To share your e-Eso experience use:
#e_ESO

Soft tissue tumors in childhood

Expert: **Dr Andrea Ferrari**, National Cancer Institute - IRCCS Foundation, Milan, Italy

Discussant: **Dr Andishe Attarbaschi**, St. Anna's Chidren's Hospital, Vienna, Austria

SOFT TISSUE TUMORS IN CHILDHOOD

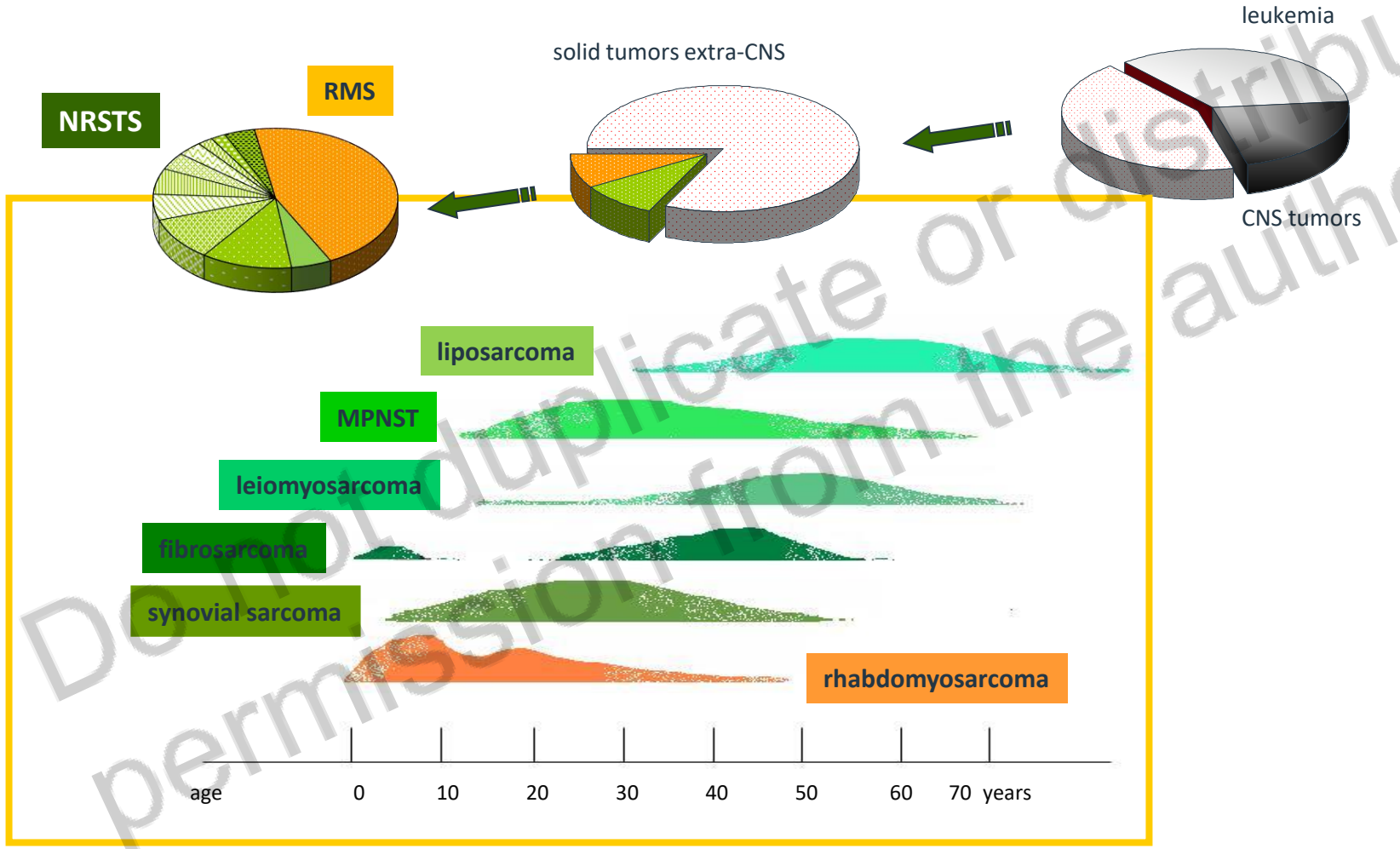
Andrea Ferrari

andrea.ferrari@istitutotumori.mi.it

SOFT TISSUE TUMORS
IN CHILDHOOD… in 30 minutes?

PEDIATRIC SOFT TISSUE SARCOMAS

very heterogeneus group of different mesenchymal malignancies (over 50 distinct histologic subtypes, classified on a histogenic basis according to the adult tissue they resemble), that account for approximately 4-5% of childhood cancers, with a different biology and clinical behaviour varying from relatively benign to highly malignant



RHABDOMYOSARCOMA (RMS)

- typical embryonal tumor of childhood
- high grade of malignancy, local invasiveness and a marked propensity to metastasize…

  …all RMS patients should be assumed to have micrometastatic disease at diagnosis, so systemic therapy is definitely recommended for all patients
- (generally) good response to chemotherapy (90% response rate) and radiotherapy

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

- rare tumors
- most are tumor entities typically found in adults
- extremely heterogeneus tumors
- scarcely sensitive to chemotherapy

PEDIATRIC SOFT TISSUE SARCOMAS

- Adult medical oncologists and pediatric oncologists do mean different things when they talk about STSs
- Patient outcomes vary according to age, and survival rate drops are observed as age increases

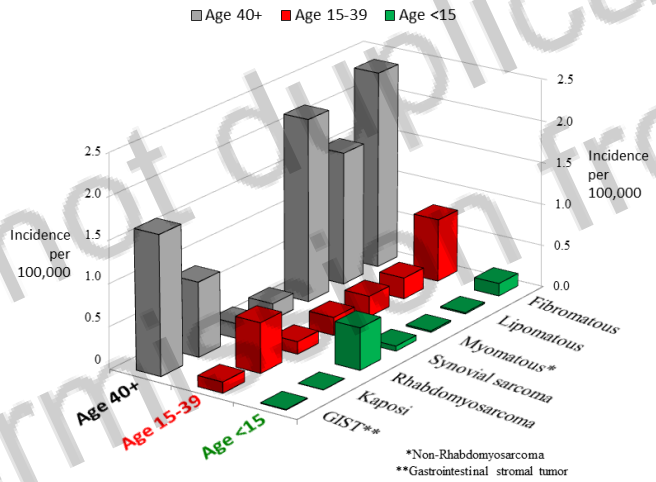
Received: 20 December 2017 | Revised: 16 January 2018 | Accepted: 24 January 2018
DOI: 10.1002/pbc.27013

REVIEW

WILEY Pediatric Blood & Cancer

The challenge of the management of adolescents and young adults with soft tissue sarcomas

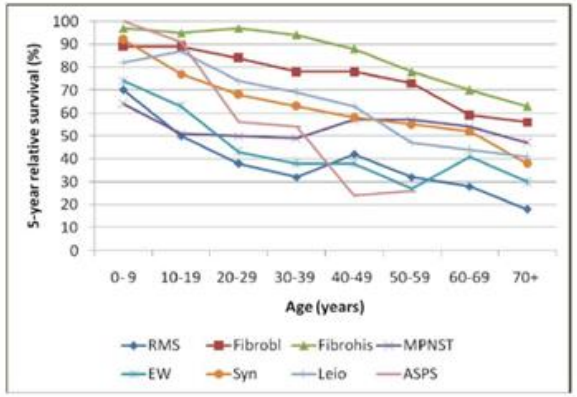
Andrea Ferrari[1] | Archie Bleyer[2] | Shreyaskumar Patel[3] | Stefano Chiaravalli[1] | Patrizia Gasparini[4] | Michela Casanova[1]



Pediatr Blood Cancer 2011;57:943–949

Soft Tissue Sarcoma Across the Age Spectrum: A Population-Based Study From the Surveillance Epidemiology and End Results Database

Andrea Ferrari, MD,[1] Iyad Sultan, MD,[2*] Tseng Tien Huang, PhD,[3] Carlos Rodriguez-Galindo, MD,[4] Ahmad Shehadeh, MD,[5] Cristina Meazza, MD,[1] Kirsten K. Ness, PhD,[3] Michela Casanova, MD,[1] and Sheri L. Spunt, MD[6,7]

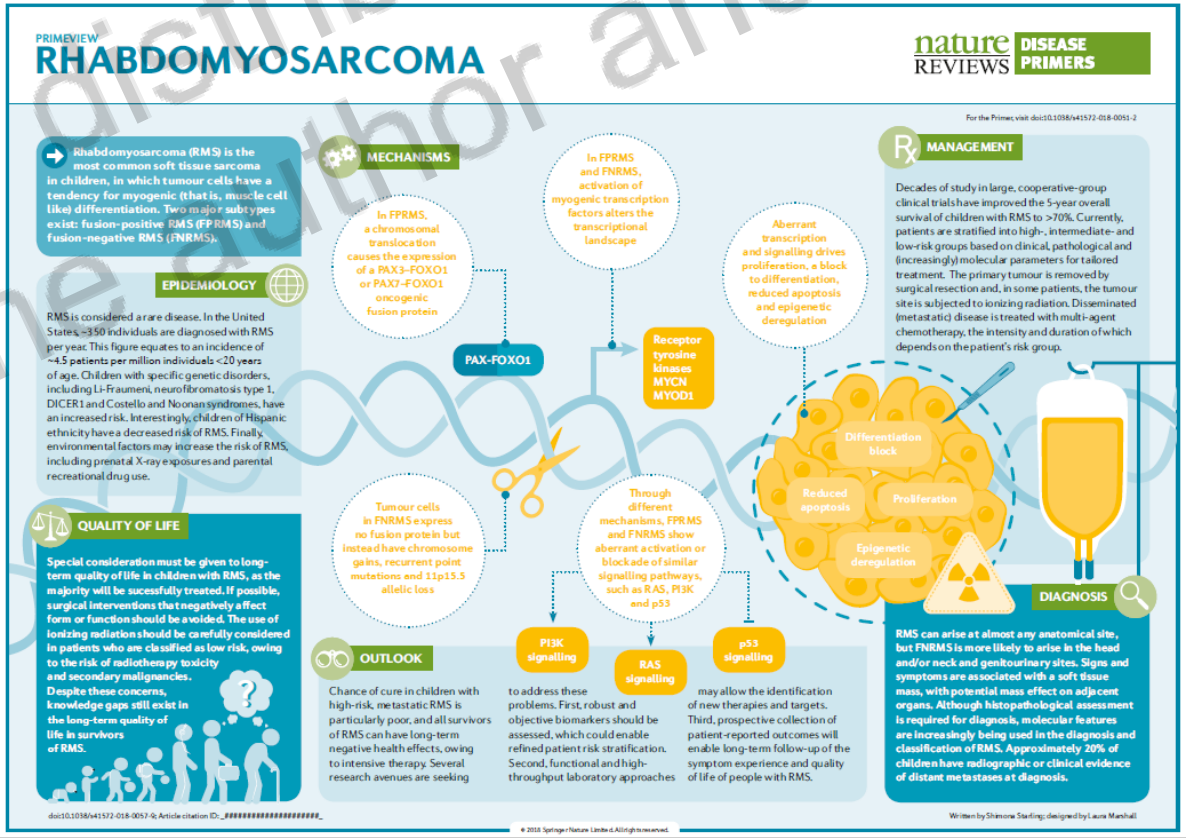


RHABDOMYOSARCOMA (RMS)

NATURE REVIEWS | DISEASE PRIMERS | Article citation ID: (2019) 5:1

Rhabdomyosarcoma

Stephen X. Skapek[1,2], Andrea Ferrari[3], Abha A. Gupta[4], Philip J. Lupo[5], Erin Butler[1], Janet Shipley[6], Frederic G. Barr[7] and Douglas S. Hawkins[8]*



RHABDOMYOSARCOMA (RMS)

Improvement in survival achieved in the past decades has been related to a treatment strategy based on the following aspects:

1) **Centralization of care** in specialized centers and wide collaboration on a national and international level

2) **High rate of inclusion** in **cooperative multi-institutional clinical trials**, in order to collect a large number of patients

1) A risk-adapted treatment strategy, i.e. different prognostic factors are used to stratify treatment intensity in order to improve cure rates in patients with less favorable disease by using more intensive therapy, while avoiding over-treatment and containing side effects without jeopardizing the results for patients with more favorable disease

