UCCH Pathway

UCCH Guideline
Squamous Cell Carcinoma of the Larynx

2.03.01 Anlage 24

Version Oct/2021

Hubertus Wald Tumorzentrum
Universitäres Cancer Center Hamburg
Ein Kompetenznetzwerk des UKE

Guideline Squamous Cell Carcinoma of the Larynx

Version 08, Oct/2021

according to TNM classification 8th edition

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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)

Version Oct/2021

Pathway: Squamous Cell Carcinoma of the Larynx

2.03.01 Anlage 24

Work up

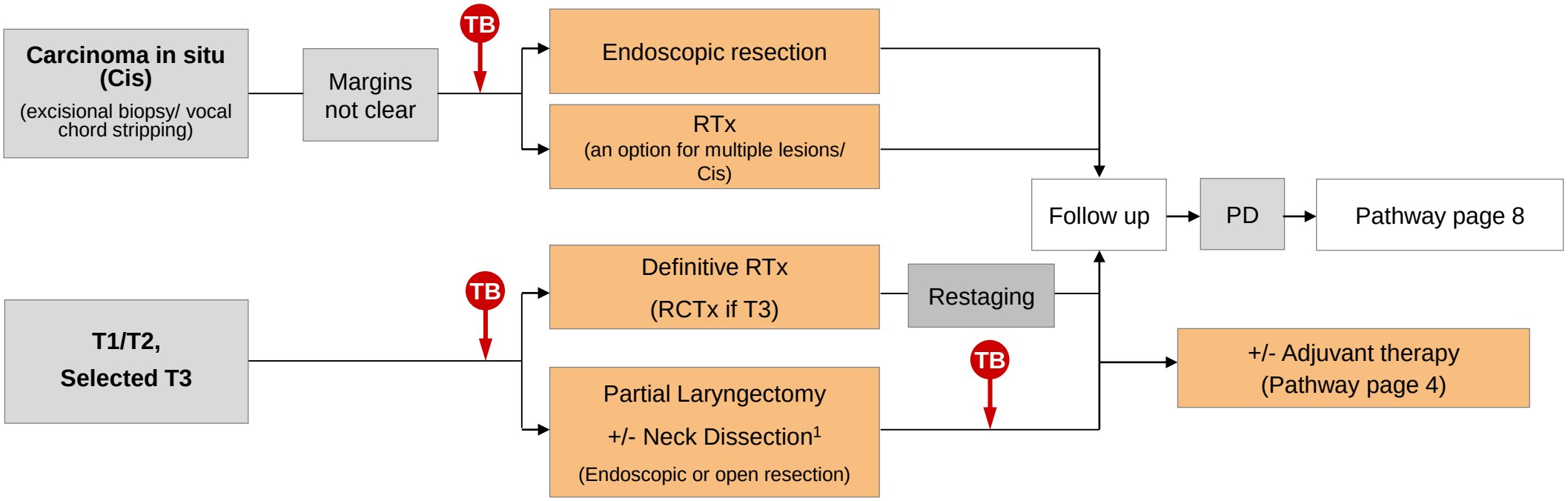
- Physical exam
- Biopsy
- T1/2: MRI head and neck or CT with contrast, chest x-ray and abdominal ultrasound, in case of N+: CT thorax/liver extension
- T3/4: MRI head and neck or CT with contrast, CT thorax/liver extension
- Dental evaluation and panoramic view
- Photodocumentation
- ORL examination
- Multidisciplinary consultation as indicated

- Supportive:
  - Offer contact to self help group
  - Screen for psychosocial distress

TB

- Resectable disease
  - Total laryngectomy not required
    - Glottic larynx → Pathway page 2
    - Supraglottic larynx → Pathway page 3
  - Total laryngectomy required → Pathway page 5
  - Non surgical treatment → Pathway page 6/7
- Unresectable
  - Performance status ECOG 0-1 → Pathway page 6
  - Performance status ECOG ≥2 → Pathway page 7
- Metastatic disease
  - Local treatment in case of symptomatic disease (e.g. surgery, radiation)
  - Systemic treatment → Pathway page 8

