

Fall 4

Kasuistisches Forum

29.04.2023

Florian Länger

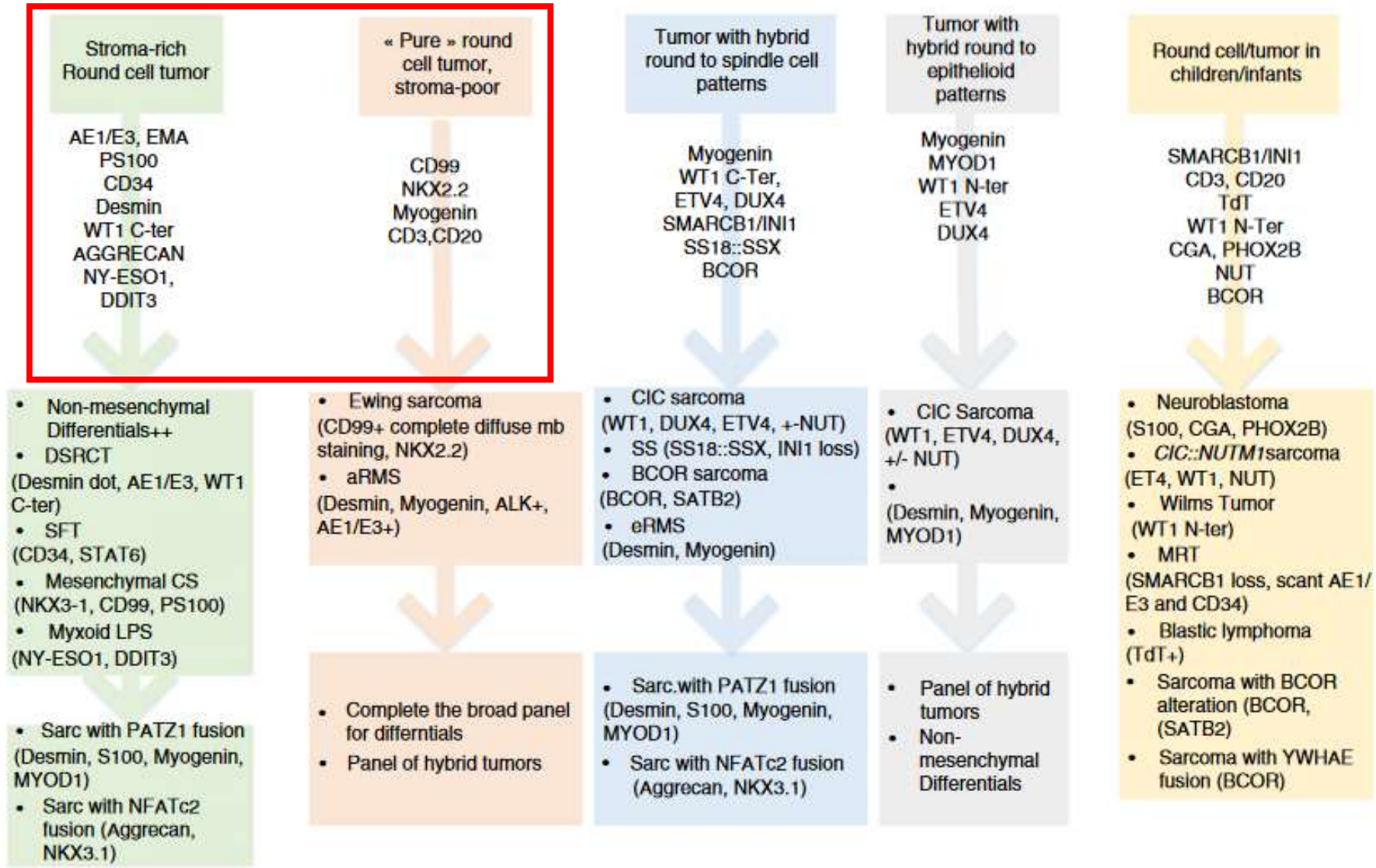
Institut für Pathologie
Medizinische Hochschule Hannover



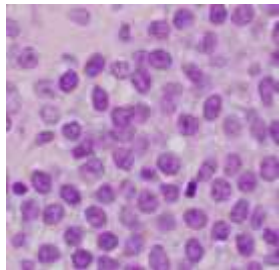
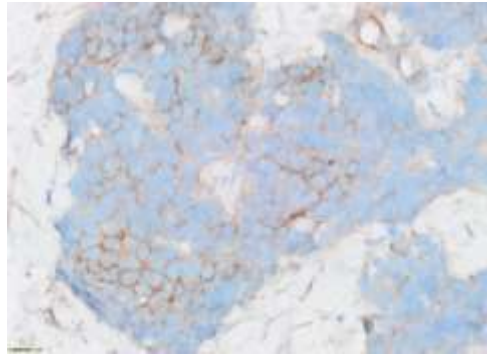
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Algorithmen

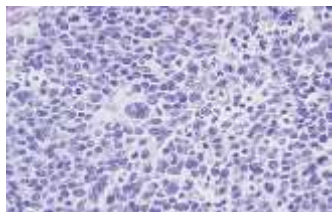
CD99
Desmin
CK8/18
NKX2.2
WT1



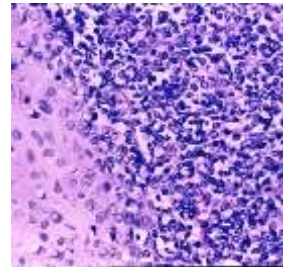
CD99



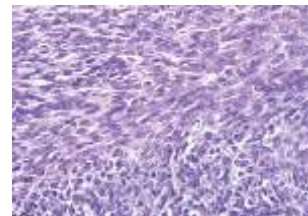
Ewing-Sarkom
Gruppe
(NKX2.2)



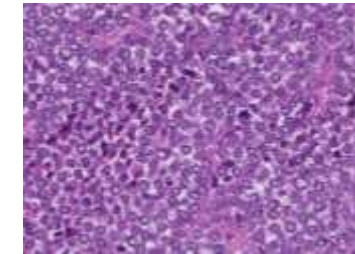
Rhabdomyosarkom
(MyoD1, Myogenin)



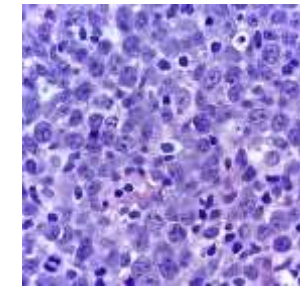
mesenchymales
Chondrosarkom
(SOX9 positiv)



Synovialzellsarkom
(SS18, TLE1 positiv)