2) A multidisciplinary treatment approach, including surgery, radiotherapy and particularly multi-agent chemotherapy

Iyad Sultan[1] and Andrea Ferrari[1]

EXPERT REVIEWS Selecting multimodal therapy for rhabdomyosarcoma

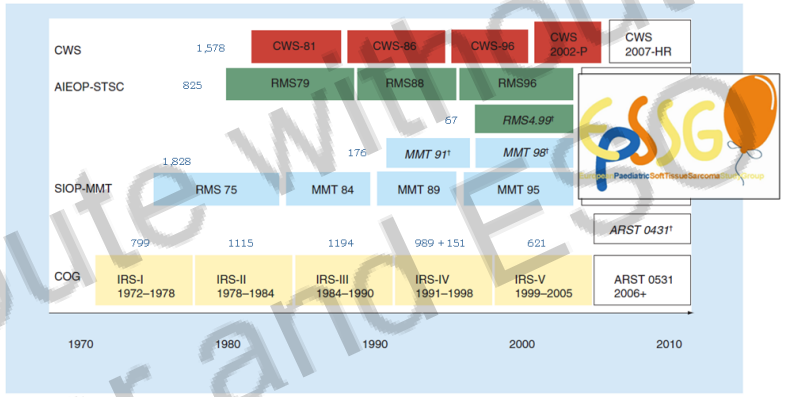


Figure 2. Major clinical trials on rhabdomyosarcoma conducted by international cooperative groups over the years. †Metastatic patients.
AIEOP-STSC: Associazione Italiana Ematologia Oncologia Pediatrica – Soft Tissue Sarcoma Committee; ARST: A Studies-Rhabdomyosarcoma Soft Tissue Sarcoma; COG: Children's Oncology Group; CWS: Co-operative Weichteilsarkomen Studie; EpSSG: European Pediatric Soft Tissue Sarcoma Study Group; IRS: Intergroup Rhabdomyosarcoma Study; MMT: Malignant mesenchymal tumor; RMS: Rhabdomyosarcoma; SIOP-MMT: International Society of Pediatric Oncology – Malignant Mesenchymal Tumor Committee.

No. Randomised Patients ~ 10,000 patients

Received: 19 July 2016 | Revised: 28 September 2016 | Accepted: 12 October 2016
DOI: 10.1002/pbc.26348

RESEARCH ARTICLE

WILEY Pediatric Blood & Cancer aspho

Access to clinical trials for adolescents with soft tissue sarcomas: Enrollment in European pediatric Soft tissue sarcoma Study Group (EpSSG) protocols

Andrea Ferrari[1] | Annalisa Trama[2] | Angela De Paoli[3] | Christophe Bergeron[4] | Johannes H. M. Merks[5] | Soledad Gallego[9] | Heidi Gemma Gatta[2] | Gianni

TABLE 2 Observed and expected cases with O/E ratio and 95% CI

	Observed	Expected	O/E ratio	95% CI	
0–14 years old					
RMS	1,139	1,488	0.77	0.72	0.81
NRSTS	615	1,234	0.50	0.46	0.54
All STS	1,754	2,722	0.64	0.61	0.68
15–19 years old					
RMS	201	315	0.64	0.55	0.73
NRSTS	163	902	0.18	0.15	0.21
All STS	364	1,217	0.30	0.27	0.33

RHABDOMYOSARCOMA (RMS)

related to the TUMOR
- histology /fusion status
- tumor size
- tumor site
- stage

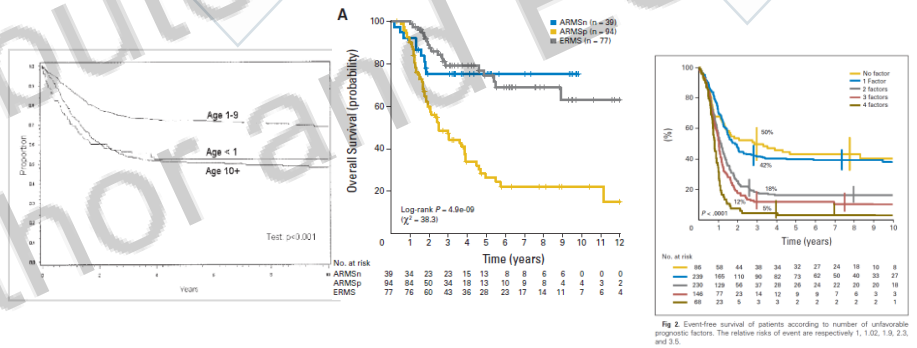
related to the PATIENT
- age
- (host biology?)

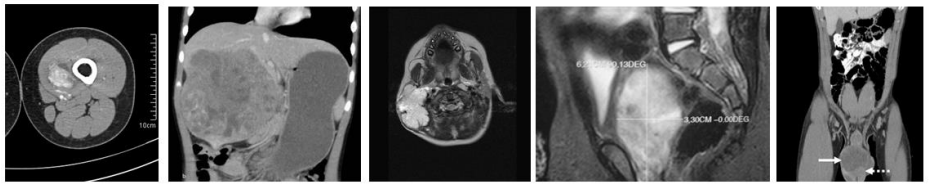
related to the TREATMENT
- modalities used
- response to therapy

Improvement in survival achieved in the past decades has been related to a treatment strategy based on the following aspects:

1) **Centralization of care** in specialized centers and wide collaboration on a national and international level

2) **High rate of inclusion** in **cooperative multi-institutional clinical trials**, in order to collect a large number of patients





1) A **risk-adapted treatment strategy**, i.e. different prognostic factors are used to stratify treatment intensity in order to improve cure rates in patients with less favorable disease by using more intensive therapy, while avoiding over-treatment and containing side effects without jeopardizing the results for patients with more favorable disease

2) A **multidisciplinary treatment approach**, including surgery, radiotherapy and particularly multi-agent chemotherapy

C	fav	II-III	N0	fav	any	18%	72% - 88%
D	fav	II-III	N0	unfav	fav	9%	80% - 85%
E	fav	II-III	N0	unfav	unfav	27%	55% - 60%
F	fav	II-III	N1	any	any	8%	50% - 60%
G	unfav	I-II-III	N0	any	any	20%	50% - 60%
H	unfav	I-II-III	N0	any	any	6%	40% - 50%

RHABDOMYOSARCOMA (RMS)

RMS 2005 – a protocol for localised RMS

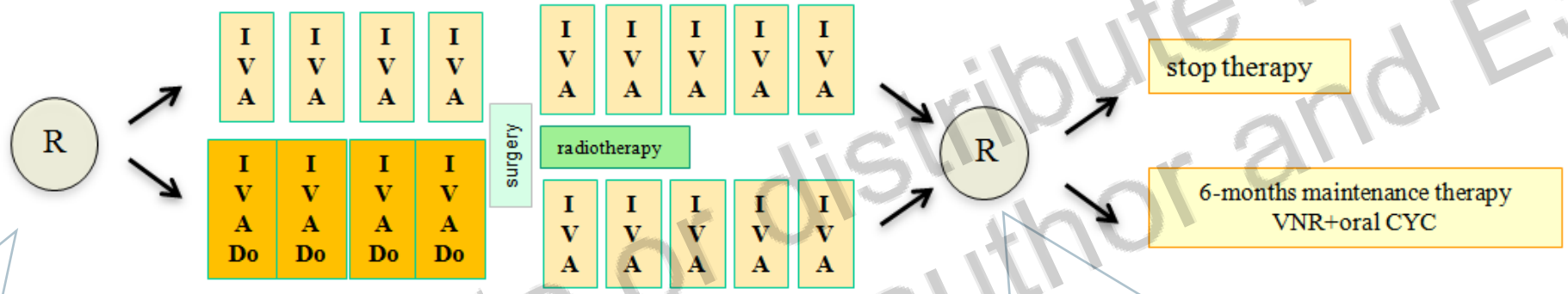
RISK GROUP	HIST	IRS	N	SITE	SIZE & AGE	%	EFS-OS	
A	fav	I	N0	any	fav	6%	90-95%	VA
B	fav	I	N0	any	unfav	6%	78% - 90%	IVA+VA or IVA ± RXT
C	fav	II-III	N0	fav	any	18%	72% - 88%	
D	fav	II-III	N0	unfav	fav	9%	80% - 85%	
E	fav	II-III	N0	unfav	unfav	27%	55% - 60%	1° random: IVA + RXT / IVADo + RXT → 2° random: stop-therapy / maintenance VNR-oral CTX
F	fav	II-III	N1	any	any	8%	50% - 60%	
G	unfav	I-II-III	N0	any	any	20%	50% - 60%	
H	unfav	I-II-III	N0	any	any	6%	40% - 50%	IVADo + RXT + VNR-oral CTX

EuropeanPaediatricSoftTissueSarcomaStudyGroup

RHABDOMYOSARCOMA (RMS)

for over 3 decades, the same standard chemotherapy, i.e. IVA for 6 months

Ifosfamide 3 g/sqm x 2 days,
Vincristine 1.5 mg/sqm, day 1
Actinomycin-D 1.5 mg/sqm, day 1



The anthracycline question
Might RMS patients benefit from a greater doxorubicin dose intensity in the initial period of their treatment?

The IVADo Regimen—A Pilot Study with Ifosfamide, Vincristine, Actinomycin D, and Doxorubicin in Children with Metastatic Soft Tissue Sarcoma

A Pilot Study on behalf of the European pediatric Soft tissue sarcoma Study Group

The maintenance treatment question
after completing the conventional chemotherapy, give regular and frequent low doses of drugs (**metronomic" therapy**), with a view to obtaining an **anti-angiogenic effect**

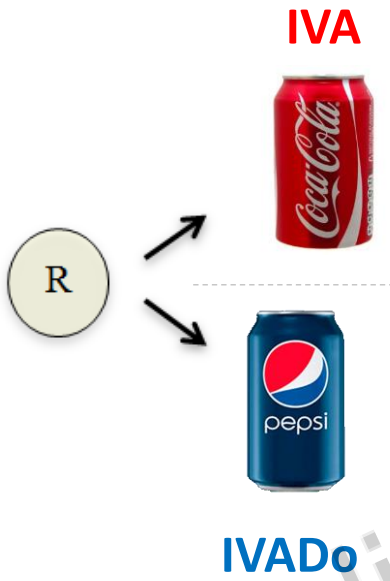
Vinorelbine in Previously Treated Advanced Childhood Sarcomas

Evidence of Activity in Rhadbomyosarcoma

Vinorelbine and Low-Dose Cyclophosphamide in the Treatment of Pediatric Sarcomas

Pilot Study for the Upcoming European Rhabdomyosarcoma Protocol

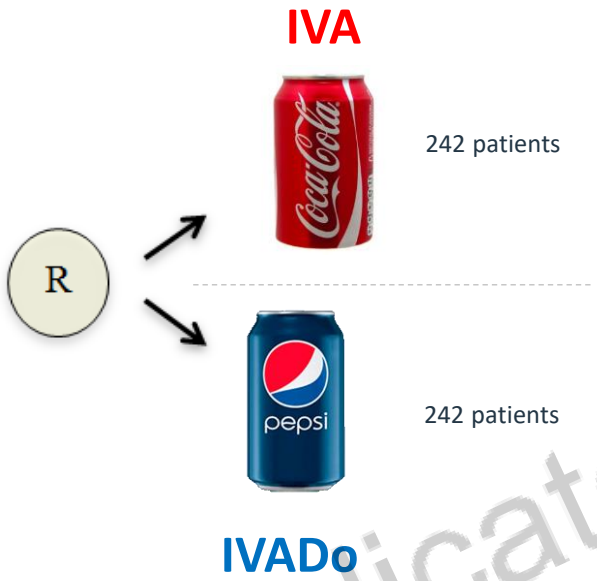
RHABDOMYOSARCOMA (RMS)



The anthracycline question

The maintenance treatment question

RHABDOMYOSARCOMA (RMS)



Doxorubin does **not** add any significant "anti RMS activity" to a standard multidrug regimen

Lancet Oncol 2018

Addition of dose-intensified doxorubicin to standard chemotherapy for rhabdomyosarcoma (EpSSG RMS 2005): a multicentre, open-label, randomised controlled, phase 3 trial

