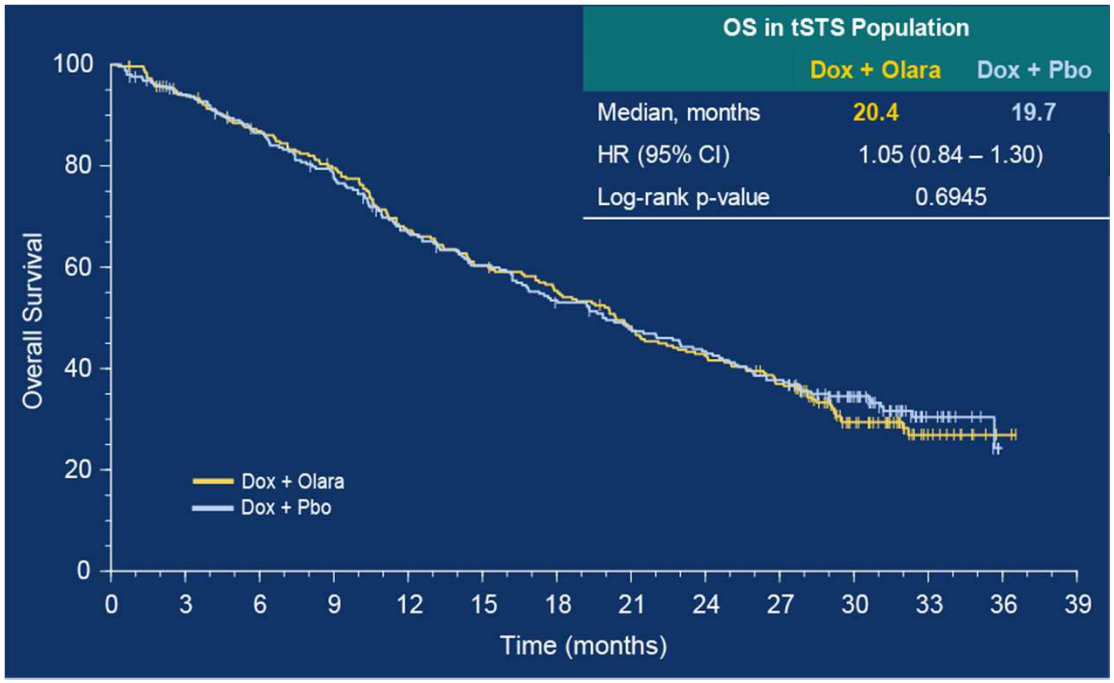
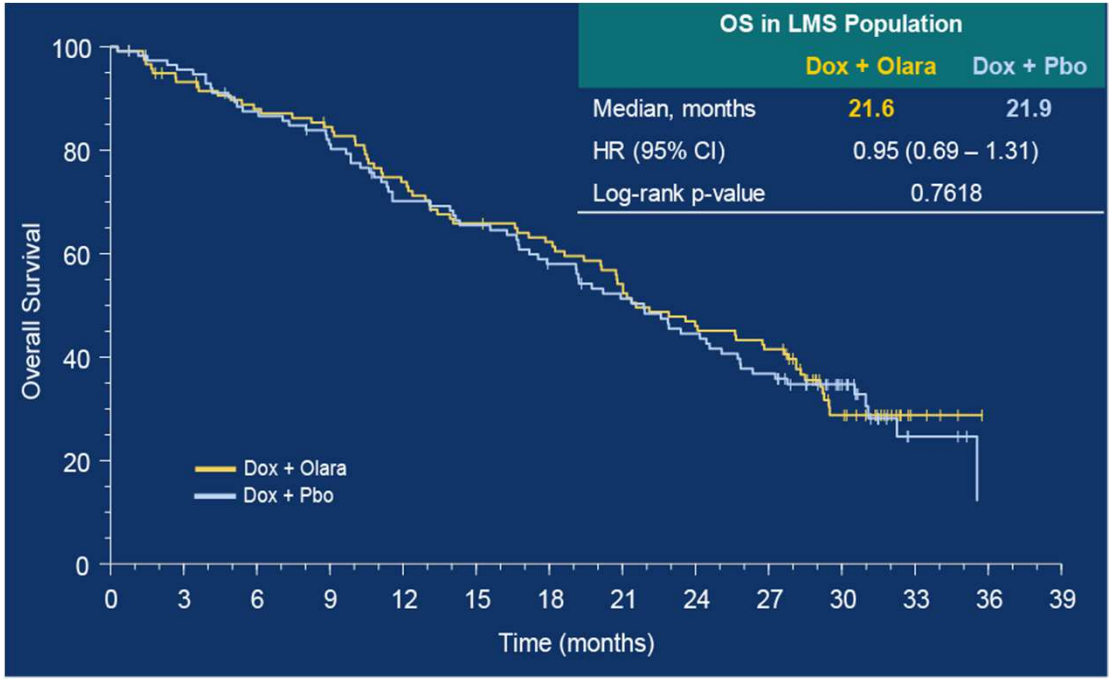
Olaratumab - Gesamtüberleben (*JGDG Phase 1b/2*)



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

Olaratumab - Gesamtüberleben (*JGDJ Phase 3 - ANNOUNCE*)





Tap WD et al. JAMA 2020; 323: 1266-1276

Phase III Studien bei metastasierten STS: A Story of Pitfalls?

2012	2014	2015	2016	2017
PALETTE[1] pazopanib vs. placebo mOS: 12.5 vs. 10.7 mo HR: 0.86 (95% CI, 0.67-1.11) PFS: 4.6 vs. 1.6 mo	EORTC-62012[2] dox vs. dox + ifosfamide mOS: 12.8 vs. 14.3 mo HR: 0.83 (95% CI, 0.67-1.03) PFS: 4.6 vs. 7.4 mo	PICASSO-III[3] dox vs. dox + palifosfamide mOS: 16.9 vs. 15.9 mo HR: 1.05 (95% CI, 0.79-1.39) PFS: 5.2 vs. 6.0 mo	ET743-SAR-3007[4] trabectedin vs. dacarbazine mOS: 13.7 vs. 13.1 mo HR: 0.93 (95% CI, 0.75-1.15) PFS: 4.2 vs. 1.5 mo	SARC 21[6] dox vs. dox + evofosfamide mOS: 19.0 vs. 18.4 mo HR: 1.06 (95% CI, 0.88-1.29) PFS: 6.0 vs. 6.3 mo
			E7389-G000-309[5] eribulin vs. dacarbazine mOS: 13.5 vs. 11.5 mo HR: 0.77 (95% CI, 0.62-0.95) PFS: 2.6 vs. 2.6 mo	GeDDiS[7] dox vs. doce + gemcitabine mOS: 17.6 vs. 15.5 mo HR: 1.14 (95% CI, 0.83-1.57) PFS: 23.3 vs. 23.7 wks

Led to drug approval

First Line | Second Line +

dox, doxorubicin; doce, docetaxel; EORTC, European Organisation for Research and Treatment of Cancer; GEDDIS, gemcitabine and docetaxel versus doxorubicin as first-line treatment in previously untreated advanced unresectable or metastatic soft-tissue sarcomas; mOS, median overall survival; mo, month; PICASSO, palifosfamide-tris with doxorubicin for soft tissue sarcoma; SARC, Sarcoma Alliance for Research Through Collaboration; STS, soft tissue sarcoma; wks, weeks.

