UCCH Universitäres Cancer Center Hamburg
UCCSH Universitäres Cancer Center Schleswig-Holstein

UCCH / UCCSH Pathway

Guideline
Soft Tissue Sarcoma

Version Mar/2023

Guideline Soft Tissue Sarcoma*

Version 09, Mar/2023
according to TNM classification 8th edition (UICC)

** Pathway does not apply to: GIST, bone sarcomas, Ewing sarcoma and small-, round- and blue cell soft tissue sarcomas, Rhabdomyosarcomas, alveolar soft part sarcoma*

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Legend of Colours

= Therapeutic procedure

= Clinical or diagnostical condition

= Diagnostic procedure

= Clinical trial

= Supportive measure

= Referral

= Tumorboard (including post tumorboard interaction with patient that follows the principles of shared decision-making)

TNM according to UICC AJCC v. 2017

Classification	Trunk and extremities (arms and legs)	Retroperitoneum	Head and neck	Abdomen and thoracic (chest) visceral organs
TX	Main tumour cannot be assessed due to lack of information			
T0	No evidence of a primary tumour			
T1	tumour ≤5 cm	tumour ≤5 cm	tumour ≤2 cm	Limited to one organ
T2a	T2 tumour >5 ≤10 cm	T2 tumour >5 ≤10 cm	T2 tumour >2 ≤4 cm	Infiltration of serous membrane of the visceral peritoneum (no breakthrough)
T2b				Infiltration of the visceral peritoneum (microscopic level)
T3	tumour >10 ≤15 cm	tumour >10 ≤15 cm	tumour >4 cm	Infiltration of the visceral peritoneum (macroscropic) or infiltration of a second organ
T4a	T4 tumour >15 cm	T4 tumour >15 cm	T4a Infiltration of eye socket, skull base, or dura, central intestines, facial bones, or musculi pterygoidei	Multifocal tumour with more than two foci in one organ
T4b			T4b Infiltration of brain/ central nervous system, prevertebral musculature, encircle A. carotis or perineural spread with inclusion of CNS	Multifocal tumour with more than two, but less than 5 foci
T4c				Multifocal tumour with more than 5 foci
NX*	Regional lymph nodes cannot be assessed due to lack of information			
N0*	not spread to nearby lymph nodes	**N1**	spread to nearby lymph nodes	
M0	not spread to distant sites	**M1**	spread to distant sites	

UICC / AJCC 2017 stages

Stage group	T	N	M	three-step grading	two-step grading
IA	T1	N0	M0	G1	Low grade
IB	T2, T3	N0	M0	G1, GX	Low grade
II	T1	N0	M0	G2, G3	High grade
IIIA	T2	N0	M0	G2, G3	High grade
IIIB	T3, T4	N0	M0	G2, G3	High grade
IIIC	any T	N1	M0	any	
IV	any T	any N	M1	any	

Pathway: Soft Tissue Sarcoma

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2.03.01 Anlage 14 UCCH*
ID: 462451 UCCSH*

Pathway page 1: Workup

Soft tissue sarcoma suspicious lesion

Initial Diagnostic Imaging:

- **MRI** of the local finding (stem or extremity lump) or **CT** (abdominal or retroperitoneal lump)

Further radiologic work up if needed

Biopsy:

- Multiple core needle biopsies (14/16G)[1] | if <3cm, superficial excision biopsy

TB

Baseline staging:

- CT thorax, abdomen, pelvis
- Histology (including histologic subtype and mandatory grading according to FNCLCC[2])

Facultative[3]:

- PET-CT
- Bone scan (consider in case of rhabdomyosarcoma and/or metastatic disease)
- cMRT (consider in case of angiosarcoma)

Offer contact to self help group/psychooncological support at each stage of the disease

	TB		
Soft tissue sarcoma Stage IA / IB	TB	Surgical resection possible	Pathway page 2
		Surgical resection not possible[4]	Pathway page 4
Soft tissue sarcoma Stage II/III	TB	Resectable w/ acceptable functional outcome	Pathway page 3
		Surgical resection not possible[4]	Pathway page 4
Embryonal/alveolar Rhabdomyosarcoma	TB	Multimodal therapy (CWS guidance)	Pathway page 5
Metastatic disease (Stage IV)	TB	Systemic therapy[5]	Pathway page 5

1 The standard approach for suspected soft tissue sarcoma is core needle biopsie planned along future resection axis. In case of superficial or epifascial lesion <3 cm or localizations (e.g.retroperitoneal) otherwise not amenable to core needle biopsie excision biopsy might be performed (risk of tumor cell dissemination).