Gianni Bisogno, Meriel Jenney, Christophe Bergeron, Soledad Gallego Melcón, Andrea Ferrari, Odile Oberlin, Modesto Carli, Michael Stevens, Anna Kelsey, Angela De Paoli, Mark N Gaze, Helene Martelli, Christine Devalck, Johannes H Merks, Myriam Ben-Arush, Heidi Glosli, Julia Chisholm, Daniel Orbach, Veronique Minard-Colin, Gian Luca De Salvo, for the European paediatric Soft tissue sarcoma Study Group

Response rate :
- IVADo 71.0%
- IVA 66.3 %

High risk Group:
results better than expected
3-year EFS
estimated: **50-55%**
observed: **66%**

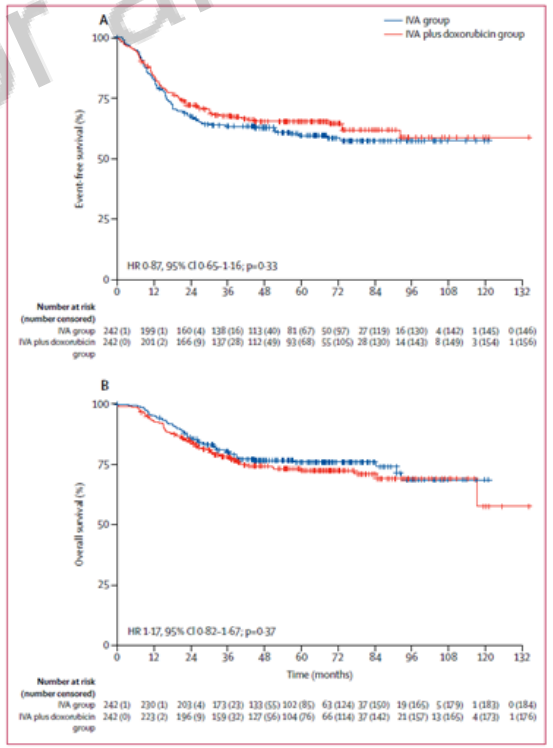


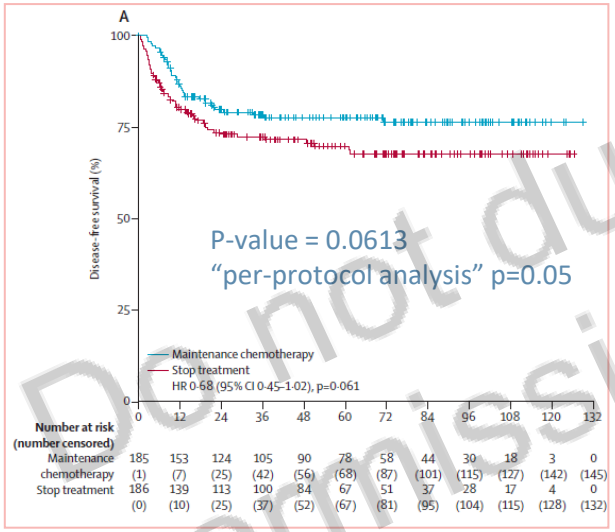
Figure 3: Kaplan-Meier plots for event-free survival (A) and overall survival (B) in the intention-to-treat population
IVA=ifosfamide, vincristine, and dactinomycin. HR=hazard ratio.

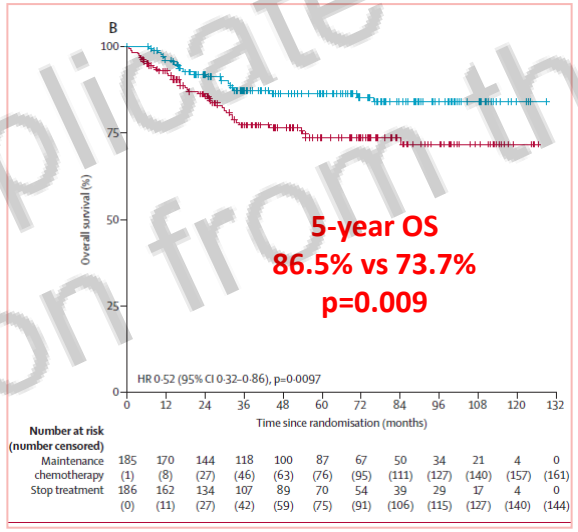
RHABDOMYOSARCOMA (RMS)

Lancet Oncol 2019; 20: 1566–75

Vinorelbine and continuous low-dose cyclophosphamide as maintenance chemotherapy in patients with high-risk rhabdomyosarcoma (RMS 2005): a multicentre, open-label, randomised, phase 3 trial

Gianni Bisogno, Gian Luca De Salvo, Christophe Bergeron, Soledad Gallego Melcón, Johannes H Merks, Anna Kelsey, Helene Martelli, Veronique Minard-Colin, Daniel Orbach, Heidi Glosli, Julia Chisholm, Michela Casanova, Ilaria Zanetti, Christine Devalck, Myriam Ben-Arush, Peter Mudry, Sima Ferman, Meriel Jenney, Andrea Ferrari*, for the European paediatric Soft tissue sarcoma Study Group*





this study demonstrated that adding maintenance treatment with vinorelbine and low-dose oral cyclophosphamide for patients with high-risk RMS in complete remission after standard treatment improves survival and is safe and well tolerated

RHABDOMYOSARCOMA (RMS)

Vinorelbine and continuous low-dose cyclophosphamide as maintenance chemotherapy in patients with high-risk rhabdomyosarcoma (RMS 2005): a multicentre, open-label, randomised, phase 3 trial

Gianni Bisogno, Gian Luca De Salvo, Christophe Bergeron, Soledad Gallego Melcón, Johannes H Merks, Anna Kelsey, Helene Martelli, Veronique Minard-Colin, Daniel Orbach, Heidi Glosli, Julia Chisholm, Michela Casanova, Ilaria Zanetti, Christine Devalck, Myriam Ben-Arush, Peter Mudry, Sima Ferman, Meriel Jenney, Andrea Ferrari*, for the European paediatric Soft tissue sarcoma Study Group*

first randomised study to demonstrate a survival benefit related to an experimental chemotherapy regimen in RMS over the past three decades

VOLUME 36 · NUMBER 27 · SEPTEMBER 20, 2018
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Addition of Vincristine and Irinotecan to Vincristine, Dactinomycin, and Cyclophosphamide Does Not Improve Outcome for Intermediate-Risk Rhabdomyosarcoma: A Report From the Children's Oncology Group

Douglas S. Hawkins, Yueh-Yun Chi, James R. Anderson, Jing Tian, Carola A.S. Arndt, Lisa Bomgaars, Sarah S. Donaldson, Andrea Hayes-Jordan, Leo Mascarenhas, Mary Beth McCarville, Jeannine S. McCune, Geoff McCowage, Lynn Million, Carol D. Morris, David M. Parham, David A. Rodeberg, Erin R. Rudzinski, Margarett Shnorhavorian, Sheri L. Spunt, Stephen X. Skapek, Lisa A. Teot, Suzanne Wolden, Torunn I. Yock, and William H. Meyer

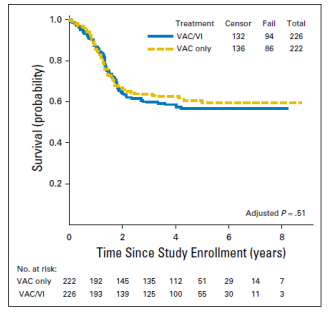
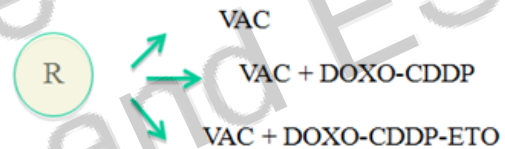


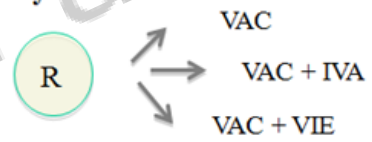
Fig 3. Event-free survival by treatment arm. VAC, vincristine, dactinomycin, and cyclophosphamide; VI, vincristine and irinotecan.

Children's Oncology Group

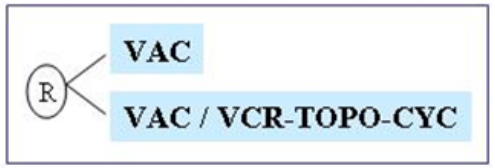
IRS-III study



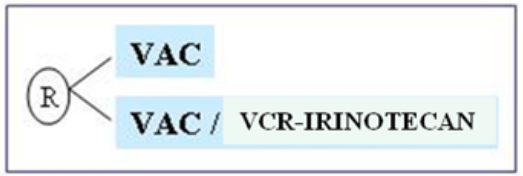
IRS-IV study



D9803 study



ARST0531 study



RHABDOMYOSARCOMA (RMS)

Comment

Vinorelbine and continuous low-dose cyclophosphamide as maintenance chemotherapy in patients with high-risk rhabdomyosarcoma (RMS 2005): a multicentre, open-label, randomised, phase 3 trial

Gianni Bisogno, Gian Luca De Salvo, Christophe Bergeron, Soledad Gallego Melcón, Johannes H Merks, Anna Kelsey, Helene Martelli, Veronique Minard-Colin, Daniel Orbach, Heidi Glosli, Julia Chisholm, Michela Casanova, Ilaria Zanetti, Christine Devalck, Myriam Ben-Arush, Peter Mudry, Sima Ferman, Meriel Jenney, Andrea Ferrari*, for the European paediatric Soft tissue sarcoma Study Group*

first randomised study to demonstrate a survival benefit related to an experimental chemotherapy regimen in RMS over the past three decades

Editorial

TJ Tumori Journal

Tumori Journal

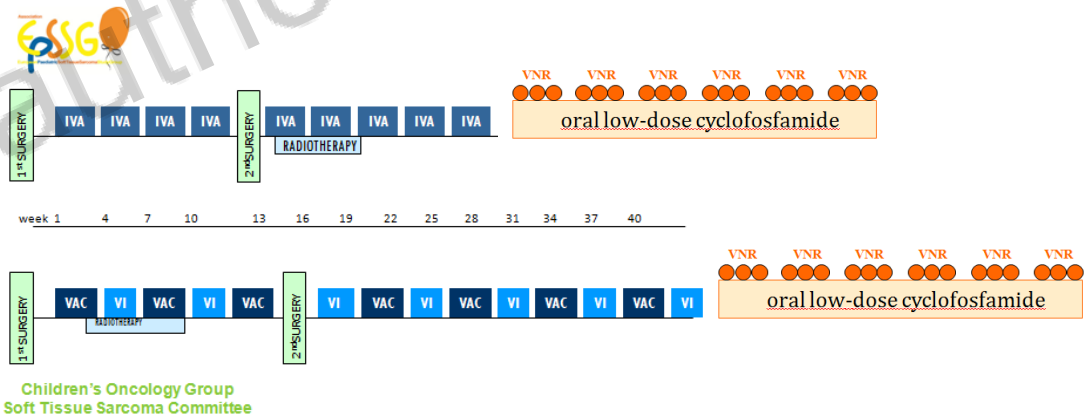
A home run for rhabdomyosarcoma after 30 years: What now?

Andrea Ferrari[1], Patrizia Gasparini[2] and Michela Casanova[1]

News > Medscape Medical News > Conference News > ASCO 2018

After 30 Years, a 'Home Run' for Treating Rhabdomyosarcoma?

