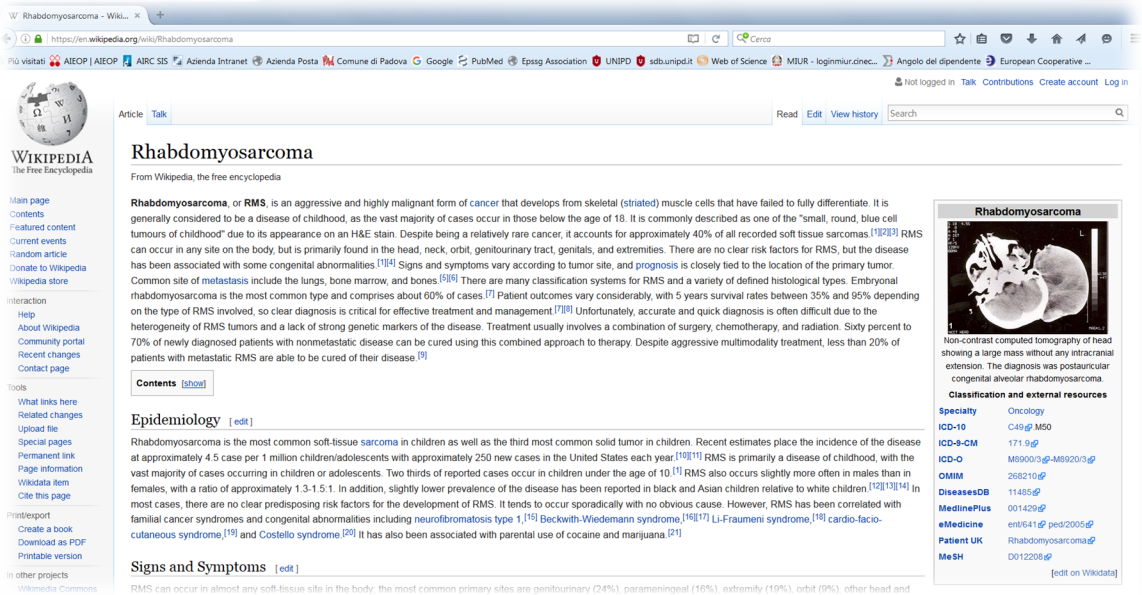
Mercoledì 4 ottobre 2023

Rabdomiosarcomi

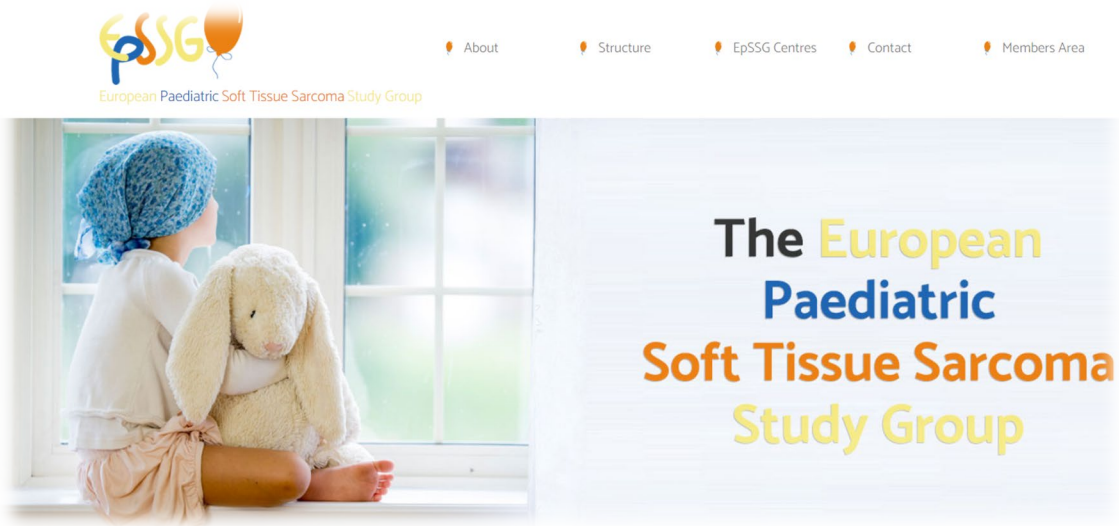
Dr.ssa M.C. Affinita

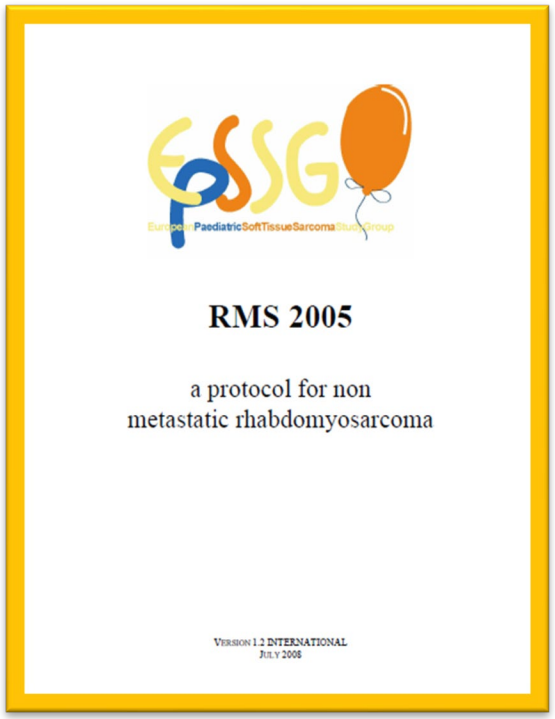
Rabdomiosarcoma

- Il Rabdomiosarcoma (RMS) è il Sarcoma delle parti molli più frequente nei bambini e adolescenti, 4-5% di tutti i tumori pediatrici.
- La sopravvivenza negli ultimi anni è migliorata per i pz con RMS localizzati (OS a 5 anni: 80%) resta insoddisfacente per i pz con RMS metastatici (OS a 3 anni del 30%) .
- 24% dei pazienti con RMS recidivano

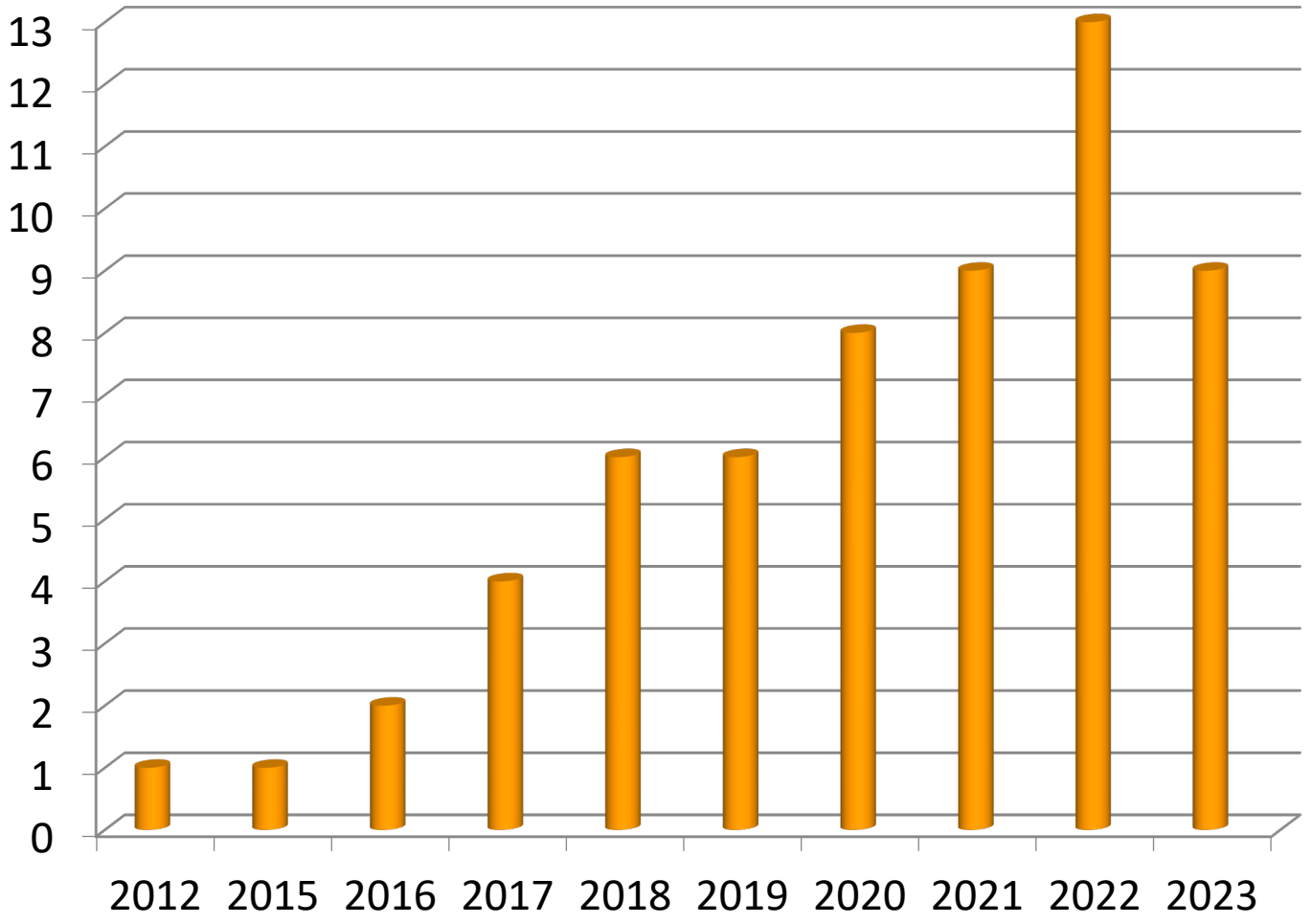


https://www.epssgassociation.it/en/





Pubblicazioni



- **60** pubblicazioni (total IF=803)
- **30** analisi ongoing (2023)
- **+9** analisi con gruppi cooperativi (2023)

Cosa e'cambiato...?

CHILDREN'S ONCOLOGY GROUP

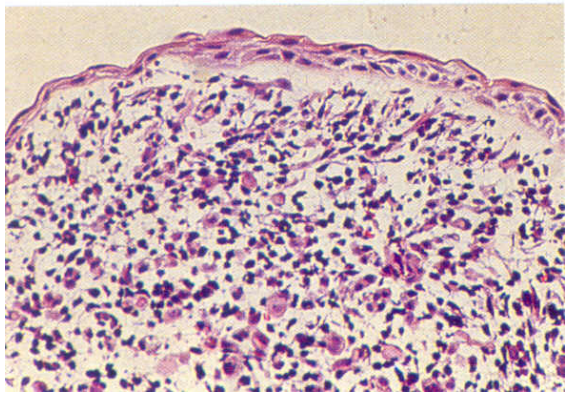
1. Classificazione del Rabdomiosarcoma

1995 (IRC) :

Tumore a piccole cellule rotonde blu con differenziazione in senso muscolare (rabdomioblasti, striature trasversali citoplasmatiche,…).

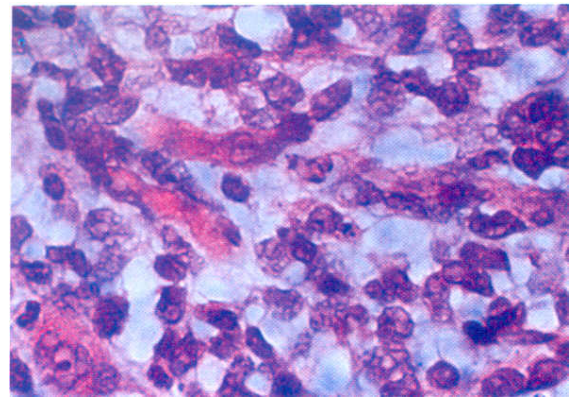
Immunoistochimica:
Identifica proteine muscolo-specifiche (desmina, actina, vimentina, mioglobina, …).

Prognosi favorevole



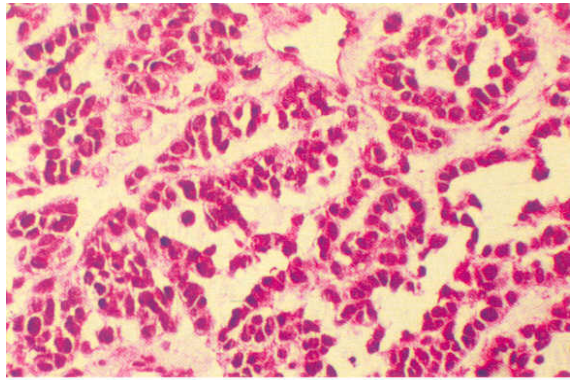
RMS Botrioide & RMS spindle cell

Prognosi intermedia



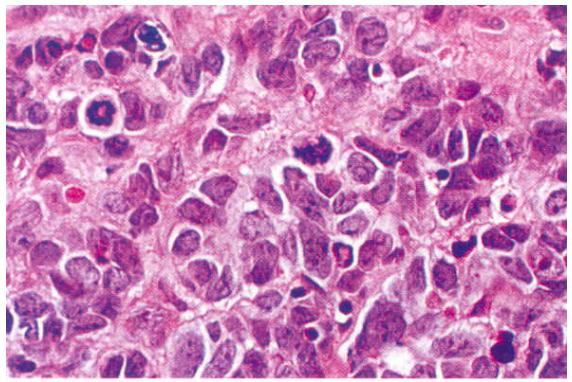
RMS Embrionale

Prognosi sfavorevole



RMS Alveolare

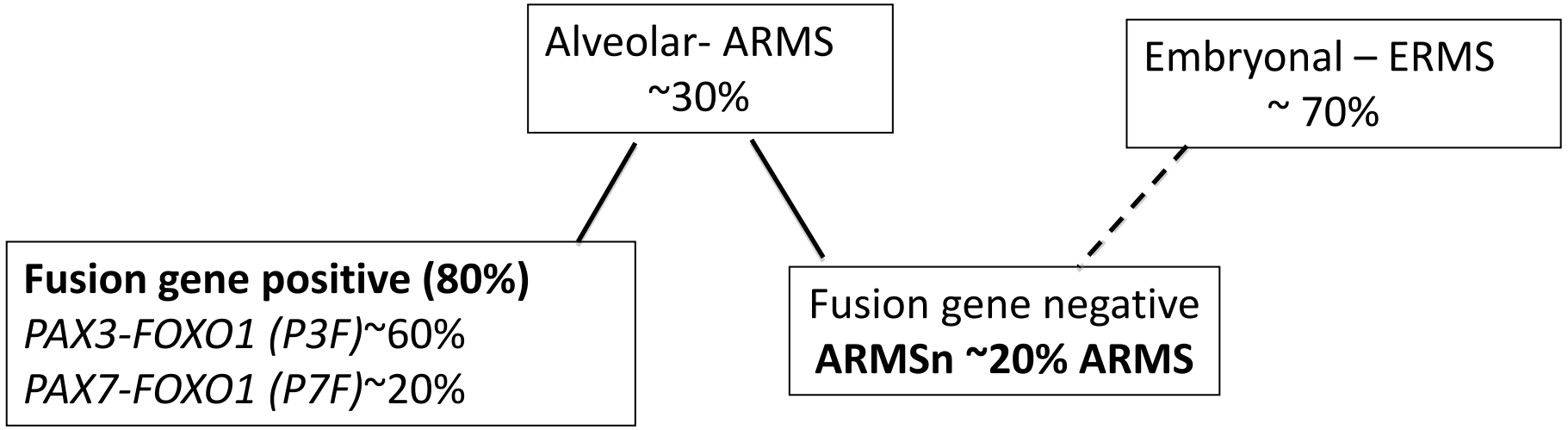
Prognosi sfavorevole



RMS Alveolare-solido

Newton WA et al. Cancer 1995

Late 90ties: Molecular Characterization by RT-PCR/FISH



VOLUME 28 · NUMBER 13 · MAY 1 2010

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Fusion Gene–Negative Alveolar Rhabdomyosarcoma Is Clinically and Molecularly Indistinguishable From Embryonal Rhabdomyosarcoma

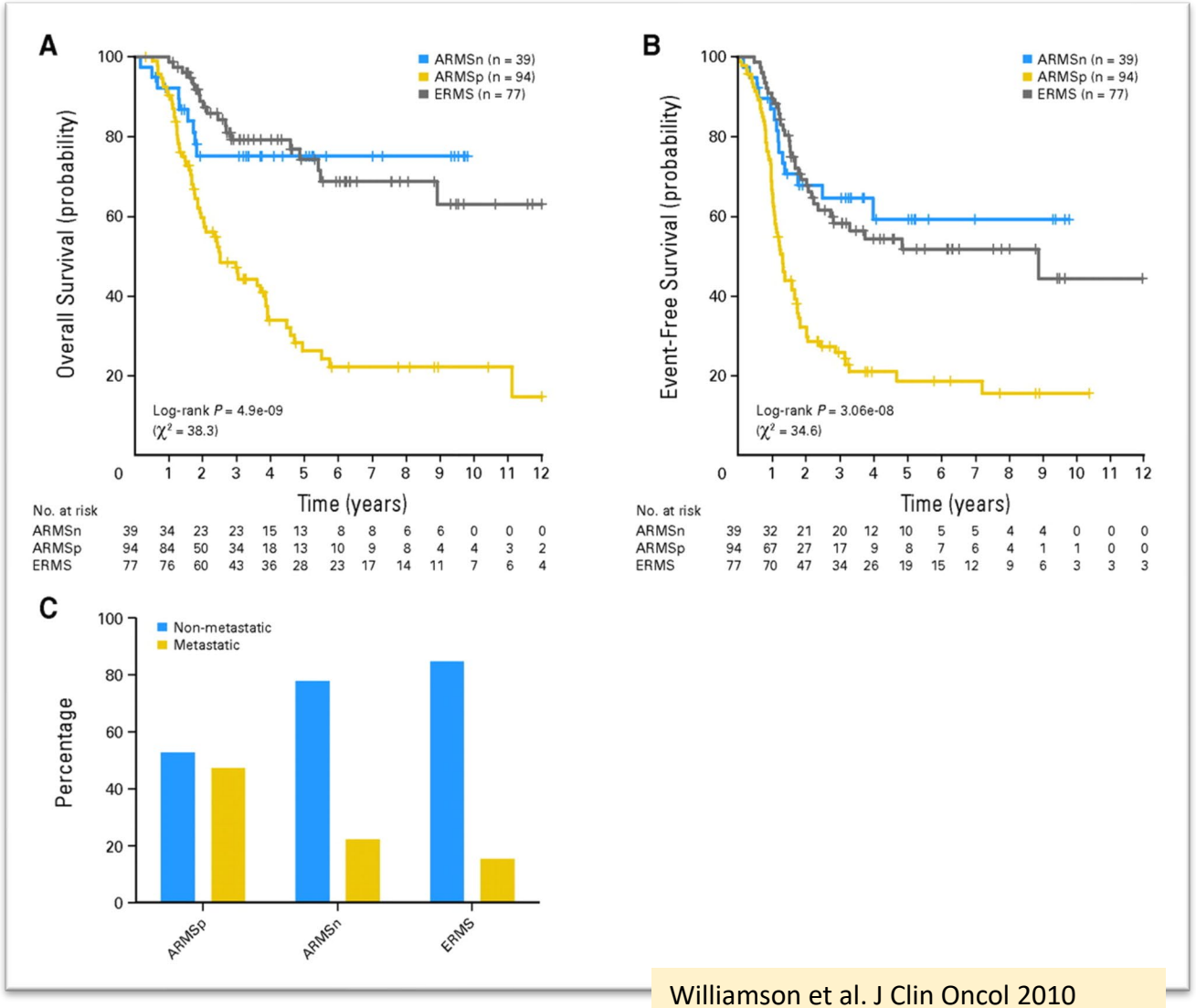
Daniel Williamson, Edoardo Missiaglia, Aurélien de Reyniès, Gaëlle Pierron, Benedicte Thuille, Gilles Palenzuela, Khin Thway, Daniel Orbach, Marick Laé, Paul Fréneaux, Kathy Pritchard-Jones, Odile Oberlin, Janet Shipley, and Olivier Delattre