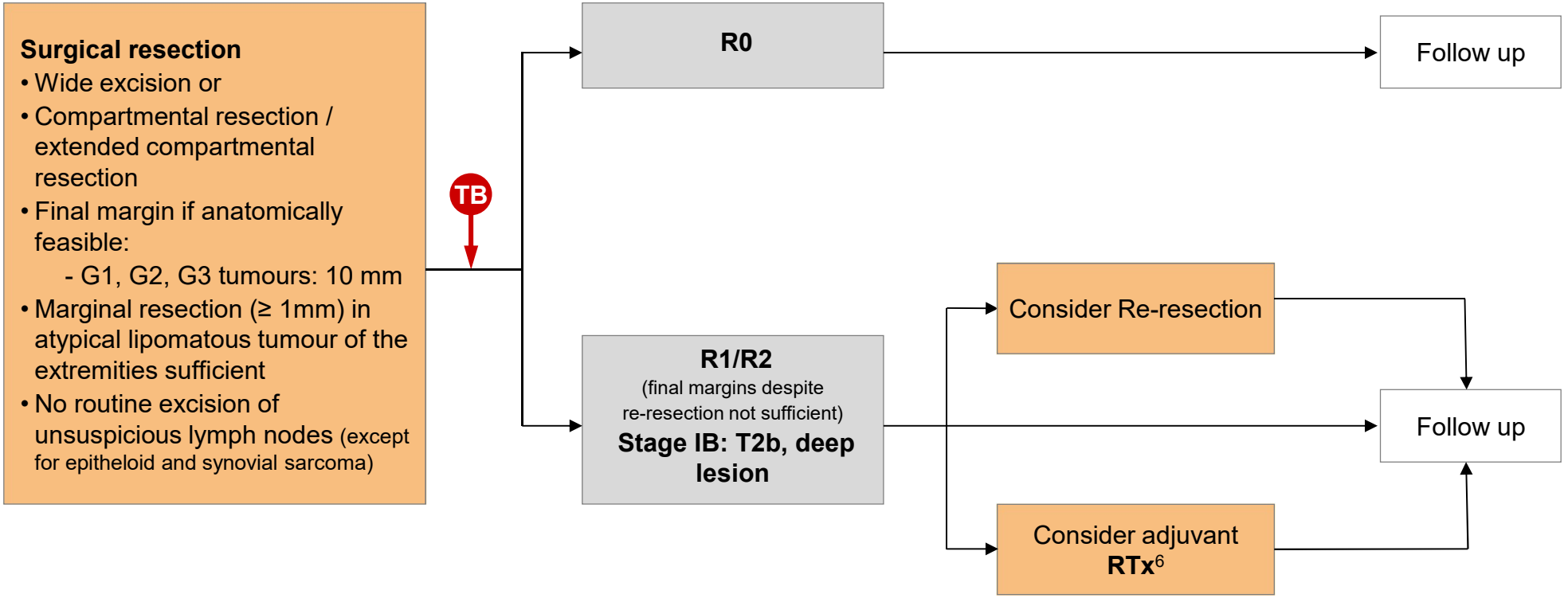
2 French Federation Nationale des Centres de Lutte Contre le Cancer, grading based upon differentiation, necrosis and mitotic rate

3 Additional imaging should be used on an individual base respecting clinical setting and subtype (i.e. PET CT before mutilating surgery, cMRT in angiosarcoma)

4 - Poor performance status
- Locally advanced, potentially resectable disease:
- Borderline resectable tumors (e.g. R0 resection not achievable, lesion technically not amenable) - Resectable with adverse functional outcomes

5 Consider multimodal therapy including metastasectomy or local ablative procedures in oligometastatic disease (1-3 metastatic lesions)