Maintenance chemotherapy in rhabdomyosarcoma: the new standard of care



Children's Oncology Group
Soft Tissue Sarcoma Committee

RHABDOMYOSARCOMA (RMS)

Vinorelbine and continuous low-dose cyclophosphamide as maintenance chemotherapy in patients with high-risk rhabdomyosarcoma (RMS 2005): a multicentre, open-label, randomised, phase 3 trial

Gianni Bisogno, Gian Luca De Salvo, Christophe Bergeron, Soledad Gallego Melcón, Johannes H Merks, Anna Kelsey, Helene Martelli, Veronique Minard-Colin, Daniel Orbach, Heidi Glosli, Julia Chisholm, Michela Casanova, Ilaria Zanetti, Christine Devalck, Myriam Ben-Arush, Peter Mudry, Sima Ferman, Meriel Jenney, Andrea Ferrari*, for the European paediatric Soft tissue sarcoma Study Group*

Received: 13 May 2020 | Revised: 12 July 2020 | Accepted: 29 July 2020

DOI: 10.1002/pbc.28649

Pediatric Blood & Cancer

ONCOLOGY: BRIEF REPORT

VIVA (vinorelbine, ifosfamide, vincristine, actinomycin-D): A new regimen in the armamentarium of systemic therapy for high-risk rhabdomyosarcoma

Andrea Ferrari[1] | Stefano Chiaravalli[1] | Marco Zecca[2] | Santina Recupero[2] | Silvia Pascale[3] | Luca Bergamaschi[1] | Michela Casanova[1]

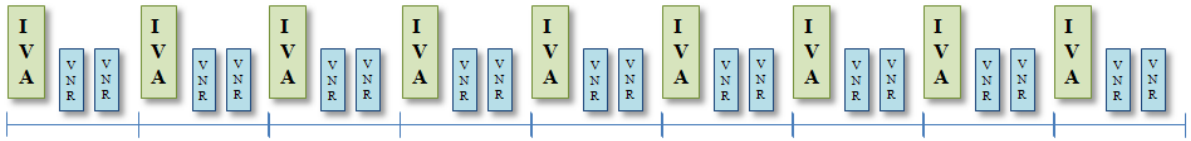
to be clarified if this is the results of the effectiveness of the drugs involved (and in particular vinorelbine)

or

it could be that simply prolonging chemotherapy cured a group of children with the persistence of a limited amount of residual disease at the end of standard treatment…

or

both..

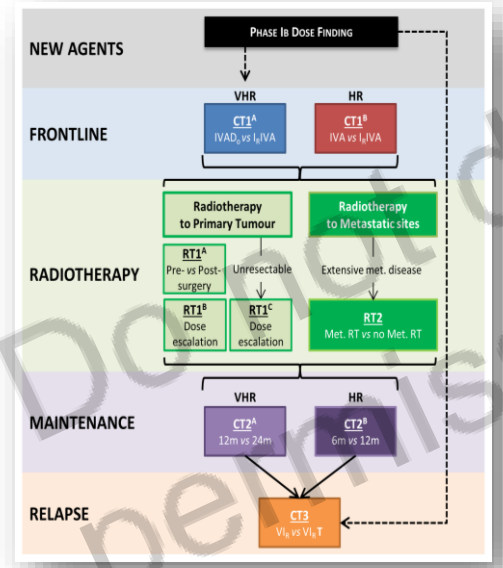


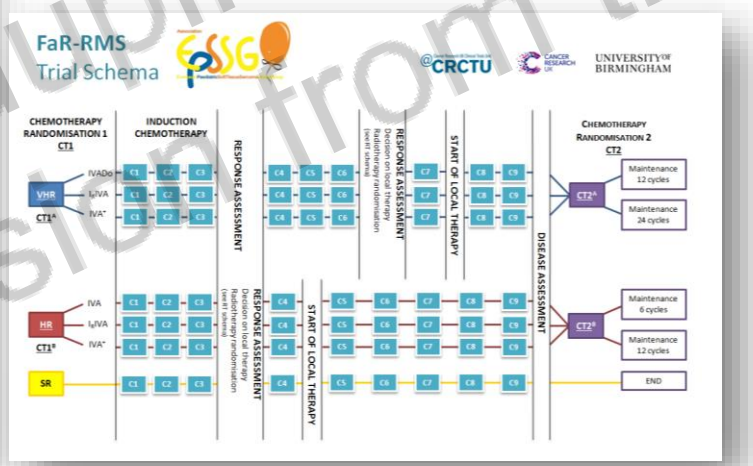
RHABDOMYOSARCOMA (RMS)

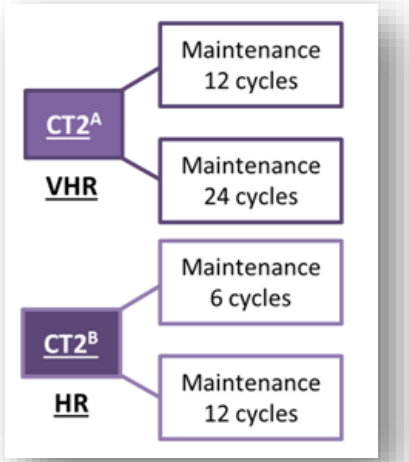
Vinorelbine and continuous low-dose cyclophosphamide as maintenance chemotherapy in patients with high-risk rhabdomyosarcoma (RMS 2005): a multicentre, open-label, randomised, phase 3 trial

Gianni Bisogno, Gian Luca De Salvo, Christophe Bergeron, Soledad Gallego Melcón, Johannes H Merks, Anna Kelsey, Helene Martelli, Veronique Minard-Colin, Daniel Orbach, Heidi Glosli, Julia Chisholm, Michela Casanova, Ilaria Zanetti, Christine Devalck, Myriam Ben-Arush, Peter Mudry, Sima Ferman, Meriel Jenney, Andrea Ferrari*, for the European paediatric Soft tissue sarcoma Study Group*

to be clarified if this is the results of the effectiveness of the drugs involved (and in particular vinorelbine)
or
it could be that simply prolonging chemotherapy cured a group of children with the persistence of a limited amount of residual disease at the end of standard treatment…
or
both..







RHABDOMYOSARCOMA (RMS)

The outcome for patients with metastatic disease or relapsing tumor remains poor

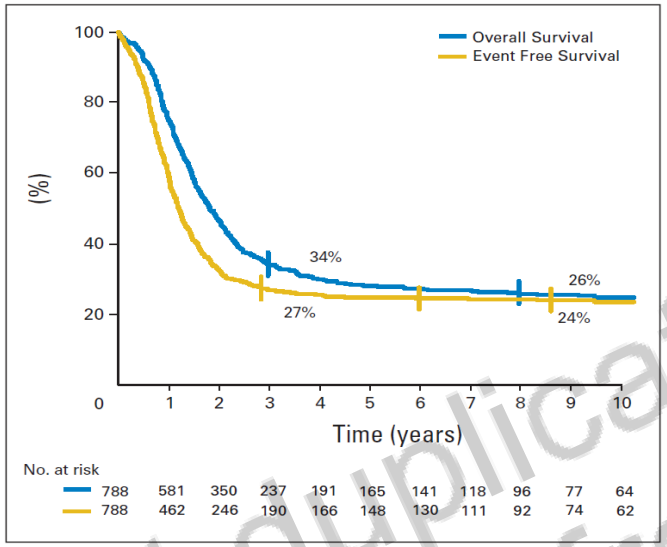


Fig 1. Overall survival and event-free survival of all 788 patients.

VOLUME 26 · NUMBER 14 · MAY 10 2008
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Prognostic Factors in Metastatic Rhabdomyosarcomas: Results of a Pooled Analysis From United States and European Cooperative Groups

Odile Oberlin, Annie Rey, Elizabeth Lyden, Gianni Bisogno, Michael C.G. Stevens, William H. Meyer, Modesto Carli, and James R. Anderson

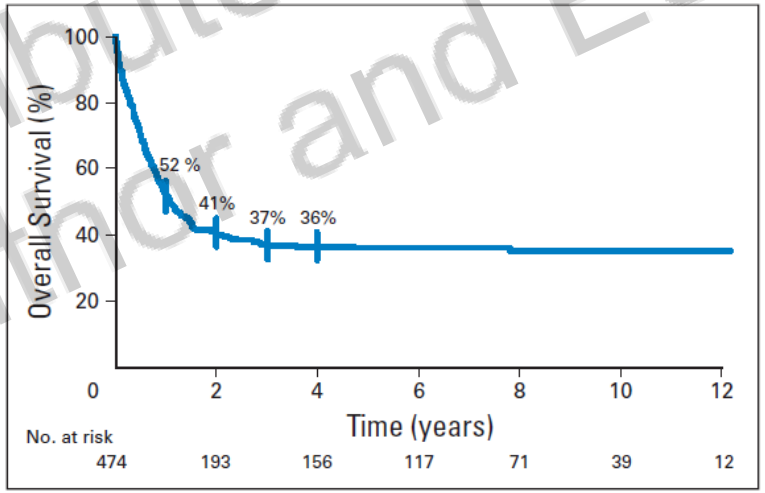


Fig 1. Kaplan-Meier curve of overall survival after last event for all 474 patients included in the study. Note that few deaths occurred > 3 years from the last event.

VOLUME 29 · NUMBER 10 · APRIL 1 2011
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Prognostic Factors After Relapse in Nonmetastatic Rhabdomyosarcoma: A Nomogram to Better Define Patients Who Can Be Salvaged With Further Therapy

Julia C. Chisholm, Julien Marandet, Annie Rey, Marcelo Scopinaro, Jose Sánchez de Toledo, Johannes H.M. Merks, Anne O'Meara, Michael C.G. Stevens, and Odile Oberlin

RHABDOMYOSARCOMA (RMS)

ARST0431: Study Design

Children's Oncology Group

WEEK	1*	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
	V	V	V	V	V	E	V	V	I		V	V	I		V	V	I		E
	Irin			Irin		VAL	DC		E		DC		E		DC		E		VAL

*Patients with evidence of intracranial extension (ICE) should receive radiation therapy starting at Week 1.

WEEK	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
		Radiation Therapy					I		V	V	I		V	V	E	V		
	V	V	V	V	V		E		D		E		D		VAL	AC		
	Irin			Irin					C				C					

WEEK	38	39	40	41	42	43	44	45	46	47#	48	49	50	51	52	53	54
	V			V	V	V	V			V	V		V	V			E
	AC			AC			AC			Irin			Irin				VAL

#Previously unirradiated metastatic sites may be irradiated during Weeks 47-51

CureSearch
Children's Oncology Group

"**dose-compression**", i.e. full-dose chemotherapy administered with a shorter interval between doses, e.g. 1-2 weeks instead of the usual 3 weeks, thereby increasing the "dose density"

Received: 13 May 2020 | Revised: 12 July 2020 | Accepted: 29 July 2020
DOI: 10.1002/pbc.28649
Pediatric Blood & Cancer | aspho | WILEY
ONCOLOGY: BRIEF REPORT

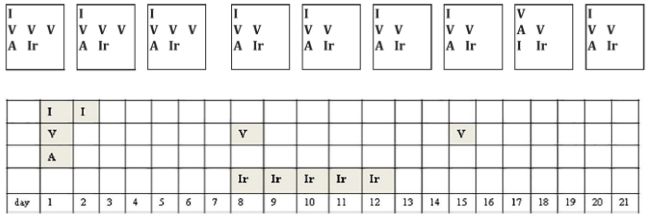
VIVA (vinorelbine, ifosfamide, vincristine, actinomycin-D): A new regimen in the armamentarium of systemic therapy for high-risk rhabdomyosarcoma

Andrea Ferrari[1] | Stefano Chiaravalli[1] | Marco Zecca[2] | Santina Recupero[2] | Silvia Pascale[3] | Luca Bergamaschi[1] | Michela Casanova[1]

Received: 18 October 2020 | Revised: 13 December 2020 | Accepted: 7 January 2021
DOI: 10.1002/pbc.28951
Pediatric Blood & Cancer | aspho | WILEY
ONCOLOGY: RESEARCH ARTICLE

Integrating irinotecan in standard chemotherapy: A novel dose-density combination for high-risk pediatric sarcomas

Gianni Bisogno[1] | Andrea Ferrari[2] | Arianna Tagarelli[3] | Silvia Sorbara[3] | Stefano Chiaravalli[2] | Elena Poli[1] | Giovanni Scarzello[4] | Federica De Corti[5] | Michela Casanova[2] | Maria Carmen Affinita[3]



RHABDOMYOSARCOMA (RMS)

temozolamide

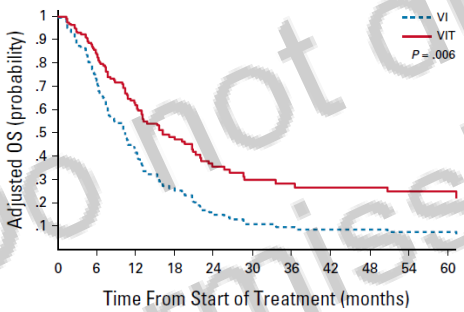
anti-VEGF

mTOR inhibitors

Journal of Clinical Oncology®

Randomized Phase II Trial of Vincristine-Irinotecan With or Without Temozolomide, in Children and Adults With Relapsed or Refractory Rhabdomyosarcoma: A European Paediatric Soft tissue Sarcoma Study Group and Innovative Therapies for Children With Cancer Trial