210 patients

ERMS
translocation negative **36%**

ARMS
translocation negative **20%**

ARMS
translocation positive **44%**



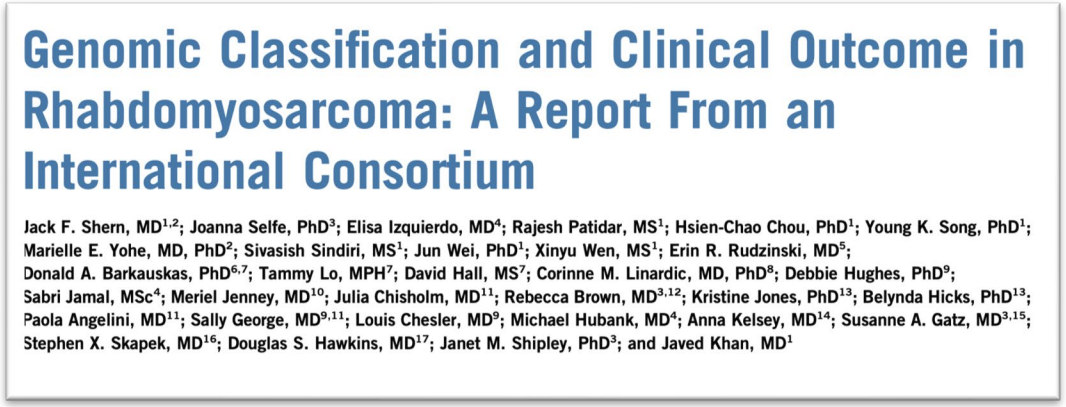
Williamson et al. J Clin Oncol 2010

WHO 2020 Classificazione Rabdomiosarcoma

RMS Embrionale	Botrioide Morfologia Classica Anaplastica Con componente Spindle Cell
RMS Alveolare	t(2;13) *PAX3-FOXO1* (70-90%) t(1;13) *PAX7-FOXO1* (10-30%) fusions of *PAX3* to *FOXO4*, *NCOA1*, or *INO80D* and *FOXO1* to *FGFR* (rare)
RMS Spindle cell/Sclerosante	*VGLL2/NCOA2/CITED2* riarrangiamento (congeniti/infantili) MyoD mutato (older children) *EWSR1*/*FUS* fused to the *TFCP2* gene; *MEIS1-NCOA2* gene fusion (osso)
RMS Pleomorfo	Rare/assente nei bambini

RMS Embrionale

ISTOLOGIA	Età (yr)	Sede	Prognosi	FUSIONS NEGATIVE /other alterations
RMS Embrionale	0-5 (18% >10 yrs) (<4% infants)	Testa/Collo (orbita) Genito-Urinario Tratto biliare, retroperitoneale Addome	Dipende dalla sede, età, stadio	Aneuploidia con perdita cromosomica Alterazione della famiglia dei geni RAS (HRAS, KRAS,NRAS), FGFR4, PIK3CA, NF1, FBXW7



Genomic Classification and Clinical Outcome in Rhabdomyosarcoma: A Report From an International Consortium

Jack F. Shern, MD[1,2]; Joanna Selfe, PhD[3]; Elisa Izquierdo, MD[4]; Rajesh Patidar, MS[1]; Hsien-Chao Chou, PhD[1]; Young K. Song, PhD[1]; Marielle E. Yohe, MD, PhD[2]; Sivasish Sindiri, MS[1]; Jun Wei, PhD[1]; Xinyu Wen, MS[1]; Erin R. Rudzinski, MD[5]; Donald A. Barkauskas, PhD[6,7]; Tammy Lo, MPH[7]; David Hall, MS[7]; Corinne M. Linardic, MD, PhD[8]; Debbie Hughes, PhD[9]; Sabri Jamal, MSc[4]; Meriel Jenney, MD[10]; Julia Chisholm, MD[11]; Rebecca Brown, MD[3,12]; Kristine Jones, PhD[13]; Belynda Hicks, PhD[13]; Paola Angelini, MD[11]; Sally George, MD[9,11]; Louis Chesler, MD[9]; Michael Hubank, MD[4]; Anna Kelsey, MD[14]; Susanne A. Gatz, MD[3,15]; Stephen X. Skapek, MD[16]; Douglas S. Hawkins, MD[17]; Janet M. Shipley, PhD[3]; and Javed Khan, MD[1]

Mutation of RAS pathway members in 50% of RMS
BCOR (15%), NF1 (15%), and TP53 (13%) mutations
P53 mutations were associated with worse outcomes
Mutations in RAS isoforms predominated in infants (64%).

Shern et al. J Clin Oncol 2021

RMS Spindle cell/Sclerosante

Istologia	Età (yr)	Sede	Prognosi	FUSIONS STATUS
SPINDLE/SCLEROSANTE RMS	Infantile (1)	back	Favorable	NCOA2,VGLL2 fusions
	Older children, adults (2,3)	Testa-collo, tronco estremità	poor	MyoD1 mut ((L122R) *
	Older children, adults	Bone, facial bones	poor	*FUS/EWSR1::TFCP2*

Congenital Spindle Cell Rhabdomyosarcoma: An International Cooperative Analysis

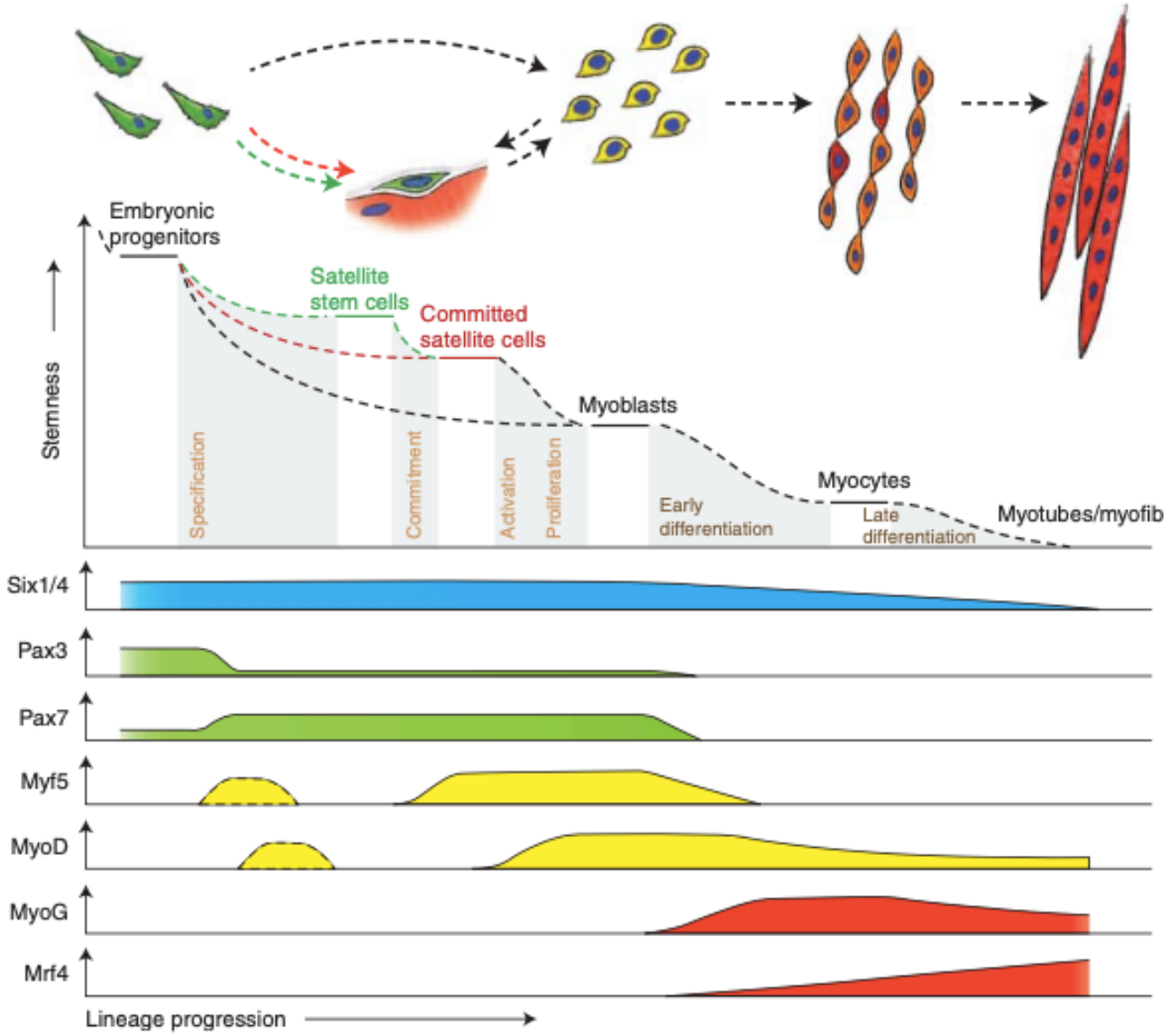
Sarah Whittle, M.D.[1,2], Rajkumar Venkatramani, M.D.[1,2], Anton Schönstein[3], Svetlana D Pack, Ph.D.[4], Rita Alaggio, M.D.[5], Christian Vokuhl, M.D.[6], Erin R. Rudzinski, M.D.[7], Anna-Lena Wulf, M.D.[6], Angelica Zin, M.D.[8], Juliana R. Gruver[4], Michael A. Arnold, M.D., Ph.D.[9,10], Johannes H.M. Merks, M.D., Ph.D.[11], Simone Hettmer, M.D.[12], Ewa Koscielniak, M.D.[13,14], Frederic G. Barr, M.D., Ph.D.[4], Douglas S Hawkins, M.D.[15], Gianni Bisogno, M.D.[16], Monika Sparber-Sauer, M.D.[13,14]

**Associated alterations of PIK3CA (53%); deep deletions in CDKN2A (24%).*

Whittle et al. Cancer 2022

Il ruolo di MYOD1

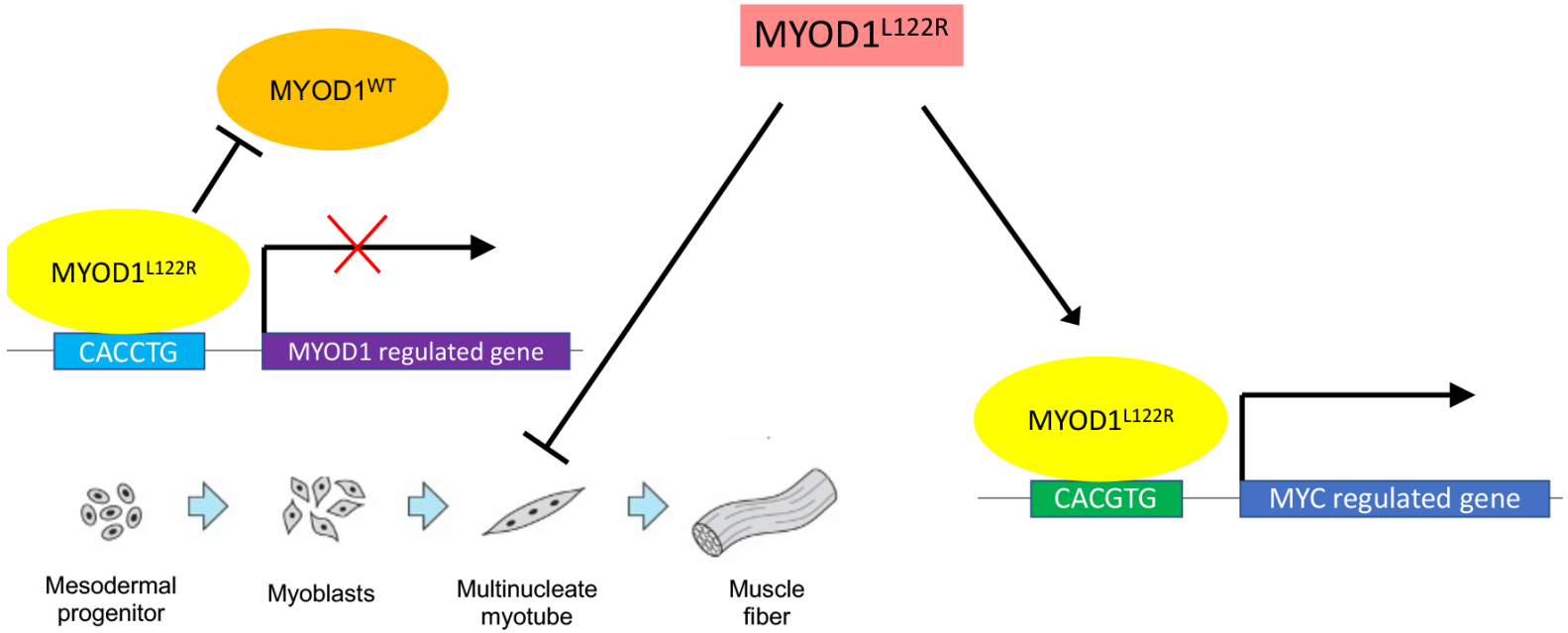
- Fattore di regolazione della miogenesi
- Differenziazione precoce
- Mioblasto → miocita
- Meccanismo «indiretto»



Bentzinger C F et al. 2012

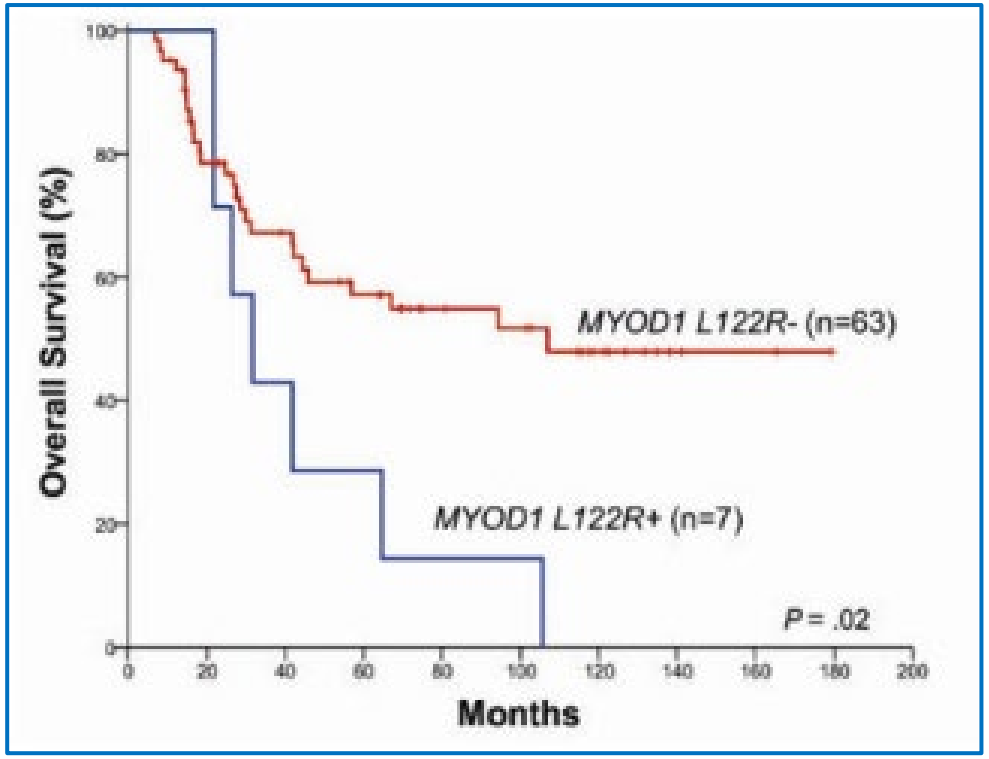
MYOD1 Mutato

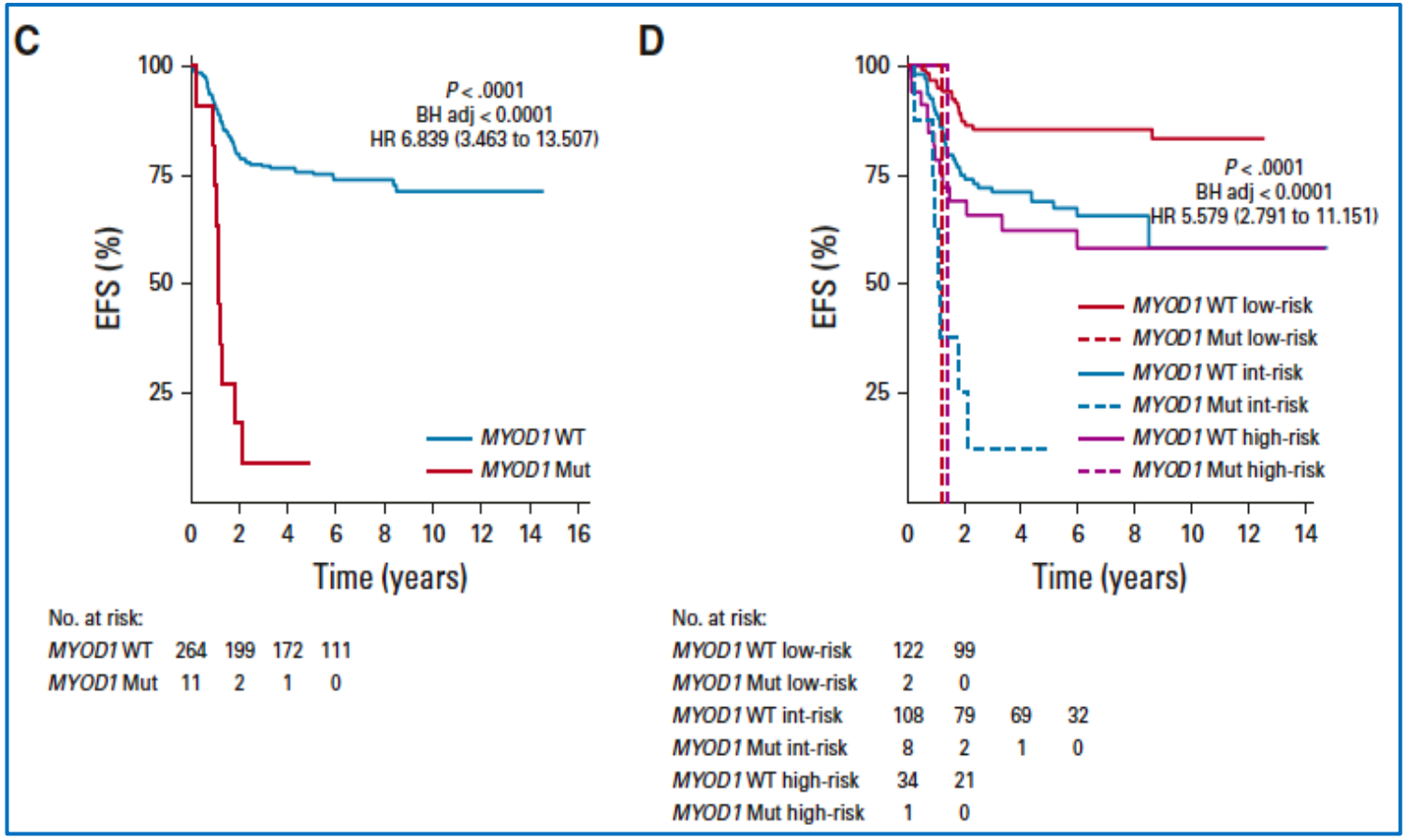
1. Perdita della capacità di favorire la differenziazione
2. MYOD1^{L122R} dominante negativo
3. Attività MYC-like



Di Carlo et al. et al. 2023

MYOD1 Mutato: Sopravvivenza





Kohsaka et al. 2014

Shern et al. 2021

MYOD1 Mutato: quali pazienti?