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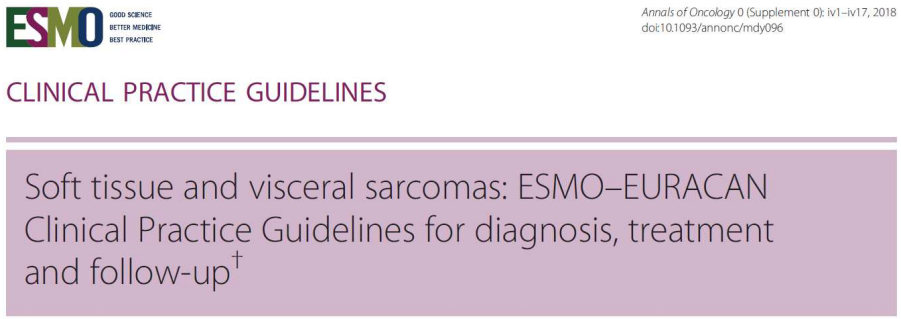
[1]Van der Graaf WTA et al. Lancet 2012; [2]Judson I et al. Lancet Oncol 2014; [3]Ryan CW et al. J Clin Oncol 2016; [4]Trabectedin US prescribing information 2019; [5]Schöffski P et al. Lancet 2016; [6]Tap WD et al. Lancet Oncol 2017; [7]Seddon B et al. Lancet Oncol 2017

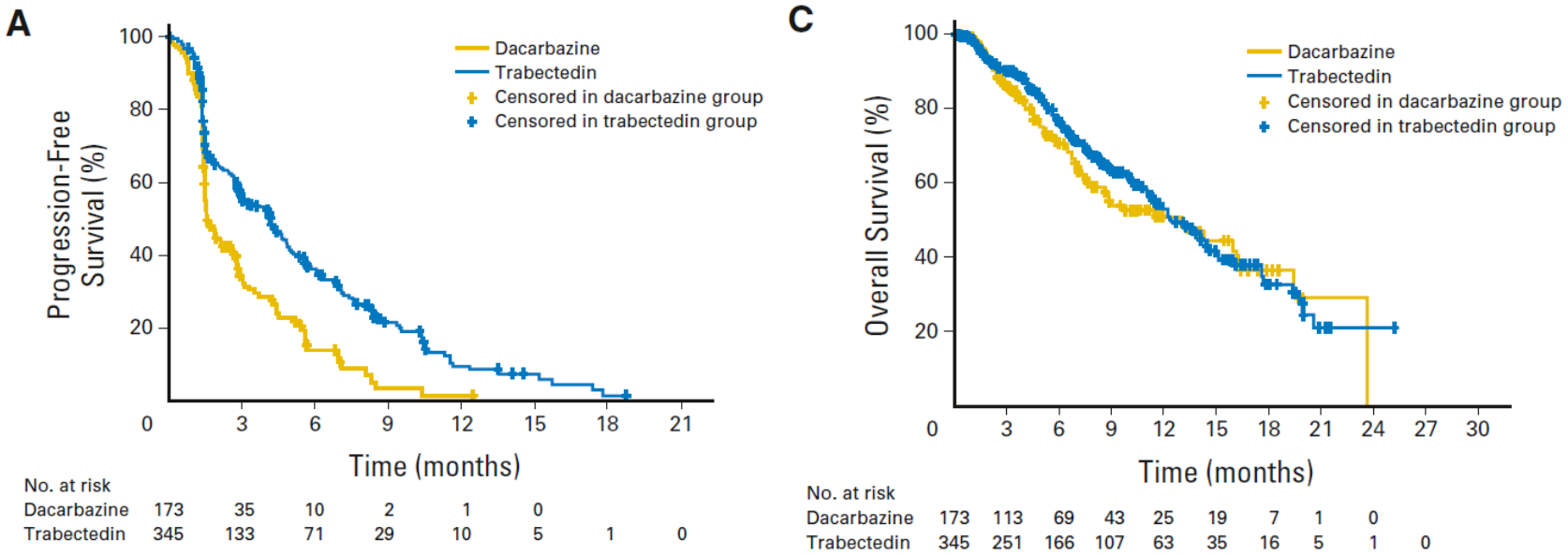
Systemtherapien bei vorbehandelten Sarkomen

• **Alle STS (Europa)** ***seit 2007***	**Trabectedin**
• **LMS + LPS (USA)** ***seit 2015***	**Trabectedin**
• **Alle STS <u>ohne</u> LPS** ***seit 2012***	**Pazopanib**
• **<u>Nur</u> Liposarkome** ***seit 2016***	**Eribulin**
Doxorubicin vorbehandelte STS	Gemcitabin/DTIC oder Gemcitabin/Docetaxel *(ESMO-EURACAN 2018)*
Vorbehandelte, nicht-adipozytäre STS	Regorafenib (*ESMO-EURACAN 2018*)
Alle STS	Einschluss in klinische Studien (*ESMO-EURACAN 2018*)



