

Sarcoma Subtypes in Children, Teens and Young Adults

Uta Dirksen, Essen

DAY 2 – SUNDAY February 4, 2018 (Room Foscolo)

08:30 – 10:00
(90)

Sarcoma subtypes in children, teens and young adults:

- Short profiles of the relevant subtypes (Osteosarcoma and Ewing sarcoma)
- Challenges of patients, parents and medical experts

Speaker: Uta Dirksen (GER)

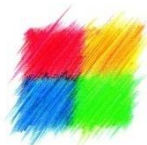
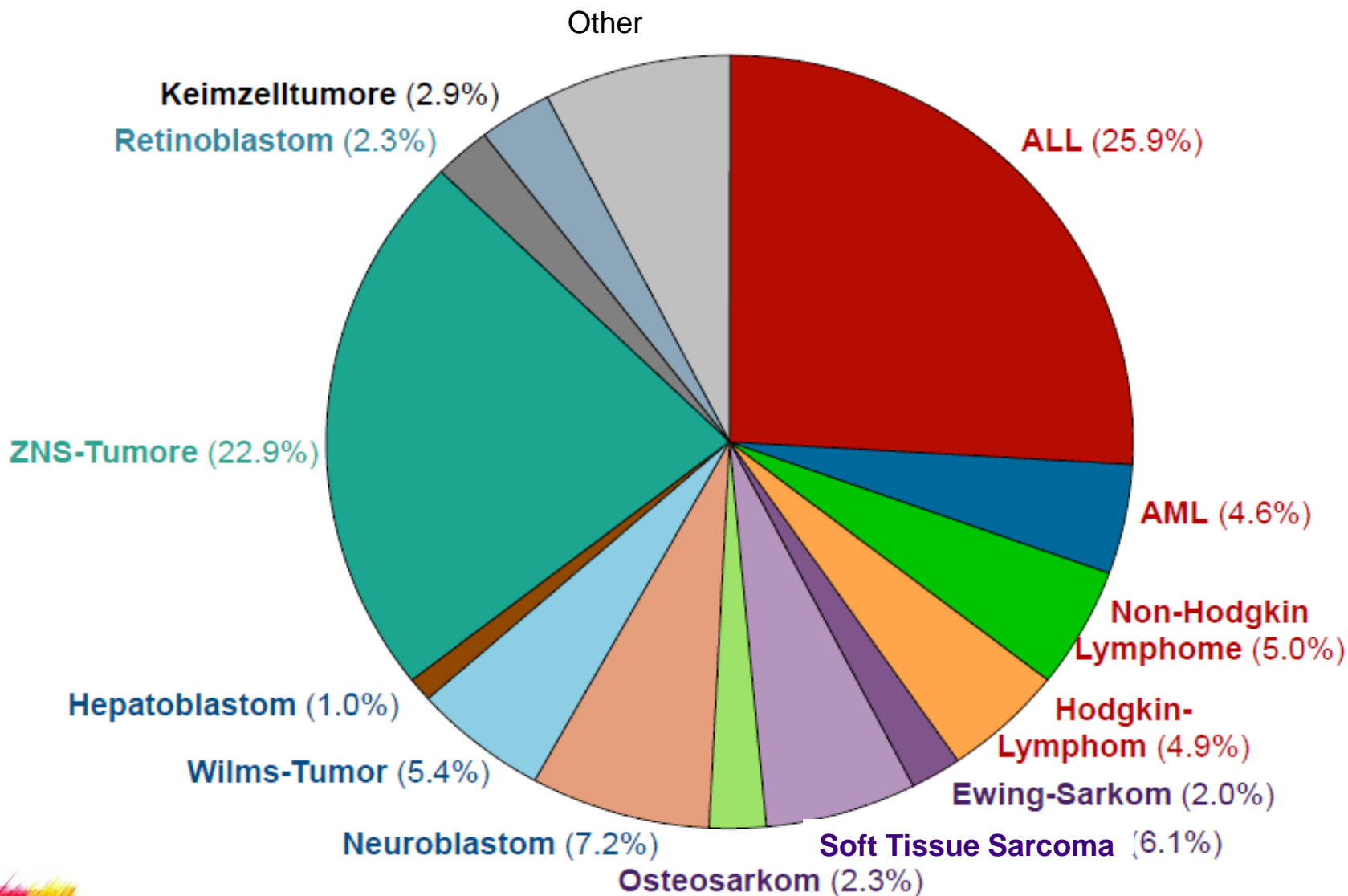
*Interview with Sami Sandakly (FR) and Angelika Sandakly (FR)
(Patient and parents perspective)*

Speaker: Winette van der Graaf (UK/NL)

