UNIVERSITÄTSKLINIKUM
Schleswig-Holstein

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

UCCH / UCCSH Pathway

Guideline
Aggressive B-Cell lymphoma

Version Jan/2024

Guideline Aggressive B-cell Lymphoma (excluding Burkitt lymphoma)
Version 01, Jan/2024

according to WHO classification 2016

Aggressive B-cell Lymphoma board members

J. Dierlamm, K. Weisel, A. Asemissen, A. Schieferdecker, M.Voigtländer , S. Ghandili (Med. Oncology)
C. Wolschke, N. Kröger, F. A. Ayuk, (BMT)
S. Klutmann, I. Apostolova (Nuclear Medicine)
M. Eggers, A. Hell (UCCH)
C. Schlüter, Stefan Bartels (KKR)
Th. Frenzel, A. Krüll, S. Brackrock (Radiooncology)
S. Weidemann (Pathology)
L. Viezens (Spine Surgery)
M. Nickelsen, V. Böhme (Onkologie Lerchenfeld)
M. Priemel (Traumatology)
J. Schulze zur Wiesch (Internal Medicine)
O. Kodalle (Patient Support)
Chr. Pott (UCCSH Med. Oncology)
N. Gebauer (UCCSH Med. Oncology)

Responsible author	V.Böhme / M.Nickelsen (ext.coop.partner Med. oncology)
Implemented	Jan/2024
Revised	
Next planned review	Jan/2026

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)

Pathway: Aggressive B-cell lymphoma

Version Jan/2024
2.03.01 Anlage 35 UCCH
ID: 487110 UCCSH

Pathway page 1:

Work up

Baseline:

History (incl. B-symptoms)

Physical examination (incl. palpation of all lymph node areas, spleen and liver)

Lab exam (including CBC with differential, LDH, uric acid, β-2 microglobulin, electrophoresis and serum immunoglobulins)

Hepatitis B[1]/C; HIV serology

PET CT (after board decision regarding indication), only if not available

- CT neck/thorax/abdomen
- Bone marrow aspirate & biopsy[2] (including cytogenetics and flow cytometry)

Biopsy[3]

Facultative:

ECG, Echocardiography and lung function test (pretreatment evaluation)

Pregnancy testing, discussion of fertility issues and sperm banking

Lumbar puncture and MRI head (mandatory for high CNS-IPI)

Gastroscopy, colonoscopy

ENT-examination

Supportive:

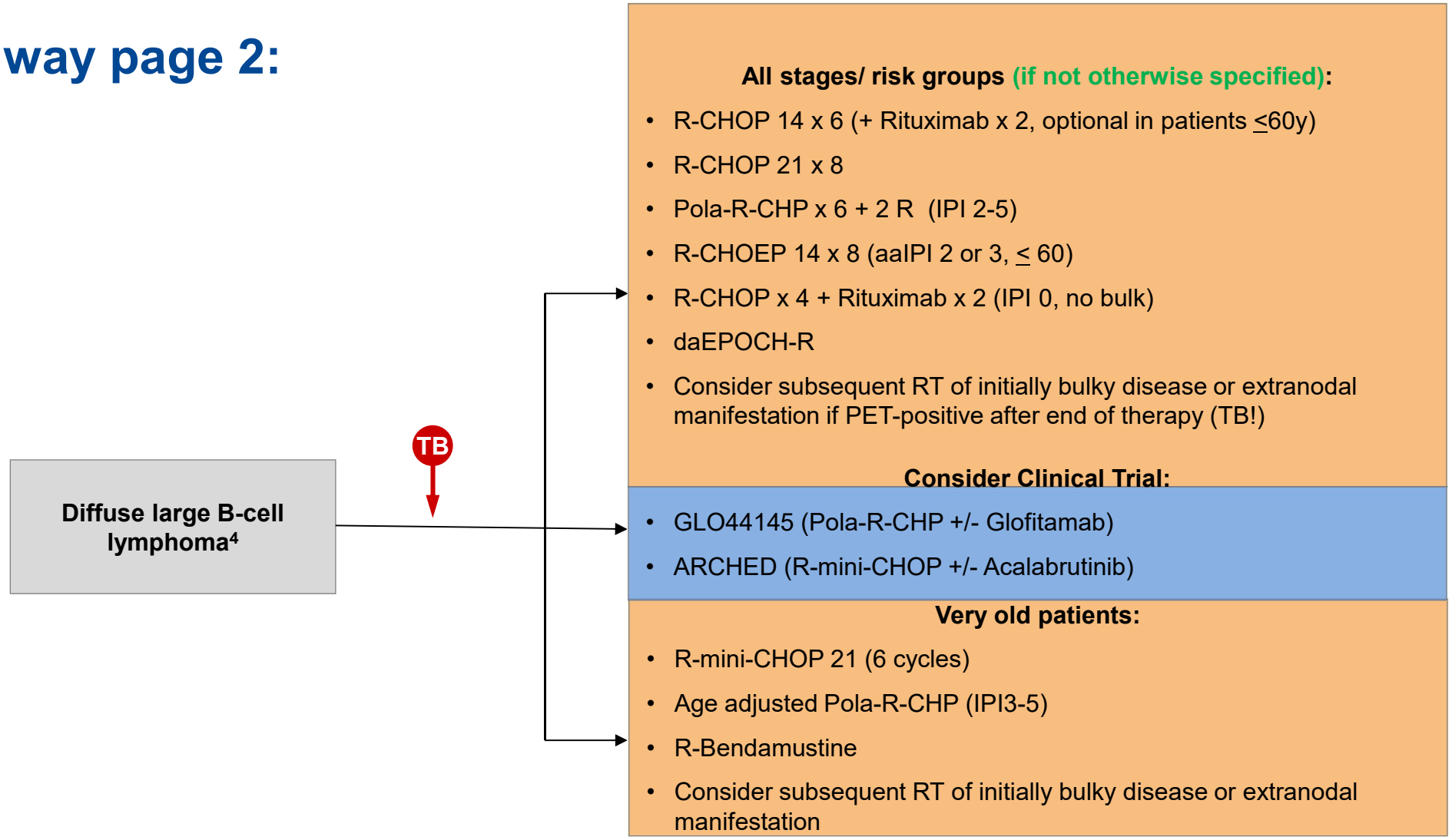
- Offer contact to self help group
- Offer psychooncological support

1 Hepatitis B testing is recommended because of the risk of reactivation with immunotherapy and chemotherapy. Antiviral prophylaxis is indicated in patients with positive Hepatitis B serology (HBs Ag positive) including occult carriers (HBs Ag negative and anti-core positive) in dependence of viral load. PCR is also recommended for patients with prior anti-B cell treatment

2 Not mandatory after PET-CT, might be considered in case of transformed aggressive lymphoma / follicular 3B (low grade bone marrow involvement might not be detected by PET-CT)