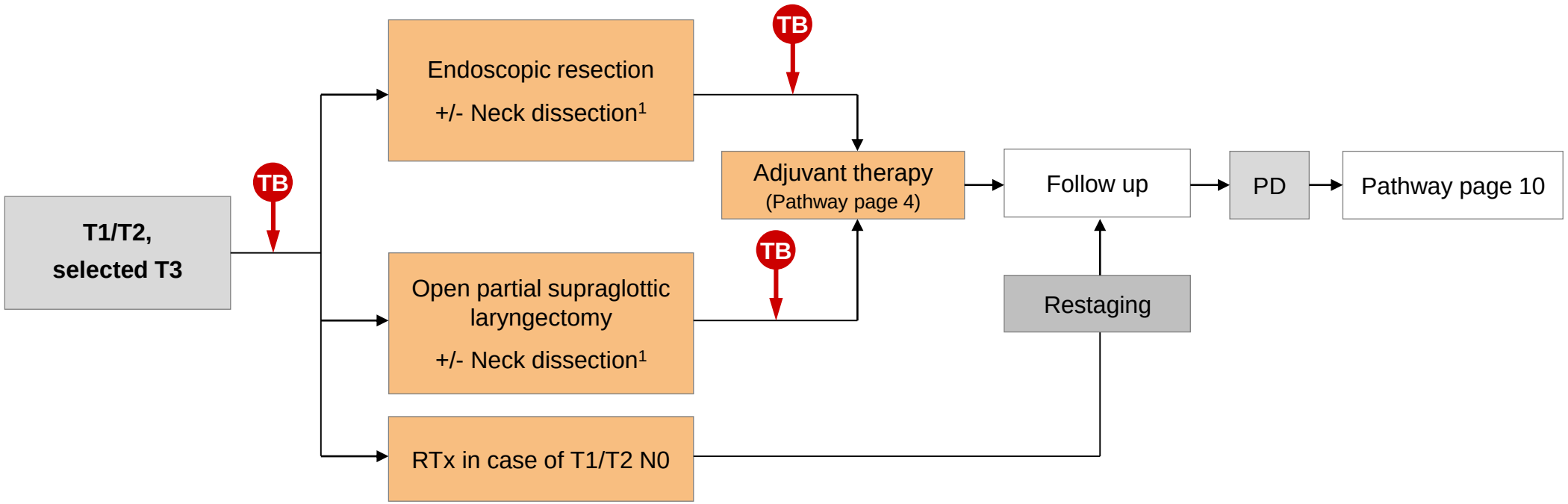
Pathway page 2: Laryngectomy not required (glottic Larynx)



RTx Radiotherapy, RCTx Radiochemotherapy, PD Progressive disease

[1] See indications for neck dissection in pathway page 11

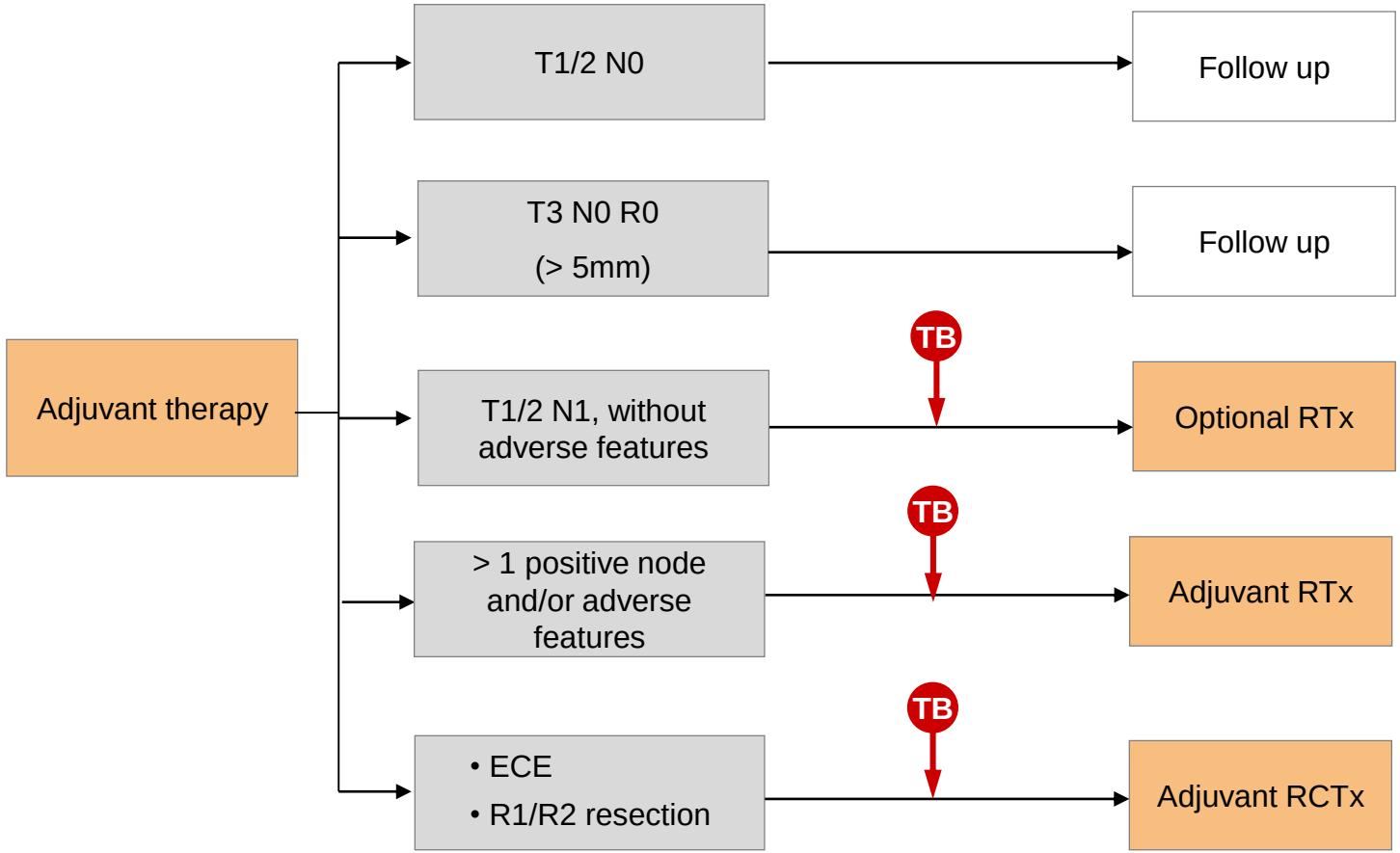
Pathway page 3: Total Laryngectomy not required (supraglottic Larynx)