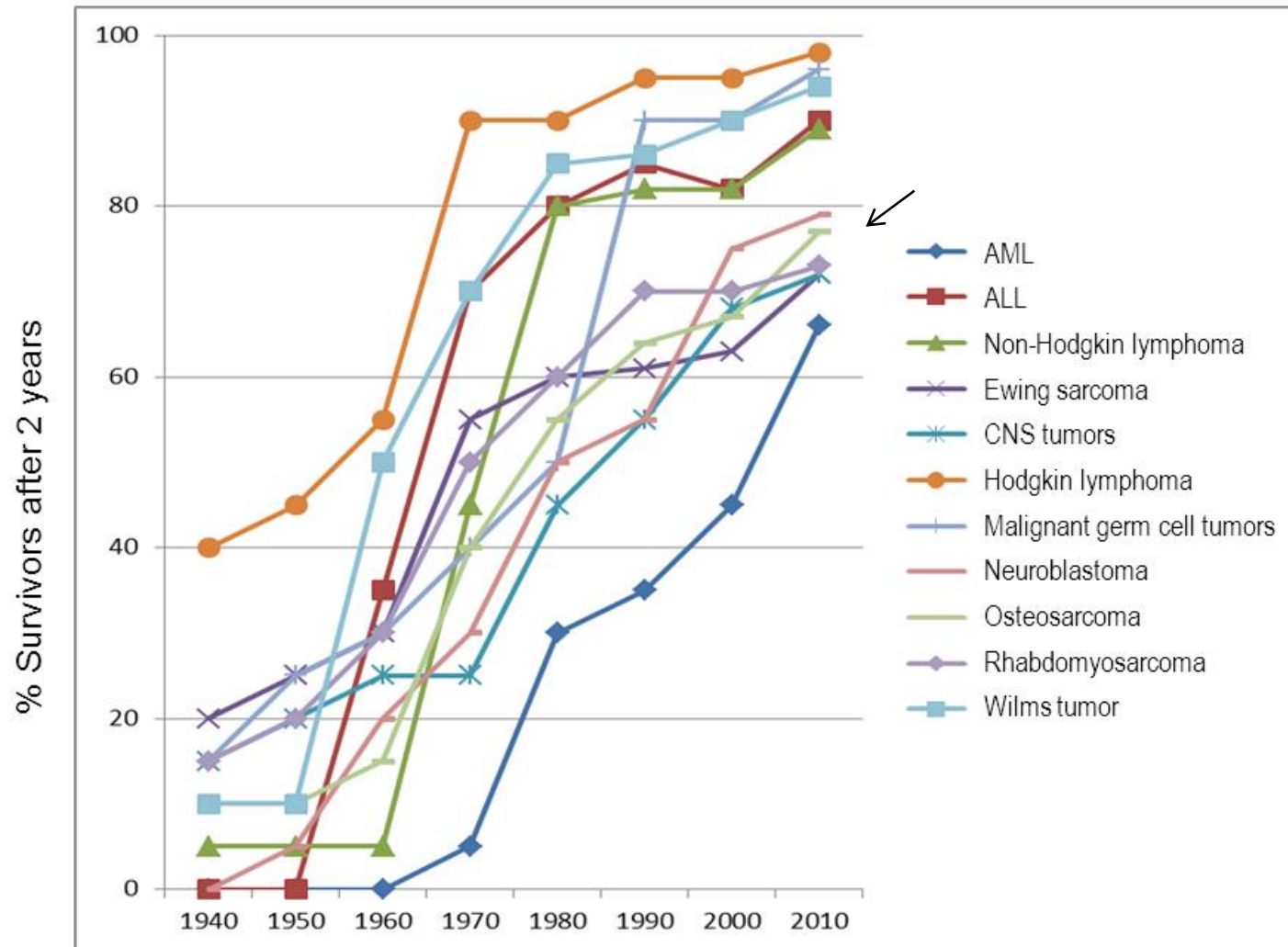
Moderator: Kathrin Schuster (GER)

10:00 – 10:30 **COFFEE BREAK (30 min.) in GAZEBO**

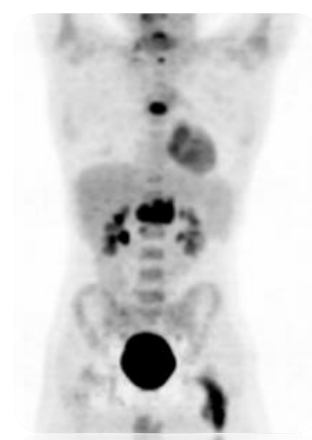
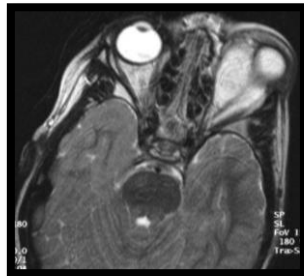
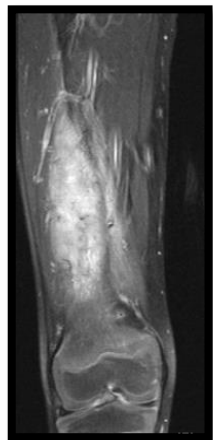