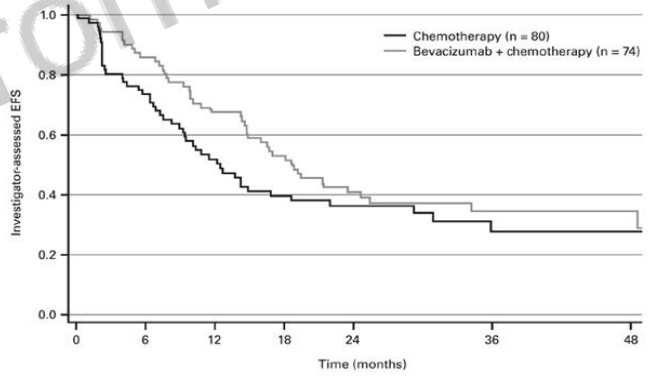
Anne-Sophie Defachelles, MD[1]; Emilie Bogart, MSc[1]; Michela Casanova, MD[2]; Johannes H. M. Merks, MD[3]; Gianni Bisogno, MD, PhD[4]; Giuseppina Calareso, MD[2]; Soledad Gallego Melcon, MD, PhD[5]; Susanne Andrea Gatz, MD[6]; Marie-Cécile Le Deley, MD[1]; Kieran McHugh, MD[7]; Alicia Probst, MSc[1]; Nathalie Rocourt, MD[1]; Rick R. van Rijn, MD, PhD[8]; Keith Wheatley, PhD[9]; Véronique Minard-Colin, MD, PhD[10]; and Julia C. Chisholm, MD[11]



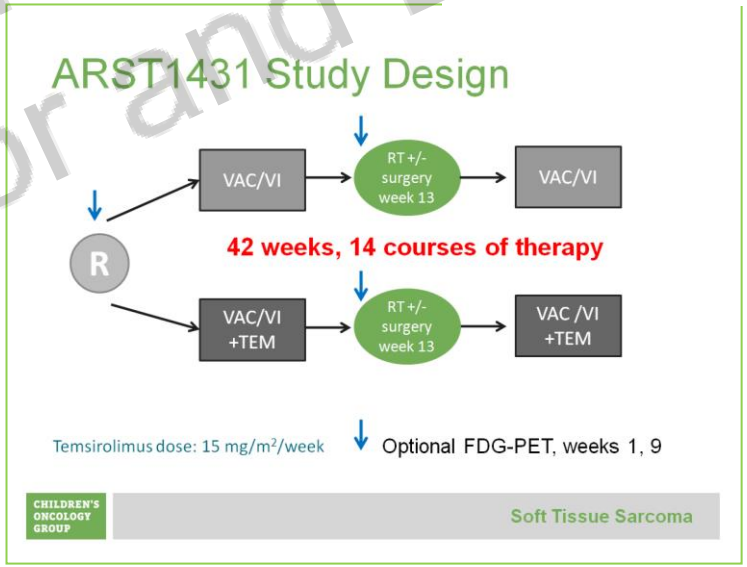
European Journal of Cancer 83 (2017) 177–184

Open-label, multicentre, randomised, phase II study of the EpSSG and the ITCC evaluating the addition of bevacizumab to chemotherapy in childhood and adolescent patients with metastatic soft tissue sarcoma (the BERNIE study)

Julia C. Chisholm [a,*,l], Johannes H.M. Merks [b,**,l], Michela Casanova [c], Gianni Bisogno [d], Daniel Orbach [e], Jean-Claude Gentet [f], Anne-Sophie Thomassin-Defachelles [g], Pascal Chastagner [h], Stephen Lowis [i], Milind Ronghe [j], Kieran McHugh [k], Rick R. van Rijn [l], Magalie Hilton [m], Jeanette Bachir [n], Sabine Fürst-Recktenwald [n], Birgit Geoerger [o,l], Odile Oberlin [o,l] on behalf of the European paediatric Soft tissue sarcoma Study Group (EpSSG) and the European Innovative Therapies for Children with Cancer (ITCC) Consortium



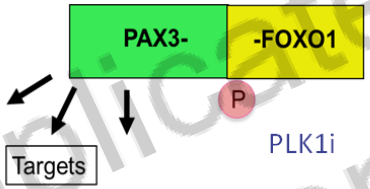
Children's Oncology Group



RHABDOMYOSARCOMA (RMS)

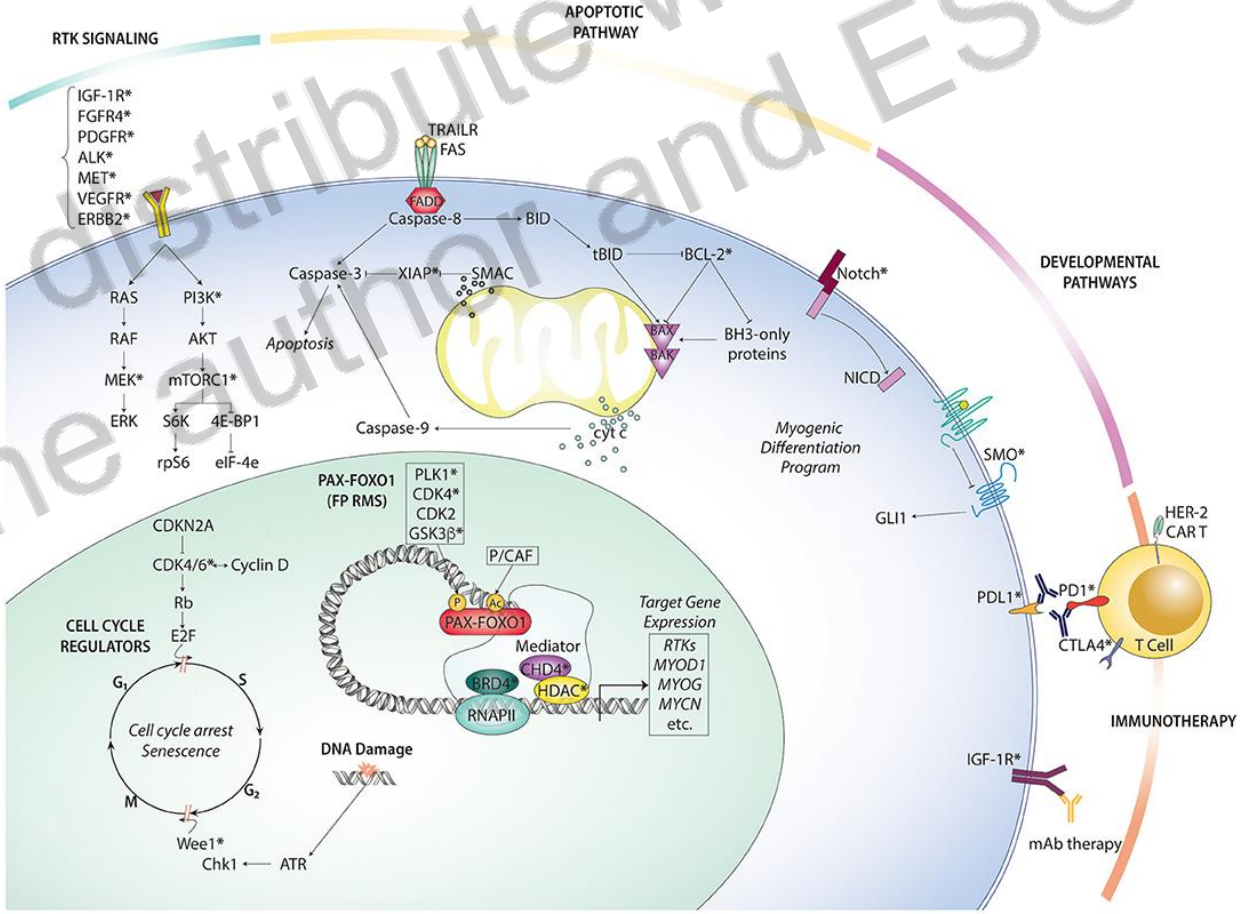
RMS targeting possibilities

- Target: actionable mutations and/or activated/altered pathways — FGFRi, mTORi, MEKi
- Target: altered chromatin — EZH2i, BRD4i, HDACi
- Target fusion proteins



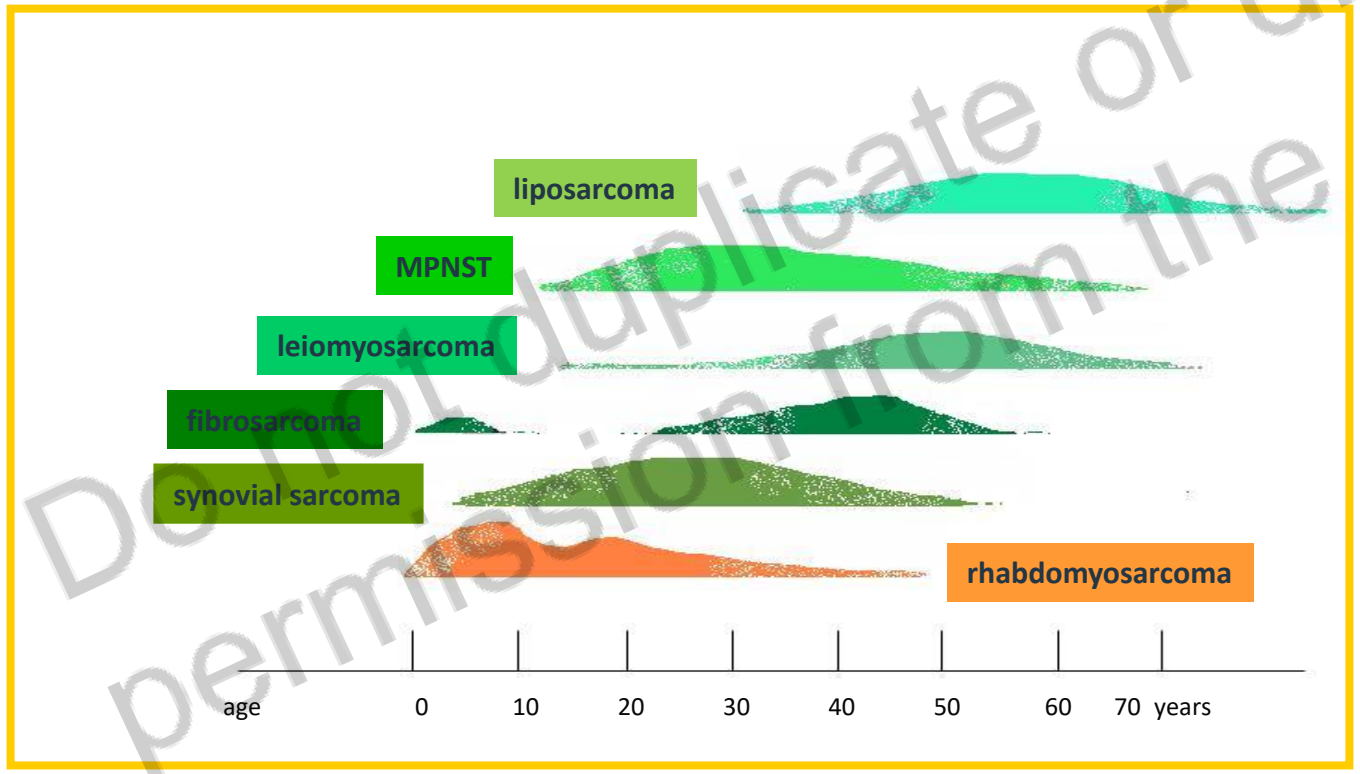
PLK1i

- Target sarcoma features or cancer specific features
  - ❑ hypoxia -> Th-302/ Evofosfamide
  - ❑ Angiogenesis/microenvironment -> bevazicumab, Regorafenib and other multi-TKI
  - ❑ DNA damage response -> DNA repair inhibitors (PARPi, WEE1…)
  - ❑ immune system



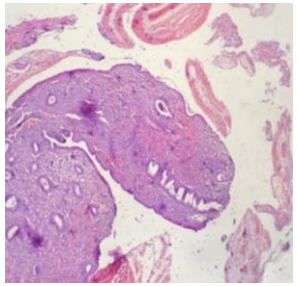
NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