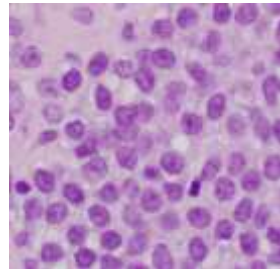
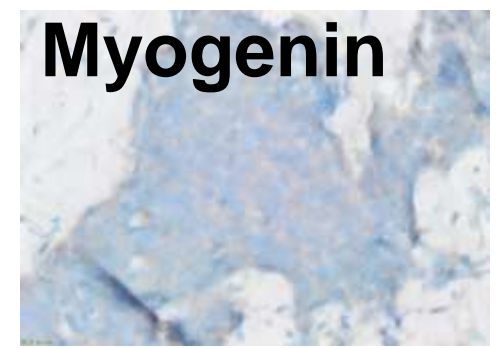
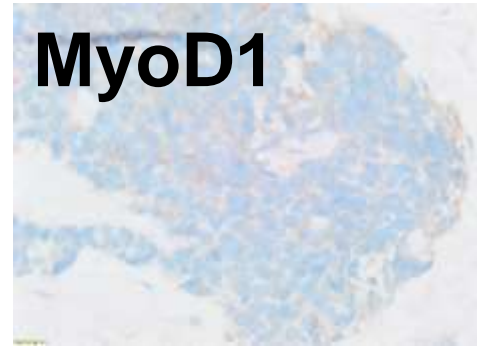
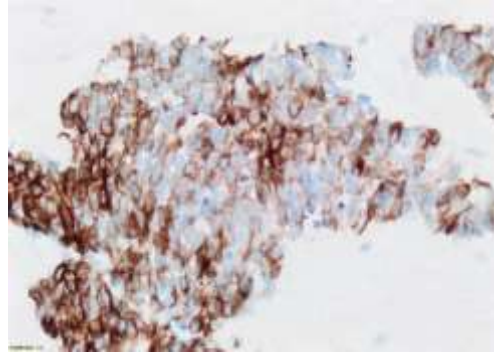


NUT-Karzinom
(NUT, p40)

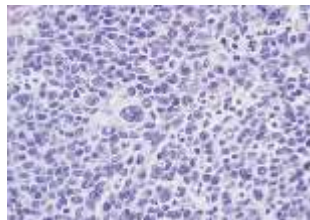


Lymphom
(CD3, CD20,
TdT, CD30)

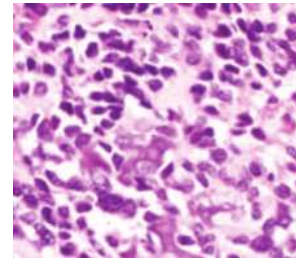
Desmin



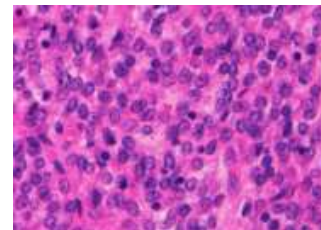
Ewing-Sarkom
Gruppe
(NKX2.2)



Rhabdomyosarkom
(MyoD1, Myogenin)

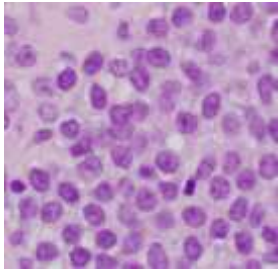
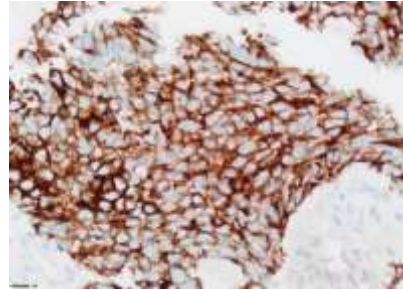


kleinzelliges
Osteosarkom
(Matrix, SATB2)

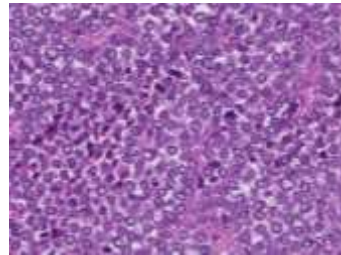


Stromasarkom
(CD10, Cyklin D1)

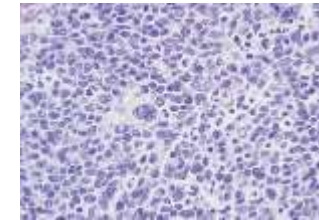
Keratin



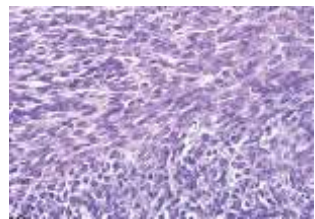
Ewing-Sarkom
Gruppe
(NKX2.2)



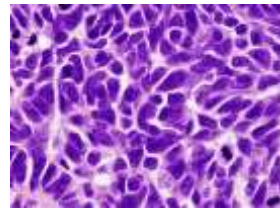
NUT-Karzinom
(NUT, p40)



Rhabdomyosarkom
(MyoD1, Myogenin)

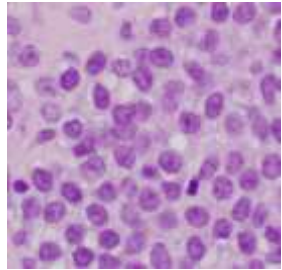
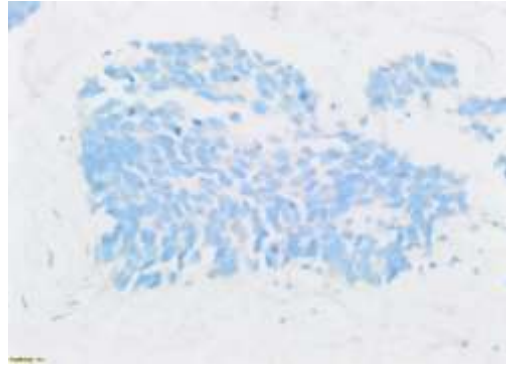


Synovialzellsarkom
(SS18, TLE1 positiv)



Kleinzeller
(TTF1, INSM1)

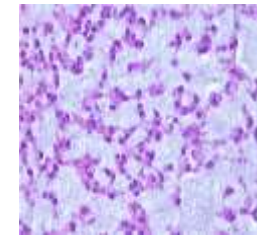
NKX2.2



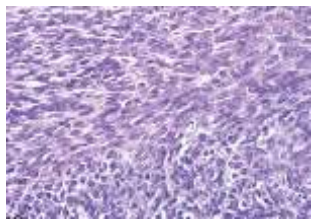
Ewing-Sarkom
Gruppe
(variabel NKX2.2)



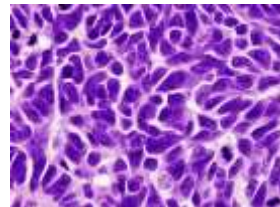
Neuroblastom
(PHOX2B)



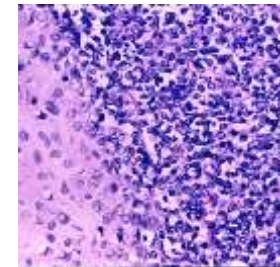
Extraskeletales
myxoides
Chondrosarkom
(NR4A3)