Published in final edited form as:
Genes Chromosomes Cancer. 2014 September ; 53(9): 779–787. doi:10.1002/gcc.22187.

Recurrent *MYOD1* Mutations in Pediatric and Adult Sclerosing and Spindle cell Rhabdomyosarcomas – Evidence for a Common Pathogenesis

Narasimhan P Agaram[1], **Chun-Liang Chen**[1], **Lei Zhang**[1], **Michael P LaQuaglia**[2], **Leonard Wexler**[3], and **Cristina R Antonescu**[1]

[1]Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY

[2]Department of Pediatric Surgery, Memorial Sloan Kettering Cancer Center, New York, NY

[3]Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY

26 pediatric patients Sc/SCRMS

11 patients < 1 year «Congenital/infantile»

15 patients > 1 year «Older children»

Genomic Classification and Clinical Outcome Rhabdomyosarcoma: A Report From an International Consortium

Jack F. Shern, MD[1,2]; Joanna Selfe, PhD[3]; Elisa Izquierdo, MD[4]; Rajesh Patidar, MS[1]; Hsien-Chao Chou, PhD[1]; Young K. Song Marielle E. Yohe, MD, PhD[2]; Sivasish Sindiri, MS[1]; Jun Wei, PhD[1]; Xinyu Wen, MS[1]; Erin R. Rudzinski, MD[5]; Donald A. Barkauskas, PhD[6,7]; Tammy Lo, MPH[7]; David Hall, MS[7]; Corinne M. Linardic, MD, PhD[8]; Debbie Hughes, PhD[9]; Sabri Jamal, MSc[4]; Meriel Jenney, MD[10]; Julia Chisholm, MD[11]; Rebecca Brown, MD[3,12]; Kristine Jones, PhD[13]; Belynda Hicks, Paola Angelini, MD[11]; Sally George, MD[9,11]; Louis Chesler, MD[9]; Michael Hubank, MD[4]; Anna Kelsey, MD[14]; Susanne A. Gatz, I Stephen X. Skapek, MD[16]; Douglas S. Hawkins, MD[17]; Janet M. Shipley, PhD[3]; and Javed Khan, MD[1]

Gene	No. of Cases	Age (median), years	Low (n = 220)	Intermediate (n = 299)	High (n = 115)	Bladder/prostate (n = 50)	Extremity (n = 92)	Female GU (n = 18)	Head and Neck (n = 57)	Orbital (n = 45)	Others (n = 21)	Parameningeal (n = 127)	Paratesticular (n = 125)	Peritoneum/trunk (n = 101)
NRAS	88	6.4	25	9	5	16	2	22	26	20	5	9	22	9
BCOR	85	6.7	20	11	7	12	3	11	16	27	10	12	18	14
NF1	80	5.1	11	14	10	22	3	11	7	13	19	14	13	16
TP53	74	4.2	11	12	11	8	16	17	19	18	10	9	2	16
FGFR4	65	4.7	11	11	6	16		11	9	18	5	17	6	12
KRAS	45	4.6	9	6	5	4	1		7	2		8	11	13
HRAS	44	2.8	8	7	4	14	3	11	2	2	10	2	12	9
CTNNB1	32	4.3	6	5	3	10		6	4	4		2	7	11
PIK3CA	28	5.1	3	5	4	2	2	6	5	2		9	2	6
MDM2	27	6.6	5	4	3	4	8	6	2	2		4	6	3
CDKN2A	23	7.6	3	4	4		3		5	7		6		6
FBXW7	18	6.7	6	1	3	2			2	2		1	8	4
MYOD1	17	10.8	2	4	2		1		7			9		
CDK4	17	11.3		2	10		12		2			2		3
MYCN	13	10.5		2	5		4		2		10	2		4
DICER1	12	6.0	2	2	2			33			10			4
ARID1A	11	8.2	2	2		2			2	4		3	1	2

1% 5% 10% Percentage of cases with a mutation in that group

Consensus
COG - EpSSG - CWS

European Journal of Cancer 172 (2022) 367–386

Review

Molecular testing of rhabdomyosarcoma in clinical trials to improve risk stratification and outcome: A consensus view from European paediatric Soft tissue sarcoma Study Group, Children's Oncology Group and Cooperative Weichteilsarkom-Studiengruppe

Simone Hettmer [a,1], Corinne M. Linardic [b,c,1], Anna Kelsey [d], Erin R. Rudzinski [e,f], Christian Vokuhl [g], Joanna Selfe [h], Olivia Ruhen [h], Jack F. Shern [i,j], Javed Khan [i], Alexander R. Kovach [c], Philip J. Lupo [k], Susanne A. Gatz [l], Beat W. Schäfer [m], Samuel Volchenboum [n], Véronique Minard-Colin [o], Ewa Koscielniak [p,q], Douglas S. Hawkins [r], Gianni Bisogno [s], Monika Sparber-Sauer [p,q], Rajkumar Venkatramani [t], Johannes H.M. Merks [u], Janet Shipley [h,*]

We also propose DNA sequencing to include high priority genes (including but not limited to *MYOD1*, *TP53*, *CDKN2A*, *CDK4* and *MYCN*). The poor survival rates associated with *MYOD1* L122R mutations, which is not limited to the spindle/sclerosing pathology, is either being used or considered for escalating treatment intensity. Ultimately, new treatments options need

Spindle Cell: non solo riarrangiamenti sfavorevoli..

Congenital Spindle Cell Rhabdomyosarcoma: An International Cooperative Analysis

Sarah Whittle, M.D.[1,2], Rajkumar Venkatramani, M.D.[1,2], Anton Schönstein[3], Svetlana D Pack, Ph.D.[4], Rita Alaggio, M.D.[5], Christian Vokuhl, M.D.[6], Erin R. Rudzinski, M.D.[7], Anna-Lena Wulf, M.D.[6], Angelica Zin, M.D.[8], Juliana R. Gruver[4], Michael A. Arnold, M.D., Ph.D.[9,10], Johannes H.M. Merks, M.D., Ph.D.[11], Simone Hettmer, M.D.[12], Ewa Koscielniak, M.D.[13,14], Frederic G. Barr, M.D., Ph.D.[4], Douglas S Hawkins, M.D.[15], Gianni Bisogno, M.D.[16], Monika Sparber-Sauer, M.D.[13,14]

[1]Texas Children's Cancer and Hematology Centers, Texas Children's Hospital, Houston, Texas.

[2]Department of Pediatrics, Baylor College of Medicine, Houston, Texas.

[3]Network Aging Research, Heidelberg University, Heidelberg, Germany.

[4]Laboratory of Pathology, Center for Cancer Research, National Cancer Institute, Bethesda, MD, USA.

- 39 pz. Rabdo Spindle Cell, età mediana alla dgn 2,5 mesi
- 13/26 pz. NCOA e/o VGLL
- EFS e OS a 5 aa per pz. infants con malattia localizzata : 86% (±11; CI 95%) e 91% (±9; CI 95%)
- EFS e OS a 5 aa del 100 % nei pz. R1.

Infantile Rhabdomyosarcomas With *VGLL2* Rearrangement Are Not Always an Indolent Disease

A Study of 4 Aggressive Cases With Clinical, Pathologic, Molecular, and Radiologic Findings

Joanna Cyrta, MD, PhD, Arnaud Gauthier, MD,* Marie Karanian, MD,† Andre F. Vieira, PhD,* Liesbeth Cardoen, MD,‡ Nina Jehanno, MD,§ Mégane Bouvet, BSc,‖ Corinne Bouvier, MD, PhD,¶ Mina Komuta, MD, PhD,#** François Le Loarer, MD, PhD,†† Daniel Orbach, MD, PhD,‡‡ Angélique Rome, MD,§§ Véronique Minard-Colin, MD, PhD,‖‖ Bénédicte Brichard, MD, PhD,¶¶ Claire Pluchart, MD, PhD,## Estelle Thebaud, MD,*** Marleen Renard, MD, PhD,¶¶ Stéphanie Pannier, MD, PhD,††† Hervé Brisse, MD, PhD,‡ Philippe Petit, MD,‡‡‡ Camille Benoist, PhD,§§§ Gudrun Schleiermacher, MD, PhD,‡‡ Birgit Geoerger, MD, PhD,‖‖ Anne Vincent-Salomon, MD, PhD,* Paul Fréneaux, MD,* and Gaëlle Pierron, PhD‖*

FaR-RMS
Frontline and Relapse RhabdoMyoSarcoma study

PAX3/7-FOXO1 fusion y/n
MANDATORY
at diagnostic level

Risk Group	Subgroup	Fusion gene status#	Post-surgical stage
Low (LR)	A	Neg.	I
Standard (SR)	B	Neg.	I
	C	Neg.	II, III
High (HR)	D	Neg.	II, III
	E	Neg.	II, III
	F	Pos.	I, II, III
Very High (VHR)	G	Pos.	I, II & III
	H	Any	IV

Site	Node Stage	Size & Age
Any	N0	Favourable
Any	N0	Unfavourable
Favourable	N0	Any
Unfavourable	N0	Favourable
Unfavourable	N0	Unfavourable
Any	N1	Any
Any	N0	Any
Any	N1	Any

Received: 10 September 2021 | Revised: 1 November 2021 | Accepted: 20 November 2021

DOI: 10.1002/pbc.29511

Pediatric Blood & Cancer | aspho | WILEY

REVIEW

An update on rhabdomyosarcoma risk stratification and the rationale for current and future Children's Oncology Group clinical trials

Josephine H. Haduong[1] | Christine M. Heske[2] | Wendy Allen-Rhoades[3] | Wei Xue[4] | Lisa A. Teot[5] | David A. Rodeberg[6] | Sarah S. Donaldson[7] | Aaron Weiss[8] | Douglas S. Hawkins[9] | Rajkumar Venkatramani[10]

CHILDREN'S ONCOLOGY GROUP

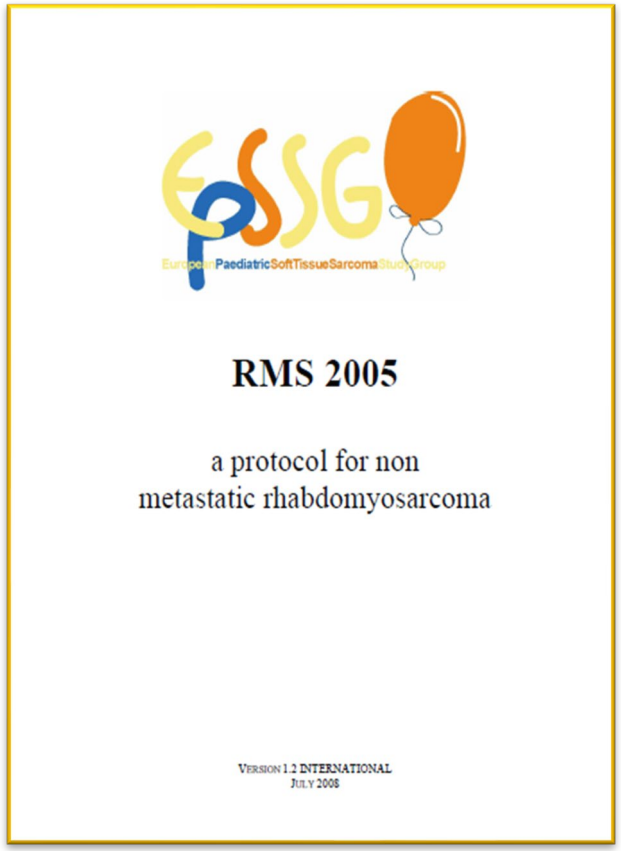
TABLE 4 Current and planned Children's Oncology Group rhabdomyosarcoma studies

Risk group	Stage	Clinical group	Age	Fusion status	COG study	Therapy
Very low	1	I	Any	FOXO1	ARST2032[a]	VA x 24 weeks
Low	1	II, III (orbit only)	Any	FOXO1–	anticipated activation spring 2022)[a]	VAC/VA x 24 weeks
Low	2	I, II				VAC/VA x 24 weeks
Intermediate	1	III (non-orbit)	Any	FOXO1–	ARST1431	Randomization to:
	1, 2, 3	I, II, III		FOXO1+		VAC/VI x 42 weeks vs.
	2, 3	III		FOXO1–		VAC/VI/Temsirolimus x 42 weeks
	3	I, II		FOXO1–		+
	4	IV	<10 years	FOXO1–		Maintenance (CPM^{PO}Vino) x 24 weeks (all patients)
High	4	IV	>10 years	FOXO1–	ARST2031	Randomization to:
			Any	FOXO1+		VAC x 42 weeks vs.
						VinoAC x 42 weeks
						+
						Maintenance (CPM^{PO}Vino) x 24 weeks (all patients)

Abbreviations: CPM^{PO}, daily oral cyclophosphamide; VAC, vincristine, dactinomycin, cyclophosphamide regimen using cyclophosphamide dose of 1.2 g/m^2/cycle; Vino, vinorelbine; VinoAC, vinorelbine, dactinomycin, cyclophosphamide regimen using cyclophosphamide dose of 1.2 g/m^2/cycle.

[a]Patients treated on VLR or LR arms of ARST2032 must have MYOD1/TP53 wildtype tumors.

2. Stadiazione



- **CT scan or MRI** of the primary site (+ initial ultrasound if follow-up with ultrasound is possible).

CT or MRI examination should be carried out with the use of contrast.
The investigation will need to be performed (again) after surgical excision biopsy if significant volume has been resected
Imaging of the primary site should include tumour volume measurement and examination of regional lymph nodes especially if not evaluable clinically or if clinically suspicious.

- **Chest CT scan:** the presence of lung metastases must be evaluated in all patients at diagnosis by CT scan *and* Postero-Anterior and Lateral **Chest X-Ray.**

Intravenous-contrast enhancement is mandatory for limb or abdominal primaries (and ideally for other primaries)

- **Abdomen-pelvic CT scan** (during same acquisition as chest CT)

For abdominal, pelvic primaries if MRI has not been performed. To assess the presence of abdominal lymphadenopathy in case of paratesticular or lower limb primaries.
Intravenous-contrast enhancement is mandatory.

- **Abdomen US**

If abdominal CT is equivocal regarding lymphadenopathy or liver metastases

- **Radionuclide Bone Scan** (with plain X rays and / or MRI of any isolated abnormal site).

Mandatory in all patients at diagnosis

- **Craniospinal MRI**

If intraspinal extension or suspected meningeal involvement
Optional investigation:

- **PET-CT:** According to local availability and local protocols

PET-TC

- Studio retrospettivo multicentrico sui pz con RMS metastatico
  (Ottobre 2008- Dicembre 2016).

- Scopo di confrontare le metodiche radiologiche standard richieste dal protocollo e la PET-CT (esame opzionale)

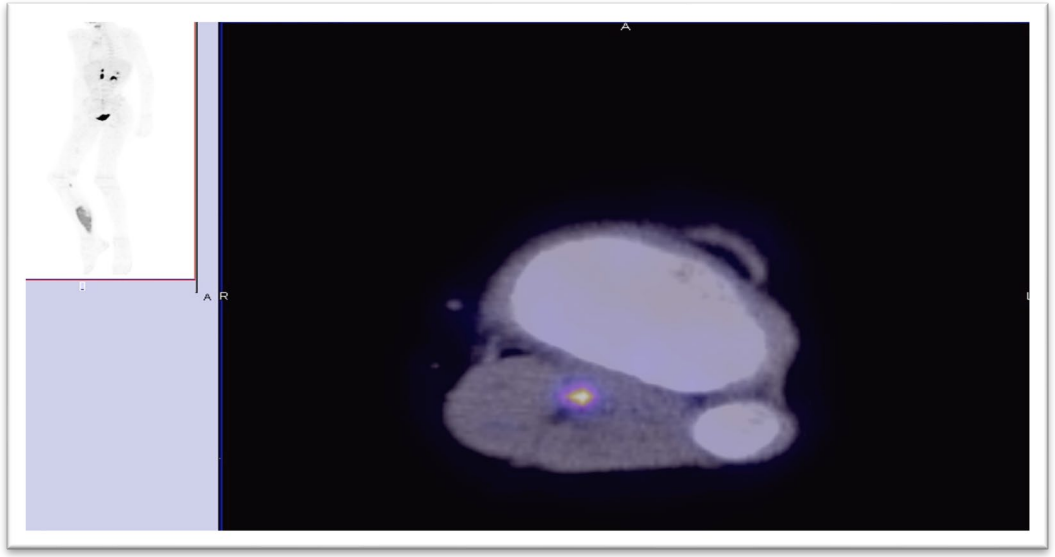
- Per identificare gli esami più specifici e sensibili per identificare i siti di MTX

Available online at www.sciencedirect.com
ScienceDirect
ELSEVIER
journal homepage: www.ejcancer.com

Original Research

Role of ^{18}F-FDG-PET/CT in the staging of metastatic rhabdomyosarcoma: a report from the European paediatric Soft tissue sarcoma Study Group

Federico Mercolini [a,*], Pietro Zucchetta [b], Nina Jehanno [c], Nadege Corradini [d], Rick R. Van Rijn [e], Timothy Rogers [f], Alison Cameron [g], Giovanni Scarzello [h], Beatrice Coppadoro [i], Veronique Minard-Colin [j], Soledad Gallego [k], Julia Chisholm [l], J.Hans Merks [m], Gianni Bisogno [i]



Mercolini et al. E. J. Oncology 2022

Comparison between ^{18}F-FDG-PET/CT (PET) and standard radiology work up (SRW) in detection of nodal and metastatic involvement.

Site of metastasis	SRW+	SRW−	*SRW sensitivity*	*PET sensitivity*
Locoregional nodes			78.5%	96.2%
PET+	59	17		
PET−	3	39		
Distant nodes			79.3%	94.8%
PET+	43	12		
PET−	3	60		
Lung			100%	79.6%
PET+	35			
PET−	9	74		
Pleura			100%	78.9%
PET+	15			
PET−	4	99		
Central nervous system			100%	50%
PET+	2			
PET−	2	114		
Peritoneum			86.7%	86.7%
PET+	11	2		
PET−	2	103		
Liver			100%	75%
PET+	3			
PET−	1	114		
Subcutis			66.7%	100%
PET+	4	2		
PET−		112		
Other sites			78.9%	89.5%
PET+	13	4		
PET−	2	99		

Bone involvement.

	BS+	BS−	
PET+	18	9	*Bone scintigraphy sensitivity 82.6%* *Bone scintigraphy specificity 100%*
PET−	1	18	*PET sensitivity 95.6%* *PET specificity 78.2%*

Comparison between ^{18}F-FDG-PET/CT (PET) and bone scintigraphy (BS).

Bone marrow involvement.