Survival since 1940



Sarcoma subtypes in children, teens and young adults



Osteosarcoma

Site: Extremity:Axial **9:1**
Metaphysis

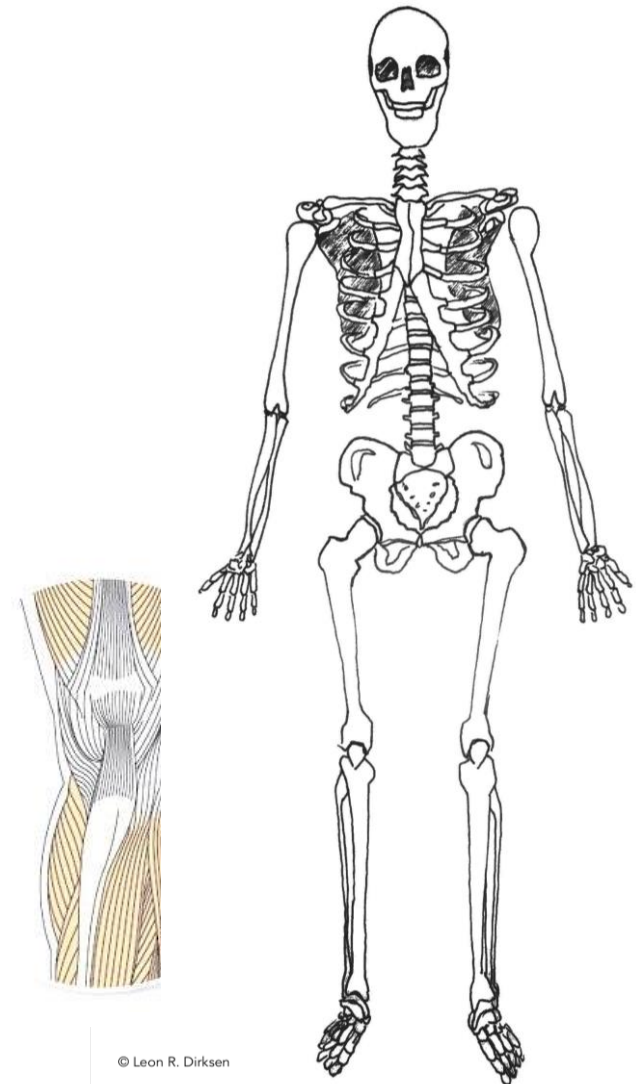
Sex: M>F

Age: TYA & Senium

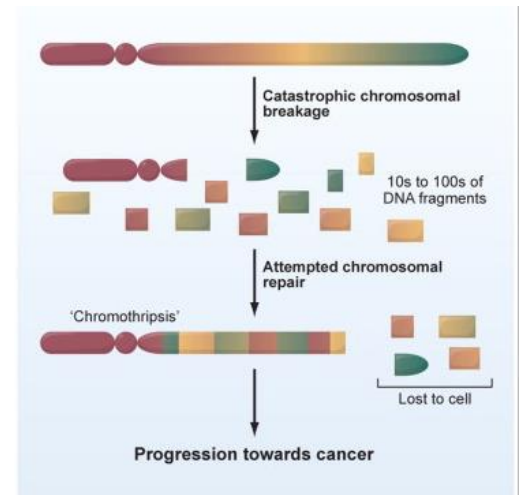
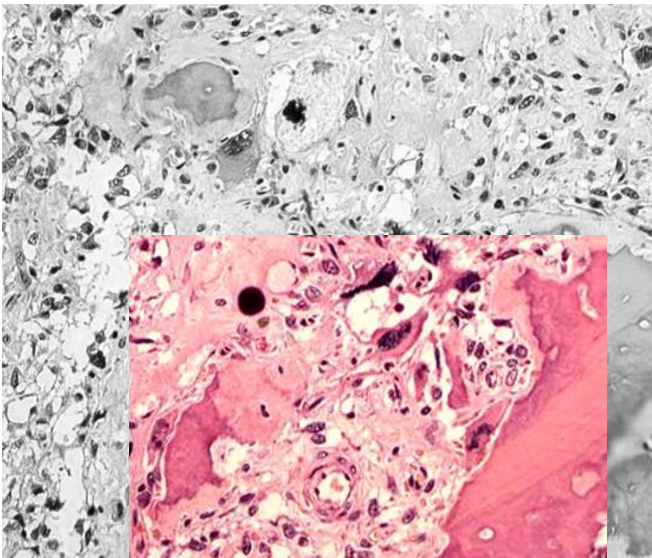
Race: All

Metastases: 20% at diagnosis

Lung:Bone 8:1



Osteosarcoma



Chemo
therapy



Chemo
therapy



1 year

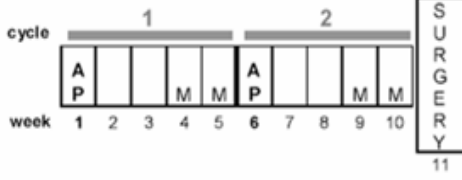
Dirksen



A = Doxorubicin 75mg/m²/course
 P = Cisplatin 120mg/m²/course
 M = Methotrexate 12g/m²/course
 E = Etoposide 500mg/m²/course
 I = Ifosfamide 14g/m²/course
 i = Ifosfamide 9g/m²/course
 Ifn = Interferon-α 0.5-1.0µg/kg weekly