RTx Radiotherapy, PD Progressive disease

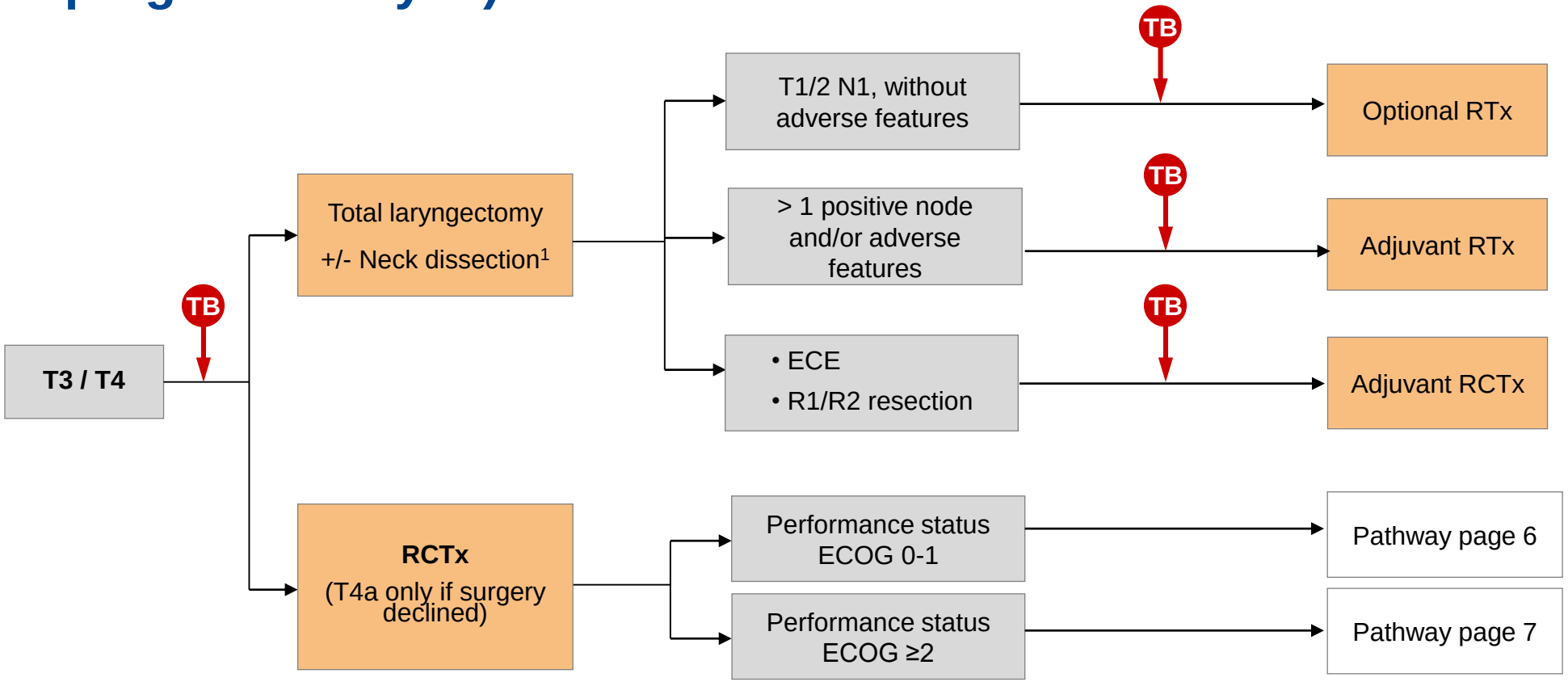
[1] See indications for neck dissection in pathway page 11