Synovialzellsarkom
(SS18, TLE1 positiv)

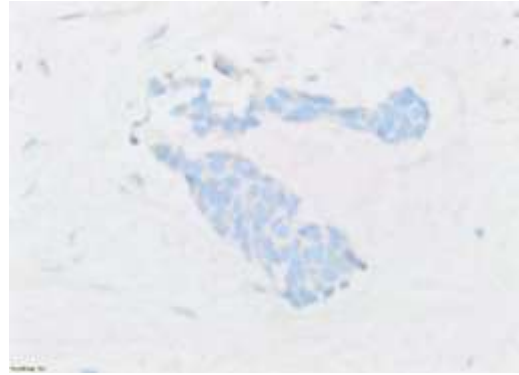


Kleinzeller
(TTF1, INSM1)

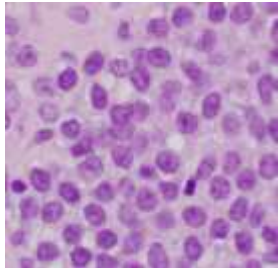


mesenchymales
Chondrosarkom
(SOX9 positiv)

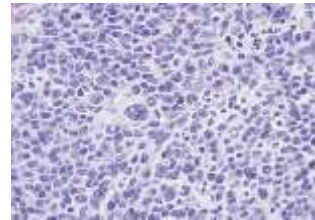
WT1



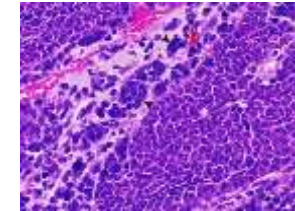
(6F-H2 aminoterminal)



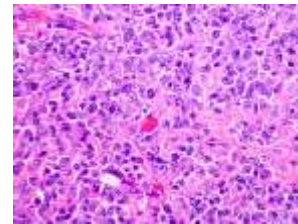
Ewing-Sarkom
Gruppe
(NKX2.2)



Rhabdomyosarkom
(MyoD1, Myogenin)

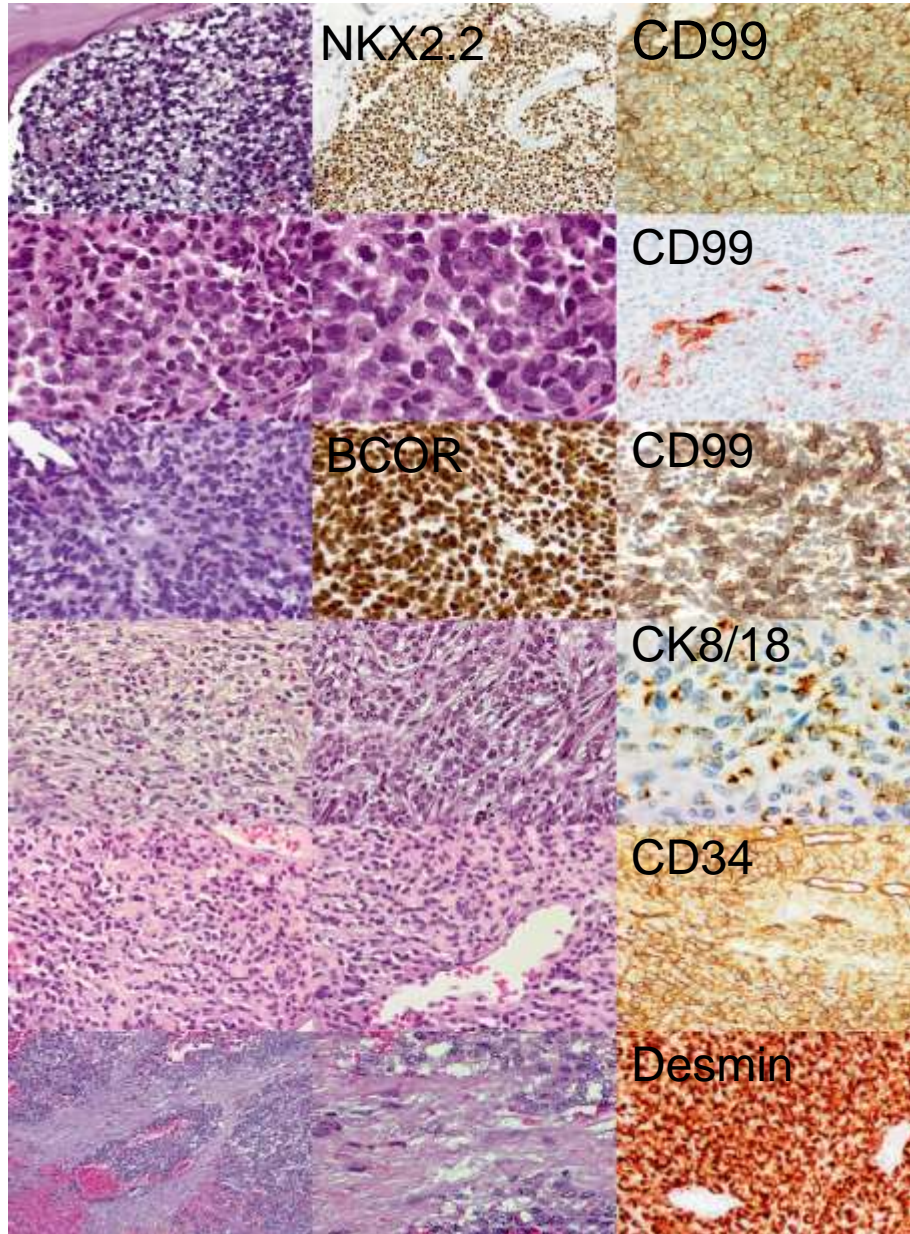


Wilms-
Tumor



Rhabdoid Tumor
(INI1-Verlust)