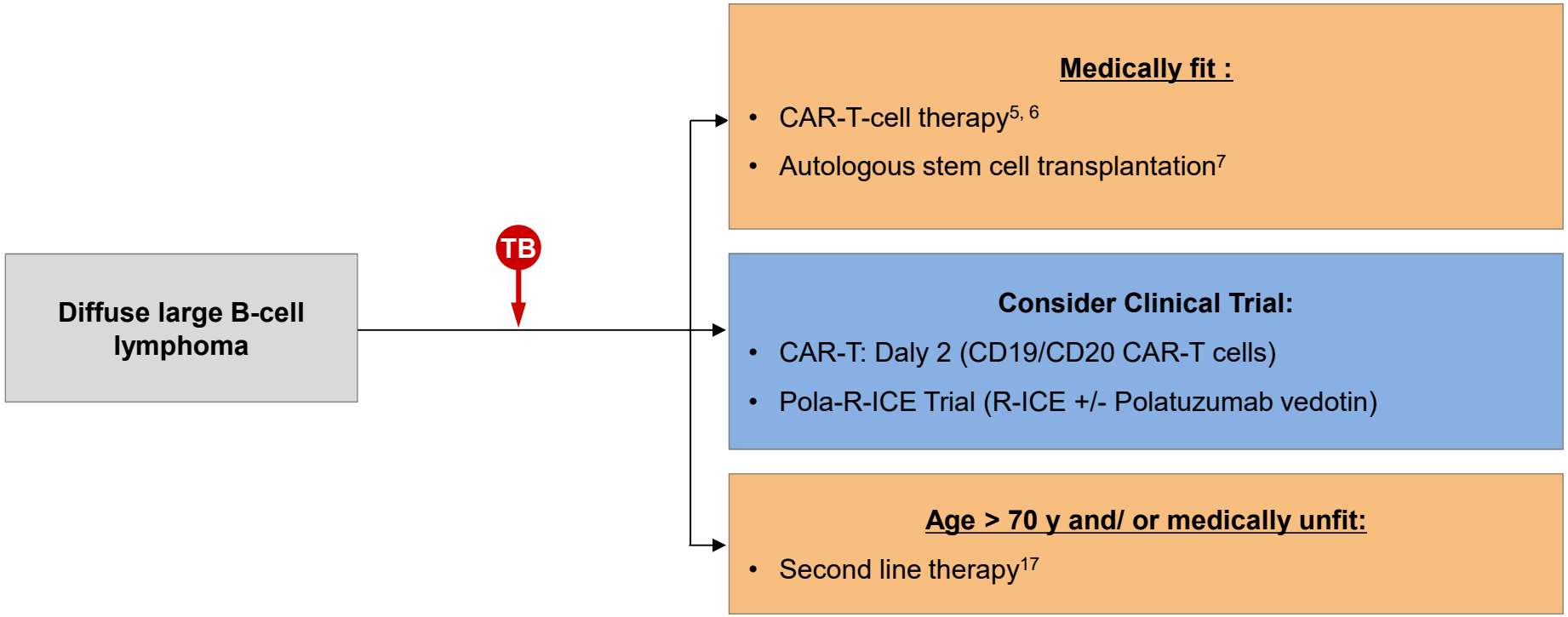
3 The histological report should give the diagnosis according to the World Health Organization classification. Fine needle aspirations are inappropiate for a reliable diagnosis. For differentiation between the NHL lymphoma subtypes cytogenetics for t14/18 and FISH t11/14 might be useful.

Pathway page 2:



[4] Consider treatment intensification for high-risk CNS-IPI (4-6 of IPI-factors and involvement of kidney/adrenal gland or involvement of testis), CNS-IPI see page 12

Pathway page 3: Relapsed or refractory disease, 1st relapse



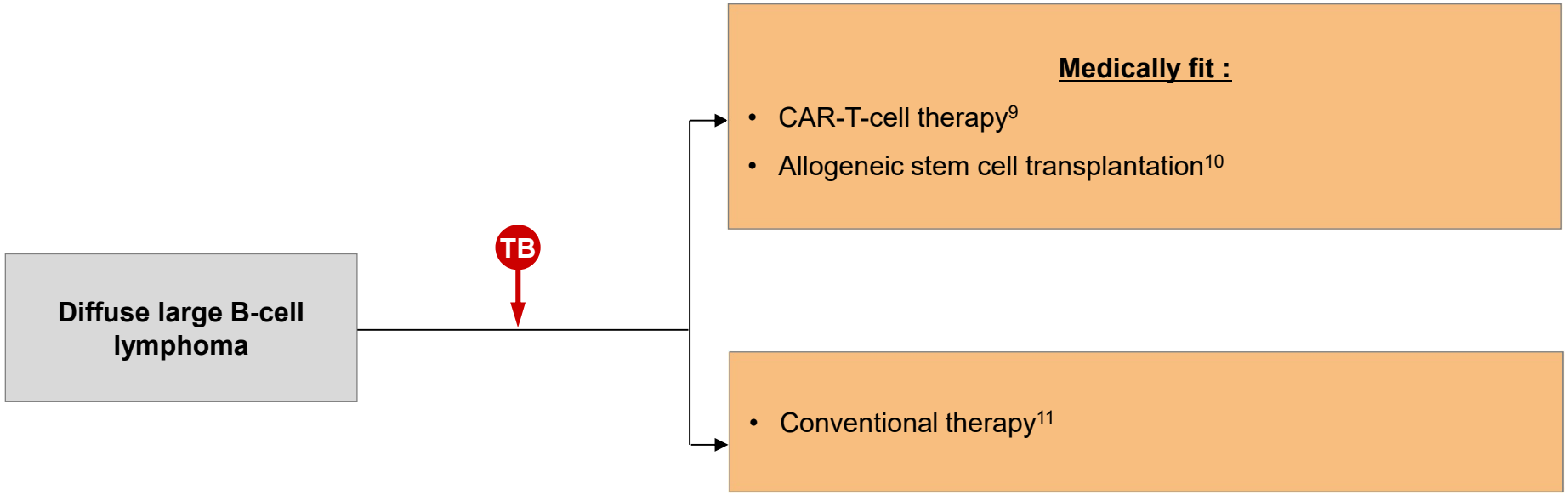
5 Consider CAR-T-cell therapy in patients with relapsed or refractory DLBCL after two or more lines of systemic therapy or if first relapse occurs within 12 months after end of first line therapy. Age > 70 alone should not be considered as contraindication for CAR-T cell therapy