Casali PG et al. Ann Oncol 2018; 29 Suppl 4: iv51-iv67

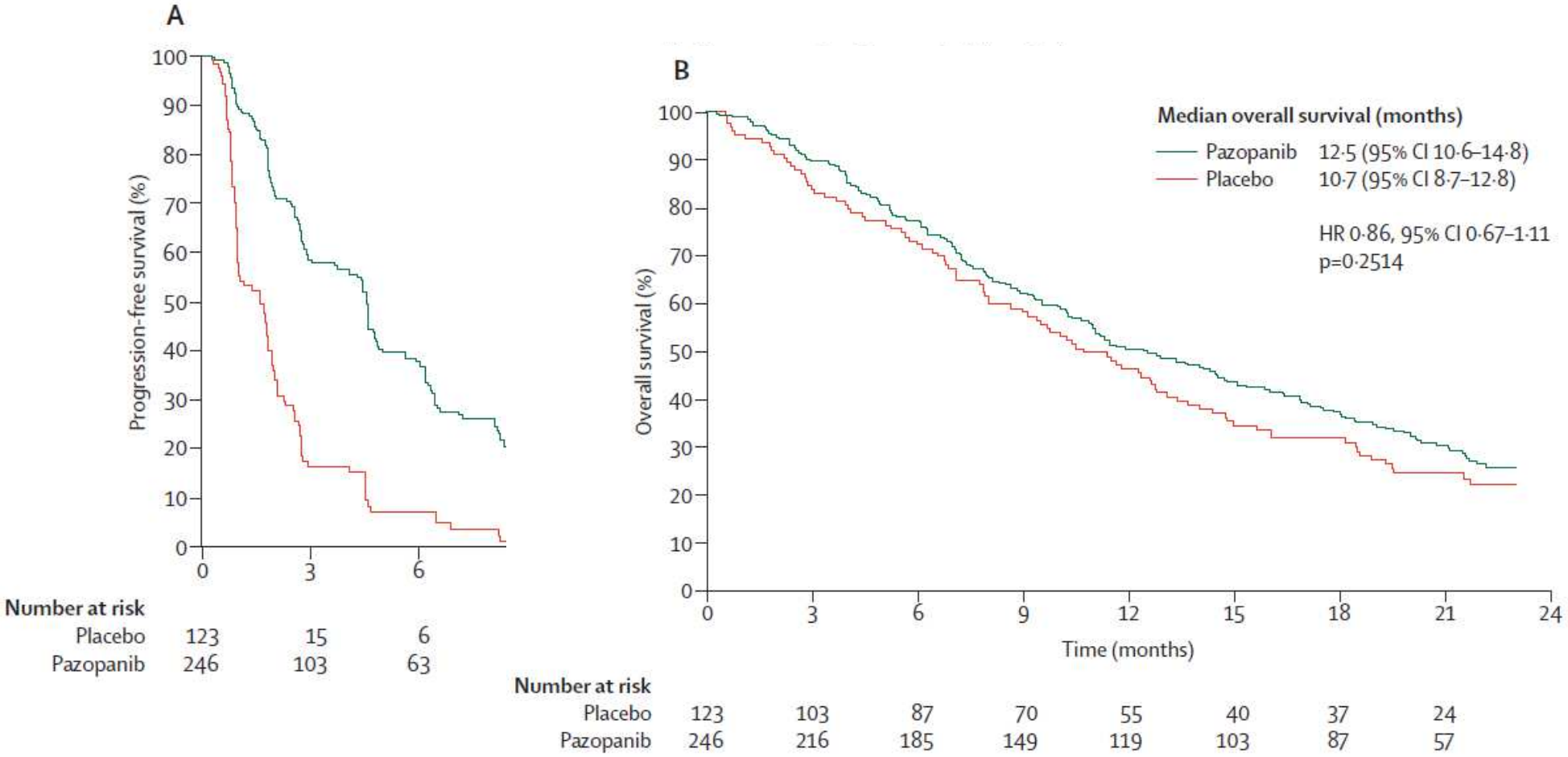
Trabectedin bei vorbehandelten STS



Conclusion
Trabectedin demonstrates superior disease control versus conventional dacarbazine in patients who have advanced liposarcoma and leiomyosarcoma after they experience failure of prior chemotherapy. Because disease control in advanced sarcomas is a clinically relevant end point, this study supports the activity of trabectedin for patients with these malignancies.

Demetri GD et al. J Clin Oncol 2016; 34: 786-793

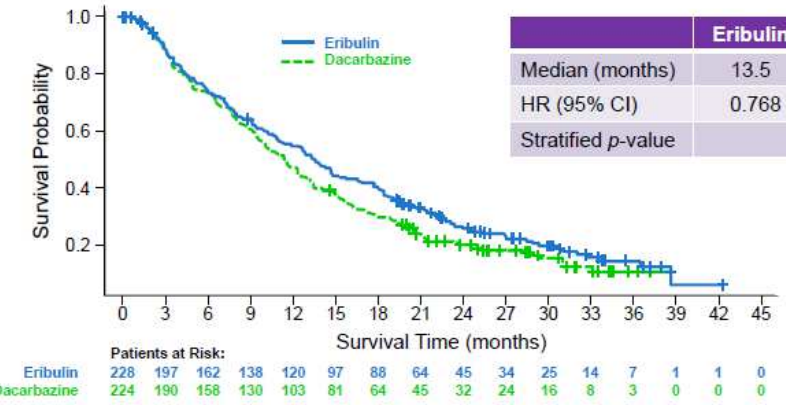
Pazopanib bei vorbehandelten STS



Van der Graaf WTA et al. Lancet 2012; 379: 1879-1886

Eribulin bei vorbehandelten STS

Primary endpoint: OS



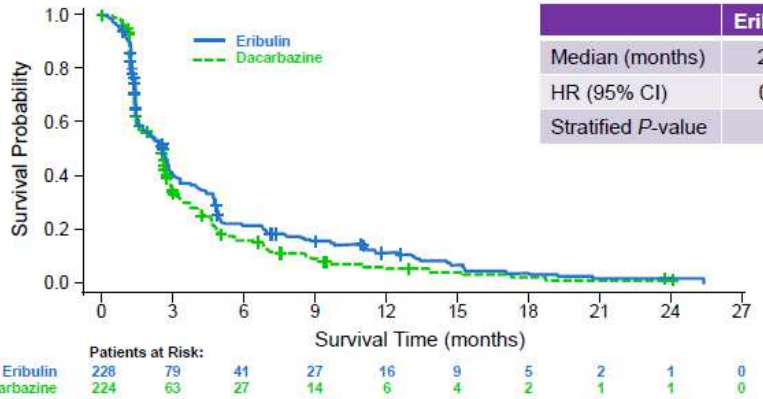
	Eribulin	Dacarbazine
Median (months)	13.5	11.5
HR (95% CI)	0.768 (0.618, 0.954)	
Stratified *p*-value	0.0169	

- The primary endpoint of OS was met, indicating a 2-month improvement in median OS with eribulin

CI, confidence interval.