Differentialdiagnose klein-rund-blauzelliger Sarkome



Ewing Sarkom

atypisches
Ewing
Sarkom

EWSR1-NFATC2 Sarkom

EWSR1-PATZ1 Sarkom

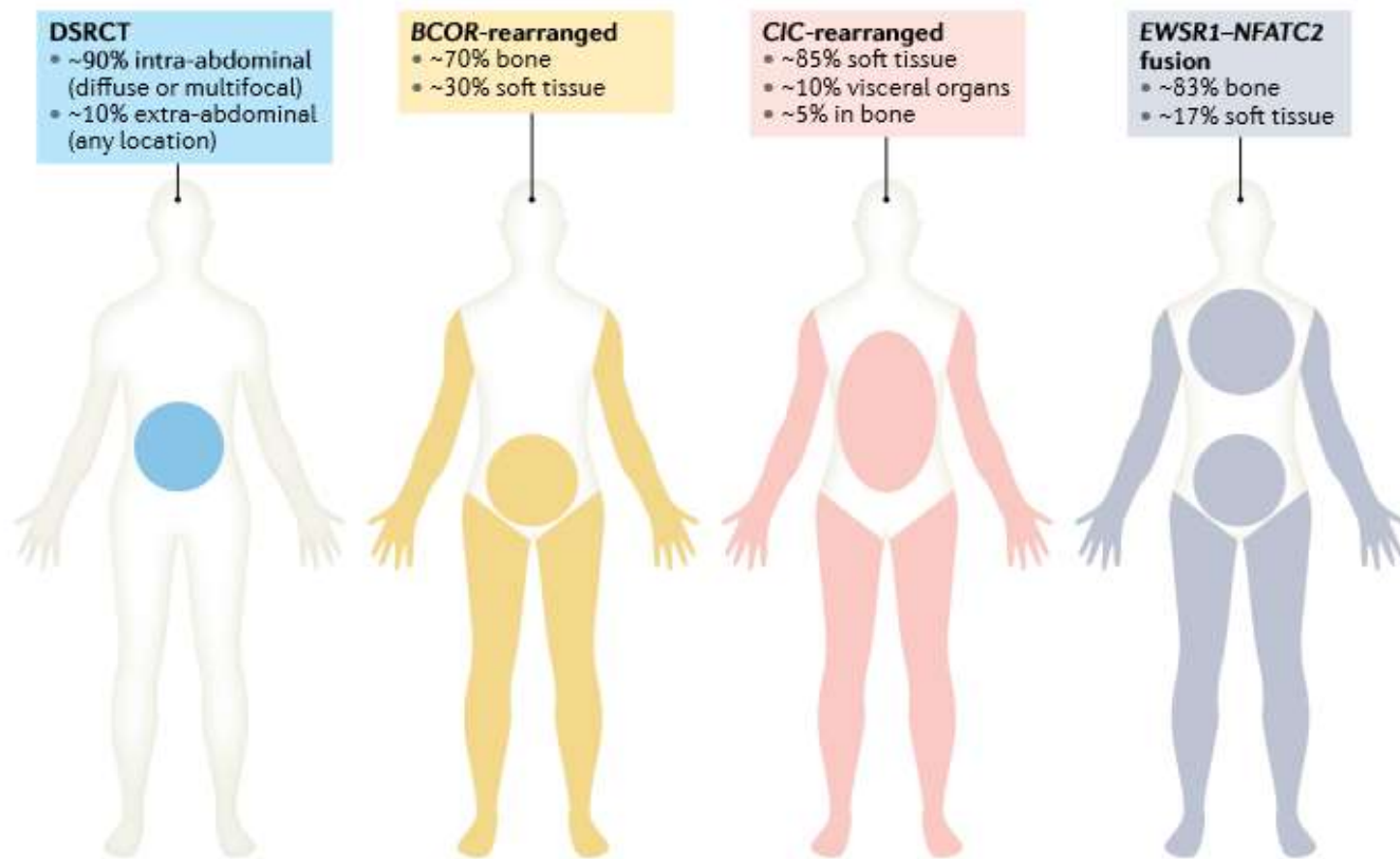
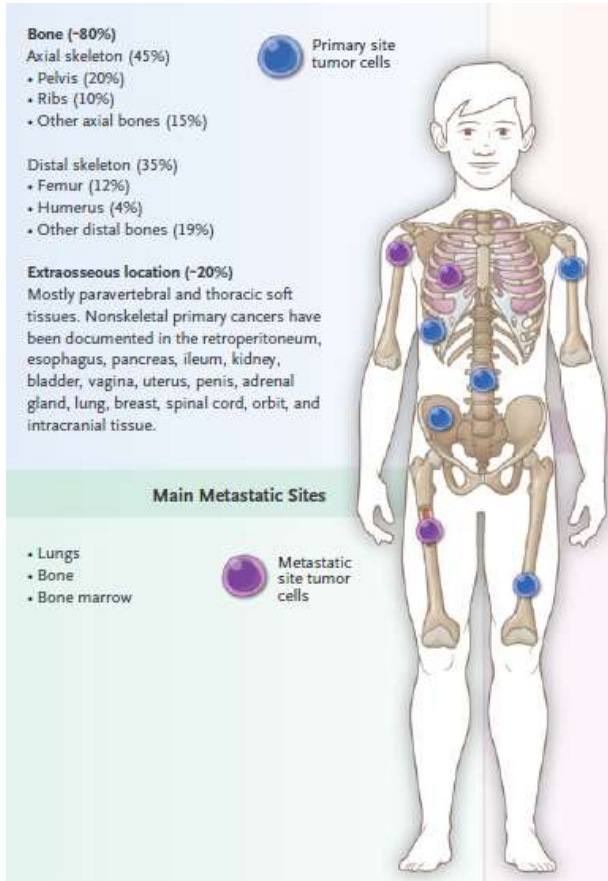
Desmoplastisches Rundzellsarkom

BCOR-transloziertes Sarkom

CIC-transloziertes Sarkom

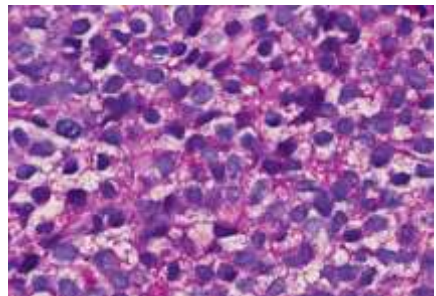
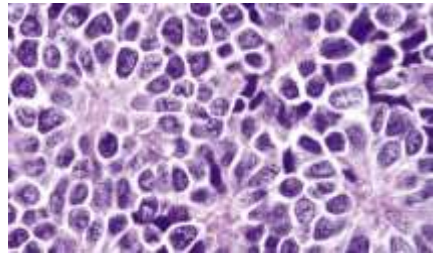
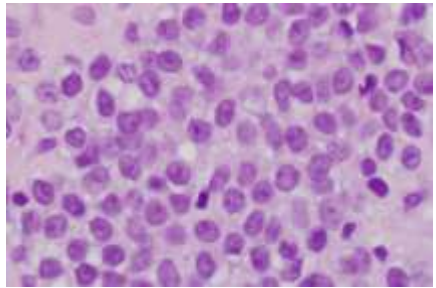
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Hilft die Klinik weiter?

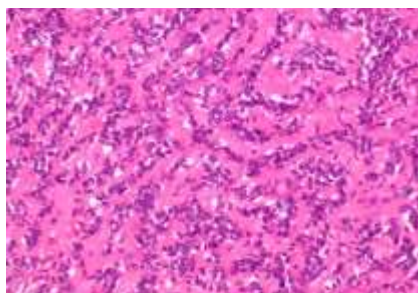
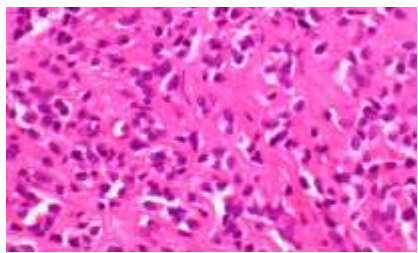
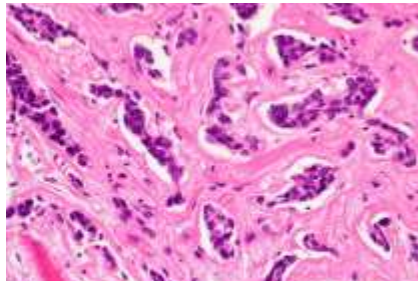


Hilft die Morphologie weiter?

