Comprehensive Cancer Center
Tübingen-Stuttgart

Bispezifische Antikörper oder CAR-T bei B-Zell-Lymphomen?

1. Tübinger Symposium für hämatologische Zelltherapie

Stefan Wirths

26. Juni 2025

EBERHARD KARLS
UNIVERSITÄT
TÜBINGEN

Comprehensive
Cancer Center
Tübingen - Stuttgart

Universitätsklinikum
Tübingen

Disclosure of conflicts of interest

1. **Employment or Leadership Position**
   None

2. **Advisory Role or Expert Testimony**
   Stemline Menarini

3. **Stock Ownership**
   None

4. **Patent, Copyright, Licensing**
   None

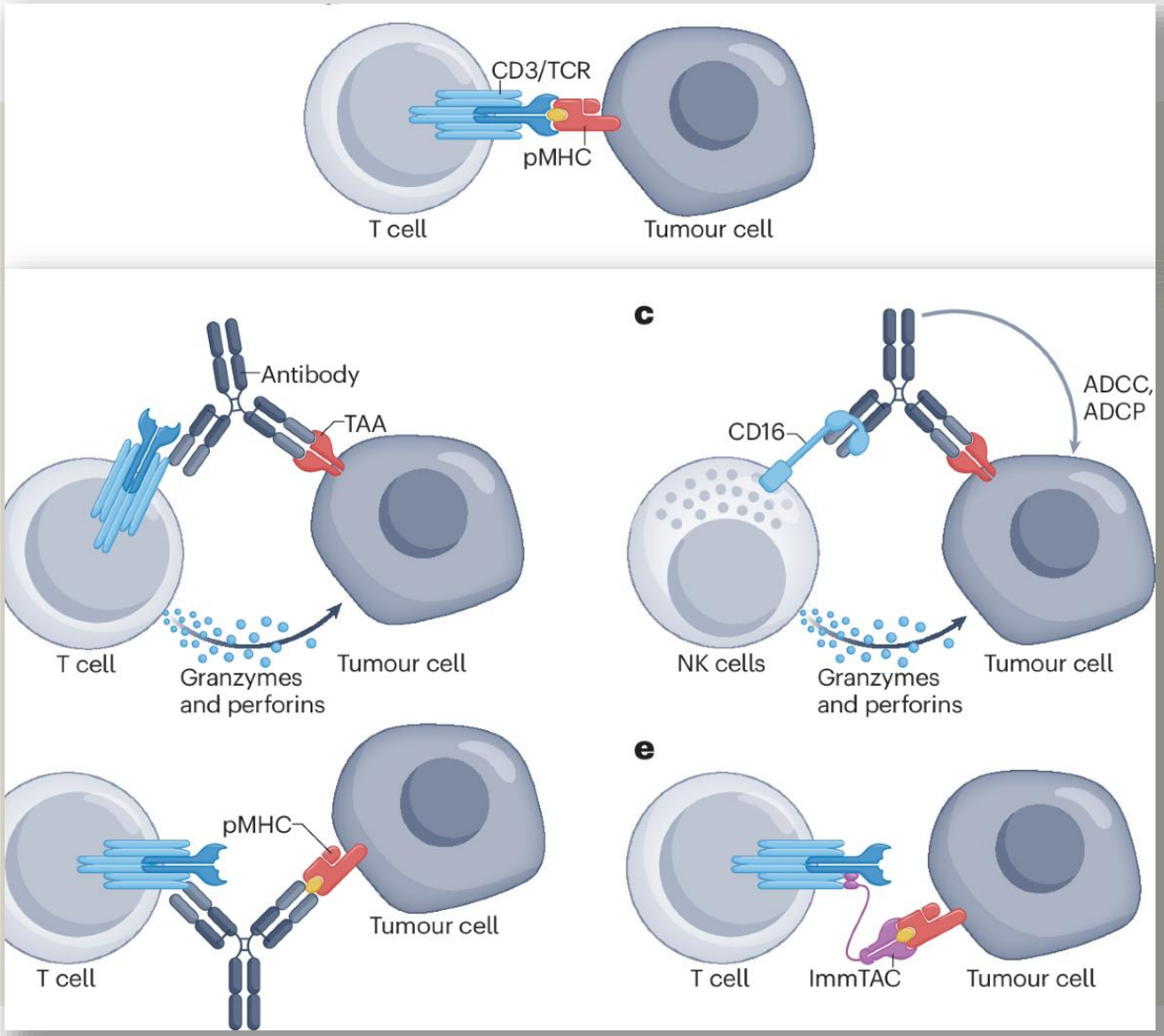
5. **Honoraria**
   AstraZeneca, Abbvie, Lilly, Roche, stemline Menarini, BeiGene