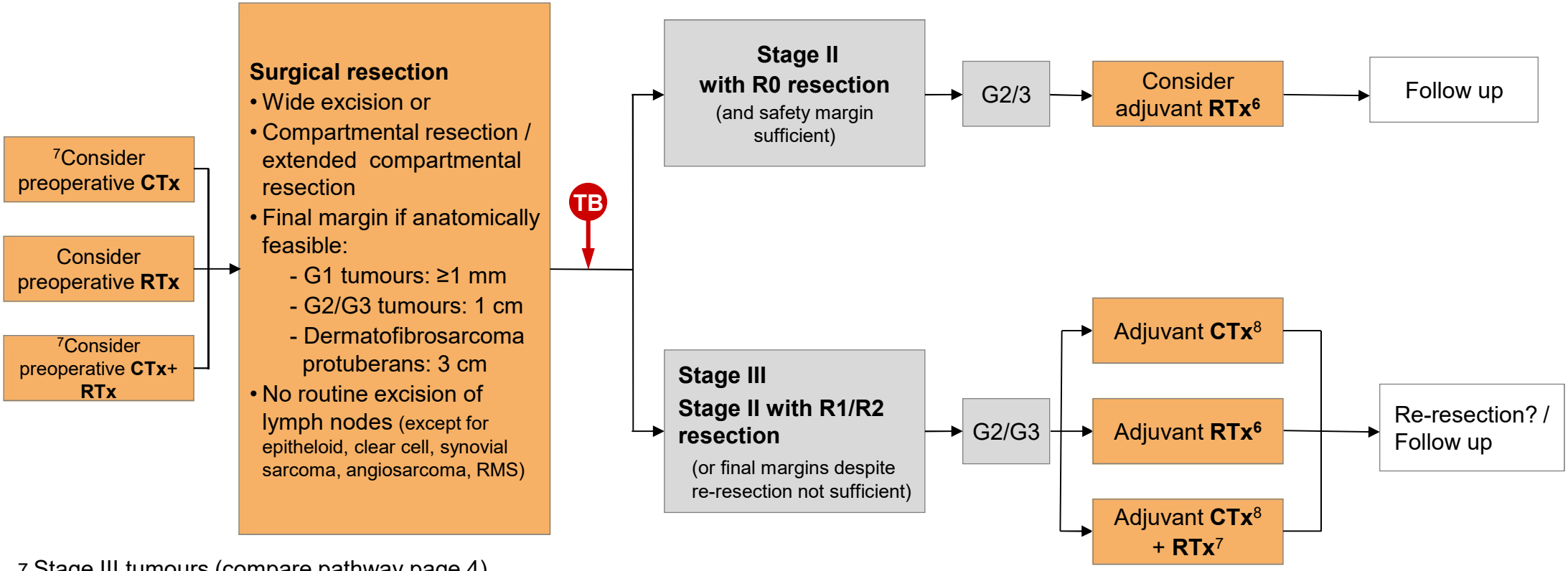
Pathway page 2: Surgical resection, UICC Stage IA / IB (Low grade)



[6] Adjuvant RTx within 6 weeks after surgery. Dose of 60 Gy, fractions of 1.8 - 2 Gy possibly with boosts up to 66-70 Gy. Patients that have undergone a compartmental resection or amputation do not require adjuvant irradiation assuming that the margins are clear.