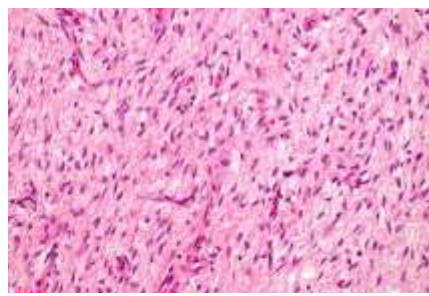
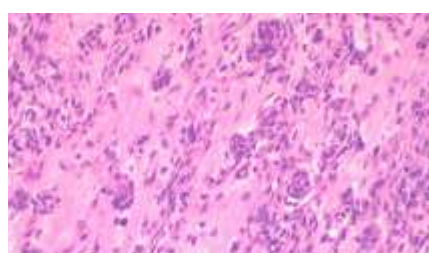
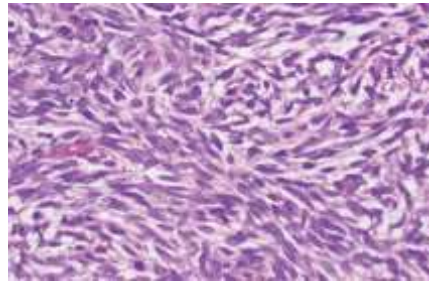
Ewing



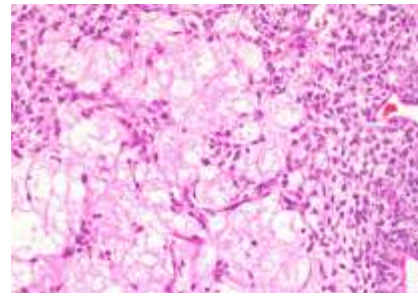
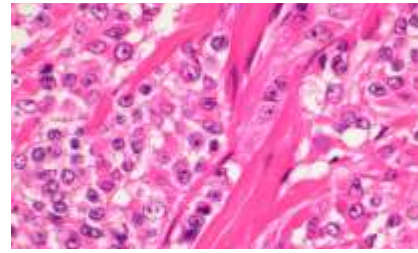
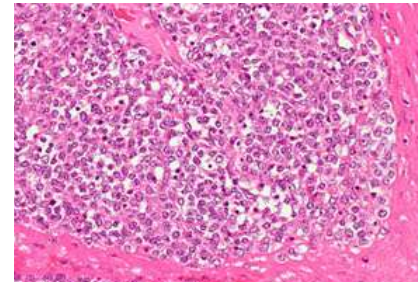
NFATC2



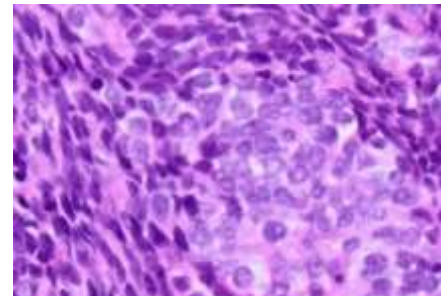
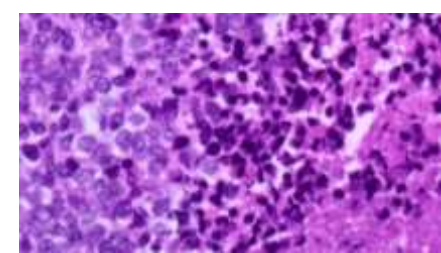
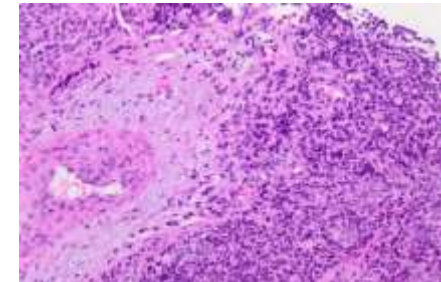
BCOR



CIC



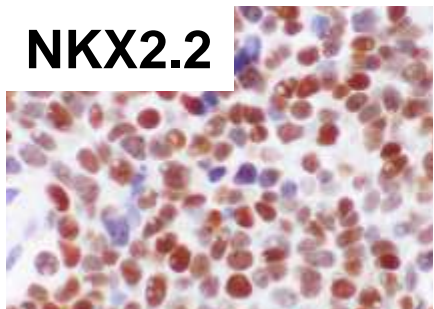
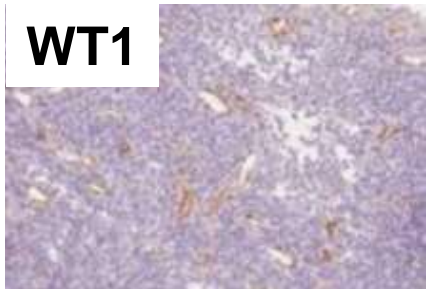
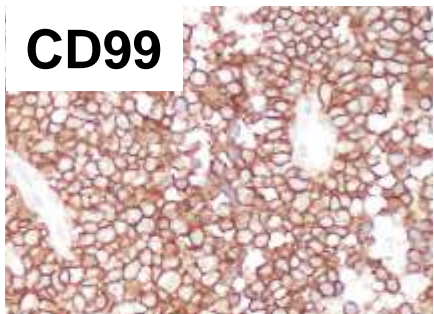
DSRCT



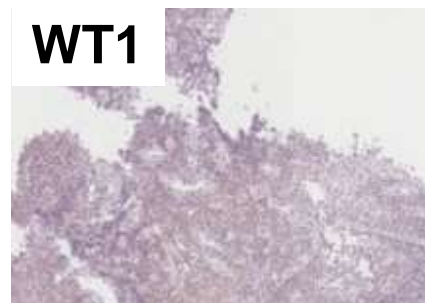
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Hilft die Immunhistologie weiter?