PRESENTED AT: ASCO Annual '15 Meeting

Secondary endpoint: PFS



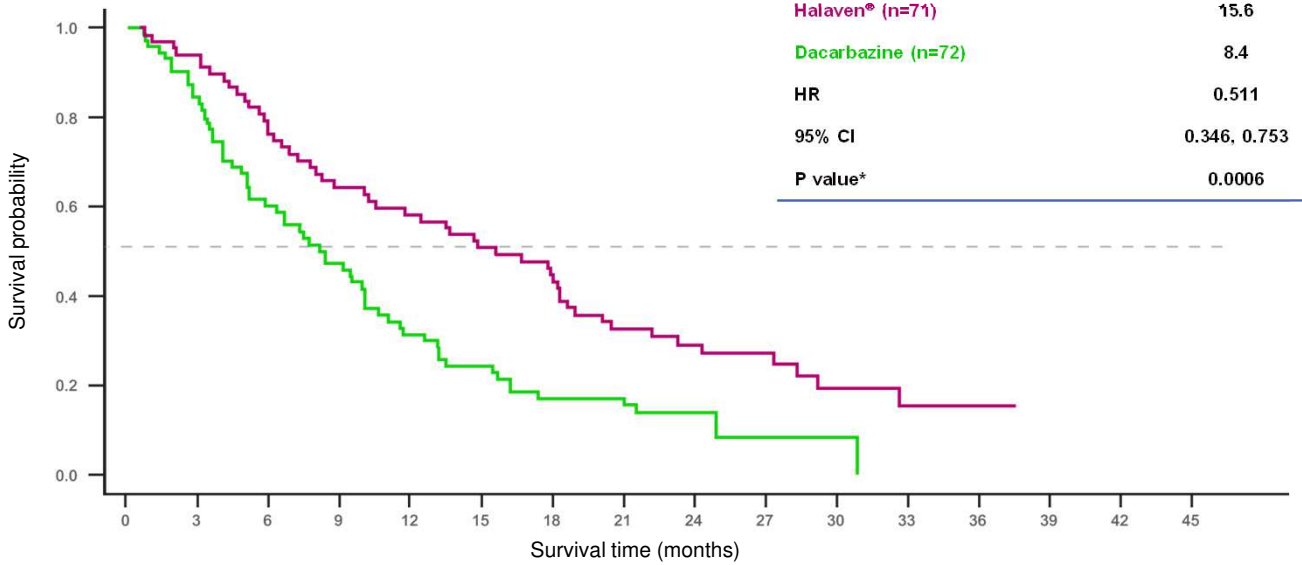
	Eribulin	Dacarbazine
Median (months)	2.6	2.6
HR (95% CI)	0.877 (0.710, 1.085)	
Stratified *P*-value	0.2287	

PRESENTED AT: ASCO Annual '15 Meeting

Schöffski P et al. Lancet 2016; 387: 1629-1637

Eribulin bei vorbehandelten STS

Liposarcoma subgroup	Median OS, months
Halaven® (n=71)	15.6
Dacarbazine (n=72)	8.4
HR	0.511
95% CI	0.346, 0.753
P value*	0.0006



Patients at risk:

Halaven®	71	63	51	43	39	34	30	20	15	12	7	4	2	0	0	0
Dacarbazine	72	59	42	42	22	17	12	11	6	3	2	0	0	0	0	0

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Schöffski P et al. Lancet 2016; 387: 1629-1637

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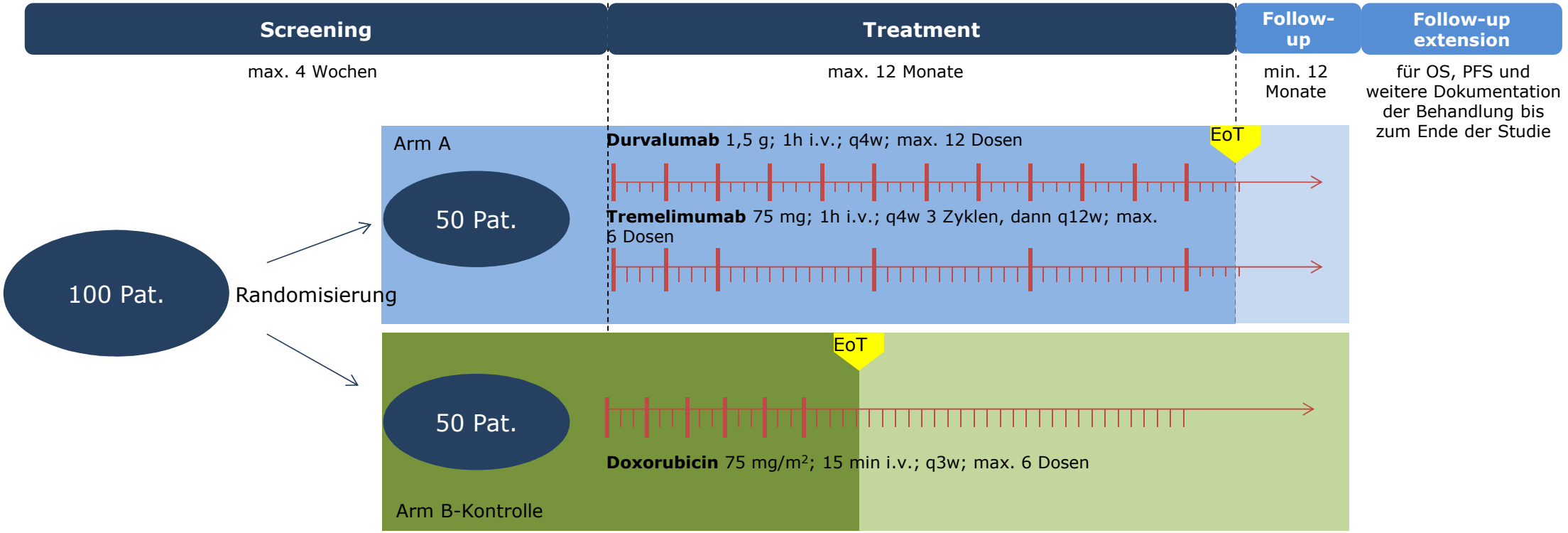
Evidenz zur Immuntherapie bei Weichgewebesarkomen

REGIMEN	n	mPFS [months]	3m-PFS	6m-PFS	ORR (RECIST)	INCLUDED SUBTYPES	RESPONDING SUBTYPES	REF
Pembrolizumab (SARC028)	42 (STS)	4.2	55 %	NA	18 %	4 (UPS, LPS, LMS, SS)	UPS, LPS, SS	Tawbi
Nivolumab	43	1.7	~35 %	15 %	5 %	> 10 (ASPS, UPS, LMS, LPS, ES, SS, MPNST, …)	ASPS, LMS	D'Angelo
Nivolumab + Ipilimumab	42	4.1	~60 %	28 %	16 %	> 10 (ASPS, UPS, LMS, LPS, ES, SS, MPNST, …)	LMS, UPS, Myxofibro, Angio	D'Angelo
Axitinib + Pembrolizumab	33	4.7	70 %	50 % (**38 %**)	25 % (**55 %**)	Several (**ASPS 36 %**)	ASPS, LMS, ES	Wilky
Sunitinib	50	1.8	39 %	22 %	2 %	Several (LMS 23 %, SS 8 %, …)	DSRCT	George
Sunitinib + Nivolumab (IMMUNOSARC)	50	5.9	69 %	50 %	11 %	Several (SS 18 %, **ASPS 6 %**)	ASPS, Angio, EMC, SS	Martin-Broto

AIO-Studien-gGmbH

DR. NOTGHI CONTRACT RESEARCH N

MEDISARC - Studiendesign



EoT= "End of Treatment"