GOOD RESPONSE

RANDOMISE

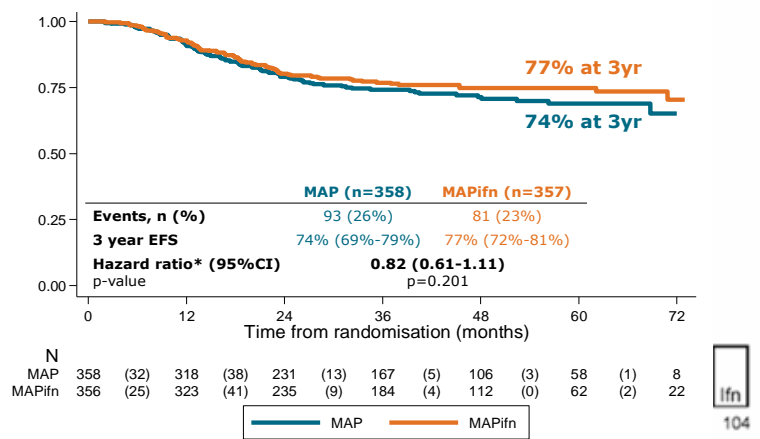


Evaluation of histological response

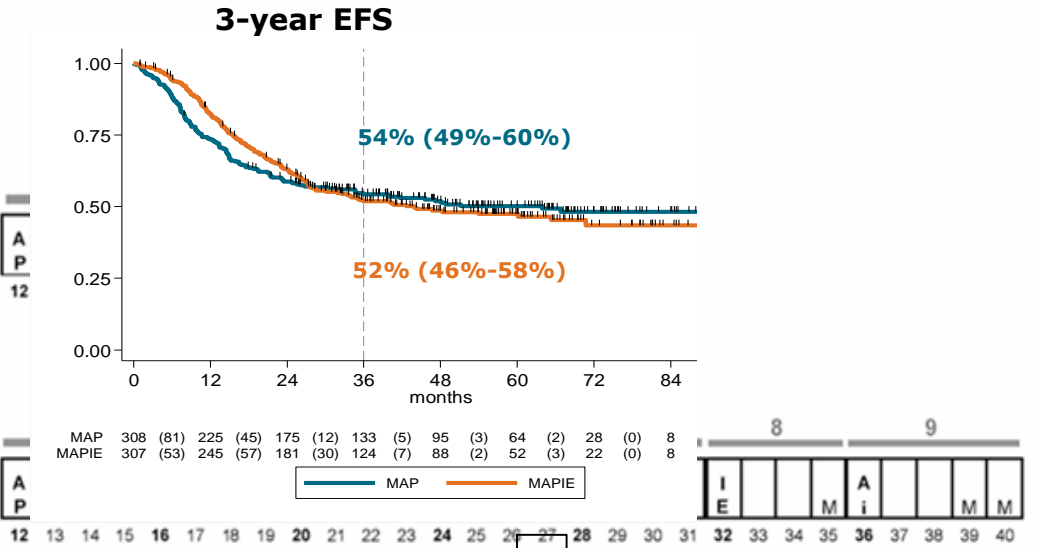
POOR RESPONSE

RANDOMISE

EFS - intention to treat



*Cox model adjusted for data center, metastases status, site and location of tumor on bone



Ewing Sarcoma

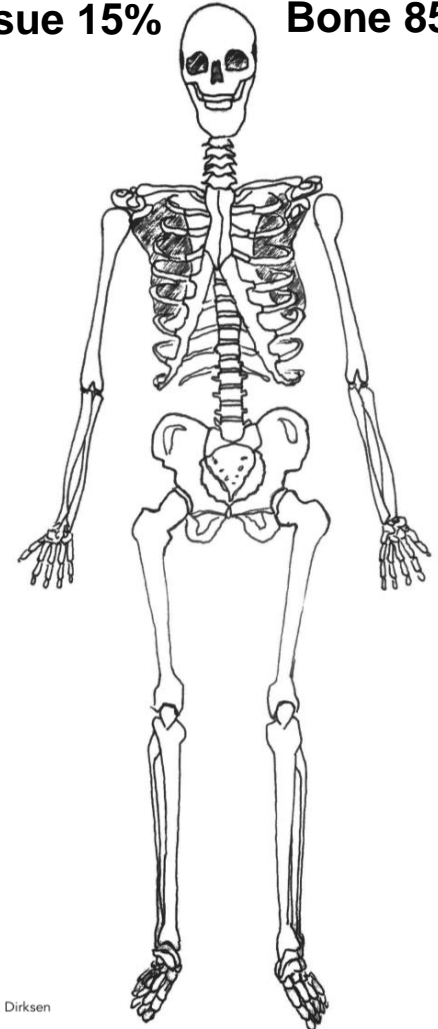
Sites: All bones
Diaphysis

Sex: M>F
Age: TYA
Race: Caucasian

Metastases: 20% at diagnosis

Bone, lung, bone marrow

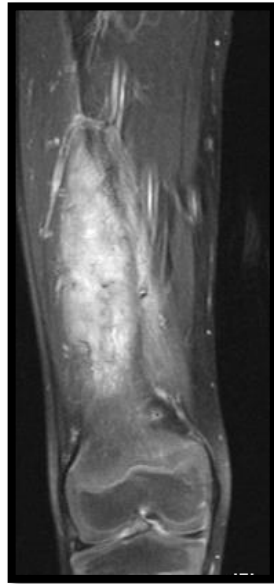
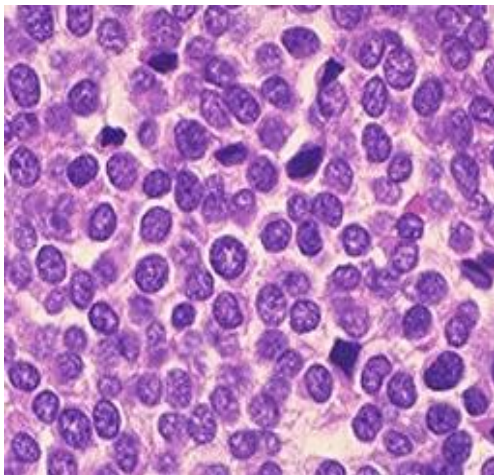
Soft Tissue 15% Bone 85%