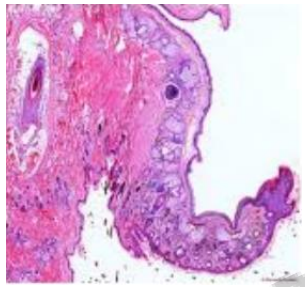
- rare tumors
- most are tumor entities typically found in adults
- extremely heterogeneus tumors
- scarcely sensitive to chemotherapy



NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

Different histology

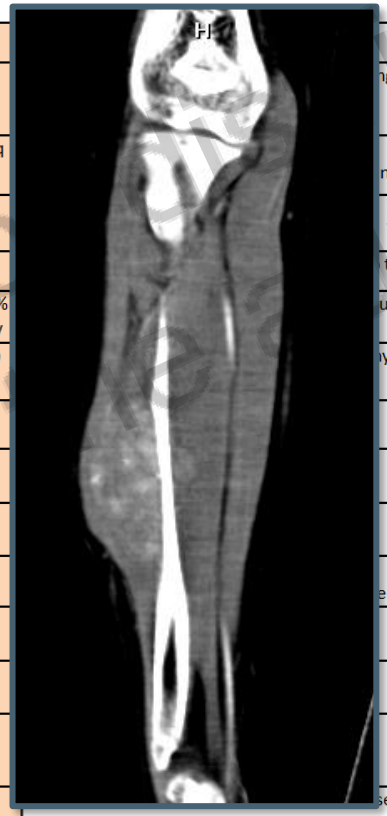


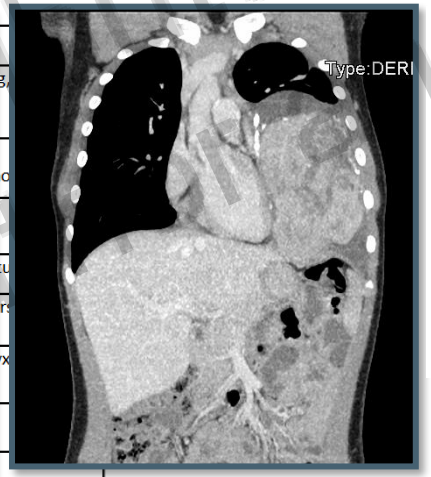


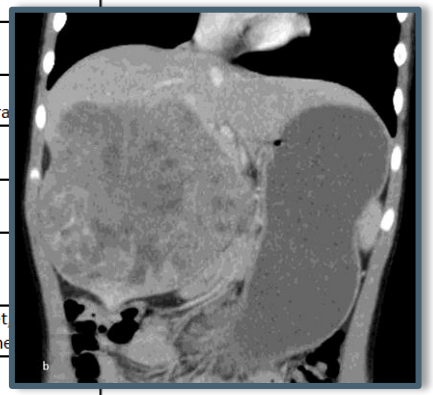
Different biology

Histotypes	Pick of incidence	Molecular finding
Synovial sarcoma	2°-3°decade	t(X;18)(p11;q11) SYT-SSX1, SYT-SSX2, SYT-SSX4
Malignant peripheral nerve sheath tumor (MPNST)	3-4° decade	loss or rearrangement of 10p, 11q, 17q and 22q
Infantile fibrosarcoma	1° year	t(12;15;)(p13;q25) ETVG(TEL)-NTRK3 *(as mesoblastic nephroma)*
Adult-type fibrosarcoma	4°-5° decade	t(2,5) and t(7,22)
Epithelioid sarcoma	3° decade	SMARCB/INI1 lost expression in 85-93% P13 K – AKT – MTOR signaling pathway
Liposarcoma	6°-7° decade	myxoid liposarcoma: t(12;16)(q13;p11) t(12;22)(q13;q12) FUS-CHOP
Leiomyosarcoma	6° decade	-
Alveolar soft part sarcoma	3° decade	t(X;17)(p11.2;q25) TFE3-ASPL
Clear cell sarcoma	3-4° decade	t(12;22)(q13;q12) t(9;22)(q22;q12) ATF1-EWS
Angiosarcoma	4°-6° decade	-
Dermatofibrosarcoma protuberans	3°-5° decade	t(17;22) t(2;17)(p23;q23) ALK-CLTC PDGFβ-COL1A1
Extraskeletal myxoid chondrosarcoma	5°-6° decade	t(9;22)(q22;q12) t(9;17)(q22;q11.2) EWS-CHN
Extraskeletal mesenchymal chondrosarcoma	2°-3° decade	complex cytogenetic alteration t(11;22) (q24;q12) (as Ewing family tumors)
Desmoplastic small round cell tumor	2°-3° decade	t(11;22) (p13;q12) EWS-WT1
Extracranial extrarenal rhabdoid tumor	infants and young children	mutated hSNF5/INI 1 gene

Different clinical aspects







peritoneal seeding, metastases, poor outcome

poor prognosis

Different outcome

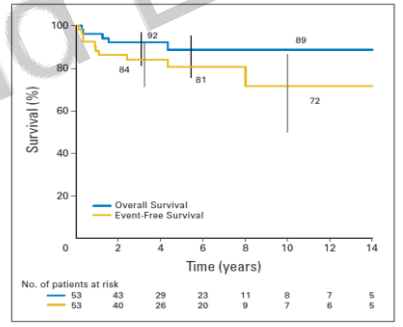


Fig 1. Overall survival and event-free survival of patients with localized infantile fibrosarcoma. Vertical bars indicate standard deviation.

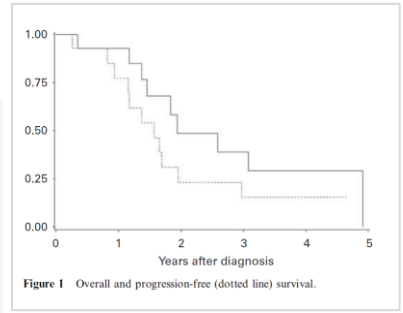


Figure 1 Overall and progression-free (dotted line) survival.

Turning points in the management of pediatric NRSTS

2005

2015

In the past, NRSTS = orphan diseases

Very few trials

- *Pratt, JCO1999 - only NRSTS randomised study in pediatric age (most pts refused randomization, i.e. 51/81)*
- *Pappo, JCO 2005 - phase 2 trial with IFO-DOXO-VCR in advance disease -39 cases*

The two largest reported series of pediatric NRSTS were single-institution experiences

- *St Jude – Spunt, JCO 1999 – 121 cases*
- *INT Milan - Ferrari, JCO 2005 – 182 cases*

NRSTS were often treated, in Europe at least, with RMS protocols

The different NRSTS entities were often treated all together, including in the same approach (and in the same analysis) very different entities as adult-type STS and extraosseous Ewing or DSRCT; or truly malignant tumors and soft tissue tumors with intermediate malignancies

Pediatric cooperative groups started to develop clinical trials specifically tailored to NRSTS, i.e. COG ARST0332 study (conducted from 2007 to 2012), EpSSG NRSTS 2005 study (2005-2016).

These multimodal risk-adapted studies were very similar in terms of their rationale, patient stratification and treatment programs

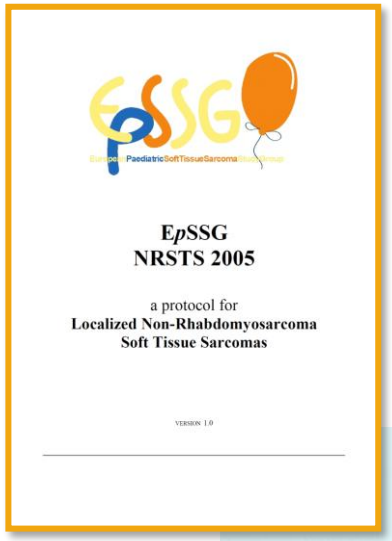
The two publications represent the benchmark for this tumor group, and defines the risk-adapted standard of care

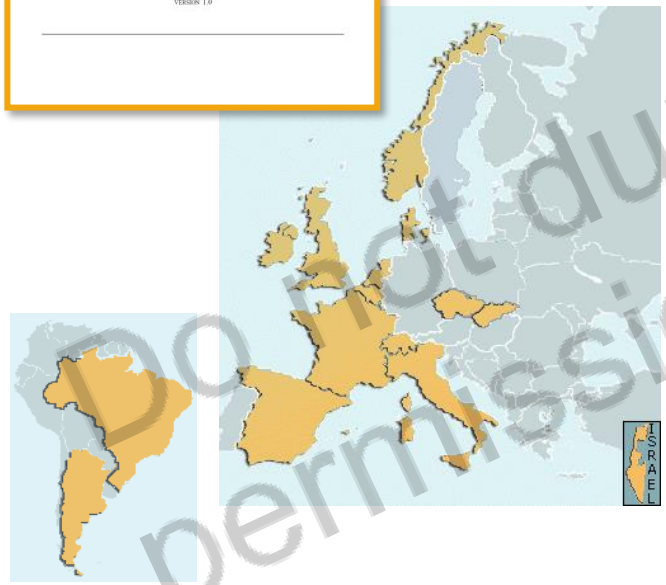
- *Spunt, Lancet Oncol 2020 – 529 cases*
- *Ferrari, Lancet Child Adolesc Health 2021 – 569 cases*

ARST1321 study
first study with a target therapy in front-line in NRSTS
first study with adults (cooperation embracing nearly the whole age spectrum are feasible... maybe)

- Weiss *Lancet Oncol 2020*

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)





- Synovial sarcoma
- "Adult-type" STS

} prospective non-randomized historically-controlled trials

- Other histotypes — guidelines

"first objective of the study is to make uniform the treatment of NRSTS patients in Europe"

Other histotypes

1. Infantile fibrosarcoma
2. Desmoplastic small round cell tumour
3. Undifferentiated sarcoma of the liver
4. Malignant ectomesencymoma
5. Mesenchymal chondrosarcoma
6. Epithelioid hemangioendothelioma
7. Myofibroblastic lesions and aggressive fibromatosis
8. Extracranial rhabdoid tumour

Second-line therapies

EuropeanPaediatricSoftTissueSarcomaStudyGroup

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

Tumor type	ref	Main features
synovial sarcoma	*Ferrari et al. Ann Oncol 26(3):567-72, 2015*	138 pts - 3-year EFS 81.9%, OS 97.2% - response rate to IFO-DOXO: 55.2%
infantile fibrosarcoma	*Orbach et al. Eur J Cancer 57:1-9, 2016*	50 pts - 3-year EFS 84%, OS 94% - response rate to VA: 70%
rhabdoid tumours	*Brennan et al. Eur J Cancer 60:69-82, 2016.*	43 pts - 3-year EFS 32.3%, OS 38.4% - poor outcome regardless of response to chemo
low-risk synovial sarcoma	*Ferrari et al. Eur J Cancer, 78:1-6, 2017*	EpSSG + COG: 60 low-risk cases (surgery alone) - 3-year EFS 90%, OS 100%
desmoid-type fibromatosis	*Orbach et al. Lancet Child Adol Health 1: 284–92, 2017*	173 pts (35% wait-and-see strategy) - 5-year PFS 36.5% - 172/173 alive - response to chemo 35% CR/PR (57% to VBL-MTX), 45% SD
alveolar soft part sarcoma	*Brennan et al. Pediatr Blood Cancer 65(4), 2018*	22 pts – for the 20 cases with localised disease, 5-year EFS 94.7%, OS 100% - response to chemotherapy in unresected/M1 cases = 0%
SYNOBIO	*Orbach et al. Cancer Medicine 7(4):1384-1393, 2018*	Genomic index in 61 cases – 5-year EFS for G1 93.8% vs G2 64.9%
epithelioid sarcoma (with COG)	*Spunt et al. Eur J Cancer 112:98-106, 2019*	EpSSG + COG: 63 cases - 5-year EFS 60.7%, OS 63.6% - response to chemotherapy: 50%
MPNST	*van Noesel et al. Pediatr Blood Cancer 66(10):e27833, 2019*	51 pts - 5-year EFS 52.9%, OS 62.1% - response rate to IFO-DOXO: 46%
inflammatory myofibroblastic tumor	*Casanova et al. Eur J Cancer 127:123-129, 2000*	60 pts – 5-year EFS 82.9%, OS 98.1% - response to chemotherapy: 55% (80% to VBL-MTX)
metastatic NRSTS	*Ferrari et al. Eur J Cancer 130:72-80, 2000*	49 pts - 2-year EFS 27.3%, 3-year OS 35.2% - response to chemotherapy: 28%
dermatofibrosarcoma protuberans	*Brennan B, et al. Pediatr Blood Cancer. 2020;67:e28351*	46 pts – most had small <*5 cm and IRS I* tumors - 5-EFS 92.6%, OS 100%