RTx Radiotherapy

Pathway page 3: Surgical resection, UICC Stage II (high grade), UICC Stage III



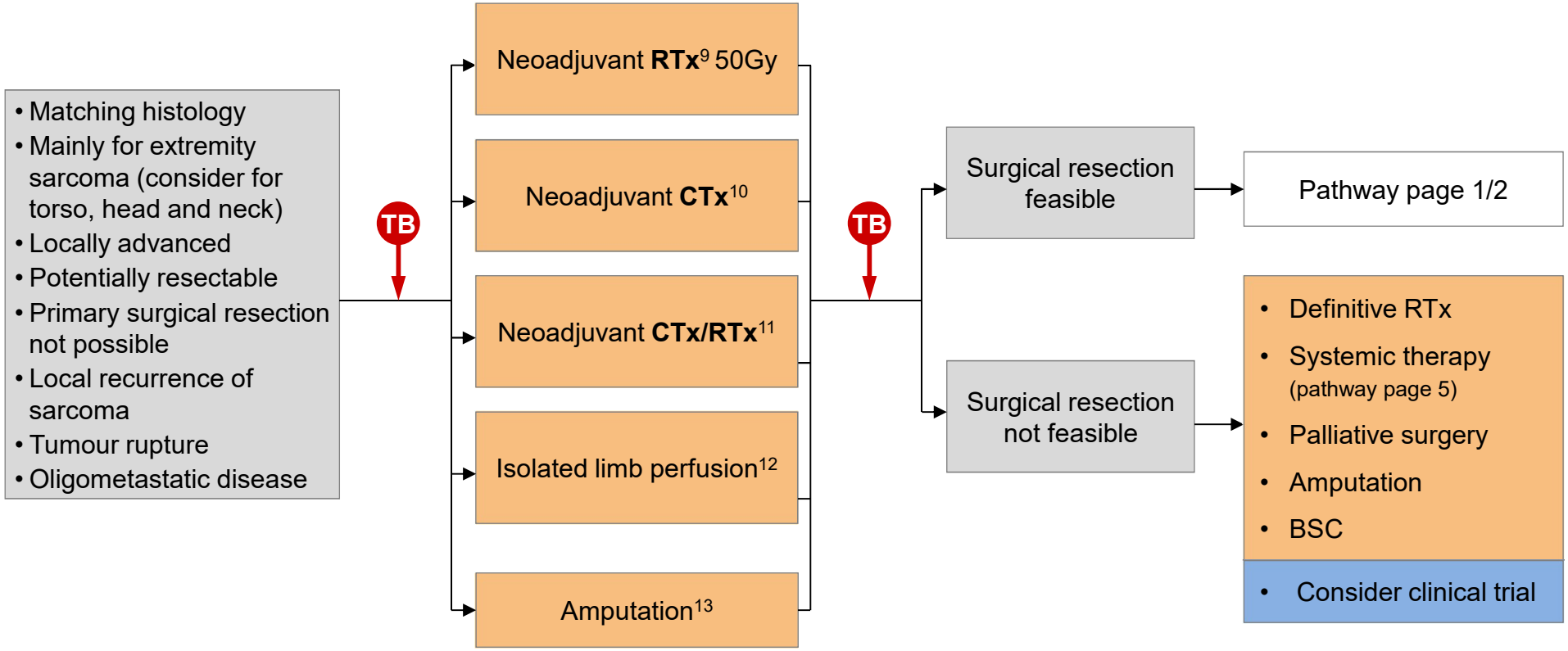
7 Stage III tumours (compare pathway page 4)

6 Adjuvant RTx within 6 weeks after surgery. Dose of 60 Gy, fractions of 1.8 - 2 Gy possibly with boosts up to 66 Gy. Patients that have undergone a compartmental resection or amputation do not require adjuvant irradiation assuming that the margins are clear.

8 If not applicated preoperatively. Adjuvant Chemotherapy with Adriamycin/Ifosfamide 4-5 courses, no Ifosfamide in case of leiomyosarcoma!. Consider Adriamycin/DTIC

CTx Chemotherapy, RTx Radiotherapy

Pathway page 4: Primary surgical R0 resection not feasible (potentially resectable, locally advanced)



9 In selected cases, i.e. in large retroperitoneal sarcomas where post-surgical RTx is difficult to apply

10 Standard Chemotherapy: 3x Adriamycin/Ifosfamide, in case of leiomyosarcoma Adriamycin/DTIC, in case of myxoid LPS Doxorubicin/Trabectedin (consider Taxane in case of angiosarcoma) Staging per CT, MRI, consider PET-CT initially

11 Combined RTx/CTx (MAID concepts), only in exceptional cases with a high requirement of local control

12 Isolated limb perfusion might be performed to permit limb salvage in cases where amputation is the only other option. 1 x Melphalan / TNF with hyperthermia, Staging MRI after six weeks

13 Occasionally performed to achieve adequate margins and the best chance of cure

CTx Chemotherapy, RTx Radiotherapy

Pathway page 5: Metastatic disease (UICC stage IV), systemic therapy

Surgical Resection of primary
(see pathway 2 and 3)
and
Metastasectomy / local ablation if oligometastatic
(surgical resection, RFA, embolization)