© Leon R. Dirksen

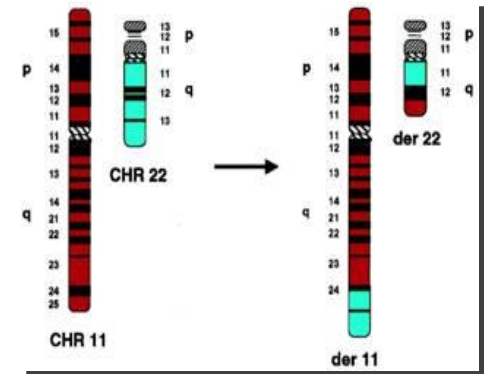


Ewing Sarcoma



Classical TET/ETS

EWS-FLI1
EWS-ERG
EWS-ETV1
EWS-ETV4
EWS-FEV
FUS-ERG
FUS-FEV
EWS-ZSG
EWS-POU5F1
EWSR1-NFATc2



Bona fide EwS – like

EWS-POU5F1
EWSR1-NFATc2
EWS-PATZI
EWS-SP3
BCOR-CCNB3
FUS-NFATc2
CIC-FOXO4
CIC-DUX4



Ewing Sarcoma

Chemo
therapy

Surgery

Radio
therapy

Chemo
therapy

High dose



Stem cell collection

1 year



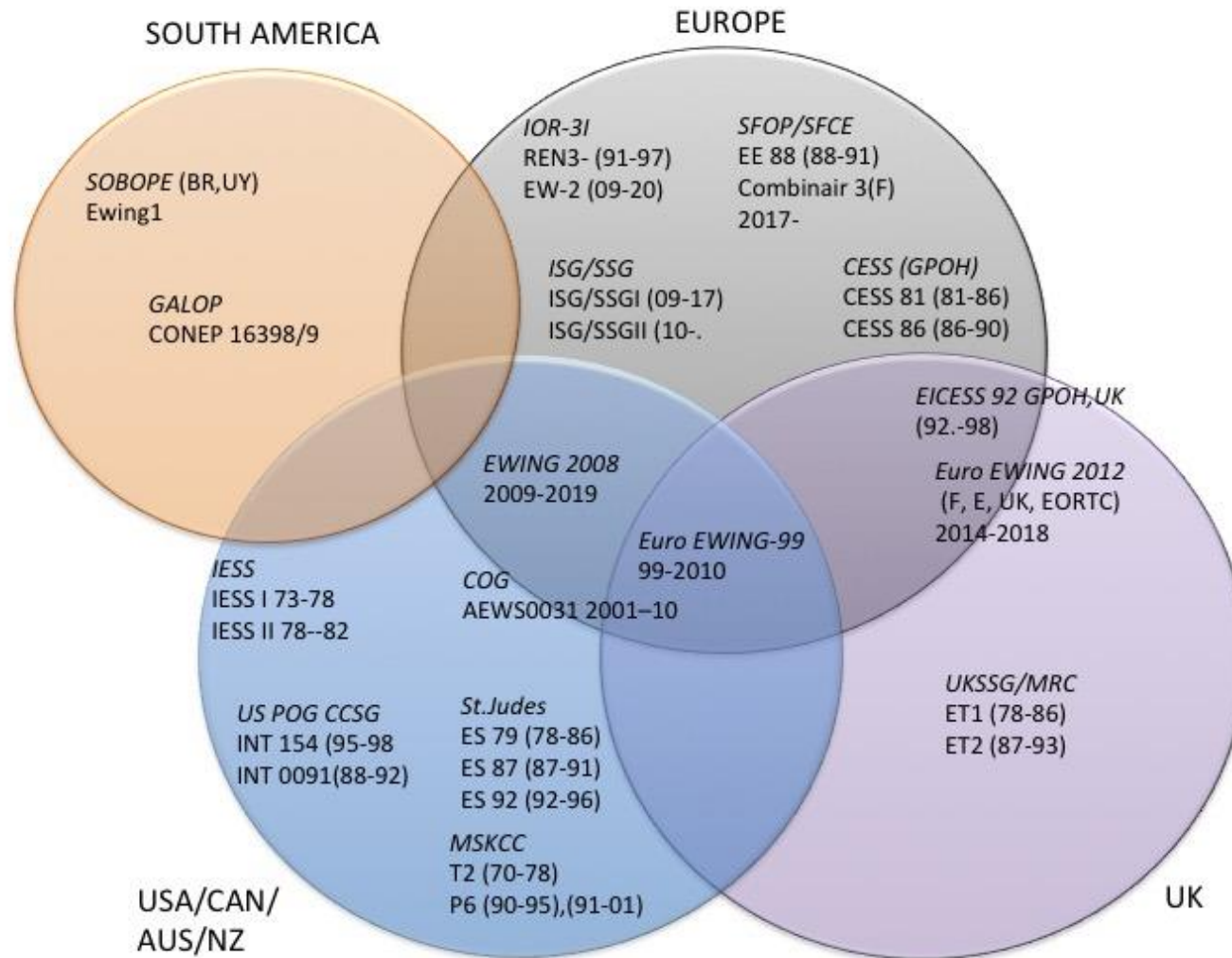
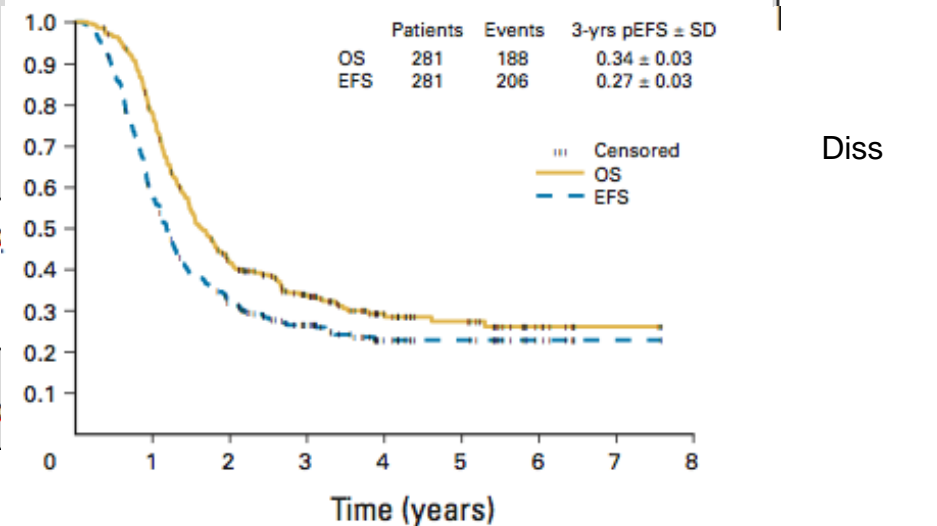
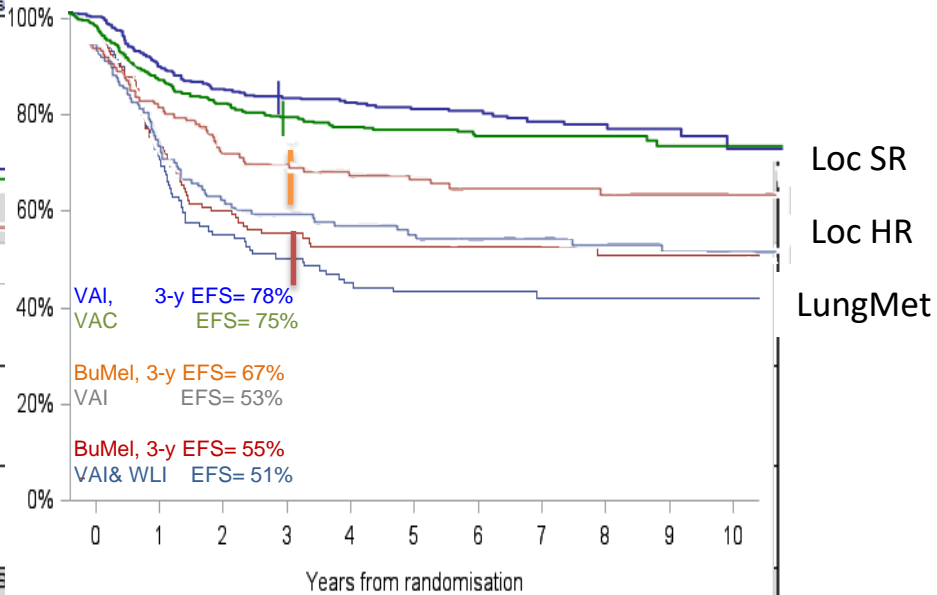