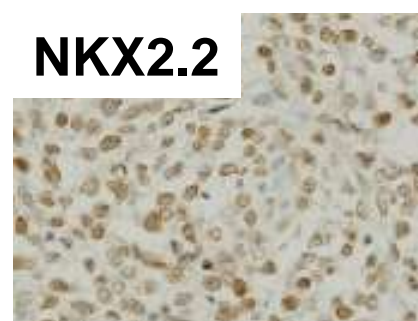
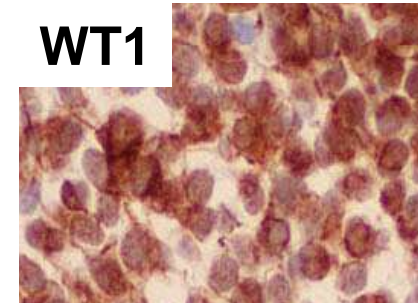
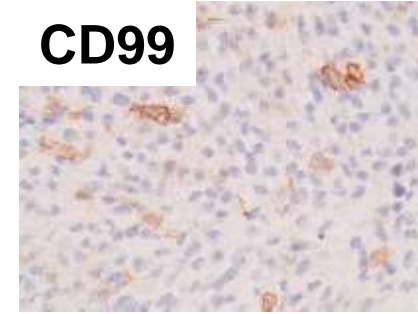
Ewing



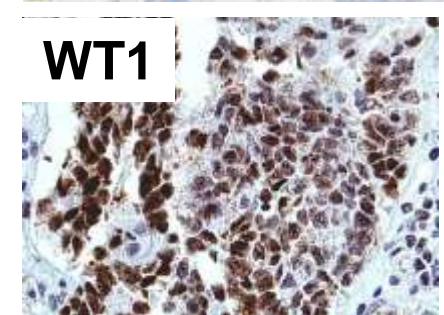
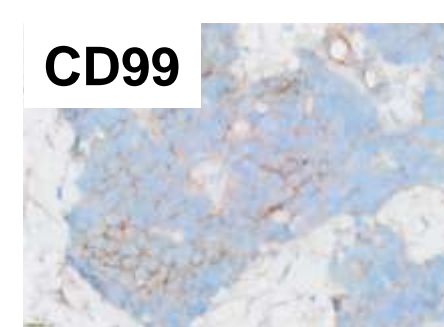
BCOR



CIC



DSRCT



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Hilft die FISH oder MolPath weiter?

Molekularzytogenetischer Befund:

Es kam eine für den Genlocus 22q12 (EWSR1) spezifische Sonde zum Einsatz (ZytoLight SPEC EWSR1, ZytoVision). Es wurden 100 Zellkerne ausgezählt: 100% der Zellkerne zeigten 1-4 Fusionsignale und 1 Split-Signal.

Karyotyp (ISCN): `nuc ish (EWSR1x2-5,5'EWSR1con3'EWSR1x1)[100]`

Bewertung:

Zusammenfassend ergibt sich ein Rearrangement des EWSR1-Gens in einem signifikanten Anteil der untersuchten Zellkerne.

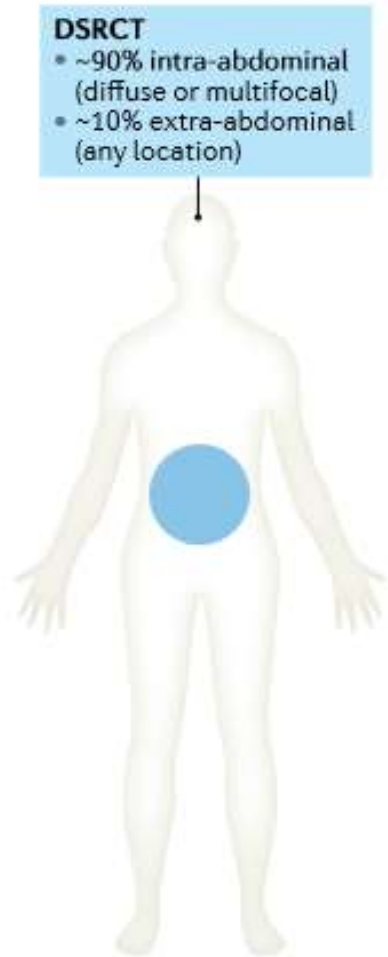
EWS1(exon7)-WT1(exon7) Fusion nachzuweisen.

Bruchpunkt chr22:29683123,chr11:32414301 mit 506

RNA-Reads mit 85 unabhängigen Startpunkten.

Entitäten mit EWSR1 Fusion	Fusionspartner
Ewing & atypische Ewing	FLI1, ERG, ETV1, ETV4, FEV, NFATC2, POU5F1, SMARCA5, PTAZ1, SP3
Desmoplastic small round cell tumor	WT1
Myxoides Liposarkom	DDIT3
Extraskellettales myxoides Chondrosarkom	NR4A3
Angiomatoides fibröses Histiozytom	CREB1, ATF1
Klarzellsarkom Weichteile	ATF1
Klarzellsarkom GIT	CREB1
Pulmonales myxoides Sarkom	CREB1
Myoepitheliale Tumore	ATF1, POU5F1, PBX1, ZNF444
Angiosarkom	ATF1
Fibromyxosarkom	CREB3L1
Rhabdomyosarkom	TFCP2

Desmoplastic small round cell tumor (DSRCT): Klinik



Adoleszente & junge Erwachsenen (meist männlich)

0,5 Fälle / 1 Million Einwohner

90% im Abdomen, meist multifokal

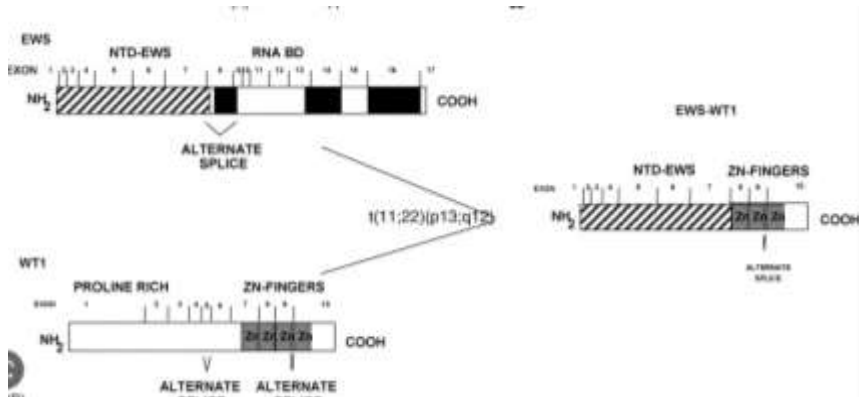
sehr selten Ovar, Schädel, Gehirn

zum Diagnosezeitpunkt 30-50% mit Metastasen (Leber, Lunge)