TB

Consider **neoadjuvant CTx**[14,15] or **RTx or adjuvant CTx/RTx**

TB

Follow up

Not resectable
(e.g. disseminated metastasis)

TB

Consider palliative care and palliative intervention[16] at each stage of the disease

CTx with Adriamycin (conventional or liposomal) +/-Ifosfamide
(Staging after each two courses)

Soft tissue sarcoma with entity specific therapy[17]:
- Leiomyosarcoma: Gemcitabine/DTIC
- Angiosarcoma: Paclitaxel
- Myxoid liposarcoma: Trabectedin
- Dermatofibrosarcoma protuberans: Imatinib
- See also pathway page 8

• Consider clinical trial

PD

TB

Salvage chemotherapy[18]**:**
- Trabectedin
- Eribulin (LPS only)
- Pazopanib
- DTIC
- Trofosfamid
- Gemcitabine +/- Docetaxel
- See also pathway page 6

• Consider clinical trial

Other options:
- Palliative RTx (EBRT, SBRT)
- Palliative Surgery (Debulking)
- BSC

[14] In case of neoadjuvant chemotherapy 5 courses Adriamycin/Ifosfamid.
[15] Significance of chemotherapy not proven in randomized trials
[16] See palliative care screening tool on page 9
[17] See complete list of soft tissue sarcoma with entity specific therapy on page 7
[18] Depending on histologic subtype, pretreatment and therapy free intervall

CTx Chemotherapy, RTx Radiotherapy, PD Progressive disease, BSC best supportive care, EBRT external beam radiation therapy, SBRT Stereotactic body radiotherapy, RFA Radiofrequency ablation

Pathway page 6: Metastatic disease, conclusion - systemic therapy

First-line
(regardless of subentity, chemo-sensitive)

- Doxorubicin / liposomal Doxorubicin
- Trofosfamide (elderly >65 yrs, frail)
- Doxorubicin/Ifosfamid only if need for remission induction (CAVE FN)
- Doxorubicin/DTIC for Leiomyosarcoma
- Gemcitabin/Docetaxel, Pazopanib, or Trabectedin if Doxorubicin contraindicated

≥ 2nd Line
for Leiomyosarcoma

- Trabectedin
- Gemcitabin mono or
- Gemcitabin/DTIC or
- Gemcitabin/Docetaxel

→ Pazopanib

≥ 2nd Line
for Liposarcomas

- Eribulin → Trabectedin
- Trabectedin → Eribulin

≥ 2nd Line
Others

- Trabectedin (also: mSFT, Chondrosarcoma)
- Gemcitabin mono (+/- DTIC)
- Gemcitabin mono (+/- Ifosfamid)