GISG Study Portfolio

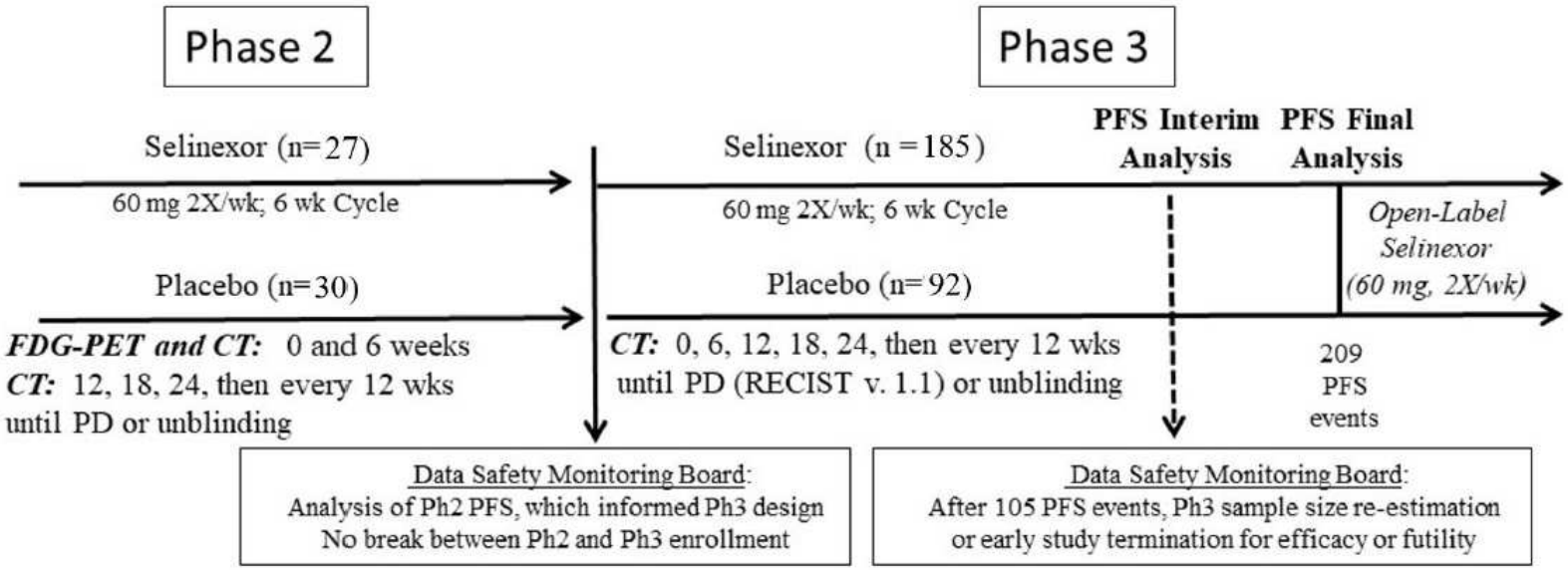
- **GISG-10:** Trabectedin combined with regional hyperthermia as 2nd line treatment for advanced STS (**Hyper-TET**, Issels / Lindner)
- **GISG-11:** QoL in patients with STS undergoing palliative chemotherapy or treatment with Pazopanib (**PazoQoL**, Schuler)
- GISG-12: Patient directed intervention towards a multidimensional recommendation guideline to improve the QoL for STS patients under palliative treatment with Trabectedin (**YonLife**, Schuler)
- **GISG-13:** 1st line Trabectedin in elderly "unsuited" patients incl. geriatric assessment (**E-TRAB,** Kasper)
- GISG-14: Data collection of STS patients treated with Trabectedin (**ReTraSarc**, Pink / Reichardt)*
- ➢ **GISG-15:** Immunotherapy with Nivolumab plus Trabectedin in advanced STS (**NiTraSarc**, Pink)
- **GISG-16:** Trabectedin plus Olaparib in solid tumors harboring DNA repair deficiencies (**Top-Art**, Fröhling)
- GISG-17: Doxorubicin Rechallenge plus Olaratumab (**OlaReDo**, Pink) > **DexraReDo**
- **GISG-18:** German Interdisciplinary Sarcoma Registry (**GISAR**, Pink / Reichardt)
- GISG-19: Predictive value of liquid biopsy (cfDNA) in high-risk GIST patients (**cfDNA GIST**, von Bubnoff)

*Pink D et al. J Clin Oncol 2020; 38 (suppl; abstr 11554)

SEAL: Selinexor (Karyopharm) bei Liposarkomen (DDLS)

Study Design Overview:

This is a Phase 2-3, multicenter, randomized, double-blind, placebo-controlled study. Approximately 334 total patients will be randomized (57 patients in Phase 2 and approximately 277 patients in Phase 3). Enrollment in Phase 2 has been completed. There was no break between Phase 2 and Phase 3 enrollment. The study overview is presented in the figure below:

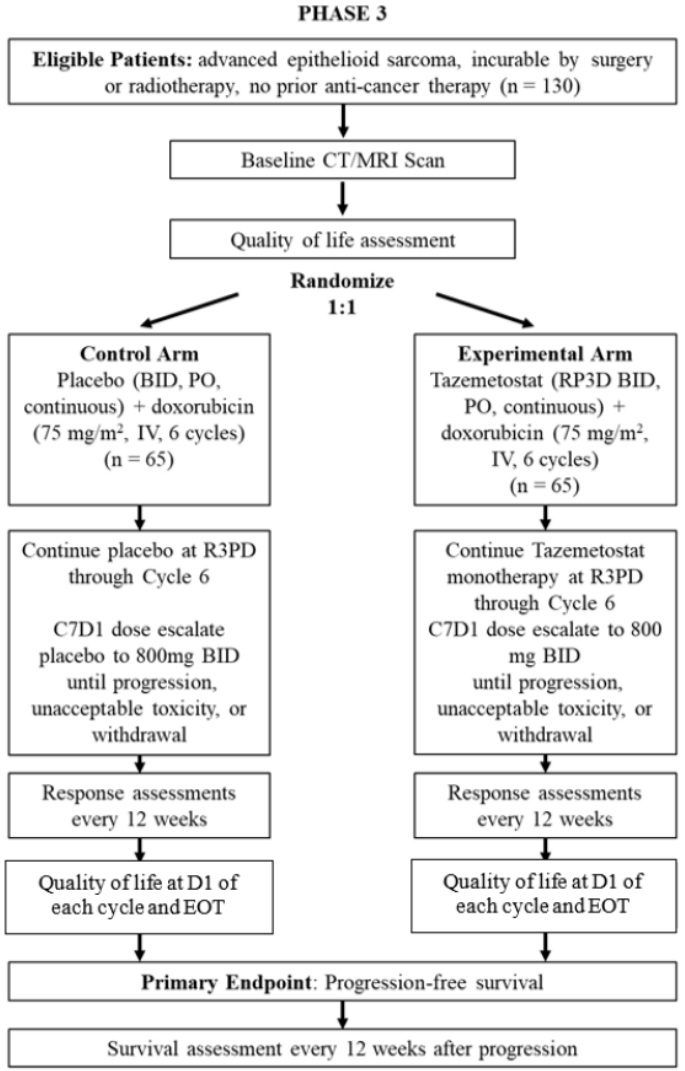


Patients in the placebo arm who have PD will have the option to cross over to open-label selinexor.