Pathway page 4: Adjuvant therapy



RTx Radiotherapy, RCTx Radiochemotherapy, Adverse features: pT3/T4, Pn1, L1, V1

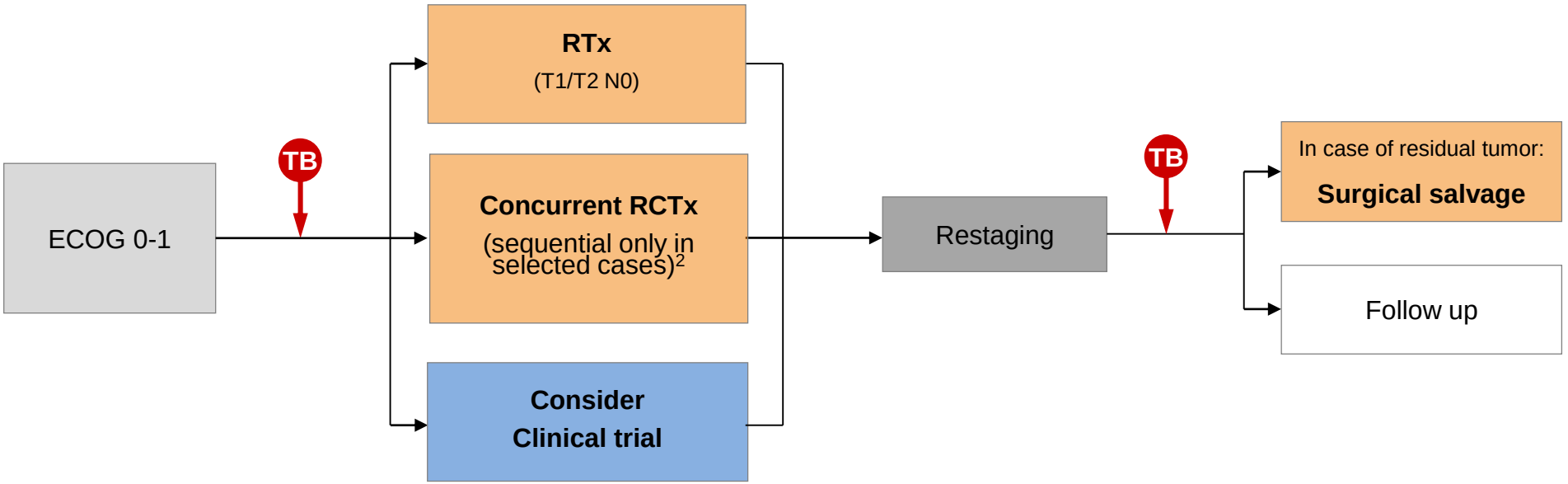
Pathway page 5: Total Laryngectomy required (glottic and supraglottic Larynx)



RTx Radiotherapy, RCTx Radiochemotherapy. ECOG The Eastern Cooperative Oncology Group

[1] See indications for neck dissection in pathway page 11

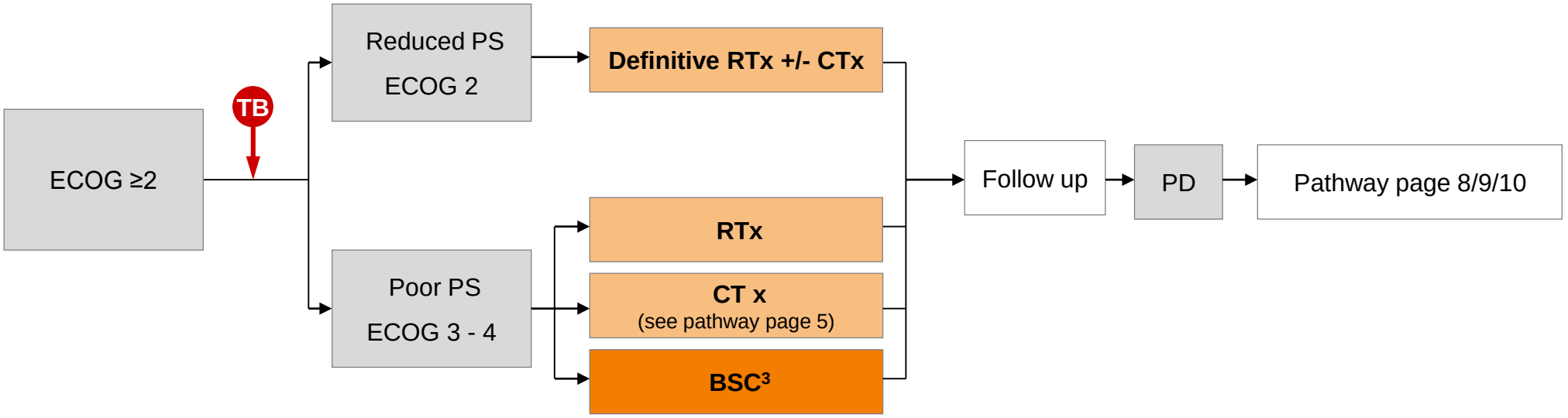
Pathway page 6: Non-surgical treatment SCC and PS (ECOG) 0-1



ECOG The Eastern Cooperative Oncology Group, RTx Radiotherapy, RCTx Radiochemotherapy