	BMA + and/or BMB+	BMA − and BMB -	
PET+	43	2	*BMA + BMB sensitivity* 95.9% *BMA + BMB specificity* 100%
PET−	4	65	*PET sensitivity* 91.8% *PET specificity* 93.8%

Comparison between ^{18}F-FDG-PET/CT (PET) and bone marrow aspirates (BMA)-bone marrow biopsy (BMB).

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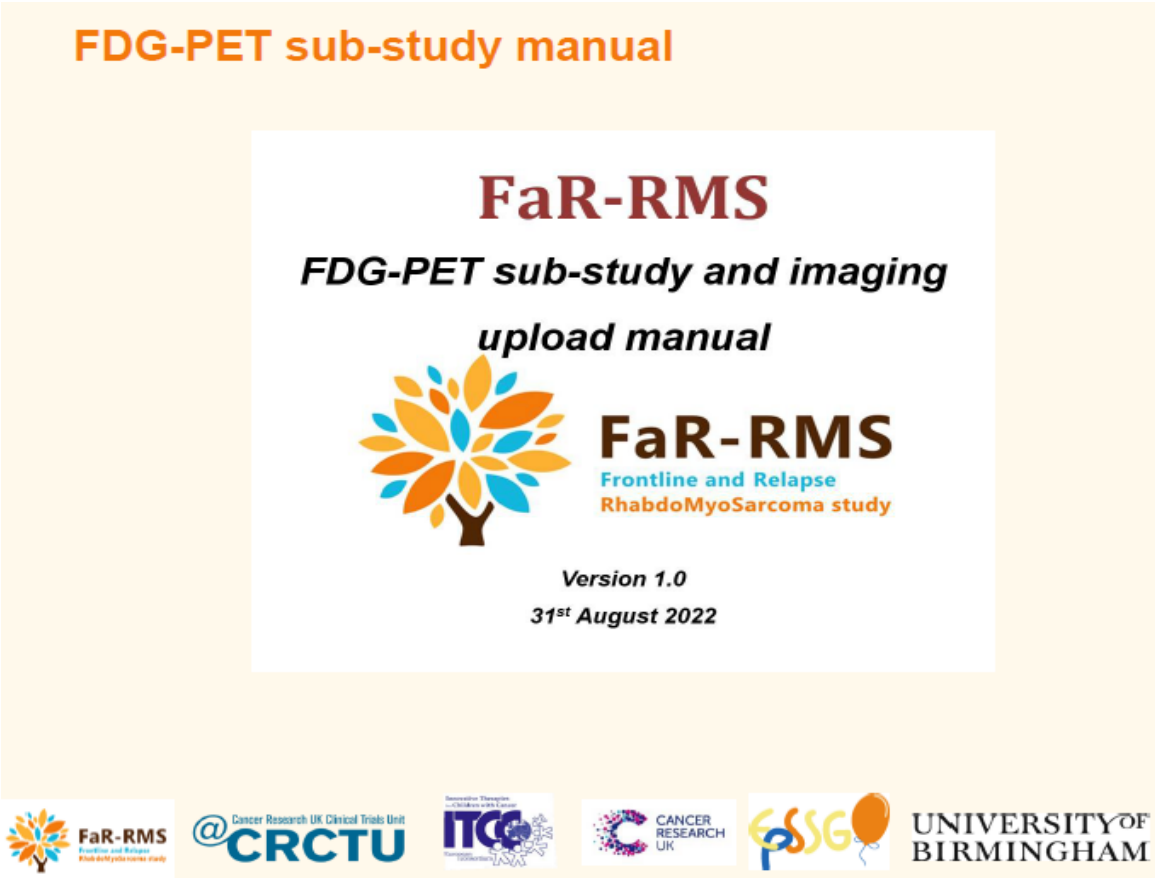
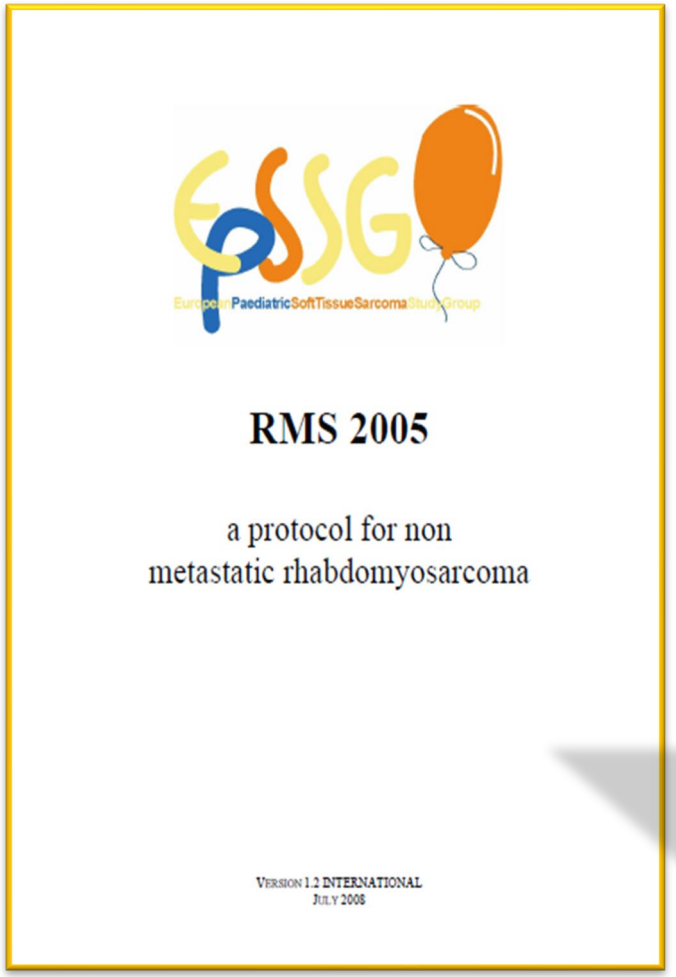


SCOPO: Valutare il valore prognostico della PET-TC/RMN per i pazienti con diagnosi di RMS Very Hight Risk e Hight Risk.

- Ottobre 2022 attivata la piattaforma di imaging Keosys FaR RMS
- Novembre 2022: revisione delle immagini da parte di 5 Medici nucleari.
- L'esame PET revisionato sarà quello eseguito alla diagnosi e dopo 3 cicli di chemioterapia di induzione.

3. Trattamento



Risk Group	Subgroups	Pathology	Post surgical Stage (IRS Group)	Site	Node Stage	Size & Age
Low Risk	*A*	Favourable	I	Any	N0	Favourable
Standard Risk	*B*	Favourable	I	Any	N0	Unfavourable
	C	Favourable	II, III	Favourable	N0	Any
	D	Favourable	II, III	Unfavourable	N0	Favourable
High Risk	*E*	Favourable	II, III	Unfavourable	N0	Unfavourable
	F	Favourable	II, III	Any	N1	Any
	G	Unfavourable*	I, II, III	Any	N0	Any
Very High Risk	*H*	Unfavourable	I, II, III	Any	N1	Any

clinical trial updates

Nonmetastatic Rhabdomyosarcoma in Children and Adolescents: Overall Results of the European Pediatric Soft Tissue Sarcoma Study Group RMS2005 Study

Gianni Bisogno, MD, PhD[1,2]; Veronique Minard-Colin, MD, PhD[3]; Ilaria Zanetti, BSc[2]; Andrea Ferrari, MD[4]; Soledad Gallego, MD, PhD[5]; Raquel Dávila Fajardo, MD, PhD[6,7]; Henry Mandeville, MD[8]; Anna Kelsey, MD[9]; Rita Alaggio, MD[10]; Daniel Orbach, MD, PhD[11]; Sheila Terwisscha van Scheltinga, MD[7]; Gabriela Guillén Burrieza, MD[12]; Myriam Ben-Arush, MD[13]; Heidi Glosli, MD[14]; Peter Mudry, MD[15]; Sima Ferman, MD[16]; Christine Devalck, MD[17]; Anne Sophie Defachelles, MD[18]; Johannes Hendrikus Maria Merks, MD, PhD[7,19]; and Meriel Jenney, MD, PhD[20]

J Clin Oncol 00.

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

Lancet Oncol 2018; 19: 1061–71

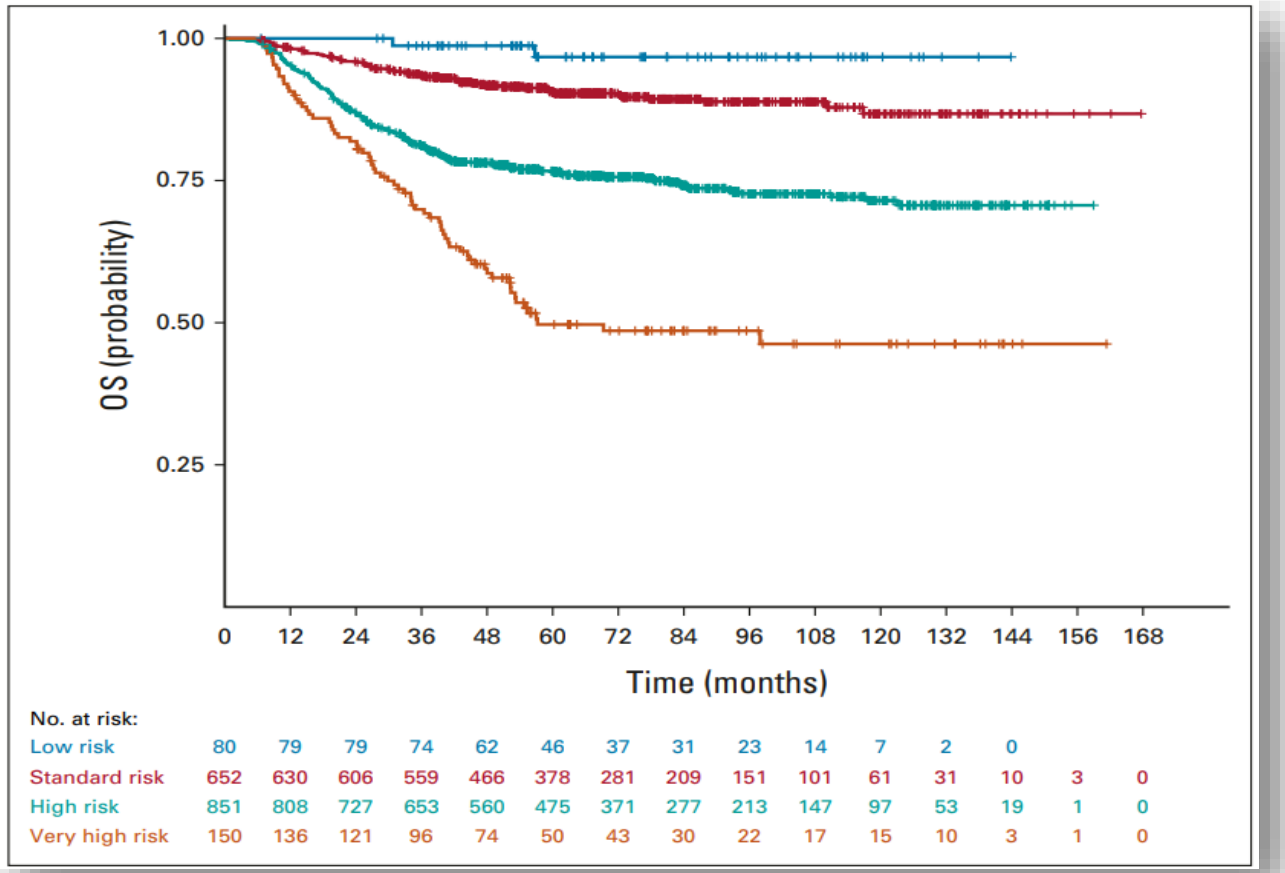
Vinorelbine and continuous low-dose cyclophosphamide as maintenance chemotherapy in patients with high-risk rhabdomyosarcoma (RMS 2005): a multicentre, open-label, randomised, phase 3 trial

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*

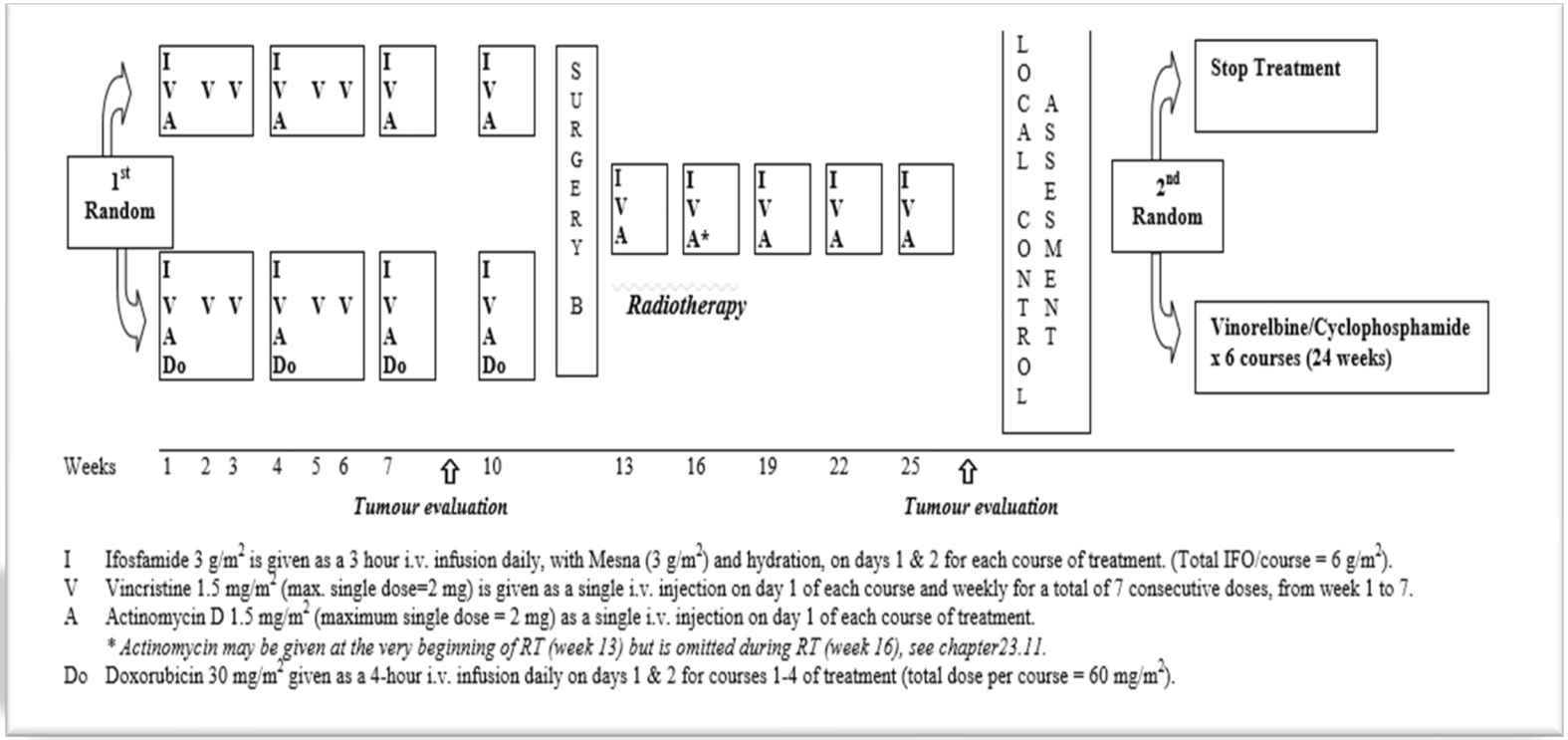
Lancet Oncol 2019; 20: 1566–75

Conclusioni sul trattamento

- EFS e OS dei pz non metastatici: 70,7% (range 68,5-72,8) e 80,4% (range 78,4-82,3)
- Pz LR possono effettuare un regime privo di alchilanti per 22 settimane
- La dose cumulativa di ifosfamide può essere ridotta nel gruppo SR
- Le antracicline possono essere omesse nei pazienti del sottogruppo D e HR senza comprometterne la prognosi

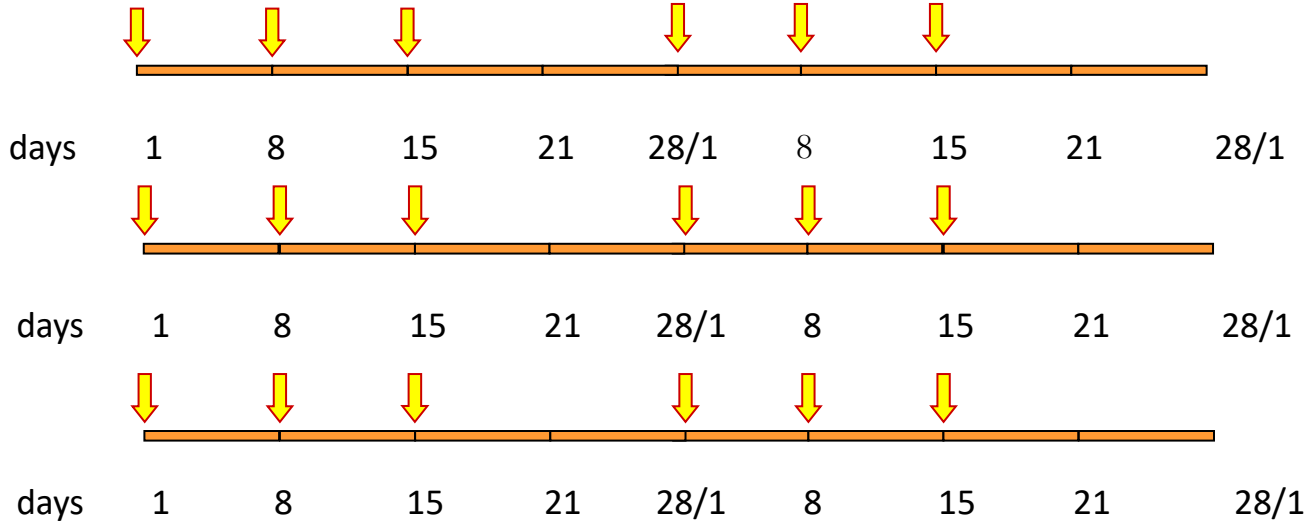


Arm	*EFS*	*OS*
Low risk	93,7% (885,5-97,3)	96,7% (87,2-99,2)
Standard risk	77,4% (73,9-80,5)	90,6 % (87,9-92,7)
High risk	67,3% (64-70,4)	76,7% (73,9-79,4)
Very high risk	48,8% (40,4-56,7)	49,7% (40,8-57,9)



I Ifosfamide 3 g/m^2 is given as a 3 hour i.v. infusion daily, with Mesna (3 g/m^2) and hydration, on days 1 & 2 for each course of treatment. (Total IFO/course = 6 g/m^2).
V Vincristine 1.5 mg/m^2 (max. single dose=2 mg) is given as a single i.v. injection on day 1 of each course and weekly for a total of 7 consecutive doses, from week 1 to 7.
A Actinomycin D 1.5 mg/m^2 (maximum single dose = 2 mg) as a single i.v. injection on day 1 of each course of treatment.
** Actinomycin may be given at the very beginning of RT (week 13) but is omitted during RT (week 16), see chapter23.11.*
Do Doxorubicin 30 mg/m^2 given as a 4-hour i.v. infusion daily on days 1 & 2 for courses 1-4 of treatment (total dose per course = 60 mg/m^2).