6. **Financing of Scientific Research**
   None

7. **Other Financial Relationships**
   None

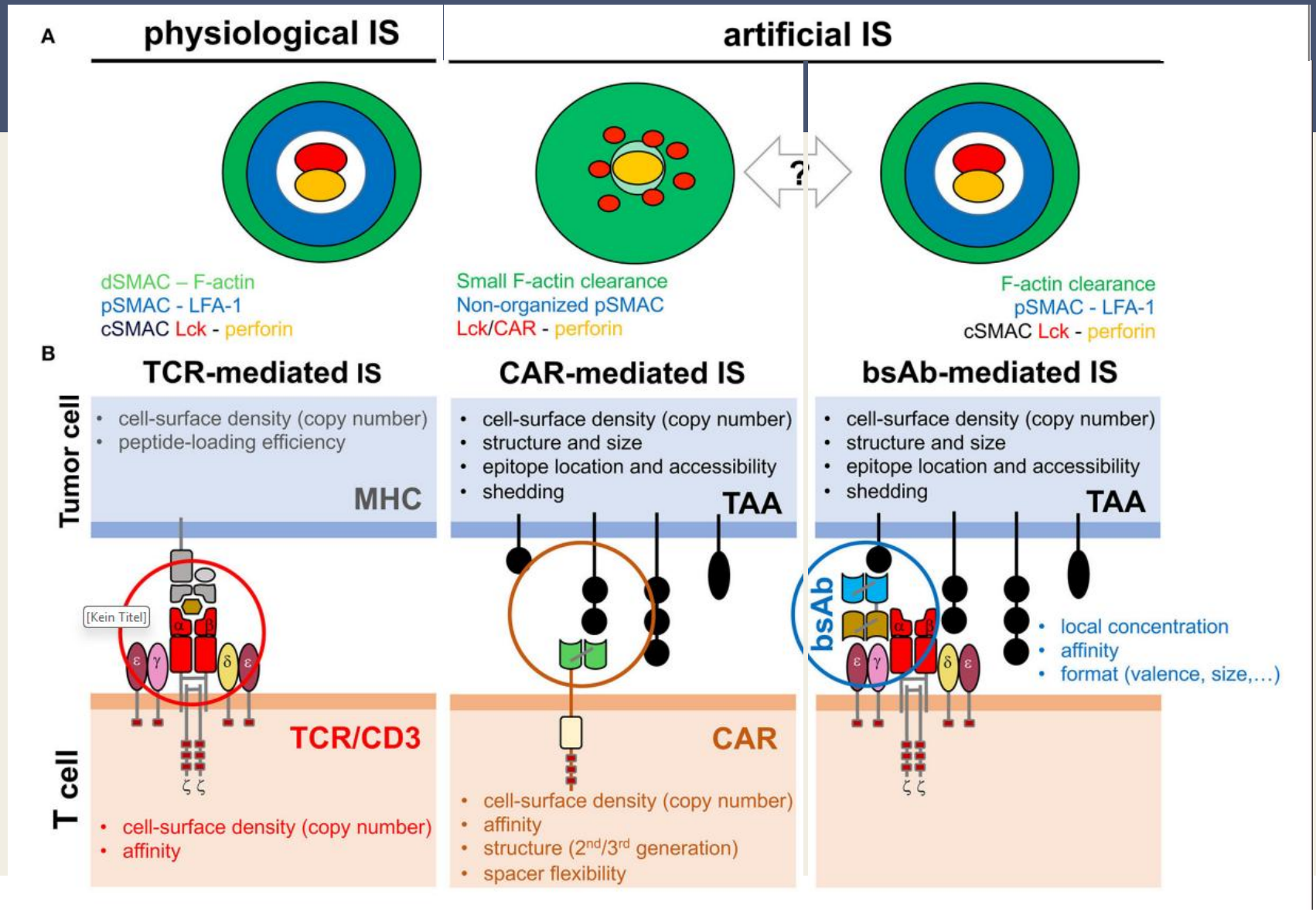
8. **Immaterial Conflicts of Interest**
   None