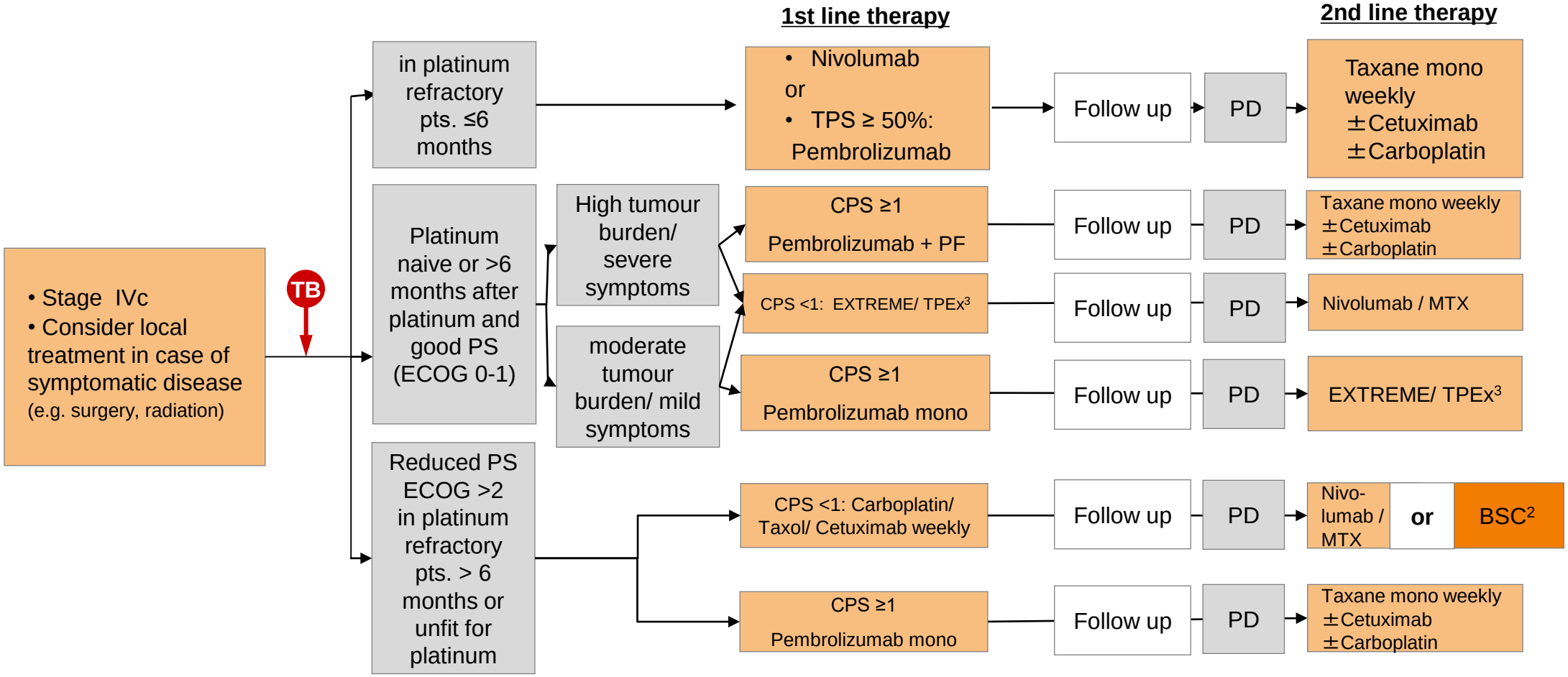
[2] See preconditions for Protocoll Sequential Therapy on page 20-22

Pathway page 7: Non-surgical treatment and PS (ECOG) ≥ 2



PS Performance Status, ECOG The Eastern Cooperative Oncology Group, BSC best supportive care
RTx Radiotherapy, CTx Chemotherapy, PD Progressive Disease
[3] See palliative care screening tool on page 15

Pathway page 8: Metastatic disease (systemic treatment)



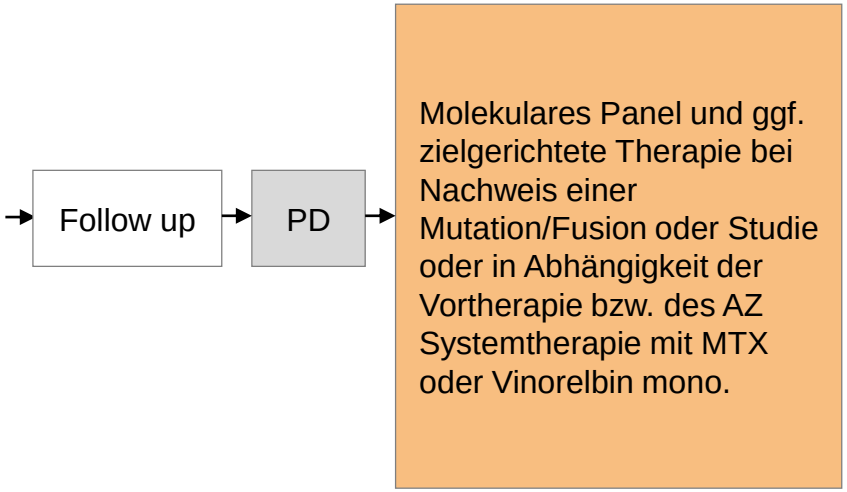
PS Performance Status, ECOG The Eastern Cooperative Oncology Group, BSC Best supportive care, PD Progressive Disease, CPS combined proportion score