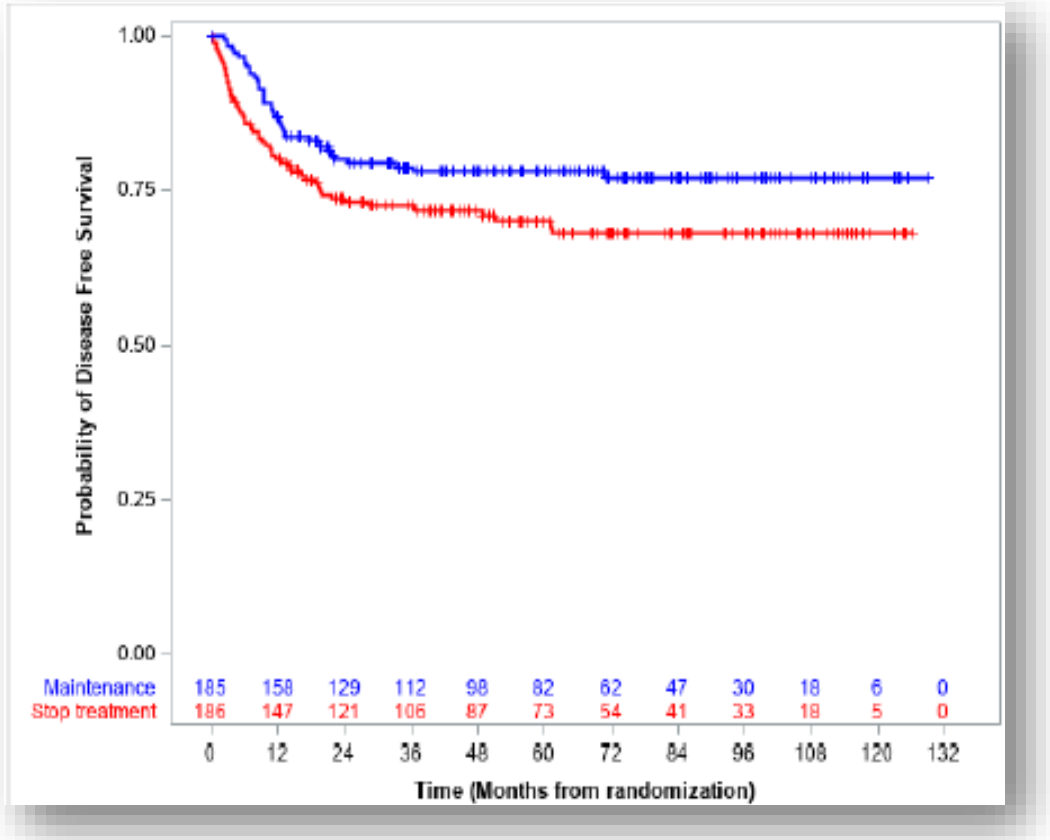
Vinorelbine
Cyclo



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

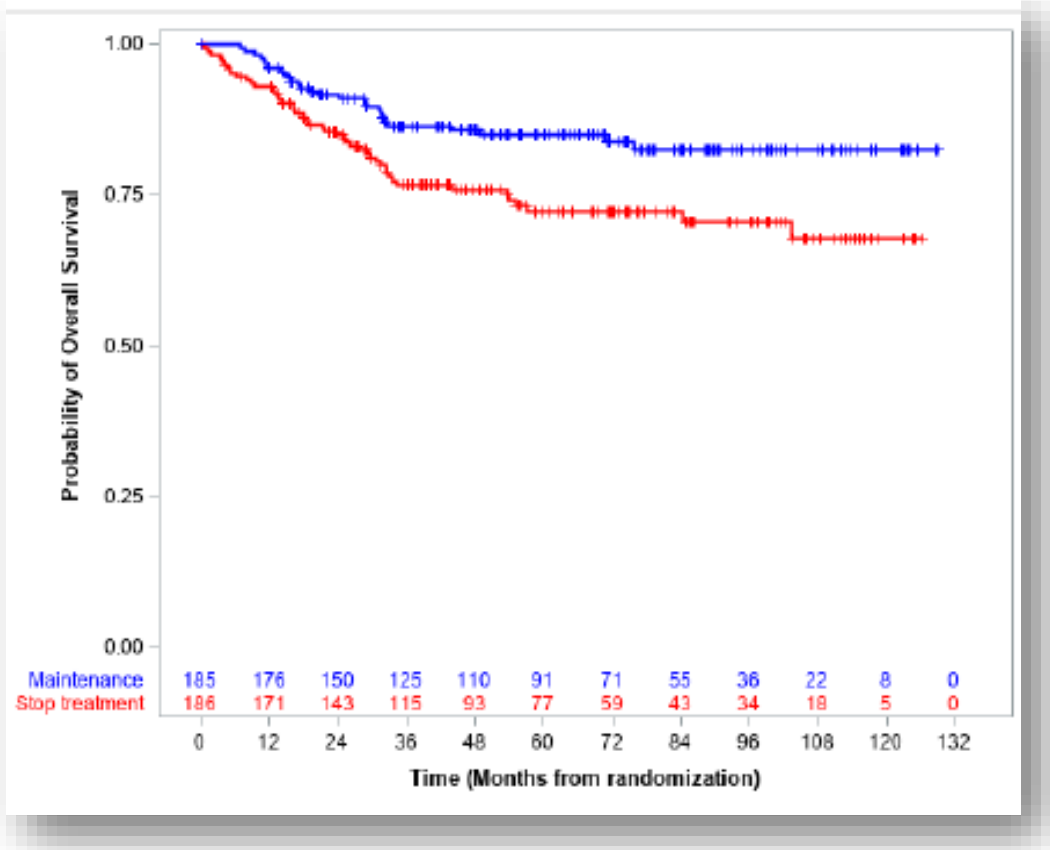
5-yrs DFS



Arm	*N*	*Events*	*5-yrs DFS*
Maintenance	185	40	78,1% (71,2-83.5)
No Maintenance	186	54	70,1% (62.6-76.3)

p-value: 0.056

5-yrs OS



Arm	*N*	*Events*	*5-yrs OS*
Maintenance	185	24	85 (78,5-89,6)
No Maintenance	186	42	72,4 (64,6-78,7)

p-value: 0.008

cancers

MDPI

Review

Maintenance Chemotherapy for Patients with Rhabdomyosarcoma

Gianni Bisogno [1,2,*], Veronique Minard-Colin [3], Meriel. Jenney [4], Andrea Ferrari [5], Julia Chisholm [6], Daniela Di Carlo [1], Lisa Lyngsie Hjalgrim [7], Daniel Orbach [8], Johannes Hendrikus Maria Merks [9,10] and Michela Casanova [5]

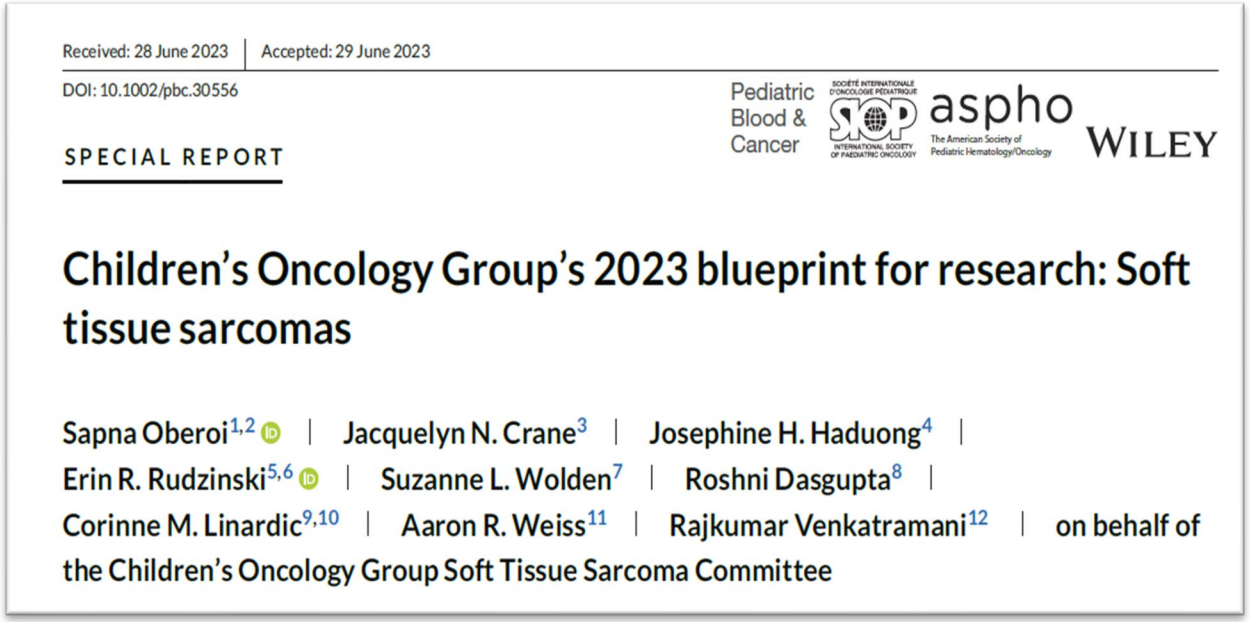
Table 1. Published trials exploring maintenance chemotherapy for patients with rhabdomyosarcoma.

Author, Year of Publication (Reference)	Study	Patients	Type of Study (No of Pts)	Maintenance Chemotherapy	Conclusion
Bisogno et al., 2019 [8]	RMS2005—international multicentre	High-risk localized RMS	Randomized (371 pts enrolled, 185 received MC)	6 cycles of i.v. vinorelbine 25 mg/m^2 on days 1, 8, 15 and oral cyclophosphamide 25 mg/m^2/day, on days 1 to 28.	Maintenance chemotherapy significantly increases patient OS (DFS increase was evident but not statistically significant)
Gallego et al., 2018 [19]	RMS2005—international multicentre	Very high risk localized RMS	Prospective (103 pts)	Same as RMS2005 study	The contribution of MC to OS and EFS difficult to establish. Prognostic impact of fusion status
Schoot et al., 2022 [20]	MTS2008—international multicentre	Metastatic RMS	Prospective (270 pts)	Same as RMS2005 study but longer (12 cycles)	The outcome remains poor. Not possible to determine whether the addition of MC improved the outcome in comparison with historical cohorts.
Chisholm et al., 2017 [21]	BERNIE—international multicentre	Metastatic soft tissue sarcomas	Randomized phase II	Same as in MTS2008 study with the addition of Bevacizumab in the experimental arm	The outcome was not improved by the addition of Bevacizumab
Klingebiel et al., 2008 [22]	HD CWS-96—international multicentre	Metastatic RMS	Prospective non randomized (96 pts enrolled, 51 received MC)	4 cycles of trofosfamide (2 × 75 mg/m^2/day) and idarubicine (1x5 mg/m^2/day 1, 4, 7, 10) alternating with 4 cyles of trofosfamide and etoposide (2 × 25 mg/m^2/day)	Significantly superior survival for patients receiving oral MC vs. those receiving high-dose chemotherapy
Dantonello et al., 2010 [23]	CWS-91, CWS-86, CWS-91, CWS-96—international multicentre	Embryonal RMS with isolated lung metastasis	Retrospective (29 pts, 8 received MC)	Same as HD CWS-96 study	5-years EFS was significantly superior in patients receiving MC
Koscielniak et al., 2022 [24]	CWS2002P—international multicentre	High-risk localized soft tissue sarcomas	Prospective non randomized (204 pts enrolled, 155 pts received MC)	7 cycles of i.v. vinblastine 3 mg/m^2 on days 1, 8, and 15 and oral cyclophosphamide 2× 25 mg/m^2/day on days 1–21. One week pause between the cycles	EFS and OS were significantly superior for patients receiving MC
Koscielniak et al., 2022 [25]	CWS-2007 HR—international multicentre	High-risk localized soft tissue sarcomas	Randomized 195 enrolled, 96 received MC)	As in the HD CWS-96 study	OS and EFS were not different in the 2 groups
Tramsen et al., 2023 [26]	CWS IV-2002 and CWS DOK IV 2004—international multicentre	Metastatic RMS	Prospective non randomized (176 pts enrolled, 89 received MC)	Same as in the HD CWS-96 study (14 pts) or as in the CWS2002P study (75 pts)	MC produces better results than allogenic bone marrow transplant and similar results when compared to high-dose chemotherapy but with a less therapeutic burden
Devadas et al., 2019 [27]	Institutional study	Relapsed/refractory or metastatic sarcomas	Retrospective (13 RMS pts)	Oral tamoxifen 40 mg/m^2/day divided twice every day, associated with etoposide and cyclophosphamide, both drugs were given orally at the dose of 50 mg/m^2 for 21 days every 28 days, for at least 1 year.	MC is a low-cost treatment that can induce long-term remission in few patients
El Kababri M et al., 2020 [28]	Multicentre study	Refractory or relapsing solid tumors	Prospective (14 RMS pts)	cyclophosphamide (30 mg/m^2) and etoposide (25 mg/m^2) days 1–21, followed by a break of one week and daily valproic acid (20 mg/kg) days 1–28. All drugs were given orally	The regimen demonstrated activity against sarcoma (3 responses in RMS pts)
Lan Y et al., 2023 [29]	Institutional study	Newly diagnosed high-risk and relapsed RMS	Retrospective (57 pts)	Sam as RMS2005 study (but vinorelbine was administered orally and at a lower dose) Duration 48 weeks	Interesting results in relapsed non-metastatic pts (3-year OS 70%)

Review. Bisogno et al. Cancer2023

- La maggioranza degli articoli è a favore dell'utilizzo della terapia di mantenimento nei pazienti con RMS HR;
- L'uso della terapia di mantenimento a basse dosi ha mostrato risultati migliori rispetto al mantenimento con alte dosi;
- Solo uno studio randomizzato tedesco (CWS-2007) ha dimostrato dei dati a sfavore;
- Molti aspetti della terapia di mantenimento devono essere ancora studiati (combinazione e durata)

Review. Bisogno et al. Cancer 2023



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Pediatric Blood & Cancer

SPECIAL REPORT

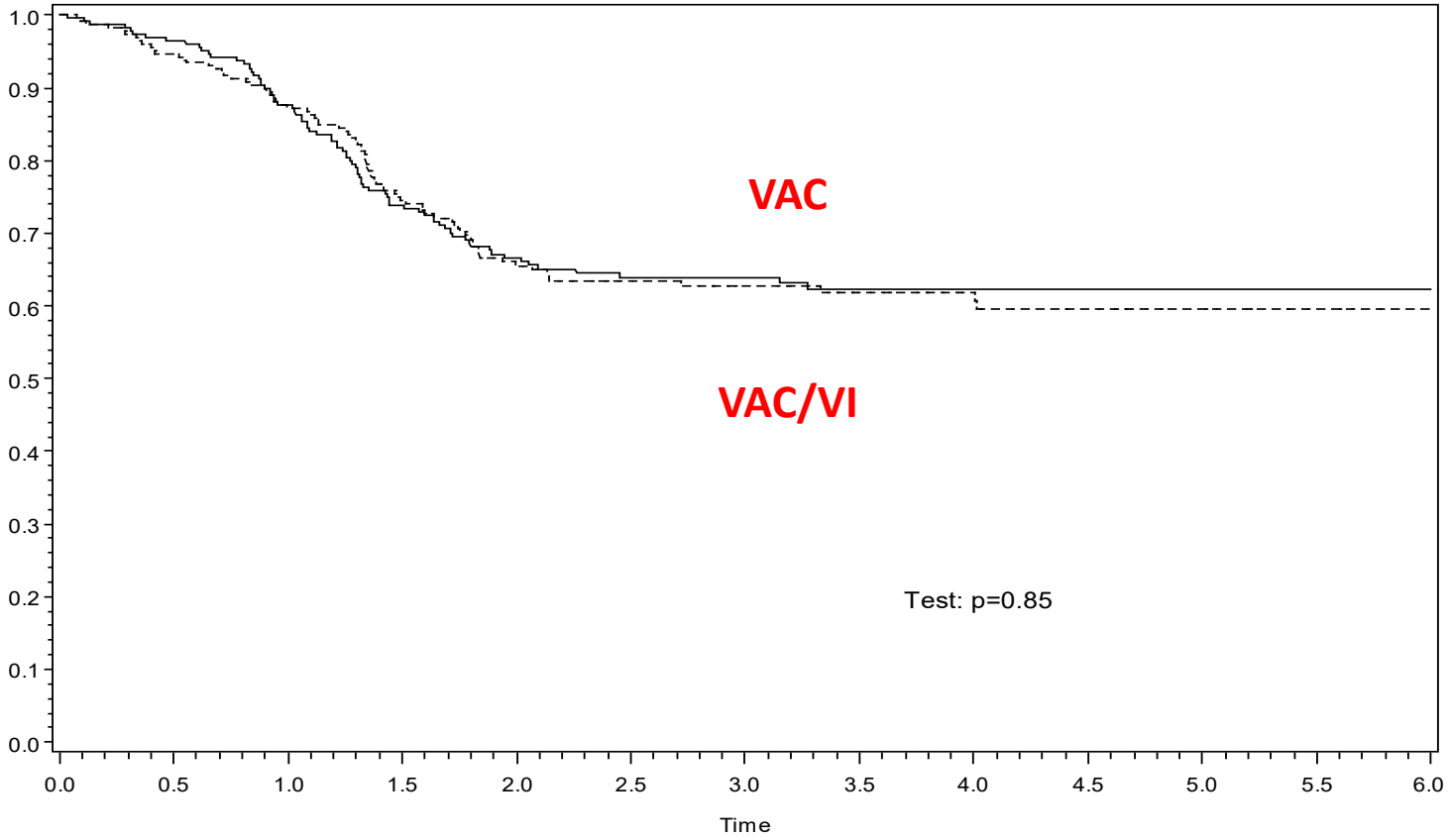
Children's Oncology Group's 2023 blueprint for research: Soft tissue sarcomas

Sapna Oberoi[1,2] | Jacquelyn N. Crane[3] | Josephine H. Haduong[4] | Erin R. Rudzinski[5,6] | Suzanne L. Wolden[7] | Roshni Dasgupta[8] | Corinne M. Linardic[9,10] | Aaron R. Weiss[11] | Rajkumar Venkatramani[12] | on behalf of the Children's Oncology Group Soft Tissue Sarcoma Committee

- Il COG per il trattamento dei pz con RMS utilizza un approccio multidisciplinare basato sulla stratificazione per rischio;
- I farmaci più utilizzati sono Vincristina e Actinomicina D ± Ciclofosfamide (VAC) e Irinotecan (VAC/VI).
- 5-year event-free survival (EFS) per tutti i pz con RMS è di circa il 70%