EuropeanPaediatricSoftTissueSarcomaStudyGroup

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

NRSTS 2005 whole series
The ultimate analysis

Paediatric non-rhabdomyosarcoma soft tissue sarcomas: the prospective NRSTS 2005 study by the European Pediatric Soft Tissue Sarcoma Study Group (EpSSG)

Andrea Ferrari, Max M van Noesel, Bernadette Brennan, Ilaria Zanetti, Nadege Corradini, Michela Casanova, Pablo Berlanga, Johannes H M Merks, Rita Alaggio, Stefan Schifflers, Gema L Ramirez-Villar, Chiara Giraudo, Gabriela Guillen Burrieza, Akmal Safwat, Gianni Bisogno, Gian Luca De Salvo, Daniel Orbach

Lancet Child Adolesc Health 2021

Published Online
June 29, 2021
https://doi.org/10.1016/
S2352-4642(21)00159-0

EpSSG NRSTS 2005 protocol
Localised NRSTS

enrolled patients = 1321

30 cases excluded due to review different from NRSTS

evaluable patients = 1291

671 cases excluded due to histological subtype included in "other categories"

Infantile fibrosarcoma	85
DSRCT	12
Undifferentiated sarcoma	36
Undifferentiated sarcoma liver	40
Malignant ectomesenchymoma	3
Chondrosarcoma	10
Epithelioid Hemangioendothelioma	13
Myofibroblastic lesions	293
IMT	*73*
Desmoid-type fibromatosis	*201*
Other Myofibroblastic lesions	*19*
Rhabdoid tumor	91
Extraskeletal Ewing sarcoma	77
Others #	11

synovial sarcoma and "adult-type" NRSTS= 620

7 cases excluded for missing data

44 cases excluded because treated in a group different from the assigned

Patients to be analysed = 569

Synovial sarcoma = 206

"Adult-type NRSTS" = 363

Alveolar Soft Part Sarcoma	19
Angiosarcoma	13
Clear cell sarcoma	17
DFSP	64
Epithelioid sarcoma	34
Fibrosarcoma – adult type	8
Leiomyosarcoma	22
Liposarcoma	35
Low grade Fibromyxoid sarcoma	18
Malignant Fibrous Histiocytoma	7
MPNST	74
Sarcoma NOS.	52

TREATMENT CATEGORIES

SURGERY ALONE group	250
ADJUVANT RADIOTHERAPY group	17
ADJUVANT CHEMOTHERAPY group (± radiotherapy)	93
NEOADJUVANT CHEMOTHERAPY group (± radiotherapy)	209

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

Paediatric non-rhabdomyosarcoma soft tissue sarcomas: the prospective NRSTS 2005 study by the European Pediatric Soft Tissue Sarcoma Study Group (EpSSG)

Andrea Ferrari, Max M van Noesel, Bernadette Brennan, Ilaria Zanetti, Nadege Corradini, Michela Casanova, Pablo Berlanga, Johannes H M Merks, Rita Alaggio, Stefan Schifflers, Gema L Ramirez-Villar, Chiara Giraudo, Gabriela Guillen Burrieza, Akmal Safwat, Gianni Bisogno, Gian Luca De Salvo, Daniel Orbach

Lancet Child Adolesc Health 2021

Published Online
June 29, 2021
https://doi.org/10.1016/
S2352-4642(21)00159-0

Surgery alone group		
Synovial sarcoma	IRS group I, tumour size ≤5 cm	Initial resection only, no adjuvant treatment
Adult-type non-rhabdomyosarcoma soft tissue sarcomas	IRS group I, tumour size ≤5 cm, any tumour grade	
	IRS group I, tumour size >5 cm, tumour grade 1	
	IRS group II, any size tumour, tumour grade 1	
Adjuvant radiotherapy group		
Adult-type non-rhabdomyosarcoma soft tissue sarcomas	IRS group I, tumour size >5 cm, tumour grade 2	Radiotherapy 50·4 Gy
	IRS group II, tumour size ≤5 cm, tumour grade 2–3	Radiotherapy 54·0 Gy
	IRS group II, tumour size >5 cm, tumour grade 2	
Adjuvant chemotherapy group (with or without radiotherapy)		
Synovial sarcoma	IRS group I, tumour size >5 cm	I+D I+D I+D I+D
	IRS group II, tumour size ≤5 cm	I+D I+D I+D Radiotherapy 50·4 Gy
	IRS group II, tumour size >5 cm	I+D I+D I+D I I Radiotherapy 54·0 Gy I+D
	Axial site or resected N1	
Adult-type non-rhabdomyosarcoma soft tissue sarcomas	IRS group I–II, tumour size >5 cm, tumour grade 3 or resected N1	
Neoadjuvant chemotherapy group (with or without radiotherapy)		
Synovial sarcoma	IRS group III (unresected disease) or unresected N1	I+D I+D I+D S I I Radiotherapy 50·4–59·4 Gy I+D ± I+D
Adult-type non-rhabdomyosarcoma soft tissue sarcomas		

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

Together with the COG ARST0332 trial, the EpSSG NRSTS 2005 study represents a **benchmark** for this tumor group, and defines the risk-adapted standard of care.

	Patients	Events	5-year event-free survival (95% CI)	p value	Deaths	5-year overall survival (95% CI)	p value
All patients	569	157	73·7% (69·7–77·2)	..	102	83·8% (80·3–86·7)	..
Treatment category	..	..	..	<0·0001	..	..	<0·0001
Surgery alone	250	26	91·4% (87·0–94·4)	..	7	98·1% (95·0–99·3)	..
Adjuvant radiotherapy	17	4	75·5% (46·9–90·1)	..	3	88·2% (60·6–96·9)	..
Adjuvant chemotherapy	93	35	65·6% (54·8–74·5)	..	25	75·8% (65·3–83·5)	..
Neoadjuvant chemotherapy	209	92	56·4% (49·3–63·0)	..	67	70·4% (63·3–76·4)	..
Age at diagnosis, years	..	..	..	0·0122	..	..	0·31
<1	19	1	94·7% (68·1–99·2)	..	1	94·7% (68·1–99·2)	..
1–9	174	44	76·6% (69·3–82·3)	..	29	84·2% (77·5–89·1)	..
10–17	343	96	73·0% (67·8–77·5)	..	63	83·2% (78·6–86·9)	..
≥18	33	16	54·3% (35·3–70·0)	..	9	81·7% (60·9–92·1)	..
Sex	..	..	..	0·37	..	..	0·67
Female	253	64	74·3% (68·2–79·4)	..	46	81·8% (76·1–86·2)	..
Male	316	93	73·2% (67·8–77·9)	..	56	85·4% (80·8–89·0)	..
Histological subtype	..	..	..	<0·0001	..	..	<0·0001
Malignant peripheral nerve sheath tumour	74	41	42·8% (31·1–53·9)	..	31	58·0% (45·4–68·6)	..
Neurofibromatosis type 1	36	23	31·1% (16·3–47·2)	..	19	42·0% (24·9–58·2)	..
Non-neurofibromatosis type 1	38	18	52·6% (35·8–67·0)	..	12	72·3% (54·7–84·1)	..
Other adult-type NRSTS	289	63	79·6% (74·3–83·9)	..	41	86·3% (81·5–89·9)	..
Synovial sarcoma	206	53	76·5% (69·9–81·8)	..	30	89·4% (83·8–93·1)	..
Primary tumour site	..	..	..	0·0014	..	..	<0·0001
Head or neck	95	35	64·2% (53·5–73·1)	..	23	76·9% (66·5–84·5)	..
Extremities	328	74	79·8% (74·9–83·9)	..	41	89·8% (85·8–92·8)	..
Trunk (thoracic and abdominal wall)	100	29	71·2% (61·1–79·2)	..	21	79·8% (70·0–86·6)	..
Intra-abdominal	46	19	56·0% (39·9–69·3)	..	17	64·9% (48·6–77·2)	..
FNCLCC tumour grade*	..	..	..	<0·0001	..	..	<0·0001
1	148	15	88·9% (82·3–93·1)	..	3	97·8% (93·4–99·3)	..
2	115	29	78·6% (69·7–85·1)	..	16	89·3% (81·5–94·0)	..
3	165	71	58·5% (50·3–65·7)	..	58	66·0% (57·9–73·0)	..
Primary tumour size†, cm	..	..	..	<0·0001	..	..	..
≤5	301	53	84·3% (79·5–88·0)	..	25	94·0% (90·4–96·3)	<0·0001
>5	258	101	61·7% (55·3–67·5)	..	75	72·3% (66·0–77·5)	..
Locoregional lymph node involvement	..	..	..	0·042	..	..	0·022
N0	551	149	74·4% (70·4–77·9)	..	96	84·5% (81·0–87·4)	..
N1	18	8	52·5% (26·5–73·2)	..	6	62·0% (33·5–81·1)	..
Intergroup Rhabdomyosarcoma Study group	..	..	..	<0·0001	..	..	<0·0001
I	252	28	90·6% (86·1–93·7)	..	15	94·5% (90·6–96·9)	..
II	108	37	67·6% (57·6–75·8)	..	20	84·7% (75·8–90·5)	..
III	209	92	56·4% (49·3–63·0)	..	67	70·4% (63·3–76·4)	..

FNCLCC=Fédération Nationale des Centres de Lutte Contre le Cancer. NRSTS=non-rhabdomyosarcoma soft tissue sarcomas. *141 patients with grading missing were excluded. †Ten patients with missing tumour size were excluded.

Table 2: **Univariable analyses**

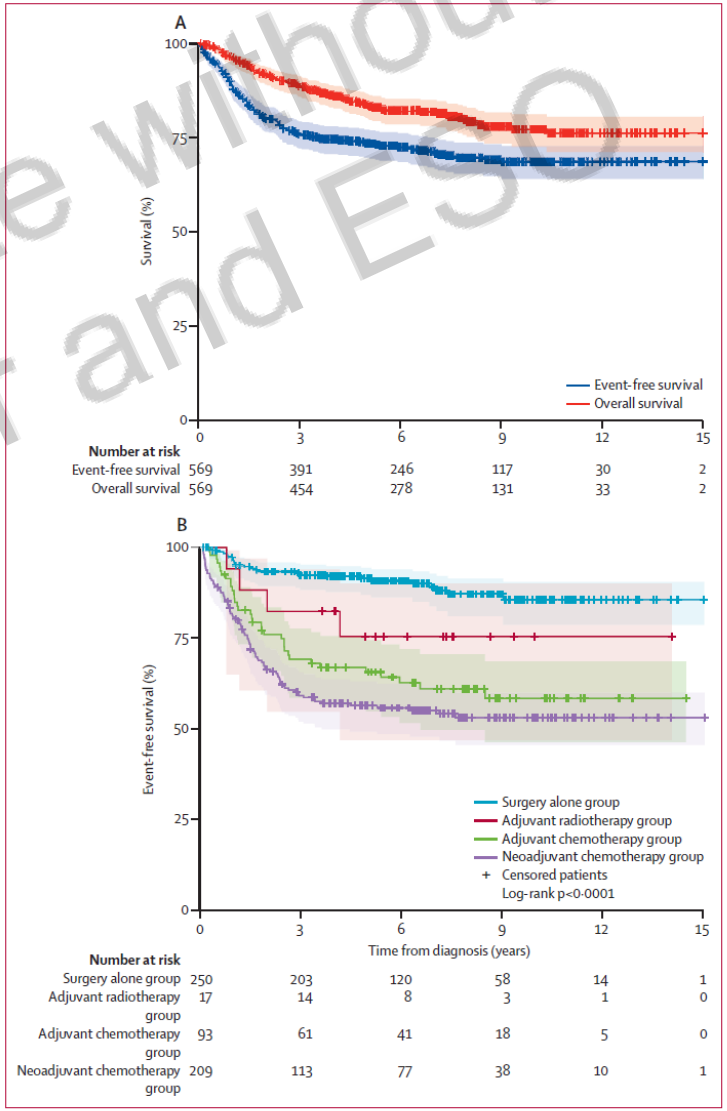


Figure 3: **Event-free survival and overall survival for the whole cohort (A) and event-free survival by treatment group (B)**
Shaded areas show the 95% CI.