[3] See palliative care screening tool on page 15

[3]See therapy protocols SCCHN on pages 17-19

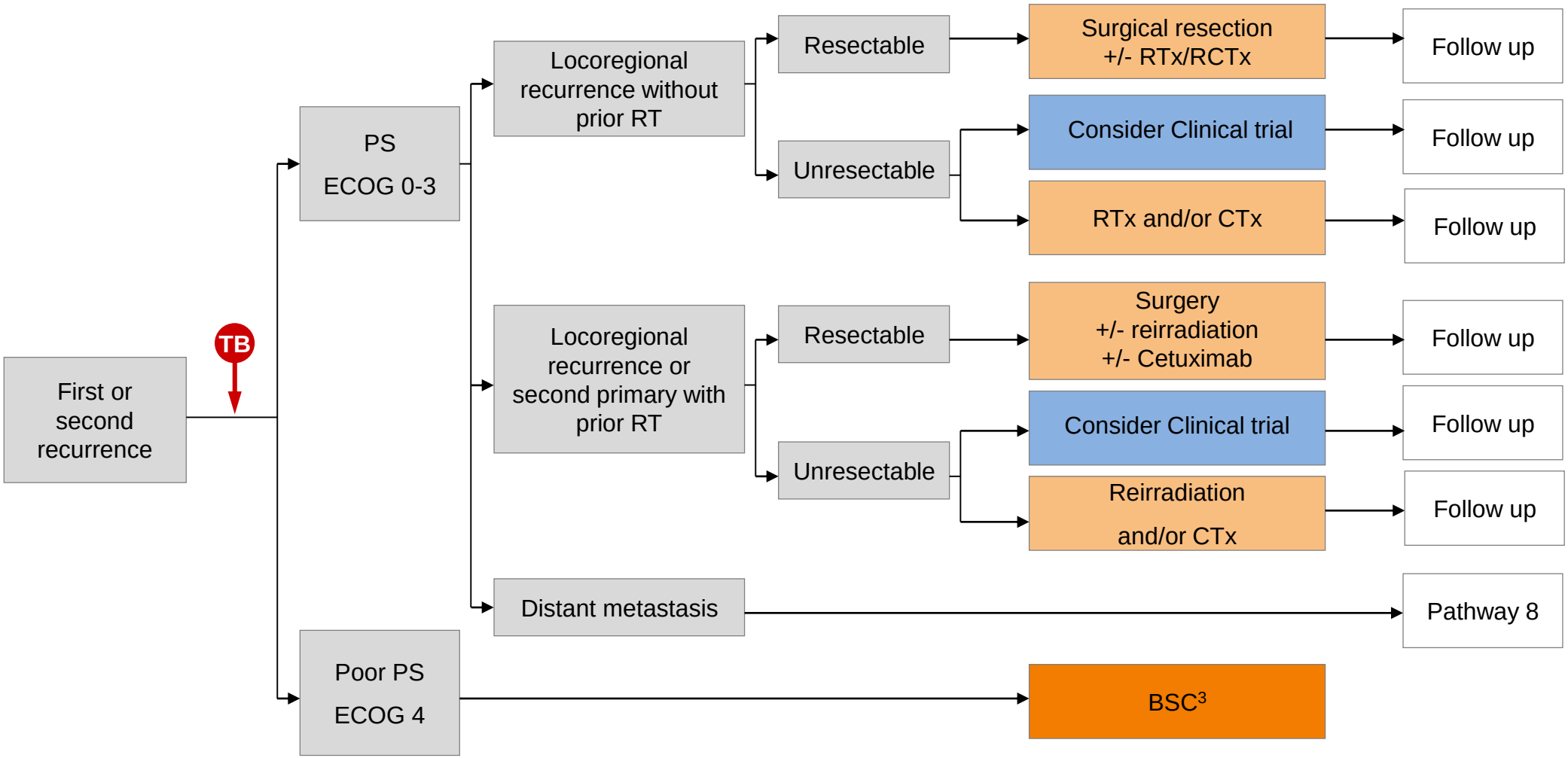
Pathway page 9: Metastatic disease (systemic treatment)

3rd line therapy



PS Performance Status, ECOG The Eastern Cooperative Oncology Group, BSC Best supportive care, PD Progressive Disease