5-20% 5-Jahres Überleben

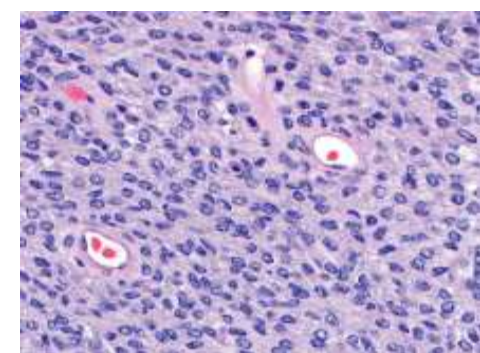
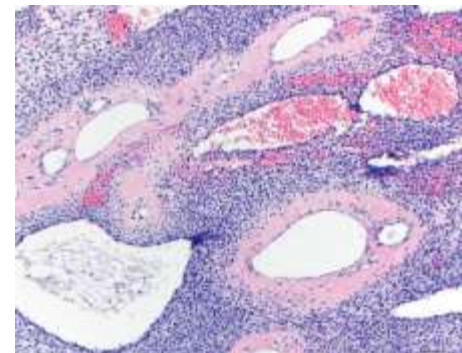
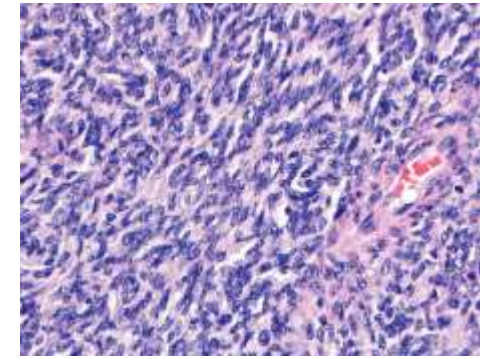
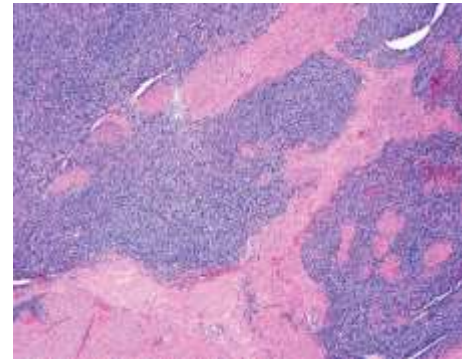
Desmoplastic small round cell tumor (DSRCT): Genetik

EWSR1-WT1 Fusion



sehr spezifisch für DSRCT

nur sehr selten in anderen Tumoren beschrieben:

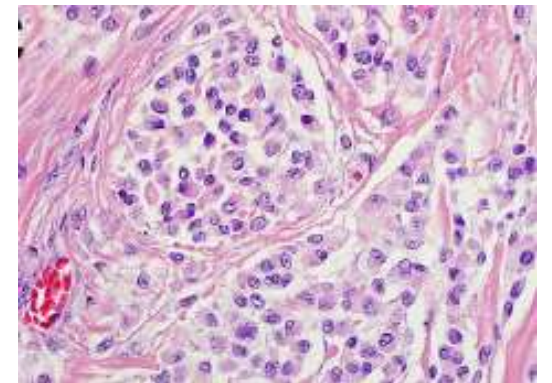
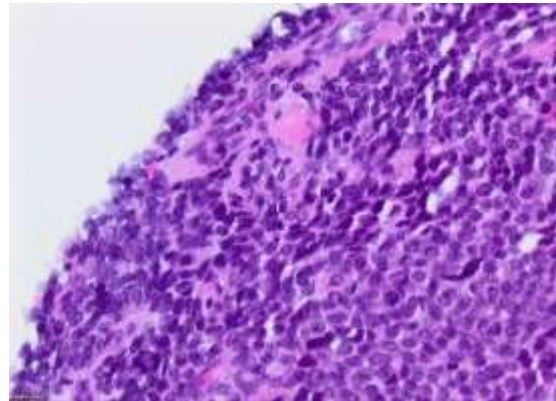
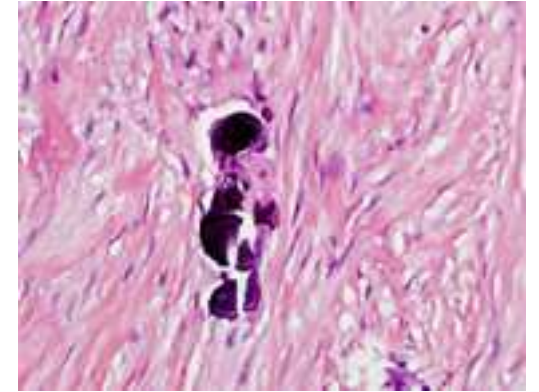
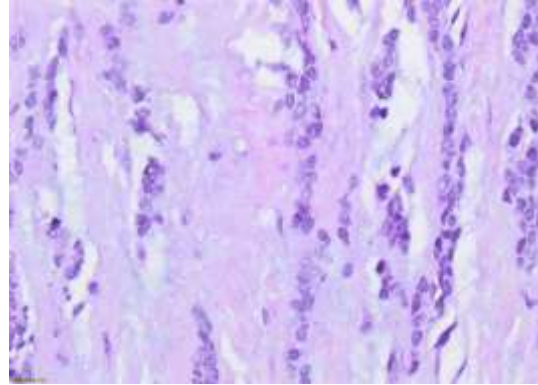
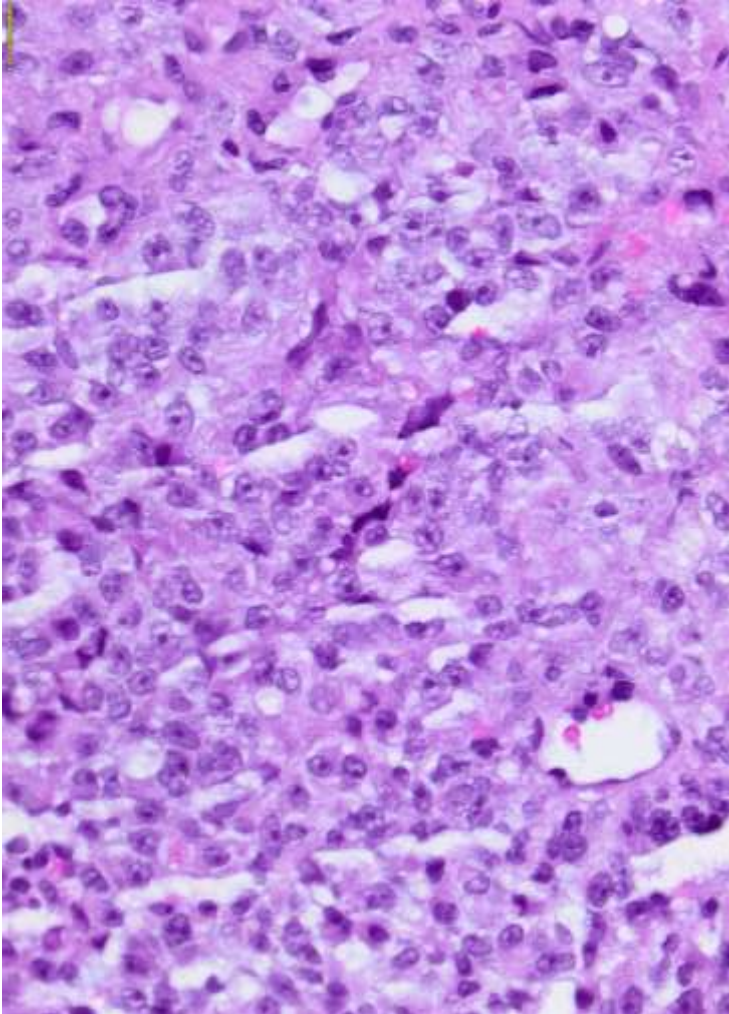


