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

UCCH / UCCSH Pathway

Guideline
Gastrointestinal Stromal Tumor (GIST)

Version Mar/2023

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Version 07, Mar/2023

according to TNM classification 8th edition, 2017

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Next planned review	Mar/2025

Legend of Colours

= Therapeutic procedure

= Clinical or diagnostical condition

= Diagnostic procedure

= Clinical trial

= Supportive measure

= Referral

TB

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

UKE HAMBURG UKSH

Pathway: Gastrointestinal Stromal Tumor (GIST)

Version Mar/2023
2.03.01 Anlage 15 UCCH*
ID: 462457 UCCSH*

Pathway page 1: Workup

GIST suspicious lesion

Workup:

Baseline:
- History
- Clinical presentation
- Laboratory tests (incl. Blood counts, liver and kidney function, coagulation, TSH)
- Abdominal/pelvic CT or MRI (w/ contrast) and chest imaging if ≥ 2cm
- Biopsy[1] (intraabdominal tumor perforation MUST be avoided)

Further diagnostic work-up:
- PET-CT in selected cases (M-status uncertain)
- Endoscopy (in case of gastric or duodenal GIST)
- Endoscopic ultrasound
- Pelvic MRI (in case of rectal GIST)
- In case of resectable disease: Postoperative histology including
  - *KIT* and *PDGFRA* mutation status
  - Mitosis count per 5mm² (≤ 5 vs. >5)
  - Miettinen risk scoring

Supportive:
Offer contact to self help group
Offer psychooncological support

TB

GIST < 2 cm
- **Gastric micro-GIST (> 50 year-olds):** • Surveillance[2] → Increase in size **≥ 2 cm** → Pathway page 2
- **Symptomatic / high risk:** • Endoscopic resection • Surgical resection (prior biopsy) → Follow up

GIST ≥ 2 cm
- Resectable → Pathway page 2
- Potentially resectable → Pathway page 3
- Not resectable → Pathway page 4

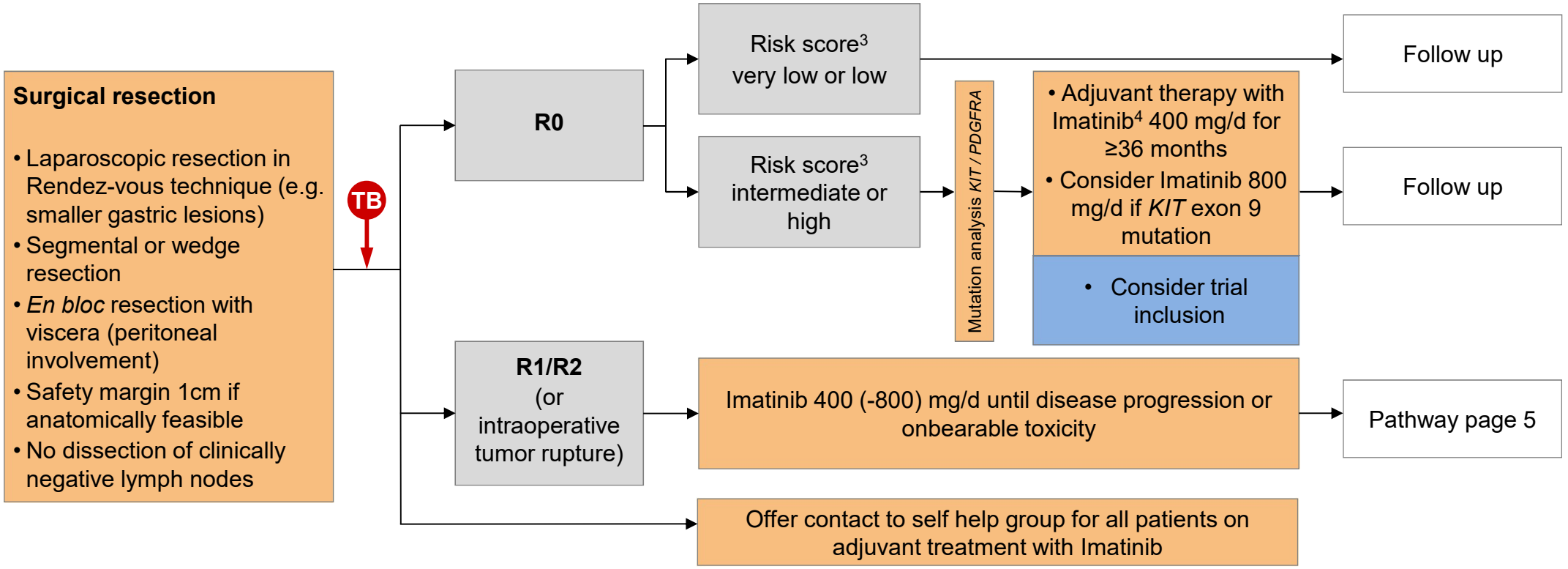
GIST Colorectal < 2 cm
- Resectable → Pathway page 2
- Potentially resectable → Pathway page 3
- Not resectable → Pathway page 4