Oberoi et al. PBC 2023

ARST0531 Study Design



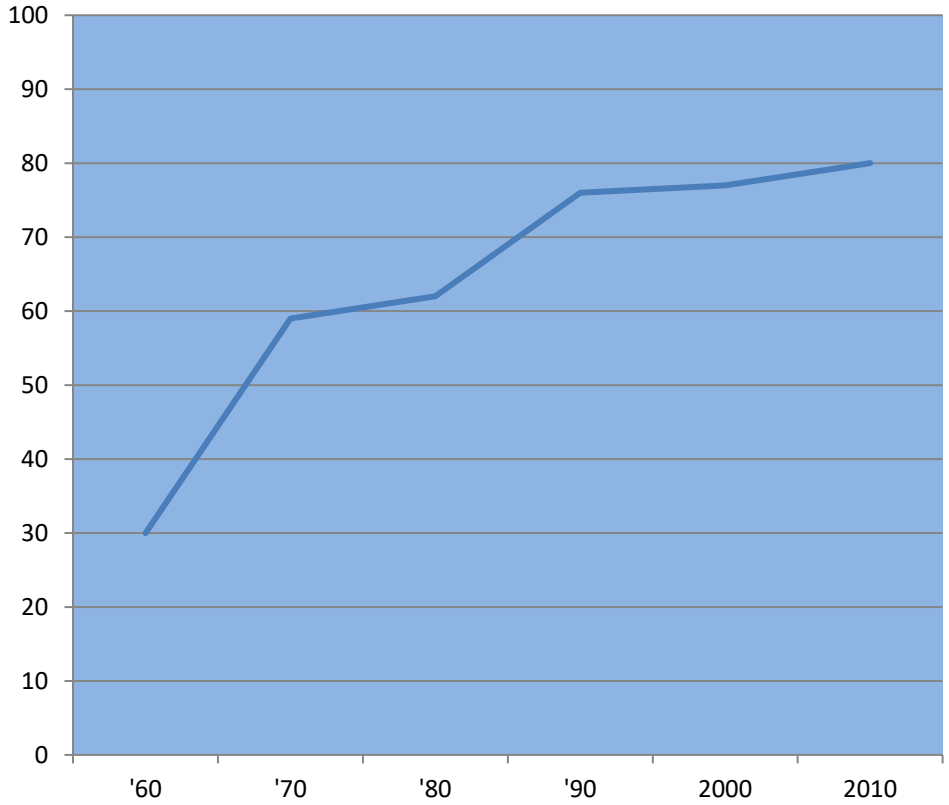
Conclusione:

- Aggiunta di VI/ VAC non migliora outcome
- Minor tossicità per il regime VAC/VI
- Minor dose di Ciclofosfamide per VAC/VI (8.4 vs. 16.8 g/m^2)

CHILDREN'S ONCOLOGY GROUP

Hawkins et al. JCO 2018

Localized RMS



Metastatic RMS

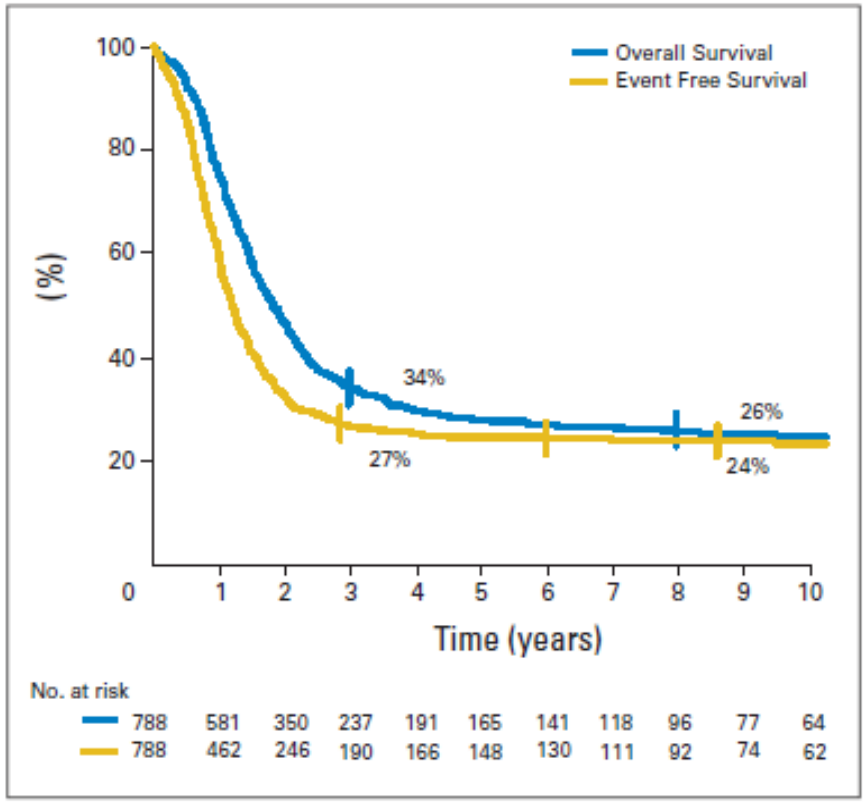


Fig 1. Overall survival and event-free survival of all 788 patients.

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

Malattia metastatica favorevole:
0-1 fattori

Malattia metastatica sfavorevole:
2-4 fattori

Oberlin score

- *Età>/= 10 aa*
- *Arti, Sito del tumore non noto, altri siti*
- *Osso/midollo osso*
- *>/= a 3 siti di metastasi*

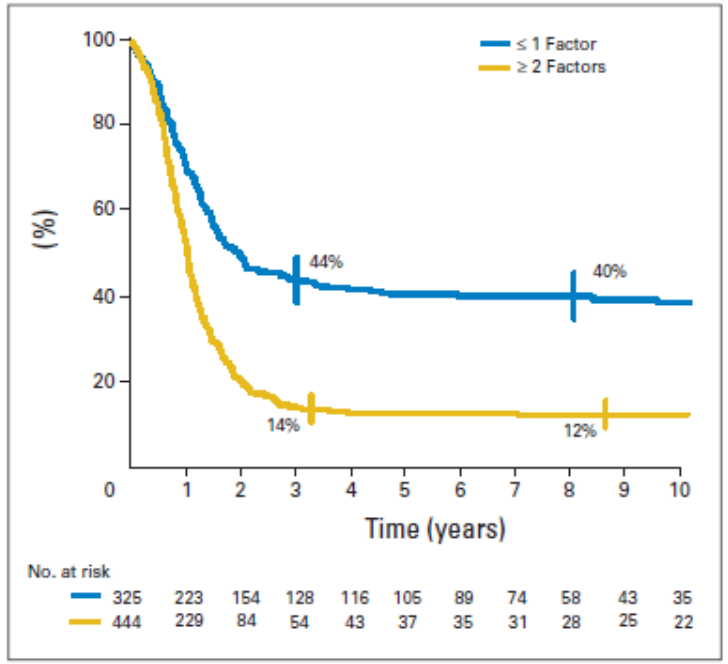


Fig 3. Event-free survival of patients according to risk score.

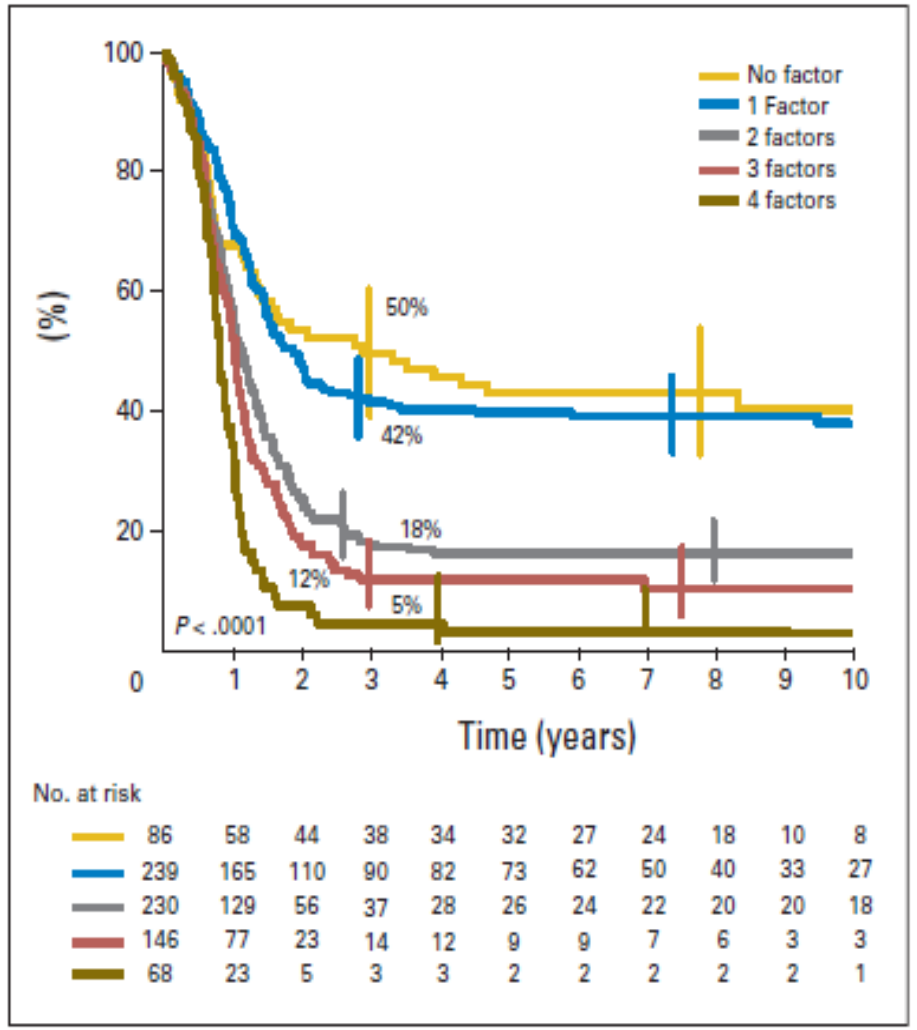


Fig 2. Event-free survival of patients according to number of unfavorable prognostic factors. The relative risks of event are respectively 1, 1.02, 1.9, 2.3, and 3.5.

European Intergroup Studies (MMT4-89 and MMT4-91) on Childhood Metastatic Rhabdomyosarcoma: Final Results and Analysis of Prognostic Factors

M. Carli, R. Colombatti, O. Oberlin, G. Bisogno, J. Treuner, E. Kosciolniak, G. Tridello, A. Garaventa, R. Pinkerton, and M. Stevens

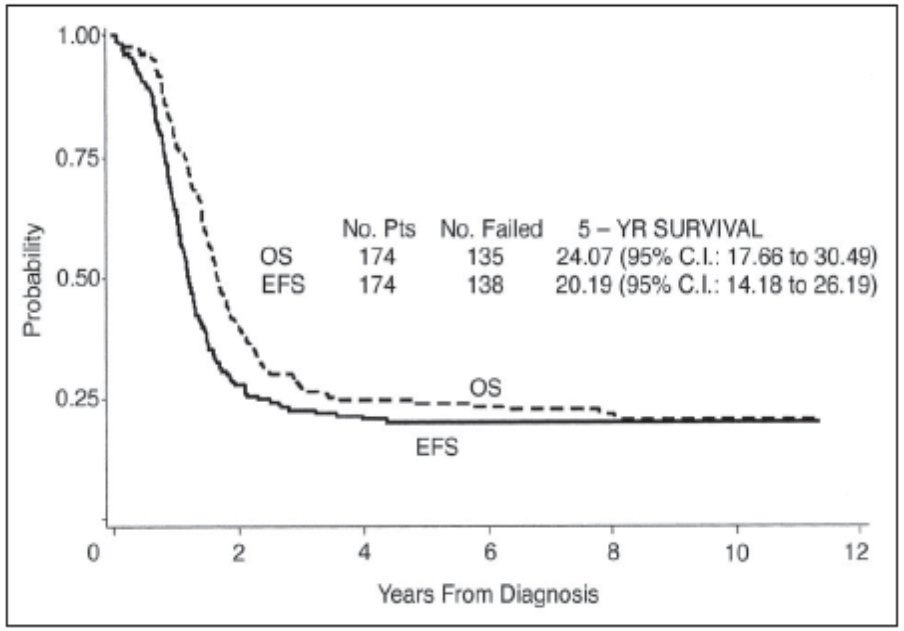
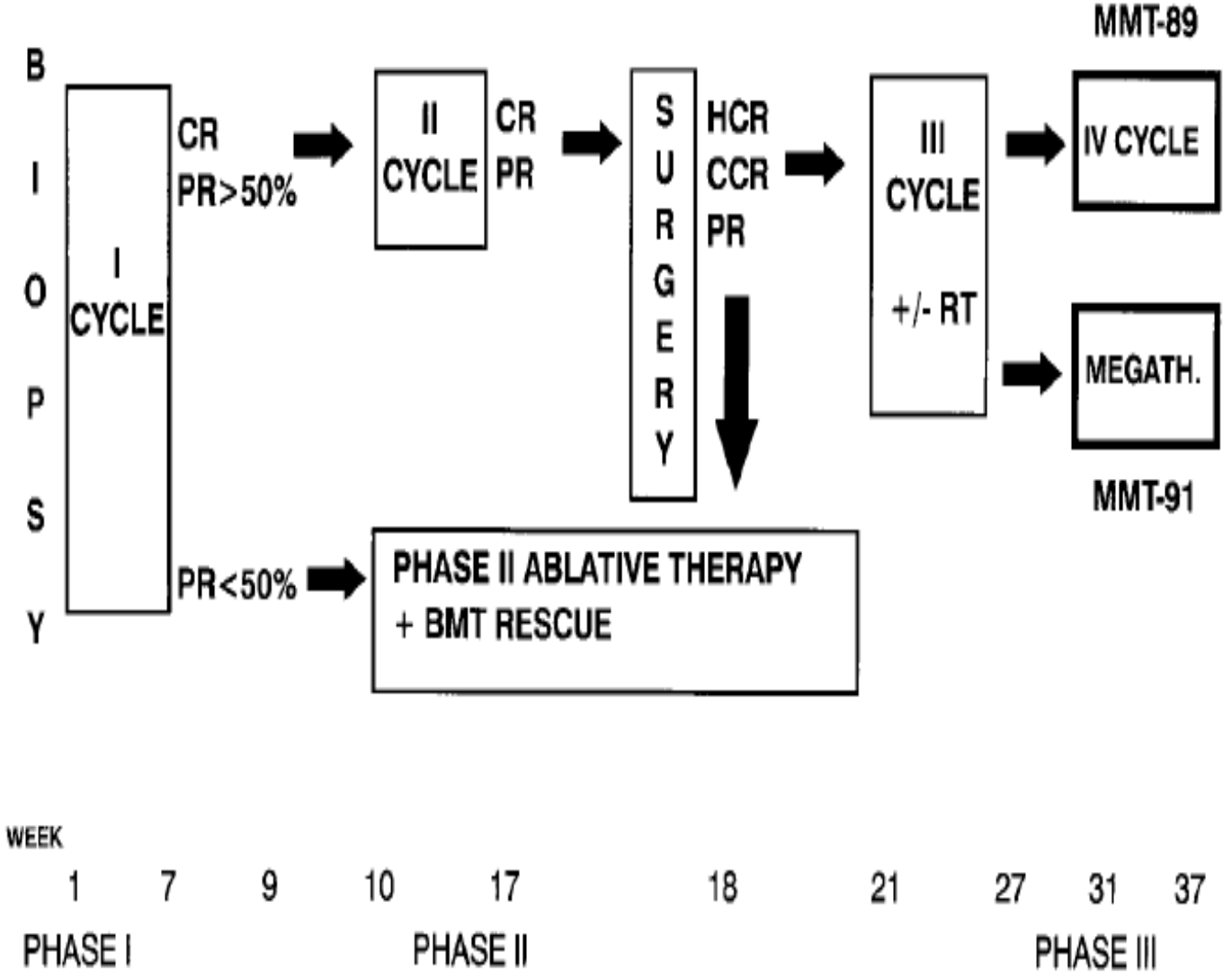


Fig 1. Overall survival (OS) and event-free survival (EFS) of 174 patients (PTS) with metastatic rhabdomyosarcoma at diagnosis. YR, year.



M. Carli et al. JCO 2004

Metastatic Rhabdomyosarcoma: Results of the European *Paediatric* Soft Tissue Sarcoma Study Group MTS 2008 Study and Pooled Analysis With the Concurrent BERNIE Study

Reineke A. Schoot, MD, PhD[1]; Julia C. Chisholm, BMBCh, PhD[2]; Michela Casanova, MD[3]; Veronique Minard-Colin, MD, PhD[4]; Birgit Geoerger, MD, PhD[4,5]; Alison L. Cameron, MB ChB, MRCP, FRCR, PGC(Ed)[6]; Beatrice Coppadoro, BSc[7]; Ilaria Zanetti, BSc[7]; Daniel Orbach, MD[8]; Anna Kelsey, MRCS, LRCP, FRCPath[9]; Timothy Rogers, MD, MBBCh, FCS(SA), FCS(paed), FRCS(paed)[10]; Cecile Guizani, MSc[11]; Markus Elze, PhD[11]; Myriam Ben-Arush, MD[12]; Kieran McHugh, MB, BCh, BAO (NUI), FRCR, FRCPI, FFRRCPI[13]; Rick R. van Rijn, MD, PhD[14]; Sima Ferman, MD, PhD[15]; Soledad Gallego, MD, PhD[16]; Andrea Ferrari, MD[3]; Meriel Jenney, MD[17]; Gianni Bisogno, MD, PhD[7]; and Johannes H.M. Merks, MD, PhD[1]