Konzepte bispezifischer Antikörper



Goebeler et al, NatRevClinOnc 2024

Immunologische Synapse - IS



SMAC

SupraMolecular Activation Complex

Roda-Navarro, Alvarez-Vallina, Front Cell Dev Biol 2020

Bispezifische Antikörper bei B-NHL – CD20-directed
- aktuell zugelassene Therapien

- **Epcoritamab**
  - > ab 3L bei DLBCL
  - > ab 3L bei FL

  Fc-silenced
  subcutan, bis zum Progress

- **Glofitamab**
  - > ab 3L bei DLBCL als Monotherapie
  - > ab 2L bei DLBCL Glofitamab-GemOx

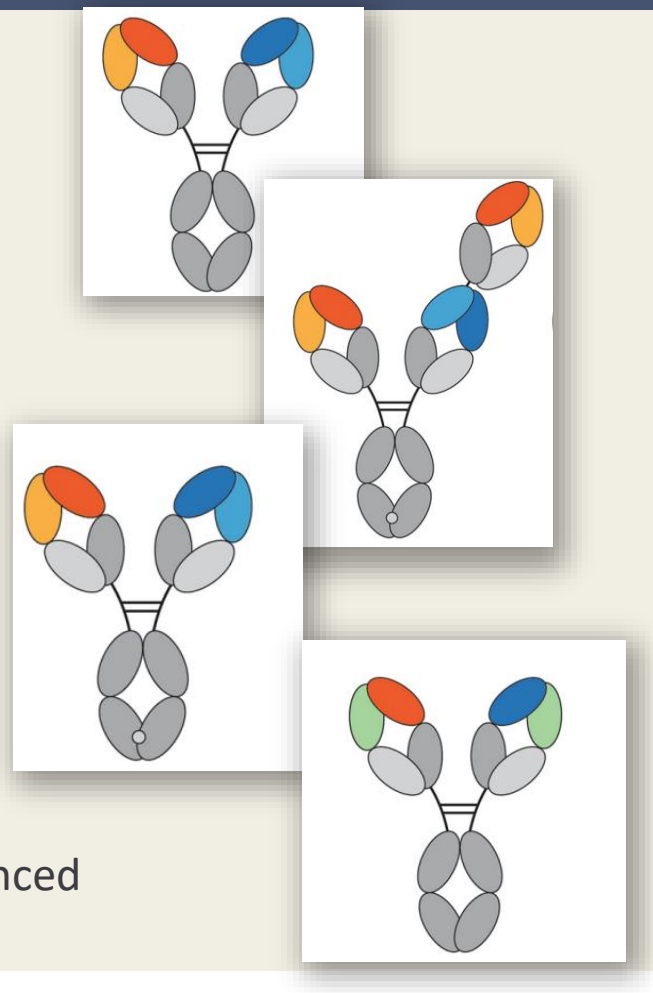
  2 anti-CD20-Domänen
  iv., zeitlich limitiert

- **Mosunetuzumab**
  - > ab 3L bei FL

  s.c., zeitlich limitiert

- **Odronextamab**
  - > ab 3L bei DLBCL
  - > ab 3L bei FL
  - >

  pos. Votum EMA
  noch nicht verfügbar, Fc-silenced
  zwei idente Leichtketten



Glofitamab bei R/R LBCL ab 3L
- Phase II – follow-up

Pivotal single-arm Phase II study in patients with R/R LBCL and ≥2 prior therapies

Key inclusion criteria

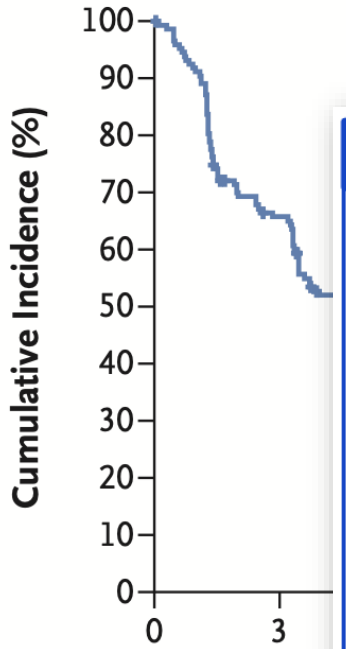
- DLBCL NOS, HGBCL, transformed FL, or PMBCL
- ECOG PS 0–1
- ≥2 prior therapies, including:
  - Anti-CD20 antibody
  - Anthracycline