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

Together with the COG ARST0332 trial, the EpSSG NRSTS 2005 study represents a **benchmark** for this tumor group, and defines the risk-adapted standard of care.

- The study demonstrated that adjuvant chemotherapy and radiotherapy can be safely omitted in the **low-risk** NRSTS
- The chances of investigating the role of **adjuvant chemotherapy** in preventing distant recurrences in patients with high-risk, initially-resected NRSTS were hindered by the limited sample size. Our study nonetheless confirmed that, despite the globally good prognosis for grossly-resected NRSTS, patients with high-grade and large tumors are at high risk of metastatic spread.
- For **unresected** cases, our study achieved better results than in historical series, possibly due to a more standardized approach. Neo-adjuvant ifosfamide-doxorubicin chemotherapy improved the resectability rate compared with previous studies.

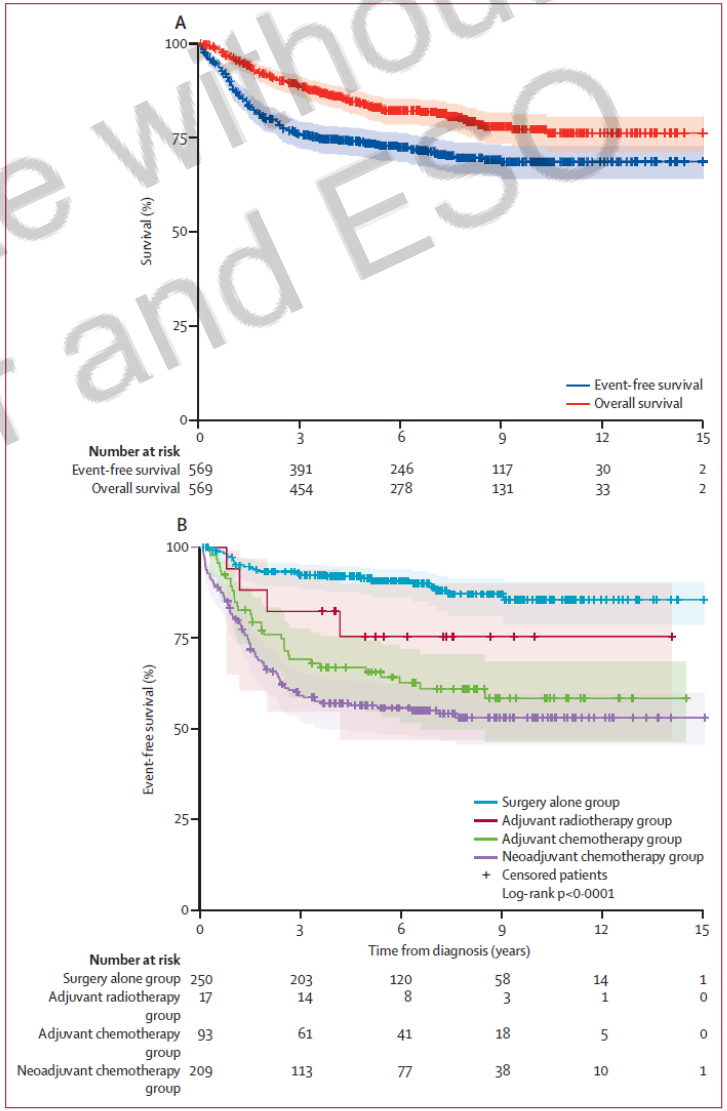


Figure 3: **Event-free survival and overall survival for the whole cohort (A) and event-free survival by treatment group (B)**
Shaded areas show the 95% CI.

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

challenges

improve the outcome for intermediate/high risk cases

better use of standard therapy

study all the NRSTSs together, or by single histotype?

AYA patients

pool resources and increase international collaborative research…
…especially with the adult sarcoma community

develop biological studies (identify new biomarkers to improve risk stratification, identification of new targets for novel therapies)

access to new drugs

how to use target therapy

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

improve the outcome for intermediate/high risk cases

better use of standard therapy

challenges

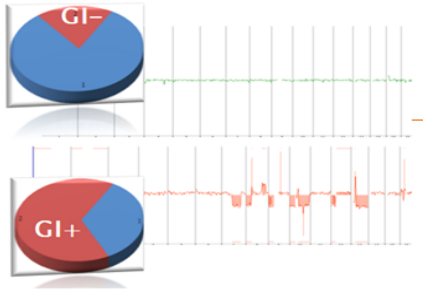
how to better use standard therapy?

patient selection based on

1. prognostic variables
in order to identify patients who are at high risk of metastatic failure and consequently in much need of systemic treatment

2. histology
in order to identify those whose histological characteristics make them more likely to respond to chemotherapy

3. tumor biology



NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

challenges

improve the outcome for int

better use of standard thera

study all the NRSTSs togethe

AYA patients

pool resources and increase
…especially with the adult sa

develop biological studies (ic
of new targets for novel ther

access to new drugs

how to use target therapy

Received: 19 July 2016 | Revised: 28 September 2016 | Accepted: 12 October 2016
DOI: 10.1002/pbc.26348

RESEARCH ARTICLE

WILEY Pediatric Blood & Cancer aspho

Access to clinical trials for adolescents with soft tissue sarcomas: Enrollment in European pediatric Soft tissue sarcoma Study Group (EpSSG) protocols

Andrea Ferrari[1] | Annalisa Trama[2] | Angela De Paoli[3] | Christophe Bergeron[4] | Johannes H. M. Merks[5] | Meriel Jenney[6] | Daniel Orbach[7] | Julia C. Chisholm[8] | Soledad Gallego[9] | Heidi Glosli[10] | Gian Luca De Salvo[3] | Laura Botta[2] | Gemma Gatta[2] | Gianni Bisogno[11] | RARECAREnet Working Group

0-14 years old	observed	expected	O/E ratio	95% CI	
RMS	1139	1488	0.77	0.72	0.81
NRSTS	615	1234	0.50	0.46	0.54
all STS	1754	2722	0.64	0.61	0.68

15-19 years old	observed	expected	O/E ratio	95% CI	
RMS	201	315	0.64	0.55	0.73
NRSTS	163	902	0.18	0.15	0.21
all STS	364	1217	0.30	0.27	0.33

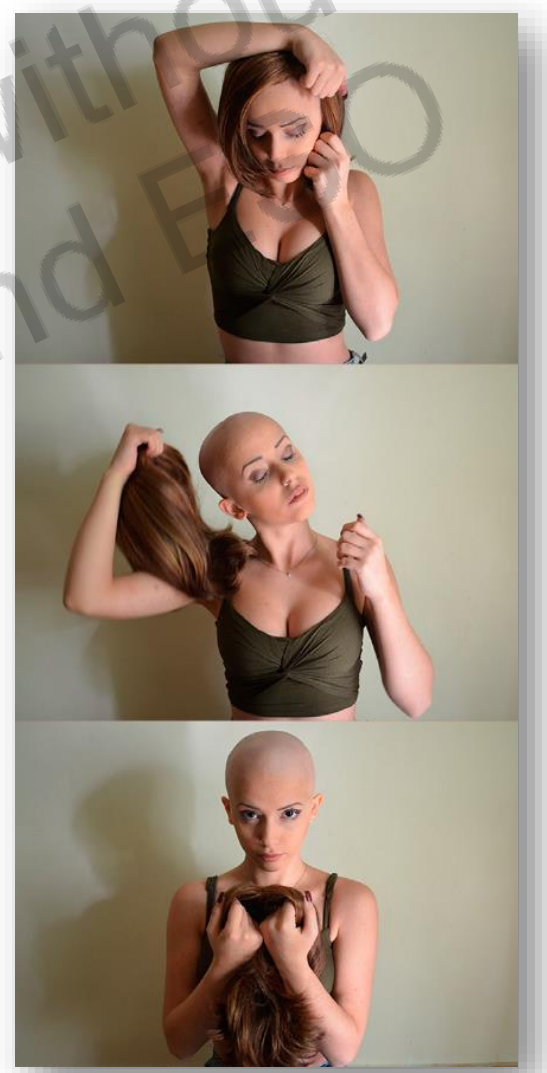
Received: 20 December 2017 | Revised: 16 January 2018 | Accepted: 24 January 2018
DOI: 10.1002/pbc.27013

REVIEW

WILEY Pediatric Blood & Cancer aspho

The challenge of the management of adolescents and young adults with soft tissue sarcomas

Andrea Ferrari[1] | Archie Bleyer[2] | Shreyaskumar Patel[3] | Stefano Chiaravalli[1] | Patrizia Gasparini[4] | Michela Casanova[1]



NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

challenges

improve the outcome for intermediate/high risk cases

better use of standard therapy

study all the NRSTSs together, or by single histotype?

AYA patients

pool resources and increase international collaborative rese
…especially with the adult sarcoma community

develop biological studies (identify new biomarkers to improve risk stratification, identification of new targets for novel therapies)

access to new drugs

how to use target therapy

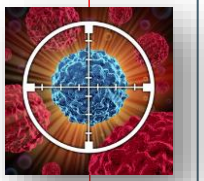
MYCKIDS: Molecular Identification and Characterization of non-Rhabdomyosarcoma Soft Tissue Sarcoma in Kids, Adolescents and Young Adults: an EpSSG NRSTS study
International sponsorship: Prinses Máxima Center, Utrecht

PI's: M van Noesel, D Orbach, A Ferrari

TUMOR ID CARD
NR-Soft Tissue Sarcoma

	Material	Number of cases	Investigations
Organization, international sponsorship, data management			
WP1	fresh	200	1. WES 2. mRNAseq 3. DNAmeth (plus clinical data)
WP2	FFPR	250	GI vs CINSARC vs grading
WP3	fresh	30	organoids
WP4	blood serum		liquid biopsies
Therapeutic Recommandations for all NRSTS histiotypes			

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)



Access to new drugs for children and adolescents with NRSTS

The impact of targeted agents on the pediatric population has not paralleled the progress seen in adult patients.
Major barriers are the small numbers of pediatric patients with NRSTS – even in large international projects - and the law regulations that offer only limited opportunities for the development of new drugs in children and orphan diseases.
Multi-level action is warranted (implement tumor sample collection and biological studies, better cooperation with adult experts, new partnerships with pharmaceutical companies and regulatory authorities…)

challenges

pool resources and increase international collaborative research…
…especially with the adult sarcoma community

develop biological studies (identify new biomarkers to improve risk stratification, identification of new targets for novel therapies)

access to new drugs

how to use target therapy

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA (NRSTS)

challenges

European Journal of Cancer 137 (2020) 183–192

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

ELSEVIER

Current Perspective

Spotlight on the treatment of infantile fibrosarcoma in the era of neurotrophic tropomyosin receptor kinase inhibitors: International consensus and remaining controversies

Daniel Orbach [a,*,1], Monika Sparber-Sauer [b,1], Theodore W. Laetsch [c], Veronique Minard-Colin [d], Stefan S. Bielack [b,e], Michela Casanova [f], Nadege Corradini [g], Ewa Koscielniak [b,h], Monika Scheer [b], Simone Hettmer [i], Gianni Bisogno [j], Douglas S. Hawkins [k], Andrea Ferrari [f]

Contents lists available at ScienceDirect

Current Problems in Cancer

journal homepage: www.elsevier.com/locate/cpcancer

ELSEVIER

Inflammatory myofibroblastic tumor: molecular landscape, targeted therapeutics, and remaining challenges

Priya Mahajan [a], Michela Casanova [b], Andrea Ferrari [b], Ashleigh Fordham [c], Toby Trahair [c,d,e], Rajkumar Venkatramani [a,*]

BJC British Journal of Cancer

www.nature.com/bjc

PERSPECTIVE

Rationale for the use of tyrosine kinase inhibitors in the treatment of paediatric desmoid-type fibromatosis

Monika Sparber-Sauer[1], Daniel Orbach[2], Fariba Navid[3], Simone Hettmer[4], Stephen Skapek[5,6], Nadège Corradini[7], Michela Casanova[8], Aaron Weiss[9], Matthias Schwab[10,11] and Andrea Ferrari[8]

access to new drugs

how to use target therapy

Short and clear take-home message

- cooperative multi-institutional clinical trials
- need for “dedicated” experts