Table 3. Clinical Trials
Newly Diagnosed

Study/author	Disease	Number of	
AEWS0031 ⁵⁹			
AEWS02P1 ⁶⁰	Metastatic	25	VDC/IfE/VBL/Celec
AEWS 1031	Localized	Ongoing	VDC/IfE VDC/IfE/C/T
AEWS 1221	Metastatic	Ongoing	VDC/IfE VDC/IfW/Gan
Euro E.W.I.N.G.-99 ⁶¹	Localized SR	856	VifDE x 6VAI x 1±RT±S followed by VAI x 7 or VAC x 7
Euro E.W.I.N.G.-99 ⁶²	Localized HR (>200 mL, ≥10% viable tumor after surgery)	240	VifDE/8x VAI ±RT±S VifDE/1xVAI/ BuMe/HR ±RT±S
Euro E.W.I.N.G.-99 ⁶³	Metastatic HR pulmonary	265	VifDE/8x VAI & WLI ±RT±S VifDE/1xVAI/ BuMe/HR ±RT±S



Bone sarcoma - surgery

Endoprosthesis



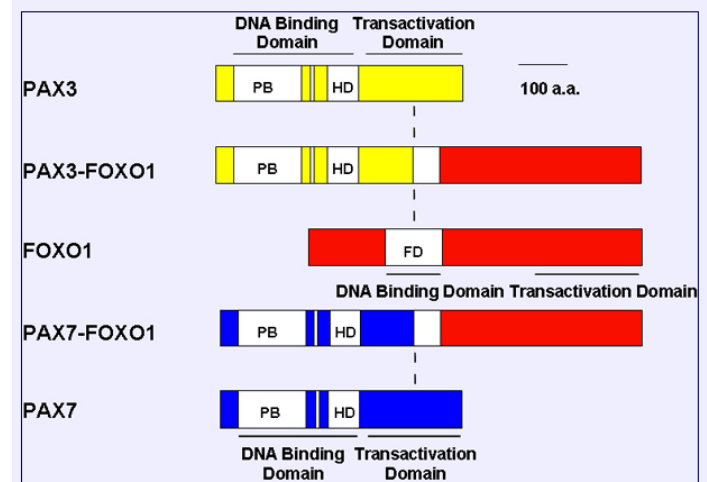
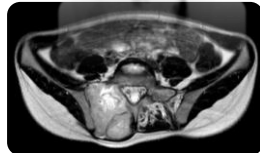
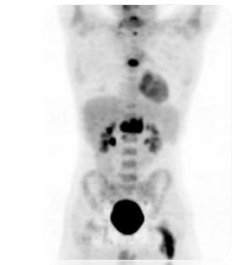
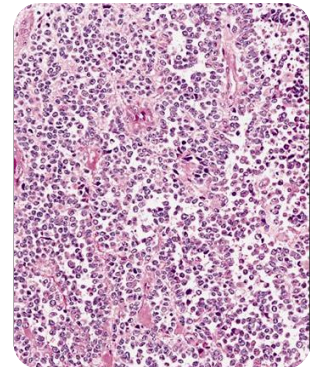
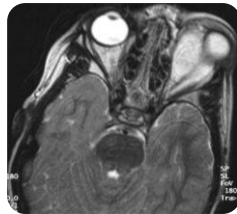
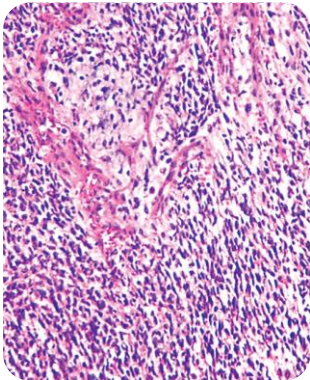
Rotation plasty



Amputation



Rhabdomyosarcoma



t 1;13 (p36; q14)

t 2;13 (q35; q14)



Rhabdomyosarcoma

Initial Loctx?