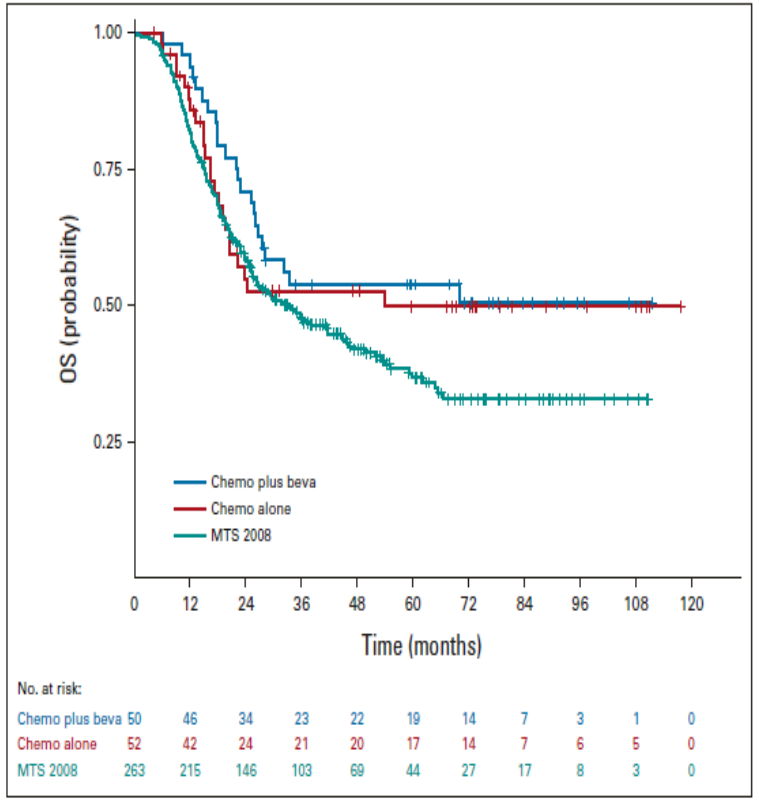
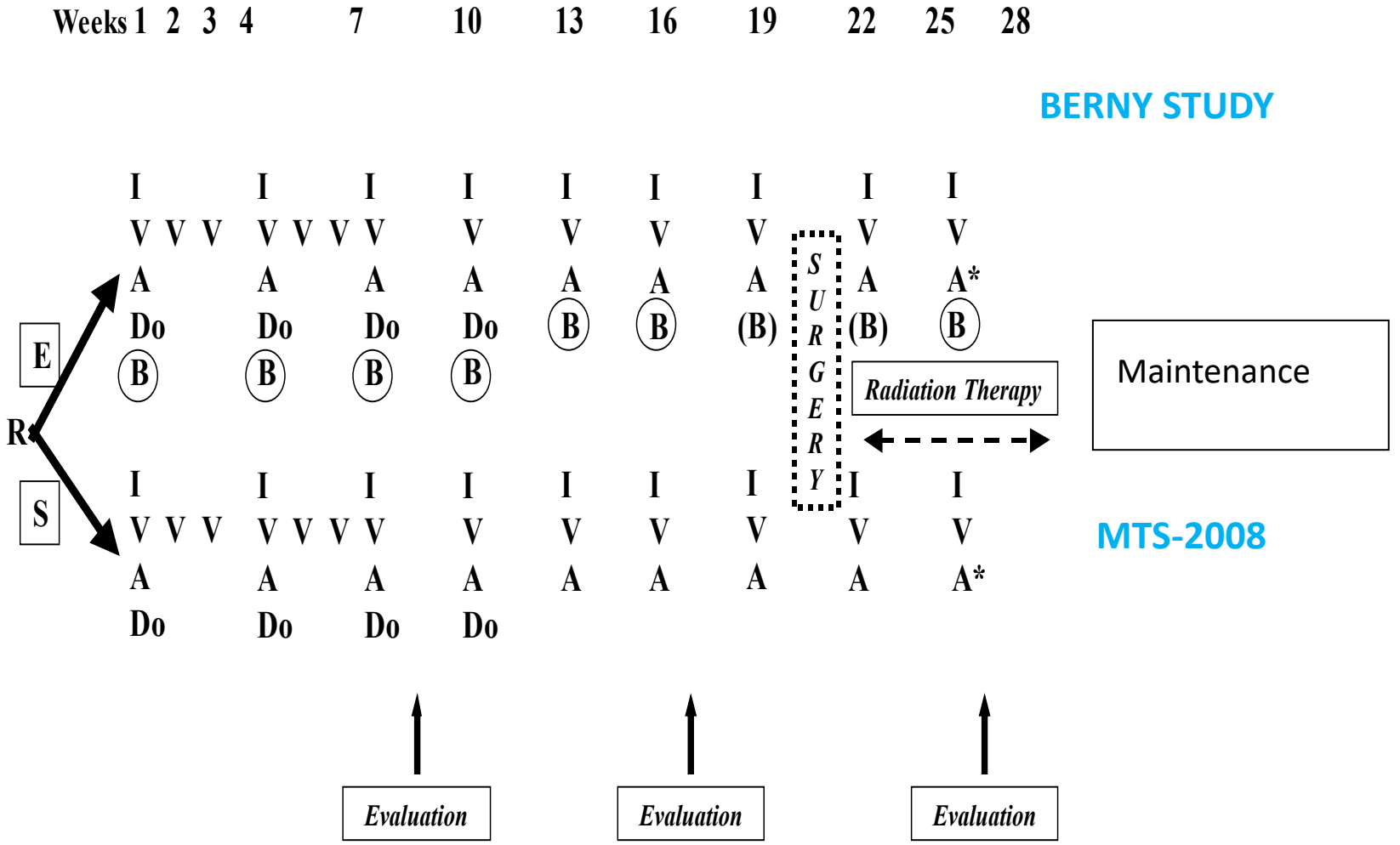


FIG 2. OS by treatment cohort. Beva, bevacizumab; chemo, chemotherapy; OS, overall survival.



Reineke A et al. JCO 2022

ARST0431

Intensive Multiagent Therapy, Including Dose-Compressed Cycles of Ifosfamide/Etoposide and Vincristine/Doxorubicin/Cyclophosphamide, Irinotecan, and Radiation, in Patients With High-Risk Rhabdomyosarcoma: A Report From the Children's Oncology Group

Brenda J. Weigel, Elizabeth Lyden, James R. Anderson, William H. Meyer, David M. Parham, David A. Rodeberg, Jeff M. Michalski, Douglas S. Hawkins, and Carola A.S. Arndt

See accompanying editorial on page 105

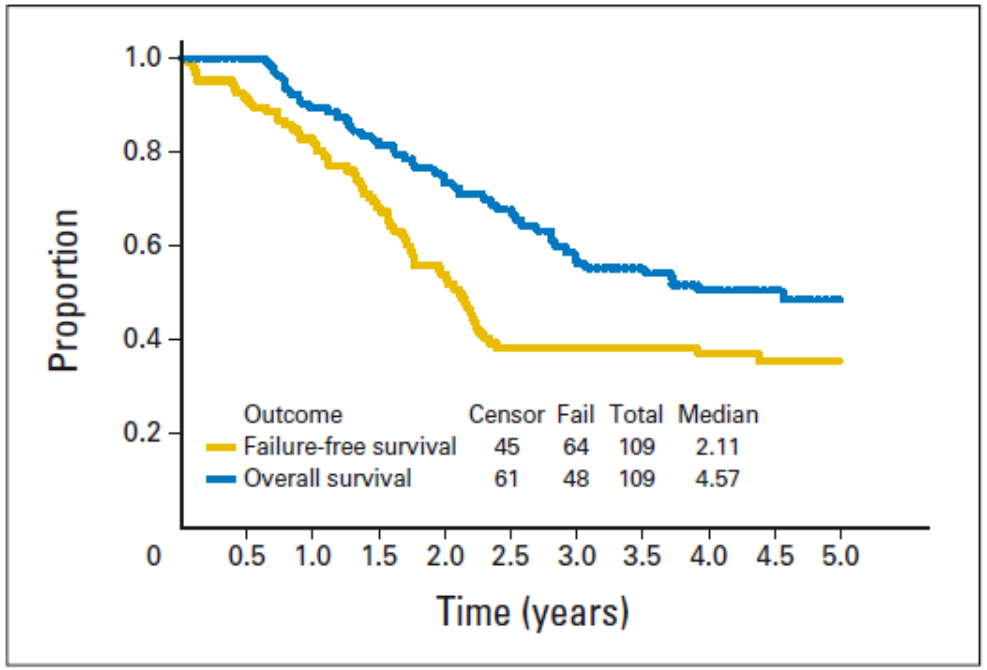


Fig 1. Outcome for all patients in ARST0431.

4.1.9 Treatment Schema

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[1]			Irin		V	D		E		D		E		D		E		V
					A	C				C				C				A
					L													L

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

[1]PG studies should be drawn before irinotecan dose

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		V	A		
Irin			Irin					C				C		A	C		
														L			

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
A			A			A			Irin			Irin				V
C			C			C										A
																L

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

CHILDREN'S ONCOLOGY GROUP

Brenda J. Weigel al. JCO 2016

Metastatic Rhabdomyosarcoma: Results of the European *Paediatric* Soft Tissue Sarcoma Study Group MTS 2008 Study and Pooled Analysis With the Concurrent BERNIE Study

Reineke A. Schoot, MD, PhD[1]; Julia C. Chisholm, BMBCh, PhD[2]; Michela Casanova, MD[3]; Veronique Minard-Colin, MD, PhD[4]; Birgit Geoerger, MD, PhD[4,5]; Alison L. Cameron, MB ChB, MRCP, FRCR, PGC(Ed)[6]; Beatrice Coppadoro, BSc[7]; Ilaria Zanetti, BSc[7]; Daniel Orbach, MD[8]; Anna Kelsey, MRCS, LRCP, FRCPath[9]; Timothy Rogers, MD, MBBCh, FCS(SA), FCS(paed), FRCS(paed)[10]; Cecile Guizani, MSc[11]; Markus Elze, PhD[11]; Myriam Ben-Arush, MD[12]; Kieran McHugh, MB, BCh, BAO (NUI), FRCR, FRCPI, FFRRCPI[13]; Rick R. van Rijn, MD, PhD[14]; Sima Ferman, MD, PhD[15]; Soledad Gallego, MD, PhD[16]; Andrea Ferrari, MD[3]; Meriel Jenney, MD[17]; Gianni Bisogno, MD, PhD[7]; and Johannes H.M. Merks, MD, PhD[1]

TABLE 3. Survival Data in Metastatic Rhabdomyosarcoma Cohorts

				≤ 1 ORF			≥ 2 ORFs		
Study	No.	3-Year EFS (95% CI)	3-Year OS (95% CI)	No.	3-Year EFS (95% CI)	3-Year OS (95% CI)	No.	3-Year EFS (95% CI)	3-Year OS (95% CI)
Oberlin[a]	788	27 (24 to 30)	34 (31 to 38)	325	44 (38 to 49)		444	14 (11 to 18)	
MTS 2008	263	35 (29 to 41)	48 (42 to 54)	113	50 (40 to 59)	61 (52 to 70)	150	24 (17 to 31)	37 (29 to 45)
BERNIE	102	37 (26 to 48)	53 (42 to 63)	44	45 (26 to 63)	72 (53 to 85)	58	31 (19 to 44)	39 (25 to 52)
MTS 2008/BERNIE	365	36 (30 to 41)	49 (44 to 55)	157	49 (40 to 57)	64 (56 to 72)	208	26 (20 to 32)	38 (31 to 45)
ARST0431[b]	109	38 (29 to 48)	56 (46 to 66)	43	69 (52 to 82)	79 (62 to 89)	66	20 (11 to 30)	14 (11 to 18)
ARST08P1[c]	168	16 (8 to 23)	41 (32 to 50)	38	38 (14 to 62)	70 (51 to 88)	130	9 (3 to 15)	33 (24 to 43)

Abbreviations: EFS, event-free survival; ORF, Oberlin risk factor; OS; overall survival.

[a]The Oberlin analyses included patients from nine studies from three international cooperative groups treated between 1984 and 2000.

between July 17, 2006, and June 13, 2008.

etween January 19, 2010, and July 19, 2013. ARST08P1 consisted of two pilot studies: in pilot 1 (N = 97), cixutumumab was added to the chemotherapy vas added to the same chemotherapy backbone.

CHILDREN'S ONCOLOGY GROUP

Reineke A at al. JCO 2018

Approcci futuri....

CHILDREN'S ONCOLOGY GROUP

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Pediatric Blood & Cancer | aspho | WILEY

REVIEW

An update on rhabdomyosarcoma risk stratification and the rationale for current and future Children's Oncology Group clinical trials

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CHILDREN'S ONCOLOGY GROUP

TABLE 4 Current and planned Children's Oncology Group rhabdomyosarcoma studies

Risk group	Stage	Clinical group	Age	Fusion status	COG study	Therapy
Very low	1	I	Any	FOXO1	ARST2032[a]	VA x 24 weeks
Low	1	II, III (orbit only)	Any	FOXO1–	anticipated activation spring 2022)[a]	VAC/VA x 24 weeks
Low	2	I, II				VAC/VA x 24 weeks
Intermediate	1	III (non-orbit)	Any	FOXO1–	ARST1431	Randomization to:
	1, 2, 3	I, II, III		FOXO1+		VAC/VI x 42 weeks vs.
	2, 3	III		FOXO1–		VAC/VI/Temsirolimus x 42 weeks
	3	I, II		FOXO1–		+
	4	IV	<10 years	FOXO1–		Maintenance (CPM^{PO}Vino) x 24 weeks (all patients)
High	4	IV	>10 years	FOXO1–	ARST2031	Randomization to:
			Any	FOXO1+		VAC x 42 weeks vs.
						VinoAC x 42 weeks
						+
						Maintenance (CPM^{PO}Vino) x 24 weeks (all patients)

Abbreviations: CPM^{PO}, daily oral cyclophosphamide; VAC, vincristine, dactinomycin, cyclophosphamide regimen using cyclophosphamide dose of 1.2 g/m^2/cycle; Vino, vinorelbine; VinoAC, vinorelbine, dactinomycin, cyclophosphamide regimen using cyclophosphamide dose of 1.2 g/m^2/cycle.

[a]Patients treated on VLR or LR arms of ARST2032 must have MYOD1/TP53 wildtype tumors.

FaR-RMS
Frontline and Relapse RhabdoMyoSarcoma study

Risk Group	Subgroup	Fusion gene status#	Post-surgical stage	Site	Nodal stage	Size & age
Low (LR)	A	Neg.	I	Any	N0	≤5cm & <10y
Standard (SR)	B	Neg.	I	Any	N0	>5cm &/or ≥10y
	C	Neg.	II, III	Favourable[1]	N0	Any
	D	Neg.	II, III	Unfavourable[2]	N0	Any
High (HR)	E	Neg.	II, III	Any	N1	Any
	F	Pos.	I, II, III	Any	N0	Any
Very High (VHR)	G	Pos.	I, II & III	Any	N1	Any
	H	Any	IV	Any	Any	Any

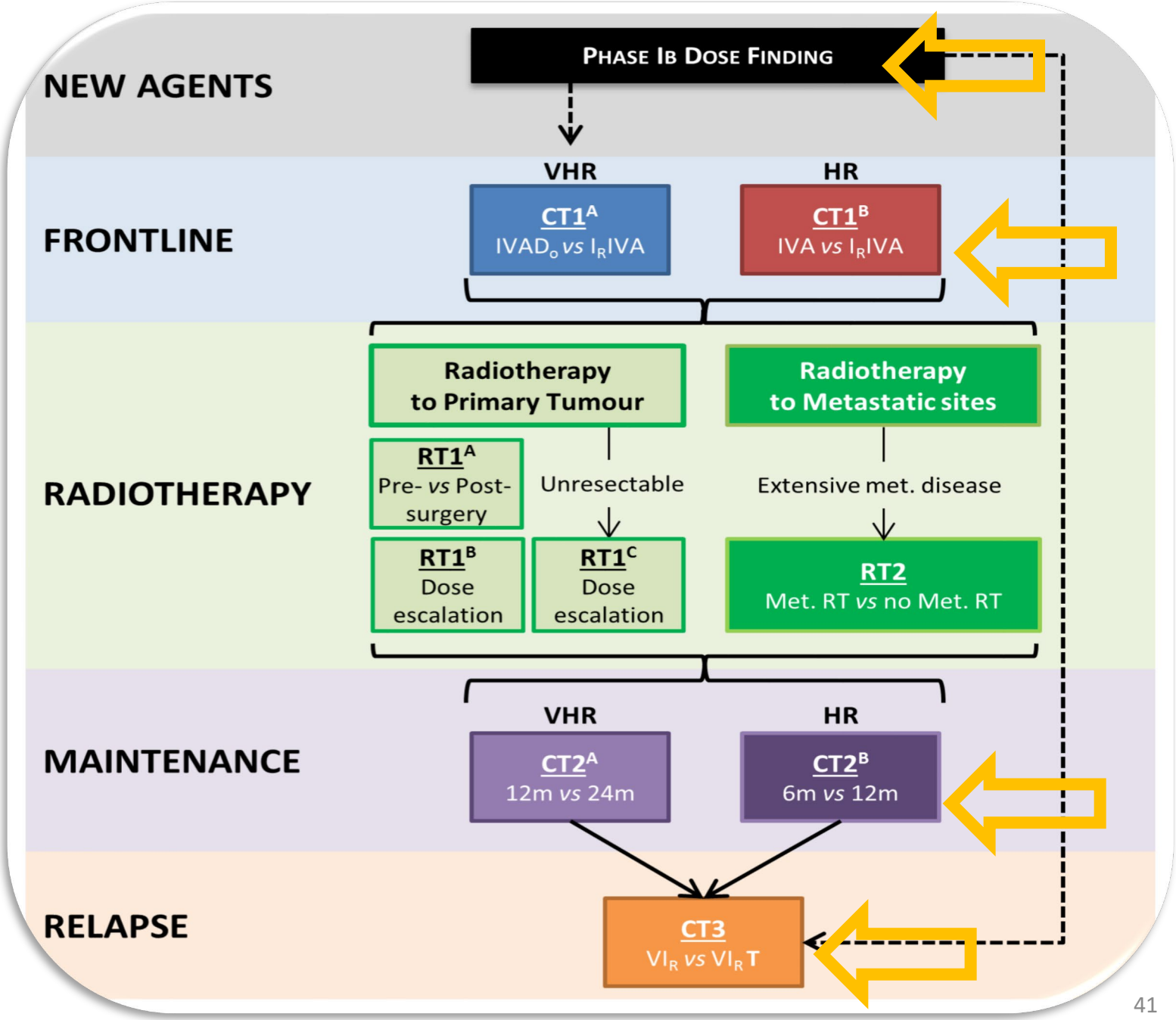
- **Fusion status**
prevale sull'istologia

- **GU- VP e biliari**
sede favorevoli

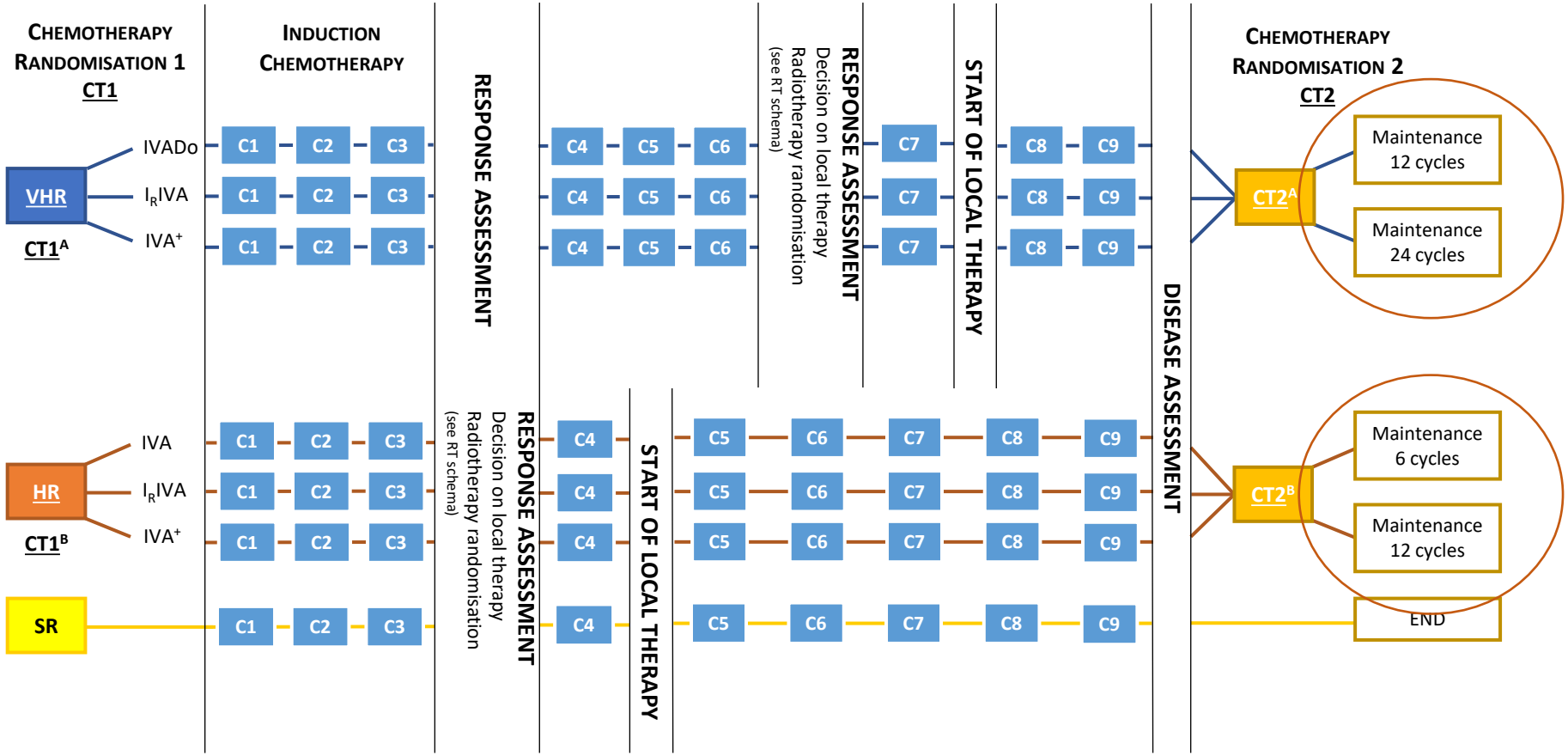
- **Sedi sfavorevole ma età/dimensioni favorevoli**
diventano high risk in FAR-RMS (es. PM con tumore < 5 cm ed età favorevole)