Metastatic disease → Pathway page 4

[1] - In case of non-intestinal GIST (<2 cm): Observation, enucleation, or endoscopic resection. Biopsy if surgery considered.
- Resectable disease: The standard approach for GIST ≥ 2 cm is biopsy if amenable to endoscopic assessment (risk of tumor cell dissemination). Otherwise laparoscopic / laparotomic excision should be performed.
- For metastatic/not resectable disease : Biopsy (from primary or metastases) including *KIT* and *PDGFRA* mutation analysis (before start of systemic treatment) mandatory.

[2] - Surveillance / EEUS at 6, 12, 18, 24 months and bi-yearly afterwards in >50 year-olds with gastric micro-GIST (< 2cm).

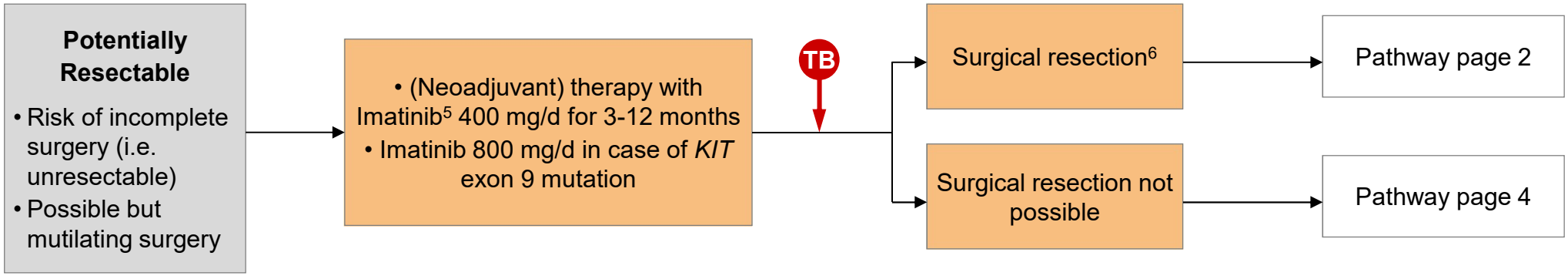
Pathway page 2: Surgical resection



[3] Risk score according to Miettinen (page 7)

[4] Imatinib is not effective in wild type GIST or in case of *PDGFRA D842V* mutation. No adjuvant treatment available for Imatinib-resistant tumors.