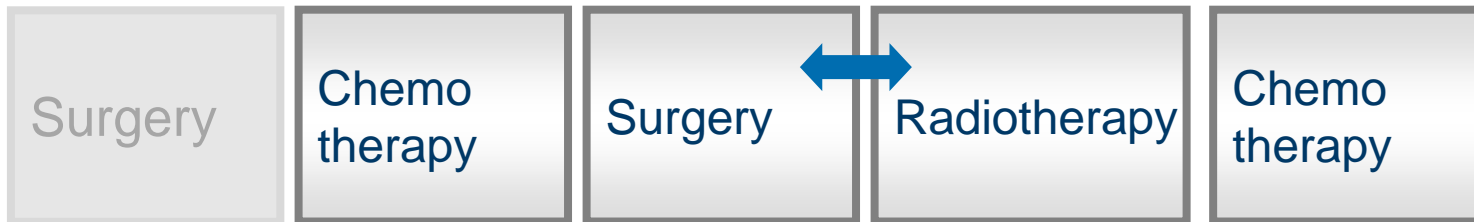


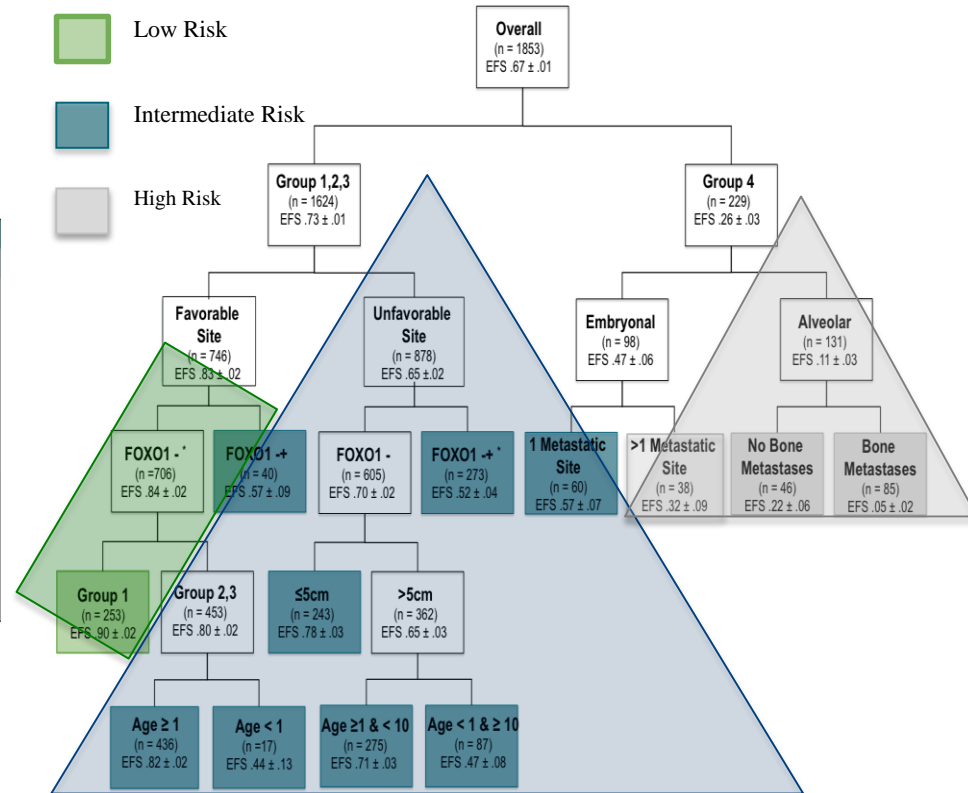
Table 1. Risk Factors Identified by the COG, Oberlin, and EpSSG					
COG Risk Assignment		Oberlin Risk Factors ^{1,2}		Clinicomolecular Risk Score ³	
		Prognostic factor	Relative risk	TNM stage/fusion status/age 5-year OS (%)	
Low	eRMSI (<i>FOXO1</i> negative): stage 1, group II stage 1, group III (orbital) stage 2, group I stage 2, group II	Age, years		CMG 1: stages I and II/fusion negative/any age; stages I and II/ <i>PAX7-FOXO1</i> /any age; stage III/ <i>PAX7-FOXO1</i> /favorable age	92
		Favorable, 1–9	1		
		Unfavorable ≤ 1 or ≥ 10	1.6		
Intermediate	eRMS: stage 1, group II (nonorbital) stage 3, group I/II stage 2/3, group III stage 4, group IV (< 10 years old) aRMS: stage 1–3, group I–III	Site		CMG 2: stage II/fusion negative/any age; stage I and II/ <i>PAX3-FOXO1</i> /any age	65
		Favorable: Orbital Non-PM PM Bladder/prostate Paratesticular/vaginal	1		
		Unfavorable: Limbs Other	1.4		
High	eRMS: stage 4, group IV (>10 years old) aRMS: stage 4, group IV	Bone or bone marrow involvement:		CMG 3: stage III/ <i>PAX3-FOXO1</i> /any age; stage IV/fusion negative or <i>PAX7-FOXO1</i> /favorable age	
		Yes	1		
		No	1.4		
		Number of metastatic sites:		CMG 4: stage IV/fusion negative or <i>PAX7-FOXO1</i> /unfavorable age; stage IV/ <i>PAX3-FOXO1</i> /any age	14
		≤ 2	1		
		≥ 3	1.4		

Abbreviations: CMG, clinical molecular risk scores; COG, Children's Oncology Group; OS, overall survival; TNM, tumor, node, metastasis.