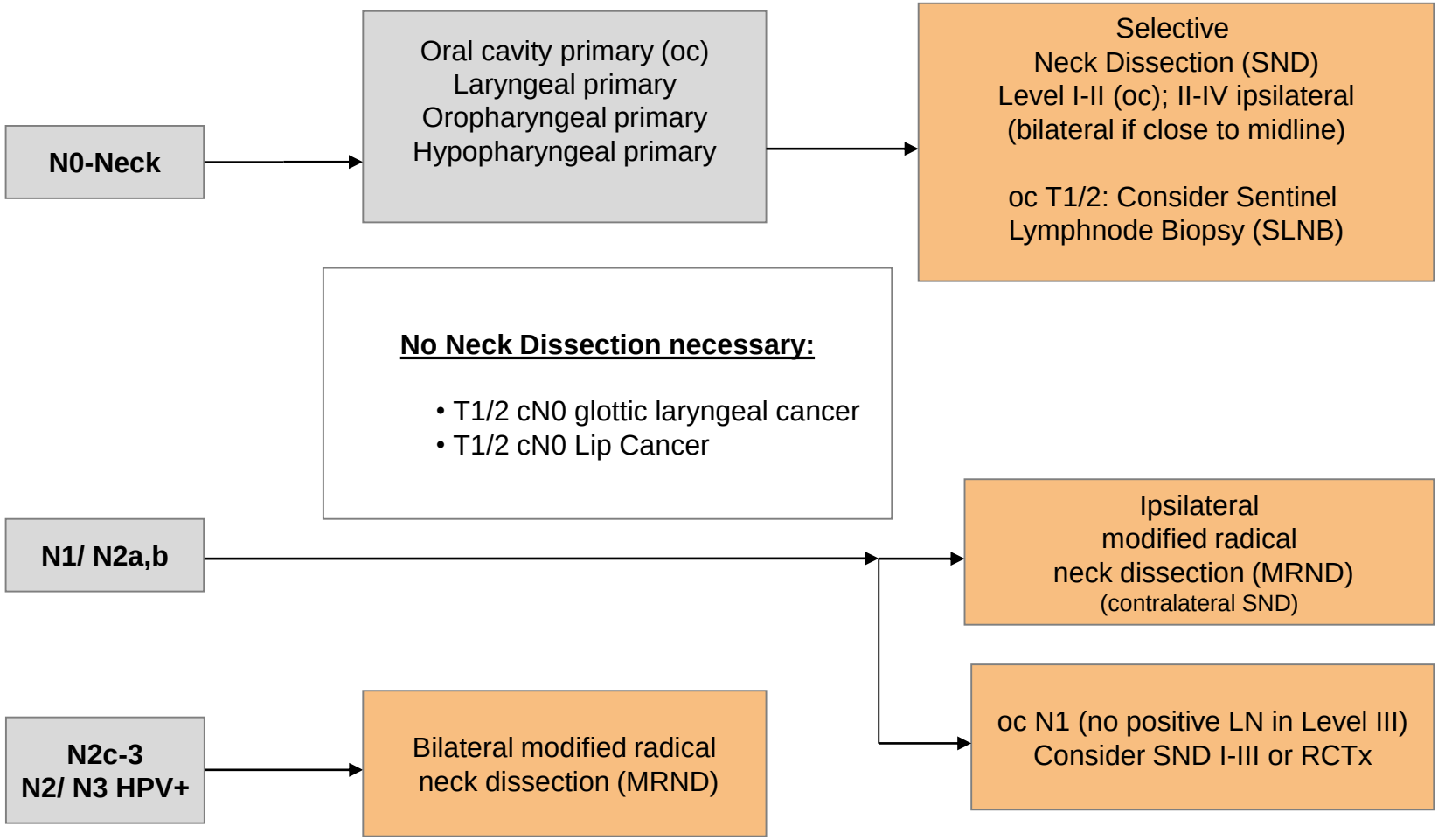
Pathway page 10: Salvage therapy



PS Performance Status, ECOG The Eastern Cooperative Oncology Group, RTx Radiotherapy, CTx Chemotherapy, RCTx Radiochemotherapy, BSC Best supportive care

[3] See palliative care screening tool on page 15

Pathway page 11: Indications for Neck Dissection



oc Oral Cavity Primary, RCTx Radiochemotherapy, SND Selective Neck Dissection

Page 12: Restaging

6 weeks after completion of therapy

- Clinical examination
- Ultrasound neck
- Examination (endoscopy) under anesthesia
- MRI neck (including primary lesion), if contraindication CT neck
- In case of unclear or suspicious lesion in thorax or abdomen: CT chest, CT/ultrasound abdomen

Palliative setting

- CT imaging after 6-8/9 weeks, depending on clinical outcome. No imaging in clinically measurable manifestation.

Page 13: Follow up

Every 3 months up to 30 months, afterwards every 6 months (5-year follow up)
Offer contact to self help group and psychooncological support whenever necessary

- Clinical examination
- Ultrasound of the neck
- Examination (panendoscopy) under anesthesia in case of suspicion of recurrence
- Thyroid function 1, 2 and 5 years after irradiation of the neck

- AJCC I/ II:
  - In case of T1/T2 glottic larynx no radiological imaging needed
  - Chest x-ray every 12 months and in case of suspicion of recurrence
  - MRI of the neck every 12 months and in case of suspicion of recurrence

- AJCC III/ IV:
  - MRI of the neck and CT of the thorax every 12 months and in case of suspicion of recurrence
  - Abdominal ultrasound

Page 14: Best supportive care

Best supportive care / palliative treatment
Consider nutritional counseling, psychological counseling, offering contact to self-help group

Upper airway obstruction:
PEG tube
Tracheostomy

Tumor associated pain:
analgetics (WHO)
palliative (chemo)radiation

Page 15: 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

Therapy Protocols RTx/ RCTx

Definitive Radiotherapy (definitive RTx)[6]:

high risk:

- ≥ 70-72 Gy (2.0 Gy/day) or equivalent or moderately accelerated in an integrated dose concept
- External-beam RT ≥ 50 Gy +/- brachytherapy

Medium risk:

- ≥ 60 Gy (2,0/die) or equivalent or moderately accelerated in an integrated dose concept

Low risk:

- ≥ 50 Gy (2,0/die) or equivalent or moderately accelerated in an integrated dose concept

Postoperative (adjuvant) Radiotherapy (RTx)[6]:

Primary:

- ≥ 60 Gy (2.0 Gy/die) or equivalent or moderately accelerated in an integrated dose concept

Neck:

- Involved nodal stations: 60 Gy (2 Gy/day) or equivalent or moderately accelerated in an integrated dose concept
- Uninvolved nodal stations: 50 GY (2 Gy/day) or equivalent or moderately accelerated in an integrated dose concept

Palliative Radiotherapy (RTx)[6]:

- Moderate Hyperfraction or moderately accelerated in an integrated dose concept

Radio-chemotherapy (RCTx)[6]:

- Definitive or high risk adjuvant 70-72 Gy, 2 Gy/die or equivalent or moderately accelerated in an integrated dose concept
- Adjuvant 66 Gy or equivalent or moderately accelerated in an integrated dose concept
- Cisplatin 40 mg/m2 every week (max. 7 cycles)

or

- Mitomycin 10 mg/m2 day 5 and day 36 and
- 5-FU 600 mg/m2 during 120 h infusion day 1-5