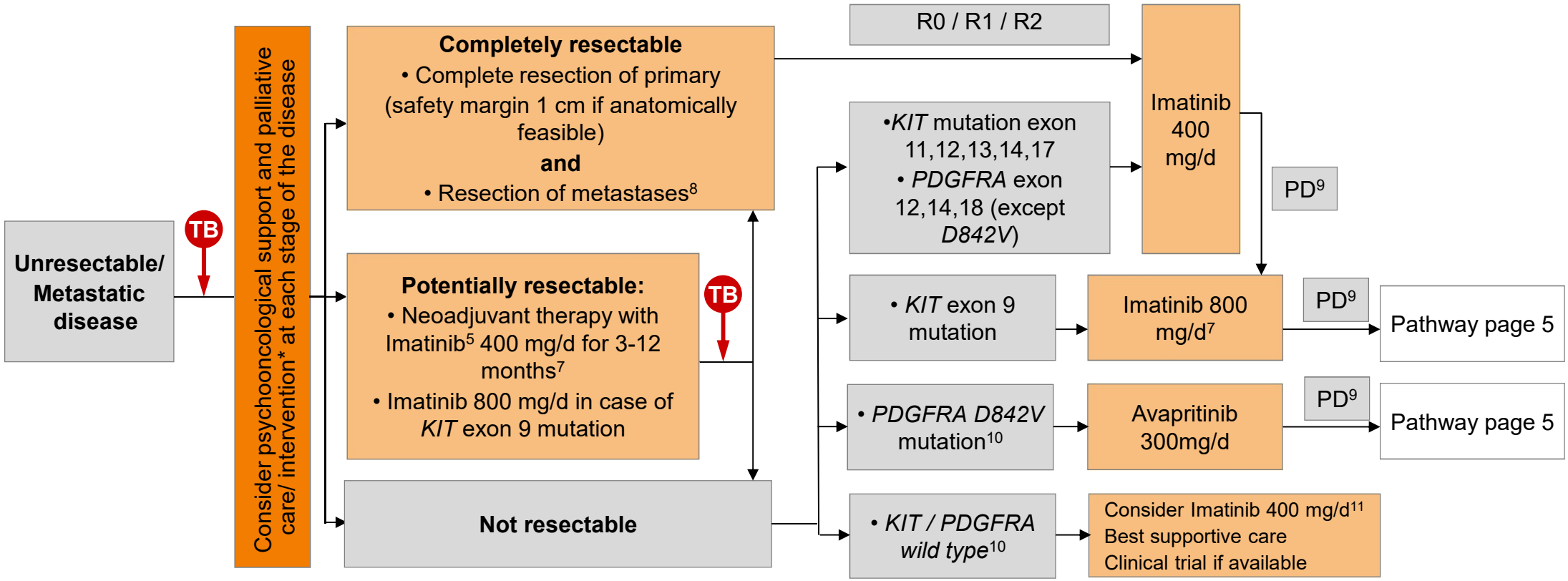
Pathway page 3: Potentially resectable



[5] Imatinib is not effective if *PDGFRA D842V* mutation. No neoadjuvant option for Imatinib-resistant tumors (see page 8).

[6] Re-staging by (thoraco-)abdomino-pelvic CT scan in 3-months-intervals. Resection after 6-12 months of treatment when no more tumor shrinkage is seen on two consecutive CT scans.

Pathway page 4: Unresectable, potentially secondarily resectable and/or metastatic disease. Systemic treatment



* See palliative care screening tool on page 8

[5] Imatinib is not effective if *PDGFRA D842V* mutation. No neoadjuvant option for Imatinib-resistant tumors (see page 8).

[7] Re-staging by (thoraco-)abdomino-pelvic CT scan in 3-months-intervals. Resection at timepoint of best response.

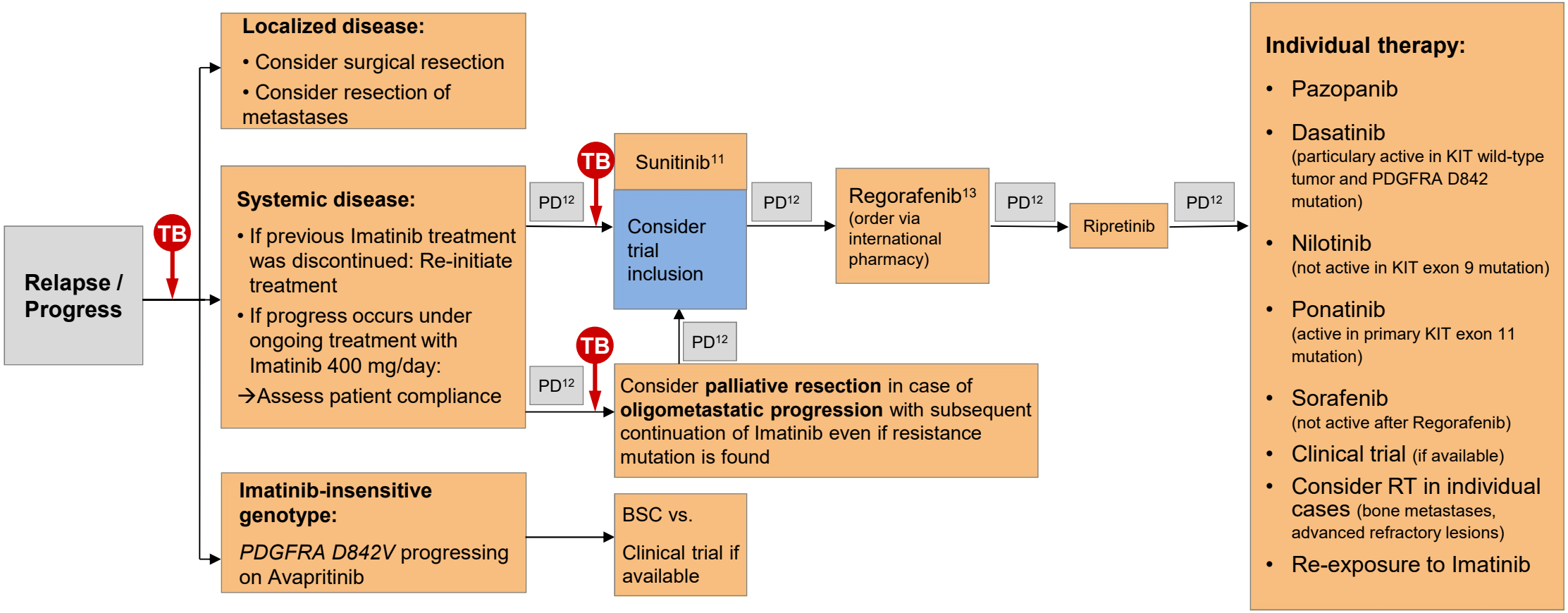
[8] Consider surgical resection in case of stable disease with progress of solitary metastases. General progress is no indication for surgery