Risk Stratification Including FOXO1 Fusion Status

Risk Group	Risk Group Assignment		
	Low	Intermediate	High
"D" series (1997-2004) (age <21)	D9602: (ERMS only) Stage 1, Grp I/II, N ₀ ; Grp II N ₁ Stage 1, Grp III, N ₀ , N _x , N ₁ ; Stage 2, Grp I, N ₀ , N _x , and Stage 2, Grp II, N ₀ , N _x ; Stage 3, Grp I/II, N ₀ , N _x , N ₁	D9803 Stage 1-3, Grp I-III ARMS; Stage 2-3, Grp III ERMS; Stage 4, Grp IV ERMS <10 yrs	D9802 Stage 4, Grp IV, except ERMS <10 yrs old
ARST series (2004-2008) (age <50)	ARST0331: (ERMS only) Stage 1, Grp I/II, N ₀ ; Stage 1, Grp III, N ₀ , N _x ; Stage 2, Grp I, N ₀ , N _x , & Grp II; Stage 3, Grp I/II	ARST0531 Stage 2/3, Grp III ERMS Stage 1-3, Grp I-III ARMS	ARST0431 Stage 4, Grp IV



Low risk-defined as $\geq 90\%$ EFS

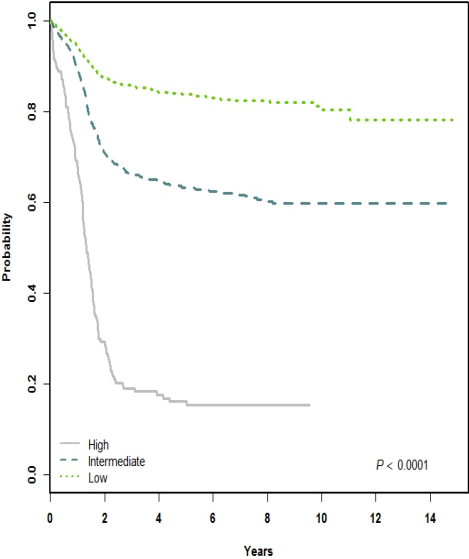
Intermediate risk-defined as $< 90\%$ and $> 40\%$ EFS

High risk-defined as $< 40\%$ EFS

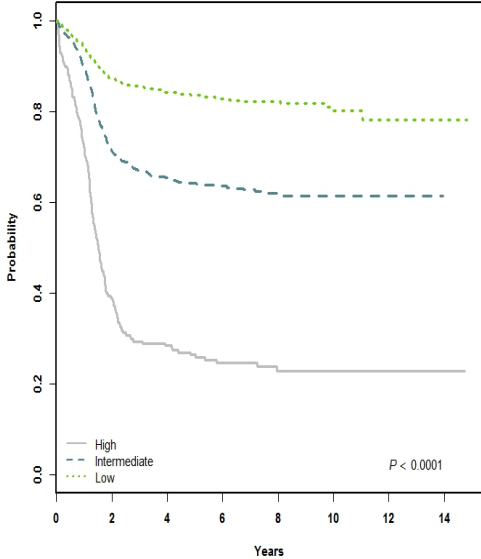


Event free survival by risk stratification

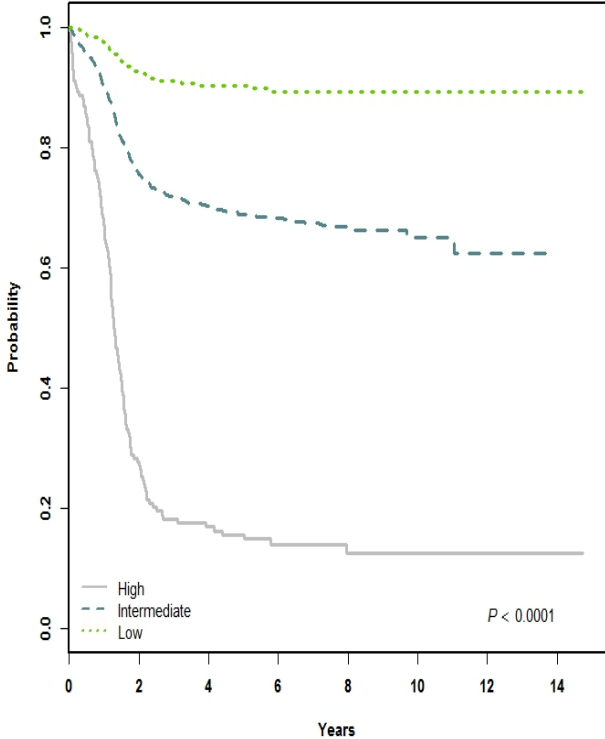
D-Series



ARST-Series



New stratification





Westdeutsches Tumorzentrum - Ambulanz

DFG



European Research Area



PanCareLIFE

wtz
westdeutsches
tumorzentrum



Essener Elterninitiative
zur Unterstützung krebskranker Kinder e.V.
Stiftung für krebskranke Kinder in Essen



Universitätsklinikum Essen