6 SIB (simultane integrated boost possible)

Therapy protocols SCCHN (1)

TPEx

- Cisplatin 75 mg/m^2 every 3 weeks
- Docetaxel 75 mg/m^2 every 3 weeks
- Cetuximab 250 mg/m^2 weekly (400 mg/m^2 loading dose)
- + G-CSF after each cycle
- Maintenance after 4 cycles TPEx: Cetuximab 500 mg/m^2 biweekly

EXTREME

- Cisplatin 100 mg/m^2 every 3 weeks (max. 6 cycles)
- 5-FU 4000 mg/m^2 during 96h infusion every 3 weeks (max. 6 cycles)
- Cetuximab 250 mg/m^2 weekly (400 mg/m^2 loading dose)
- + G-CSF after each cycle
- Maintenance after 4-6 cycles EXTREME: Cetuximab 500 mg/m^2 biweekly

Therapy protocols SCCHN (2)

Carboplatin/Paclitaxel/Cetuximab weekly (R/M-SCCHN)

- Paclitaxel 80 mg/m^2 weekly
- Carboplatin AUC2 weekly
- Cetuximab 250 mg/m^2 weekly (400 mg loading dose)
- Maintenance after 18 weeks: Cetuximab 500 mg/m^2 biweekly

TPF (Induction) (max. 3 cycles)

- Cisplatin 80-100 mg/m^2 every 3 weeks
- 5-FU 4000 mg/m^2 during 96h infusion every 3 weeks
- Docetaxel 75 mg/m^2 every 3 weeks
- + G-CSF after each cycle

Therapy protocols SCCHN (3)

Nivolumab Mono

- Nivolumab 240 mg every 2 weeks or 480 mg every 4 weeks

Pembrolizumab Mono

- Pembrolizumab 200 mg every 3 weeks or 400 mg every 6 weeks

Pembrolizumab + PF

- Pembrolizumab 200 mg every 3 weeks
- Cisplatin 100 mg/m^2 every 3 weeks (max. 6 cycles)
- 5-FU 4000 mg/m^2 during 96h infusion every 3 weeks (max. 6 cycles)
- After PF-cycles Pembrolizumab Mono maintanance

Protocol Sequential Therapy - page 1

Staging: ENT-clinic

- Physical exam
- Ultrasound neck
- Biopsy (including HPV p16 analysis)
- MRI for primary and neck (CT with contrast if contraindications against MRI)
- Chest x-ray and ultrasound abdomen **or**
- CT chest and abdomen (UICC stage III or IV and recurrent disease)
- Panendoscopy under anesthesia
- Preanesthesia studies
- Dental evaluation and panoramic view as indicated
- Voice, speech, swallowing and breathing evaluation as indicated
- Multidisciplinary consultation as indicated
- Portacath (Department of radiology, registration in angiographie phone: 54022)
- Creatinine clearance
- Audiometry
- PEG tube

Protocol Sequential Therapy - page 2

Induction chemotherapy: Medical Oncology

- 3 cycles TPF on d1, d22 and d43 (Precondition:
  - ECOG 0-1
  - Adequate bone marrow function: leucocytes > 3.0 x 10^9/L, neutrophils > 1 x 10^9/L, platelets > 80 x 10^9/L, hemoglobin > 9.0 g/dL
  - Adequate liver function: Bilirubin < 2.0 g/dL, SGOT, SGPT, AP, G-GT < 3 x ULN
  - Adequate renal function: serum creatinine <1.5 mg/dL, or if creatinin between 1.5 mg/dL and 1.8 mg/dL, creatinine clearance > 60ml
  - No serious co-morbidity, e.g. arterosclerosis + apoplexy, recent MI, high-grade carotic stenoses, unstable cardiac disease despite treatment, congestive heart failure NYHA grade 3/4, Insulin-dependent diabetes mellitus, uncontrolled hypertension, liver cirrhosis (Quick < 75%, total protein <3.0 g/dl, bilirubine >2mg/ml) or kidney insufficiency)
- Docetaxel 75 mg/m2 d1, Cisplatin 100 mg/m2 d1, 5-FU 1000 mg/m2 d1-4 (In case of dip in hearing sensitivity Cisplatin may be splitted into 50 mg/m2 on d1+2)
- Supportive therapie: GCSF (e.g. Neulasta) d6, Ciprobay 500 mg 1-0-1 in case of neutropenia < 1000/µl

Protocol Sequential Therapy - page 3

Restaging after 3 cycles TPF has to be organized by Medical Oncology within 3 weeks after 3. cycle TPF so that radiation can start on d 64-71!!

- Panendoscopie (ENT-clinic)
- MRI-neck (or CT if contraindications against MRI)
- Audiometry and Creatinine Clearance if necessary
- In case of CR/PR: combined radiochemotherapy beginning d63 (=>PEG-tube necessary)
- In case of SD/PD: salvage-resection with adjuvant radiation

↓

Radiotherapy:
Department for radiotherapy

- Radiatio: 70Gy, 2 Gy/d (five fractions per week until week seven)

↓

Follow up: Interdisciplinary tumor consultation