Glofitamab IV administration

Fixed-duration
- Q3W
- Up to 12 cyc

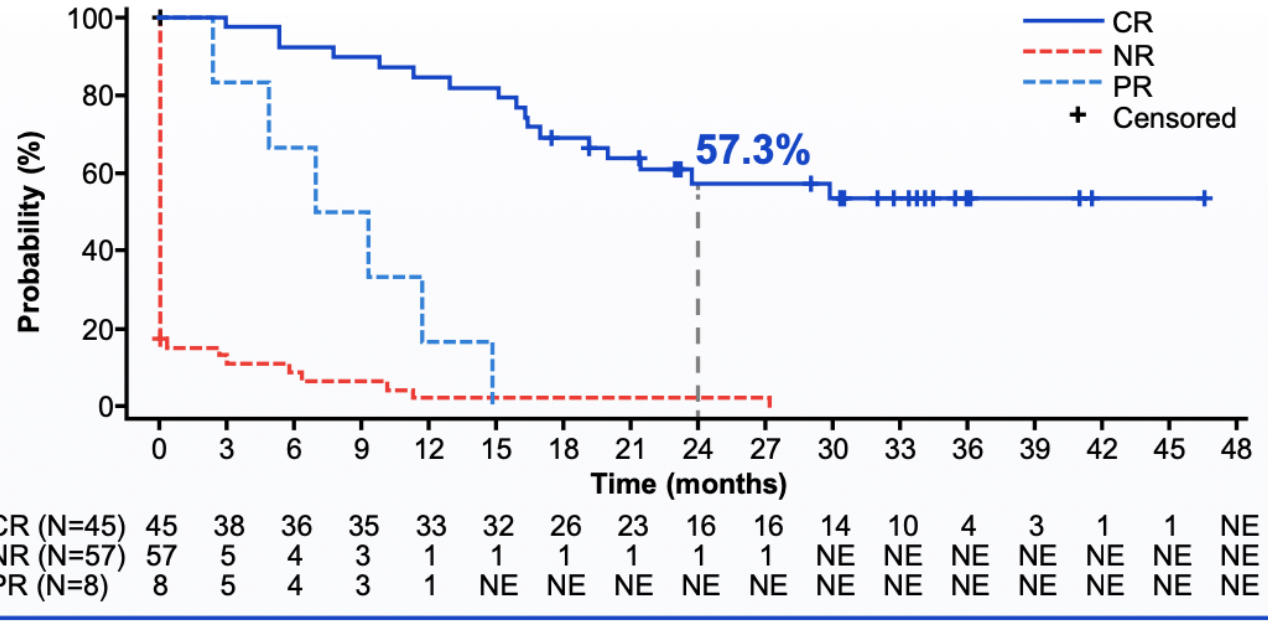
CRS mitigatio
- Obinutuzum
- C1 step-up c
- Monitoring a