EZH-301: Tazemetostat (Epizyme) bei Epithelioiden Sarkomen

FDA approves tazemetostat for advanced epithelioid sarcoma

On January 23, 2020, the Food and Drug Administration granted accelerated approval to tazemetostat (TAZVERIK, Epizyme, Inc.) for adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.



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ADP-A2M4 SPEAR T-Zell Therapie (Adaptimmune)

Phase I, “first-in-human” Dosis-eskalierende Studie (n = 38) zur ADP-A2M4 SPEAR **T-Zell Therapie** in der Subset Analyse der **Synovial Sarkome**

- **N = 16** mit Synovial Sarkomen (mittleres Alter: 49 Jahre [Range: 31-76])

- T-Zellen werden isoliert, transduziert, expandiert und re-infundiert.
  - **AEs**: Leukopenie, Neutropenie, Thrombozytopenie, Anämie, Fatigue, Übelkeit, Durchfall
  - 1 tödliche aplastische Anämie (Alter: 76 Jahre + hoch-dosiertes Konditionierungs Regime)
- RECIST **Ansprechen**: 7 PR, 7 SD, 1 PD } **ORR = 7/16 = 44 %** [**DCR ~90 %; DoR ~28 Wo]**

➢ **SPEARHEAD-1*** (Phase II Studie) bei Synovial Sarkomen und myxoid / rundzelligen Liposarkomen rekrutiert derzeit.

*Hong DS et al. J Clin Oncol 2020; 38 (suppl; abstr 102); *Araujo DM et al. J Clin Oncol 2020; 38 (suppl; abstr TPS11569)*

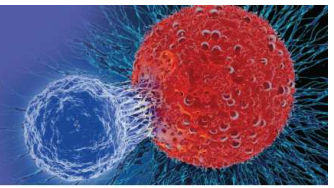
SPEARHEAD-1:

A Phase 2 Trial of ADP-A2M4 SPEAR T-Cells in Patients with Advanced Synovial Sarcoma or Myxoid/Round Cell Liposarcoma

Dejka Araujo[1], Mihaela Druta[2], Mark Agulnik[3], Sandra D'Angelo[4], Jean-Yves Blay[5], Sandra Strauss[6], Claudia Valverde[7], Albiruni Razak[8], Erin Van Winkle[9], Trupti Trivedi[9], Swethajit Biswas[9], Dennis Williams[9], Elliot Norry[9]

[1]MD Anderson Cancer Center, Houston, TX, USA, [2]Moffitt Cancer Center, Tampa, FL, USA, [3]Northwestern University, Feinberg School of Medicine, Chicago, IL, USA, [4]Memorial Sloan Kettering Cancer Center, New York, NY, USA, [5]Centre Léon Bérard, Lyon, France, [6]University College London Hospitals, London, UK, [7]Vall D'Hebron University Hospital, Barcelona, Spain, [8]Princess Margaret Cancer Centre, Ontario, Canada, [9]Adaptimmune, Philadelphia, PA, USA, and Abingdon, Oxfordshire, UK

A device-friendly version of this poster (with additional content) can be viewed by clicking here:
http://adaptimmune.posterlab.info/ASCO2020/



Background

- ADP-A2M4 SPEAR T-cells target MAGE-A4⁺ tumors (**Figure 1**)
- MAGE-A4 is highly expressed in synovial sarcoma and myxoid/round cell liposarcoma (MRCLS) in the context of HLA-A*02 (**Figure 2**)
- This Phase 2 trial was initiated based on the favorable benefit:risk profile of ADP-A2M4 observed in a Phase 1 trial (NCT03132922), which demonstrated compelling clinical responses in patients with synovial sarcoma

Figure 1. SPEAR T-cells

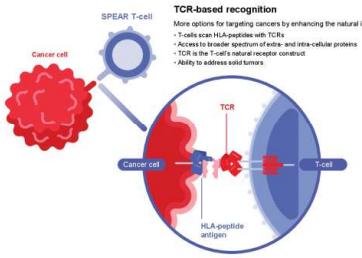
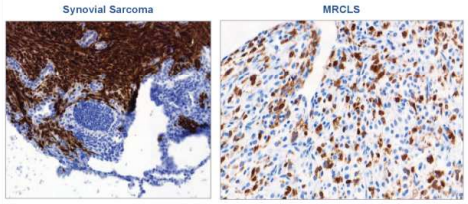


Figure 2. MAGE-A4 expression (IHC analysis)



SPEAR T-cell mechanism of action video can be viewed by clicking here:
https://youtu.be/zdI8IGXoQd0

Full trial details from ClinicalTrials.gov can be viewed by clicking here:
https://clinicaltrials.gov/ct2/show/NCT04044768

Soft tissue sarcomas

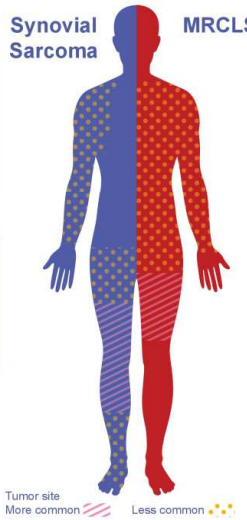
- >50 subtypes, including liposarcoma and synovial sarcoma
- Prognosis in advanced disease remains unfavorable

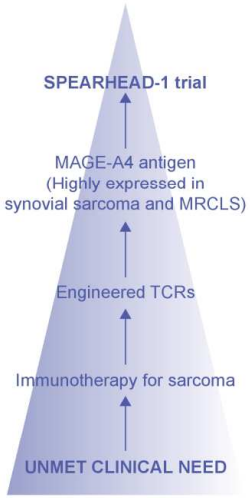
Synovial Sarcoma

- ~800–1000 new cases/year in the United States
- Often occurs in patients aged <40 years
- High metastatic potential

MRCLS

- ~750 new cases/year in the United States
- Typically presents at 35–55 years of age
- One-third MRCLS become metastatic





SPEARHEAD-1 trial (NCT04044768)

- Recruiting 45 patients from North America and Europe
- Advanced synovial sarcoma or MRCLS, prior chemotherapy, HLA-A*02 and MAGE-A4 positive

Trial Details

- Primary objective is to evaluate the efficacy of ADP-A2M4 in patients with synovial sarcoma or MRCLS
  - Determined by the Overall Response Rate, defined as incidence of complete or partial responses as assessed by independent RECIST v1.1 review
- We are currently recruiting trial participants
  - Total of 20 sites open: 14 in the US, 1 in Canada, 2 in France, and 3 in Spain
- Trial design and engineered T-cell pathway are shown below (**Figure 3** and **Figure 4**)