6 Consider allogeneic stem cell transplantation in early relapse / refractory patients not eligible for CAR-T-cell therapy

7 Consider high dose therapy and autologous stem cell transplantation in younger (<70) patients in case of late relapse (>12 months after 1st line treatment.

8 Second line therapy options depending on age, comorbidities and response duration include: Polatuzumab/BR, Tafasitamab-Lenalidomide (not in refractory patients) R-DHAP, R-ICE, R-Gem/Ox, CAR-T-cell therapy, RT of localized disease,

Pathway page 4: Relapsed or refractory disease, 2nd or further relapse



9 Age > 70 alone should not be considered as contraindication for CAR-T cell therapy. Due to missing data on T-cell exhaustion after bispecific antibody treatment CAR-T cell therapy should be considered before long term bispecific antibody treatment.

10 Consider allogeneic stem cell transplantation in younger and medically fit patients relapsed after or ineligible for CAR-T cell therapy

11 Third line therapy options depending on age, comorbidities and response duration include: Bispecific antibodies (after insurance approval depending on NUB-status!), Loncastuximab-Tesirine and all 2nd line options (see page 3) which may also be used as bridging before CAR-T or allogeneic stem cell transplantation.

Pathway page 5: Follow up

After systemic treatment:

Every 3 months for 2 years, then every 6 months until year 5, afterwards yearly

- History and clinical examination, lab exam (including full blood count and differential)
- Minimal adequate radiological or ultrasound examinations every 6 months for two years with focus on initially pathological findings, additional imaging as clinically indicated
- Annual evaluation of thyroid function in patients with irradiation of the neck
- Offer contact to self help group and psychooncological support whenever necessary
- Make recommendationens for screening measures for the early detection of cancer

After local radiotherapy:

Every 6 months for 2 years, subsequently once a year if clinically indicated:

History and physical examination
Offer contact to self help group and psychooncological support whenever necessary
Make recommendations for screening measures for the early detection of cancer

Pathway page 6: Aggressive B-cell lymphoma, risk stratification

IPI -Criteria	
Age	≥ 60 y
Extranodal sites	> 1
Ann Arbor stage	III or IV
Serum LDH level	> ULN (upper limit of normal)
Performance status	2 - 4

aaIPI –Criteria (patients ≤ 60 years)	
Ann Arbor stage	III or IV
Serum LDH level	> ULN (upper limit of normal)
Performance status	2 - 4

Risk categories according to IPI chart	
	Number of factors
Low	0-1
Low intermediate	2
High intermediate	3
High	4 - 5

Risk categories according to aaIPI chart	
	Number of factors
Low	0
Low intermediate	1
High intermediate	2
High	3

According to: A predictive model for aggressive non-Hodgkin's lymphoma. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. N Engl J Med 1993; 329: 987–994

Pathway page 7: Aggressive B-cell lymphoma, risk stratification

CNS-IPI –Criteria (each one point)[18]	
Age	≥ 60 y
Extranodal involvement	• Involvement of >1 sites
	• Kidney and/or adrenal gland
Ann Arbor stage	III or IV
Serum LDH level	> ULN (upper limit of normal)
ECOG Performance status	> 1

CNS-IPI: Sum of points[19]	
	Sum of points
Low	0-1
Intermediate	2-3
High	4 - 6

Risk of CNS relapse after two years	
Low	0.6%
intermediate	3.4%
High	10.2%

Page 8: 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