→ Pazopanib

≥ 4th Line
(TCR: 10-40%) versus BSC*

- Dacarbazin
- Trofosfamid
- high dose Ifosfamid
- Etoposid

*BSC best supportive care

Page 7: Soft tissue sarcoma with entity specific medical therapy

STS subtype	1st-line	2nd-line	3rd-line	4th-line	5th-line	6th-line
Leimyosarkom, uterin	Doxo ± Ifo	Gem/Doce	Trabectedin	Pazopanib	CPI	Regorafenib
Leiomyosarcoma, non-uterine	Doxo + DTIC or Doxo ± Ifo	Trabectedin	Gem/Doce	Pazopanib	CPI	Regorafenib
Liposarcoma, myxoid	Doxo ± Trabectedin	Trabectedin	Eribulin	CPI		
Liposarcoma, de-/differenciated	Doxo/Ifo or Doxo + DTIC	Eribulin	Trabectedin	CPI	ggf. Palbociclib	
Angiosarcoma	Paclitaxel	Gemcitabine	Doxo ± Ifo	Beva	Pazopanib	CPI
Synovial Sarcoma	HD Ifo 14g/m^2 or Doxo ± Ifo	Trabectedin	Pazopanib	Gem ± Doce or DTIC	DTIC	
MPNST	Doxo/Ifo	Gem±Vino				
Dermatofibrosarcoma protuberans	Imatinib (400-800mg)	ggf. Pexidartinib				
Endometrial Stroma Sarcoma	AI and/or GnRH analogue	Doxo ± Ifo				
Rhabdomyosarcoma, embryonal/alveolar	Please refer CWS-guidance protocol or Doxo/Ifo -> Trofo	O/TIE	Carbo/Eto	Pazopanib	Topo-I-Inh.	
Ewing sarcoma	VDC/IE -> IEVC/BuMel (EWING 2012)	TC/CE/IFOS (rEECur)	TC/CE/IFOS (rEECur)	TC/CE/IFOS (rEECur)		
Rhabdomyosarcoma, pleomorphic	VAIA or CEVAIE (age? ECOG?)					
Kaposi-Sarcoma	liposom. Doxo (Paclitaxel)	Pazopanib	Pomalidomid			
Alveolar Soft Part Sarcoma (ASPS)	Sunitinib	Pazopanib	Pembrolizumab	ggf. Cediranib		
Epithelial Hemangioendothelioma	Bevacizumab	Pazopanib	Doxo	Trabectedin		
Inflammatory Myofibroblastic Tumor	ALKi (Crizotinib/Ceritinib/…)					
Tenosynovial Giant Cell Tumor	Imatinib (400mg)					
Desmoid Tumours (Agressive Fibromatosis)	Sorafenib	Imatinib or Pazo	liposom. Doxo	Doxo+DTIC	MTX + Vinorelbin/Vinblastin	
Malignant Solitary Fibrous Tumor	Tem/Beva	Sunitinib	Pazopanib	Sorafenib		
Hemangiopericytoma / extrapleural SFT	Sunitinib	Tem/Beva	Doxo ± Ifo or DTIC	Gem/Doce	IFN-α	Axitinib
Epitheloid Sarcoma	Doxo/Ifo	Tazemezostat	Gem/Doce			
Clear Cell Sarcoma	Sunitinib					
PEComa	mTORi					
Most other STS	Doxo or Doxo/Ifo	Trabectedin	Gem/DTIC	Pazopanib	Trofosfamide	CPI

Page 8: Follow up after multimodal treatment of high grade STS

Offer contact to patient advocacy group and psychooncological support whenever necessary

	First year					Second year		Third year		Fourth year		Fifth year	
	0 mon. (OP)	3 mon.	6 mon.	9 mon.	12 mon	18 mon.	24 mon.	30 mon.	36 mon.	42 mon.	48 mon.	54 mon.	60 mon.
Physical exam Laboratory exam	X	x	x	x	x	x***	x ***	x	x	x	x	x	x
CT thorax*	x	x	x	x	x	x	x	x	x	x	x	x	x
Chest x-ray**	x		x		x	x	x	x	x	x		x	
MRI of the local finding	x	x	x	x	x	x	x	x	x	x	x	x	x
TTE after Doxo	x				x		x		x		x		x

* In case of risk factors (G 2-3, tumour size > 5 cm, subfascial (deep) localization, safety margin not sufficient, tumour recurrence, state after resection of metastases) quarterly controls are recommended in year two and three

** In case of standard risk (no risk factors) instead of CT thorax

*** In case of multiple risk factors quarterly controls are recommended for year two and three

Page 9: Palliative care screening tool

Screening items			Points
1.	• Presence of metastatic or locally advanced cancer		2
2.	• ECOG score (functional status score, performance status)		0-4
3.	• Presence of one or more serious complications of advanced cancer usually associated with a prognosis of < 12 months (e.g. brain metastases, hypercalcemia, delirium, spinal cord compression, cachexia		1
4.	• Presence of one or more serious comorbid diseases also associated with poor prognosis (e.g. moderate-severe COPD or CHF, dementia, AIDS, end stage renal failure end stage liver cirrhosis)		1
5.	• Presence of palliative care problems		1
	a.	• Symptoms uncontrolled by standard approaches	1
	b.	• Moderate to severe distress in patient or family, related to cancer diagnosis or therapy (personal targets and expectations, educational and informational requirements, cultural factors)	1
	c.	• Patient/family requests palliative care consult	1
	d.	• Team needs assistance with complex decision making or determing goals of care (benefit/side effects of treatment)	1
	e.	• Instable or deficient network especially for emergency situation or 24-h care	1

A total of > 5 points signalizes need for supportive palliative care

According to Glare et al. (2011); NCCN Clinical Practice guidelines in Oncology 2023