FaR-RMS
Frontline and Relapse RhabdoMyoSarcoma study

1° Obiettivo

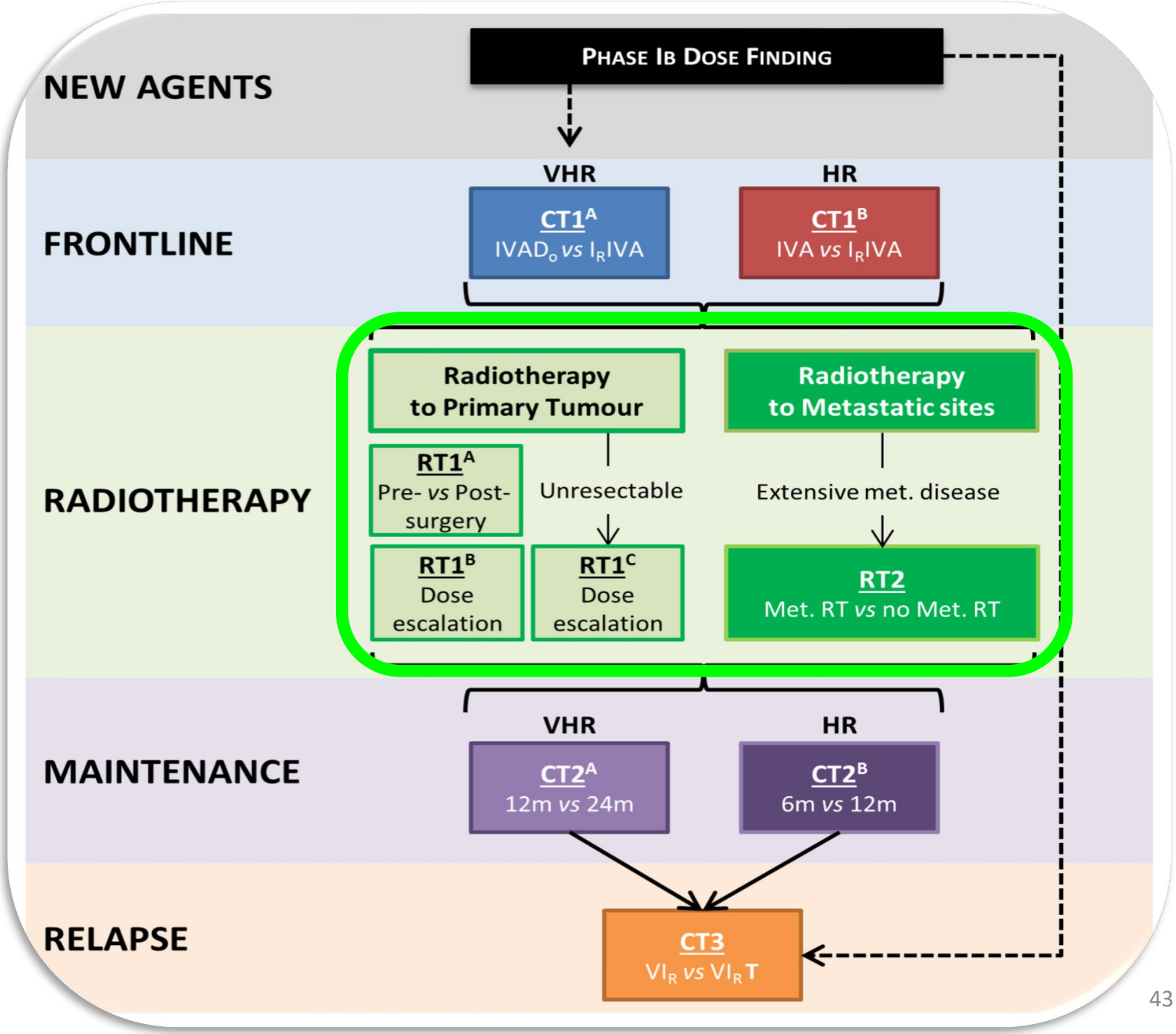


FaR-RMS
Frontline and Relapse RhabdoMyoSarcoma study

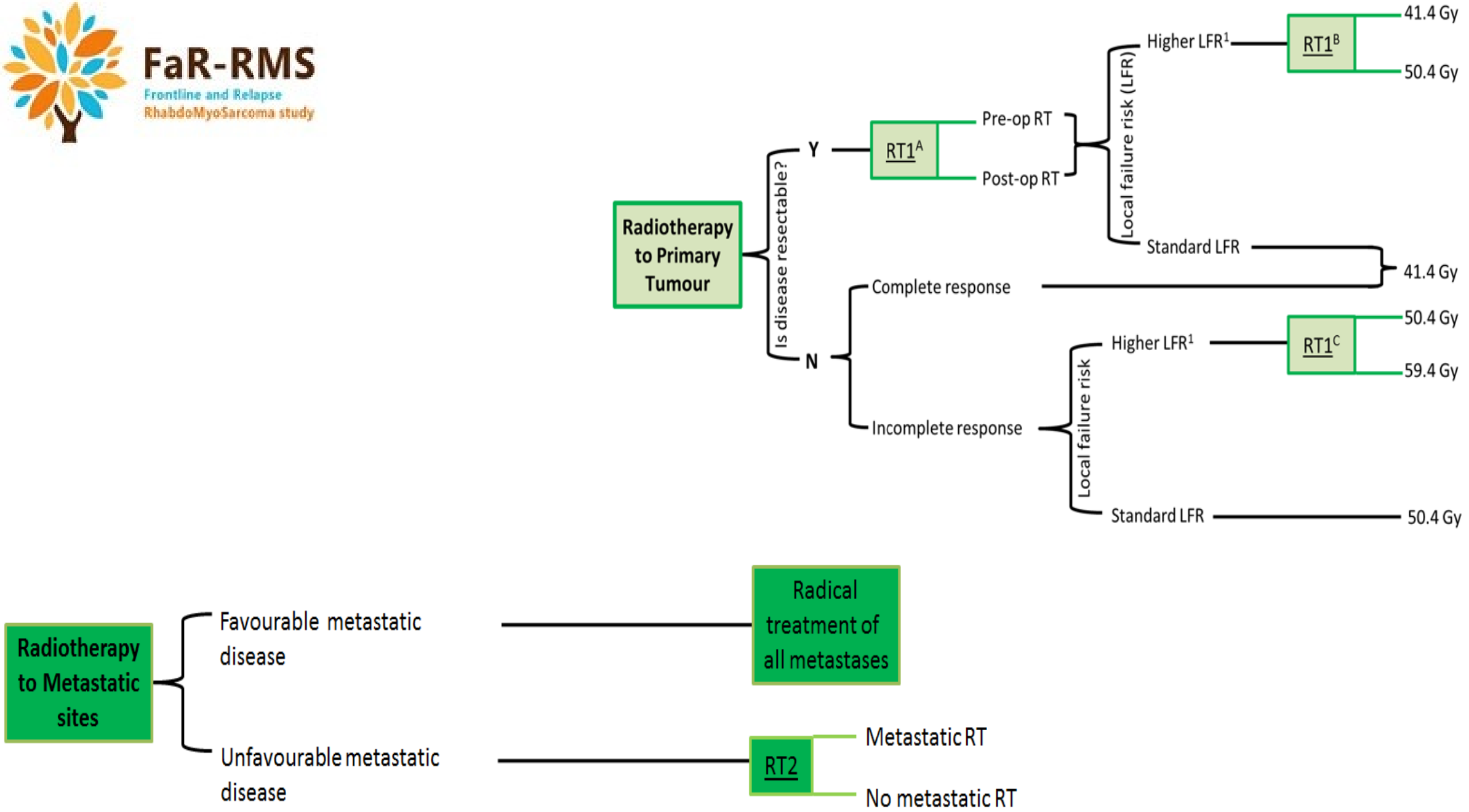


FaR-RMS
Frontline and Relapse RhabdoMyoSarcoma study

2° Obiettivo



FaR-RMS
Frontline and Relapse RhabdoMyoSarcoma study



FaR-RMS
Frontline and Relapse RhabdoMyoSarcoma study

3° Obiettivo

1) Biomarcatori radiologici (Hans Merks/Roelof van Ewijk/Alexander Leemans; Utrecht):

- *PET/TC*
- *DWI MRI*

2) Biomarcatori tumorali su tessuto (pathology lead: Anna Kelsey, Manchester; molecular profiling: Andrew Beggs (University of Birmingham))

- **mRNA seq**: signature and customized analysis of genes of interest
- **WES** for mutation analysis (panel 500 if insufficient DNA)
- **RNA fusion panel** for fusion detection
- **Germline WES** from whole blood

3) Biomarcatori molecolari su plasma including breakpoint analysis from FFPE DNA (Janet Shipley, London)

- **ct DNA analysis**

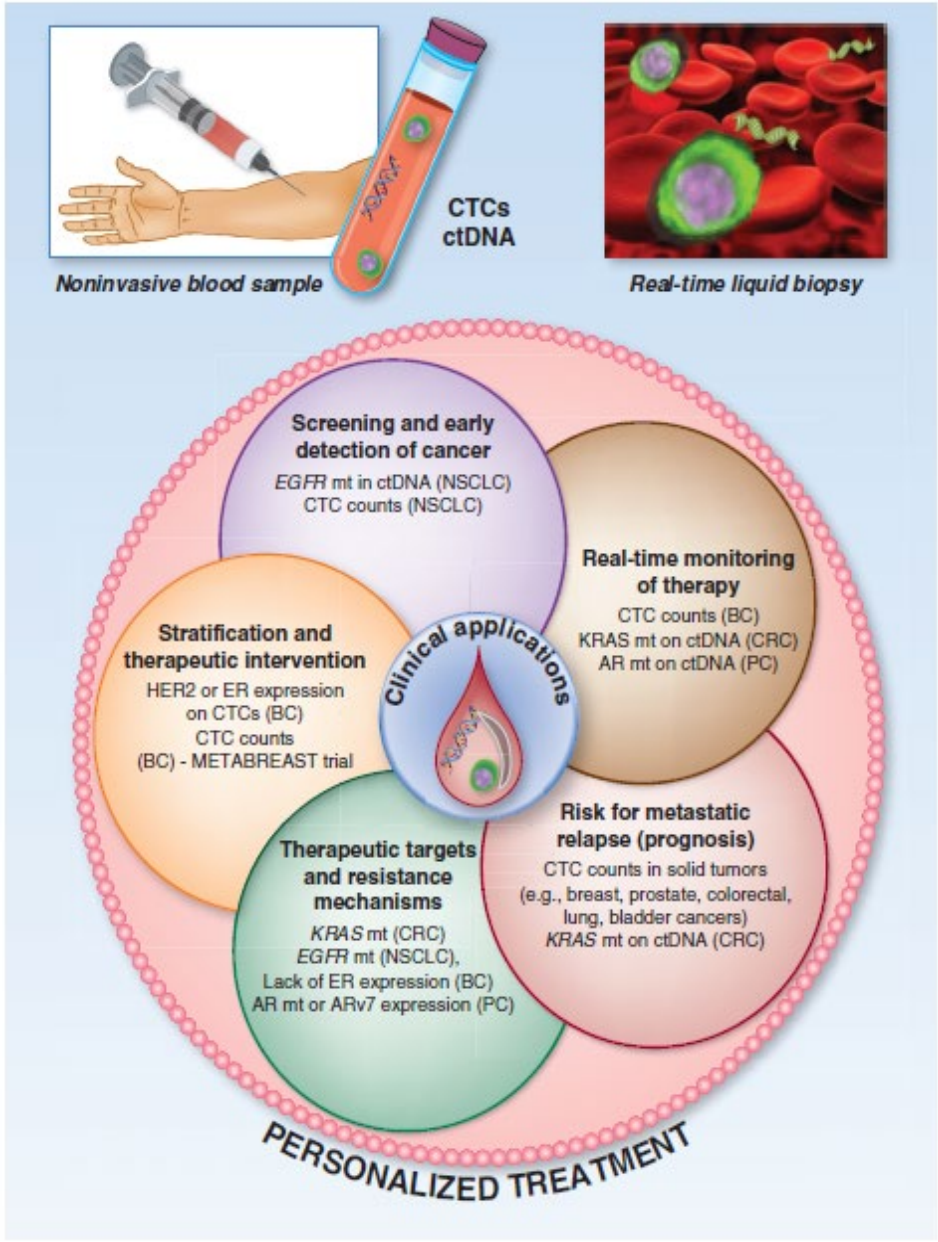
FaR-RMS
Frontline and Relapse RhabdoMyoSarcoma study

VANTAGGI

- ✓ Presenza di malattia disseminata all'esordio
- ✓ Monitorare l'evoluzione della malattia nel tempo
  - Risposta alla terapia
  - Ripresa di malattia (ricaduta)

SVANTAGGI

- ✓ Approcci metodologici in continua evoluzione
- ✓ Poco standardizzata



BIOMARKERS

Molecular Characterization of Circulating Tumor DNA in Pediatric Rhabdomyosarcoma: A Feasibility Study

Olivia Ruhen, PhD[1]; Nathalie S.M. Lak, MD[2,3]; Janine Stutterheim, MD, PhD[2,3]; Sara G. Danielli, MSc[4]; Mathieu Chicard, PhD[5]; Yasmine Iddir, PhD[5]; Alexandra Saint-Charles, PhD[5]; Virginia Di Paolo, PhD[6]; Lucia Tombolan, PhD[7]; Susanne A. Gatz, PhD[1,8]; Ewa Aladowicz, PhD[1]; Paula Proszek, MSc[1,9]; Sabri Jamal, PhD[1,9]; Reda Stankunaite, MSc[1,9,10]; Deborah Hughes, PhD[1,9]; Paul Carter, PhD[1,9]; Elisa Izquierdo, PhD[1,9]; Ajla Wasti, MD[11]; Julia C. Chisholm, MD, PhD[11,12]; Sally L. George, MD, PhD[1,11]; Erika Pace, PhD[11,13]; Louis Chesler, MD, PhD[1,11]; Isabelle Aerts, MD[5]; Gaelle Pierron, PhD[5]; Sakina Zaidi, MSc[14]; Olivier Delattre, MD, PhD[14]; Didier Surdez, PhD[14,15]; Anna Kelsey, MD[16]; Michael Hubank, PhD[1,9]; Paolo Bonvini, PhD[7]; Gianni Bisogno, MD, PhD[17]; Angela Di Giannatale, MD, PhD[6]; Gudrun Schleiermacher, MD, PhD[5,18]; Beat W. Schäfer, PhD[4]; Godelieve A.M. Tytgat, MD, PhD[2,3]; and Janet Shipley, PhD[1]

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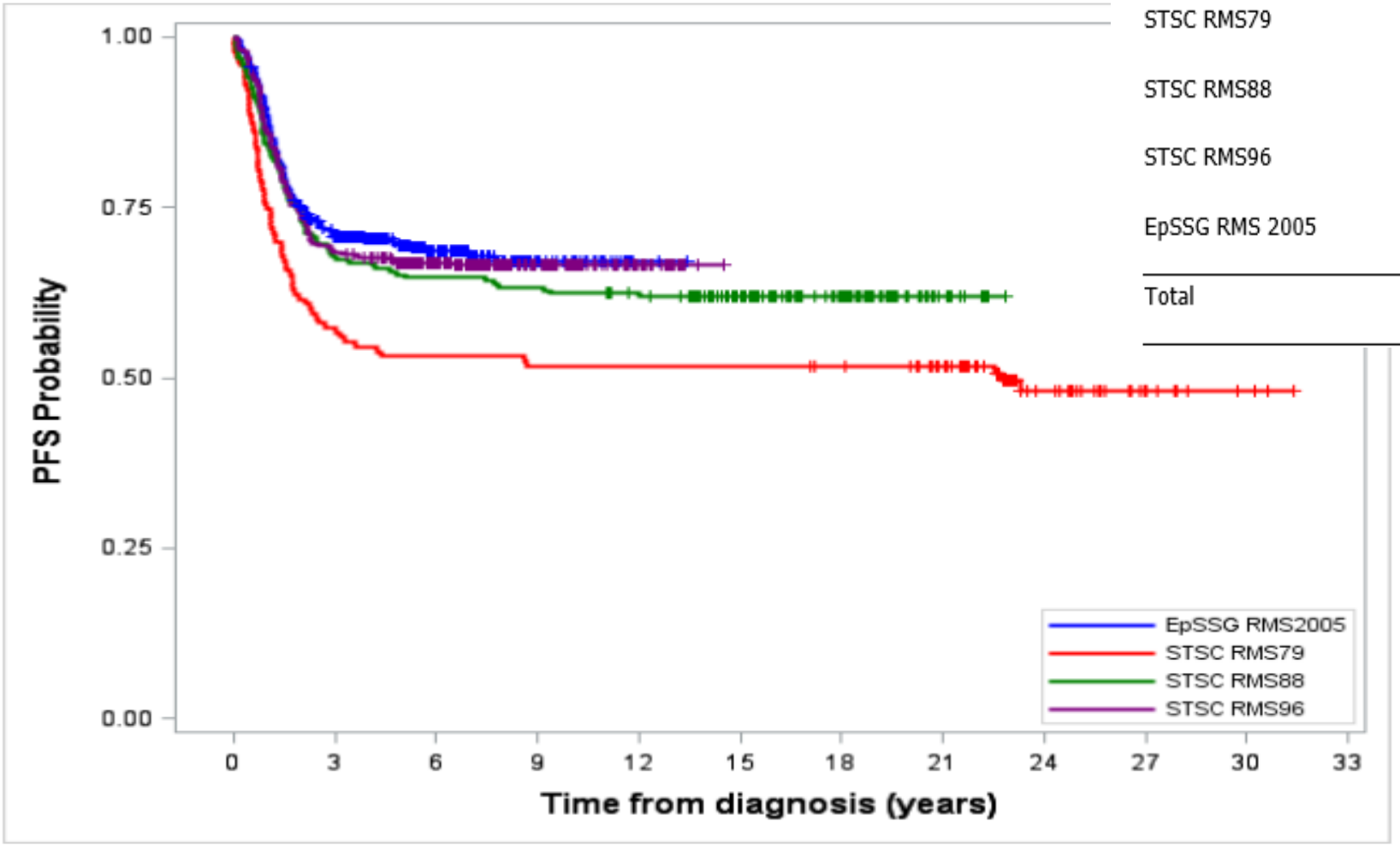
original reports

Conclusioni

PROGRESSION FREE SURVIVAL – Localised RMS Italian patients



	N patients	Failed	5-yr PFS (95%CI)	p-value
STSC RMS79	143	72	53.1 (44.6-60.9)	0.0035
STSC RMS88	218	83	65.1 (58.4-71.1)	
STSC RMS96	291	97	67.0 (61.2-72.0)	
EpSSG RMS 2005	341	106	69.5 (64.2-74.2)	
Total	993	358		


Grazie!