Figure 3. SPEARHEAD-1 trial design

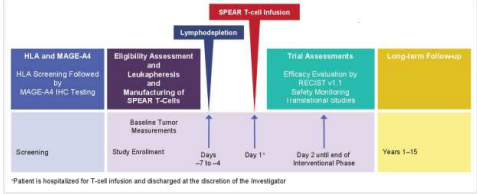
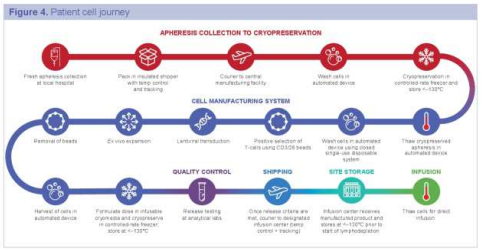


Figure 4. Patient cell journey



Principal investigator details:

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- daraujo@mdanderson.org

Abbreviations

HLA, human leukocyte antigen; IHC, immunohistochemistry; MAGE-A4, melanoma-associated antigen-A4; MRCLS, myxoid/round cell liposarcoma; PD, progressive disease; RECIST, response evaluation criteria in solid tumors; SPEAR, specific peptide enhanced affinity receptor; TCR, T-cell receptor

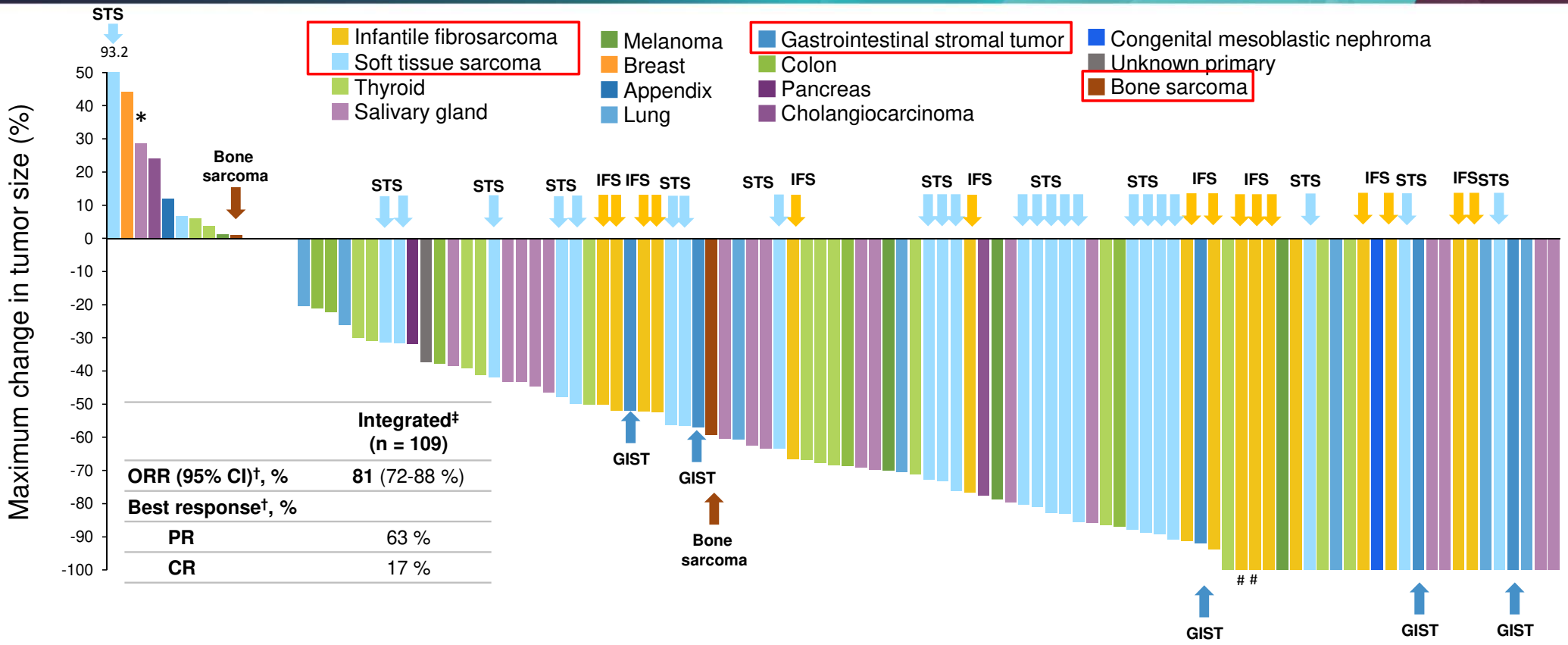
ASCO Annual Meeting, May 29-June 2, 2020 (Virtual Format)

UMM UNIVERSITÄTSMEDIZIN MANNHEIM

Araujo DM et al. J Clin Oncol 2020; 38 (suppl; abstr TPS11569)

Medizinische Fakultät Mannheim der Universität Heidelberg
Universitätsklinikum Mannheim

Larotrectinib has shown efficacy across tumor types, including Sarcomas and GIST

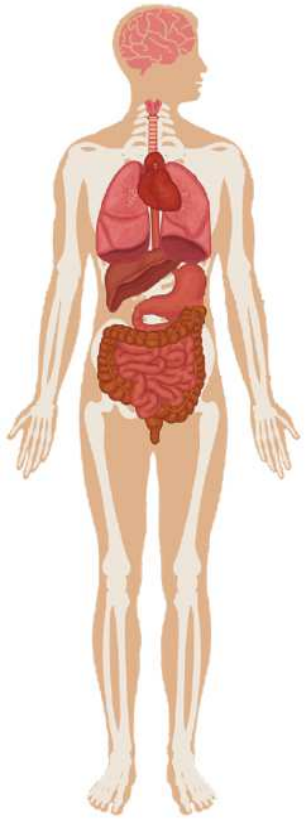


Investigator response assessments, as of July 30, 2018. Note: Two patients are not shown here; these patients discontinued treatment prior to any post-baseline tumor measurements.
*Patient had TRKC solvent front resistance mutation (G623R) at baseline due to prior therapy; †RECIST v1.1; ‡Includes 9 unconfirmed PRs pending confirmation; does not include 13 patients continuing on study and awaiting initial response assessment; #Surgical CR. CI, confidence interval; CR, complete response; GIST, gastrointestinal stromal tumor; IFS, infantile fibrosarcoma; ORR, objective response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; STS, soft-tissue sarcoma.

Lassen UN et al. ESMO 2018. Abstract 4090.