[9] Response evaluation according to CHOI criteria rather than RECIST criteria.

[10] *PDGFRA D842V*-mutated as well as *KIT/PDGFRA* wild type GIST are resistant towards all standard treatment TKIs.

[11] response rate in *KIT/PDGFRA* wild type GIST (SDH deficient) of Imatinib 2-8%.

Pathway page 5: Progressive disease, Salvage therapy



[12] Response evaluation according to CHOI rather than RECIST criteria.

[13] Consider surgical resection or local ablative treatment (RFA, TAE or SIRT) in case of unifocal or oligofocal disease progression (e.g., nodules in a cyst lesions, no more than 5 lesions). General progress is no indication for surgery.

Page 6: Follow up

Follow up under adjuvant therapy (Imatinib) in case of intermediate / high risk:

- Routine follow up by CT scanning or abdomino-pelvic MRI every 3-6 months for duration of adjuvant treatment
- Offer contact to self help group and psychooncological support

Follow up after resection / adjuvant therapy

	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 test	x	X**	x	X**	x	X***	X***	X***	X***	x	x	x	x
Abdomino-pelvic CT▼	x	X**	x	X**	x	X***	X***	X***	X***	x	x	x	x
Rectal GIST (Endoscopic ultrasound, MRI or rectoscopy)	x		x		x	x	x	x	x	x	x	x	x

* In case of small tumors (<2cm) longer intervals may be chosen.
** In case of intermediate or high risk according to Miettinen
*** In case of high risk according to Miettinen quarterly controls are recommended
**** Afterwards annually until year ten particularly in case of high-risk disease
▼ May be replaced by abdomino-pelvic MRI after longer relapse-free interval in low risk disease patients to reduce radiation exposure

Page 7: Risk stratification of primary GIST by mitotic index, size and site

		Risk of disease progression/relapse							
Mitotic index	Size	Stomach	%	Duodenum	%	Jejunum / Ileum	%	Rectum	%
≤ 5 per 50 HPF*	≤ 2cm	none	0	none	0	none	0	none	0
	> 2 ≤ 5cm	very low	1.9	low	8.3	low	4.3	low	8.5
	> 5 ≤ 10 cm	low	3.6	high	34	moderate	24	high	57
	> 10 cm	moderate	12	high		high	52	high	
> 5 per 50 HPF*	≤ 2 cm	none**	0**	high**	n.a.	high	50	high	54
	> 2 ≤ 5 cm	moderate	16	high	50	high	73	high	52
	> 5 ≤ 10 cm	high	55	high	86	high	85	high	71
	> 10 cm	high	86	high		high	90	high	

* Currently mitotic index is generally counted in 5mm^2 (equals about 18-20 HPF)
**Denotes very small number of cases

Adapted from Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. Sem Diagn Pathol 2006; 23:70–83.

Page 8: Tyrosine kinase receptor mutations and Imatinib sensitivity

Mutation	IMATINIB-responsiveness
KIT exon 11	Responsive
PDGFRA exons 12,14,18	Responsive
Other (*KIT* exons 12,13,14,17)	Responsive
KIT exon 9	Lower responses
*PDGFRA D842V** (exon 18)	100% resistant
<< wild type >>	Resistant
GIST syndromic NF1 / Carney	25% resistant

* 80-90% of metastatic GIST respond to Imatinib.

** *PDGFRA D842V*: 100% located in the stomach. 20% of gastric GIST.

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 2015