Weitere Alterationen

FGFR4 (7%), ARID1A (6%),

NF1 (3%), TP53 (3%)

Morphologische Varianten



Immunhistologie DSRCT

>80%	Cytokeratin, EMA Desmin, Vimentin NSE WT1
50%	CD15, CD57
25%	Synaptophysin, PGP 9.5 CA-125, NKX 2.2
10%	CD99 S-100, Neurofilament, GFAP sm-Aktin, α-Aktin Chromogranin A

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Relevante (neuere) diagnostische Antikörper
 bei Rundzellsarkomen

Antikörper	Hauptspezifität
NKX2.2	Ewing Sarkom
NKX3.1	NFATC2
SS18	Synovialzellsarkom
DUX4	CIC-DUX Sarkom
NUT	NUT Karzinom
PAX7	Ewing Sarkom
AGGRECAN	Non-ETS Ewing
BCOR	BCOR Sarkom
PHOXB2	Neuroblastom
NTRK 1,2,3	BCOR Sarkom

MOLECULAR ALTERATIONS: SOFT TISSUE

ADIPOCYTIC	Lipoblastoma	Rearr PLAG1 (8q12)
	Hibernoma	Rearr w/ 11q13 breakpoint
	Chondroid Lipoma	t(11;13) - c11orf95-MRTFB
	SM/PM Lipoma	Del RB1 (13q14)
	A SPLT	
	ALT/WDL	Amp MDM2, CDK4 (12q14-15)
	MLS	t(12;16) - FUS-DDIT3* t(12;22) - EWSR1-DDIT3

(PERIVASCULAR)	AVM/Hemangioma	Act MAP2K1 (15q22)
	Lymphangioma	PIK3CA (3q26) [subset]
	Glomus Tumor	Rearr NOTCH1/2/3 (9q34/1p12/19p13)
	Myopericytoma	PDGFRB (22q22)
	Myofibroma	
	Atypical Myofibroma	t(6;11) - SRF-RELA
	Anastomosing HA	Act GNAQ/GNA14 (9q21)
	Epithelioid HA	Rearr FOS (14q24) / FOSB (19p13)
	EHE	t(1;3) - WWTR1-CAMTA1* t(X;11) - YAP1-TFE3
	PMHE	t(7;19) - SERPINE-FOSB* t(7;19) - ACTB-FOSB
	TA/KHE	GNA14 (9q21) [subset]
Angiosarcoma	Amp MYC (8q24) [subset]	

(MYO)FIBROBLASTIC / FIBROHISTIOCYTIC	Nodular Fasciitis	USP rearrangements (17p13) t(17;22) - USP6-MYH9*
	Cellular FTS	
	Acral Fibromyxoma	Del RB1 (13q14)
	Cellular Angiofibroma	
	Myofibroblastoma	
	Angiofibroma (ST)	t(5;8) - AHRR-NCOA2
	CAF	t(2;5) - FN1-FGF1
	Fibromatosis	Act CTNNB1(3p22) / Inact APC (5q22)
	Lipofibromatosis	Rearr EGFR (7p11)
	Desmoplastic FB	t(2;11) - FOSL1 upreg (11q13)
	FHI	In/del EGFR exon 20 (7p11)
	Supf CD34 FBT	Rearr PRDM10 (11q24) [subset]
	SFT	Paracentric inv 12q - NAB2-STAT6
	IMT	Rearr ALK (2q23)
	Deep FH	Rearr PRKCB/D (16p12/3p21)
	TSGCT	Rearr CSF1 (1p13)
	EIMS	t(2;20;2) - RANBP2/RRBP1-ALK
	DFSP / Giant Cell FB	t(17;22) - COL1A1-PDGFB*
	IFS	t(12;15) - ETV6-NTRK3
LGFMS	t(7;16) - FUS-CREB3L2	
SEF	t(11;22) - EWSR-CREB3L1	
MIFS	t(1;10) - No fusion protein	

SMKS MUSCLE	Leiomyoma	Rearr PLAG1 (8q12) / HMGA2 (12q14)
	GIST	GoF KIT[ex11]/PDGFRA[ex18] (4q12) Inact SDH A/B/C/D
	Fetal Rhabdomyoma	LoF PTCH1 (9q22)
	ARMS	t(2;13) - PAX3-FOXO1* t(1;13) - PAX7-FOXO1
	SpC/ScI RMS	MYOD1 L122R (11p15)

PERIPHERAL NERVE SHEATH	GrCT	LoF ATP6AP1*2 (Xq28/Xp11)
	Benign Triton Tumor	CTNNB1 exon 3 (3p22)
	Perineurioma	Del NF1/NF2 (17q11/22q12)
	ScI Perineurioma	10q24 alterations
	Schwannoma	Inact/loss NF2 (22q12)
	Neurofibroma	Inact NF1 (17q11)
	MPNST	Del PRC (EED, SUZ12)
	Epithelioid MPNST	Inact SMARCB1 (22q11)
MMNST	PRKAR1 [CNC1] (17q24) / CNC2 (2p16)	

BCS	BCOR Sarcoma	BCOR ITD (Xp11) t(X;X) - BCOR-CCNB3
	CIC Sarcoma	t(4;19) / t(10;19) - CIC-DUX4
	Ewing Sarcoma	t(11;22) - EWSR1-FLI1* t(21;22) - EWSR1-ERG
	NFATC2 RCS	t(20;22) - NFATC2-EWSR1 t(16;20) - NFATC2-FUS

UNCERTAIN DIFFERENTIATION	AFH	t(2;22) - EWSR1-CREB1* t(12;16;22) - FUS/EWSR1-ATF1
	Deep Angiomyxoma	Rearr HMGA2 (12q14)
	IM Myxoma	Act GNAS (20q13)
	Myoepithelioma	Rearr EWSR1 (22q12)
	Chondroma (ST)	Rearr 12q13-25 (± HMGA3) t(2;8/10) - FN1-FGFR1/2 [subset]
	HFLT	t(1;10) - No fusion protein Inv. TGFBR1 +/-or OGA [MGEA5]
	PHAT	
	NTRK-SCN	Rearr NTRK1*2/3 (1q23/9q21/15q25)
	OMFT	Rearr PHF1 (6p21) [subset]
	PEComa	Del/LoH TSC2 (16p13)* Rearr TFE3 (Xp11)
	PMT	t(2;5/8) - FN1-FGF1/FGFR1
	ASPS	t(X;17) - ASPL-TFE3
	CCS	t(12;22) - EWSR1-ATF1
	DSRCT	t(11;22) - EWSR1-WT1
	EMC	t(9;22) - NR4A3-EWSR1/TAF15
	Epithelioid SA	Inact/Loss SMARCB1 (22q11) [Subset of MEC]
Rhabdoid Tumor		
Myoepithelial CA		
Intimal Sarcoma	Gain/Amp MDM2, PDGFRA/EGFR (12q12-15, 4q12)	
Synovial Sarcoma	t(X;18) - SS18-SSX1*2/3	

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