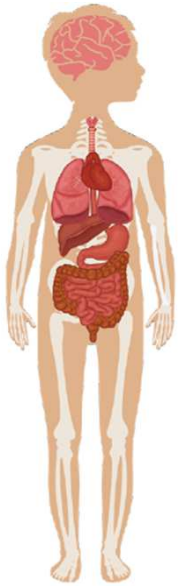
Incidence of NTRK gene fusions in different tumours varies

Adult



- Brain cancers (0.4-3.1%)[1]
- Salivary (MASC; 100%)[1]
- Secretory breast cancer (92%)[2]
- Cholangiocarcinoma (3.6%)[1]
- Thyroid cancer (1.5-14.5%)[1]
- Lung cancer (0.2-3.3%)[1]
- Colon cancer (1.5%)[1]
- Melanoma (0.3%)[1,3]
- **Sarcomas** (1%)[3]
- Spitzoid neoplasms (16.4%)[4]

Paediatric

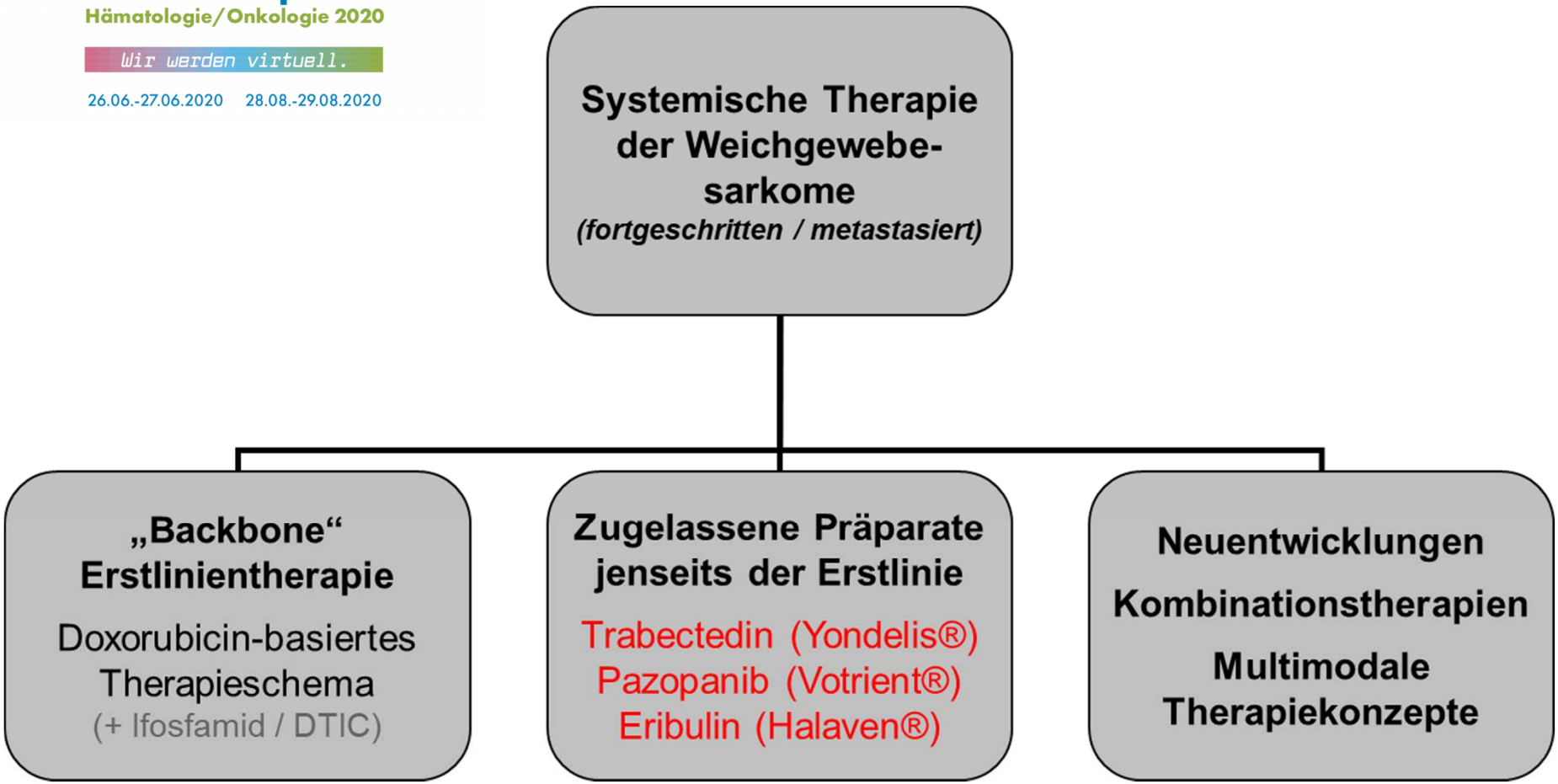


- Spitzoid neoplasms (16.4%)[4]
- Gliomas (7.1%)[1]
- Thyroid (9.4-25.9%)[5,6]
- **Infantile fibrosarcoma** (91-100%)[7]
- Congenital nephroma (83%)[1]
- Secretory breast cancer (92%)[2]
- **Sarcomas** (1%)[3]

The challenge remains how to <u>identify</u> your patients!

[1]Vaishnavi A et al. Cancer Discov 2015; 5: 25-34; [2]Tognon C et al. Cancer Cell 2002; 2: 367-376; [3]Stransky N et al. Nat Communications 2014; 5: 4846; [4]Wiesner T et al. Nat Communications 2014; 5: 3116; [5]Ricarte-Filho JC et al. J Clin Invest 2013; 123: 4935-4944; [6]Prasad ML et al. Cancer 2016; 122: 1097-1107; [7]Bourgeois JM et al. Am J Surg Pathol 2000; 24: 937-946.

Sarcoma of The Year 2020: **„NTRK fusion positive adult sarcomas“**


Systemische Therapie der Weichgewebe-sarkome
(fortgeschritten / metastasiert)
„Backbone“ Erstlinientherapie
Doxorubicin-basiertes Therapieschema
(+ Ifosfamid / DTIC)
Zugelassene Präparate jenseits der Erstlinie
Trabectedin (Yondelis®)
Pazopanib (Votrient®)
Eribulin (Halaven®)
Neuentwicklungen
Kombinationstherapien
Multimodale Therapiekonzepte

Take-Home-Messages

- **Die Doxorubicin basierte Chemotherapie bleibt der „Backbone“ in der Erstlinien-behandlung fortgeschrittener / metastasierter Weichgewebesarkome.**
- **Olaratumab konnte keinen Überlebensvorteil in Kombination mit Doxorubicin erzielen.**
- **Mit Trabectedin, Pazopanib und Eribulin stehen jenseits der Erstlinientherapie wirksame und gut verträgliche Medikamente in der metastasierten Situation zur Verfügung.**
- **Weitere Substanzentwicklungen und Therapiekonzepte (Selinexor, Immuntherapien, T-Zell Therapien) werden im Rahmen von klinischen Studien geprüft.**

Diskussion & Fragen

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Medizinische Fakultät Mannheim der Universität Heidelberg
Universitätsklinikum Mannheim