Progression-free Survival in the Main Analysis Cohort



No. at Risk 155 92

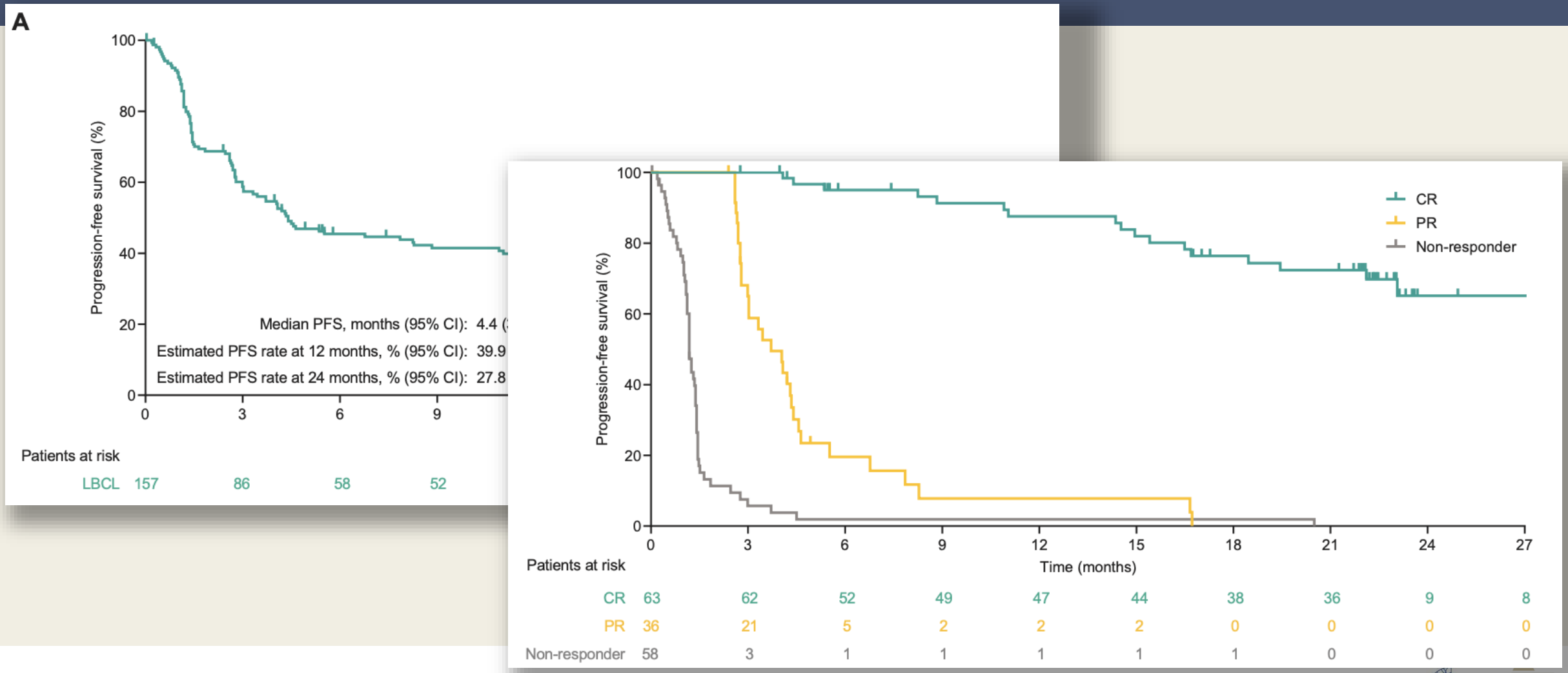
PFS



Dickinson et al, NEJM 2022 und ASH 2024

Epcoritamab bei R/R LBCL ab 3L

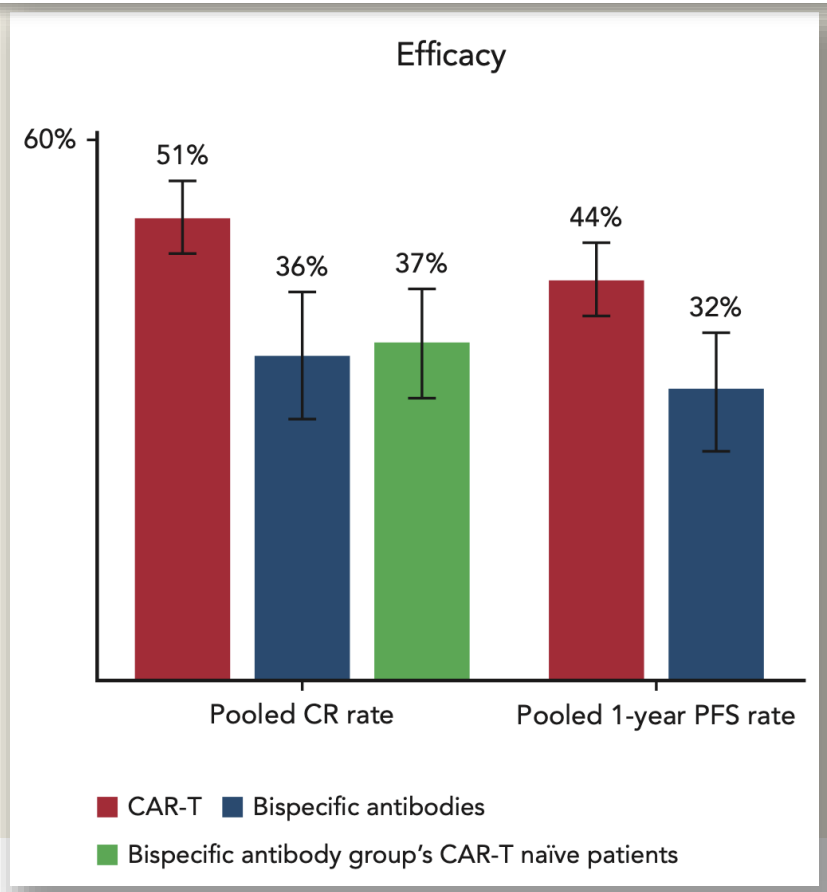
Phase II – follow up EPCORE NHL-1

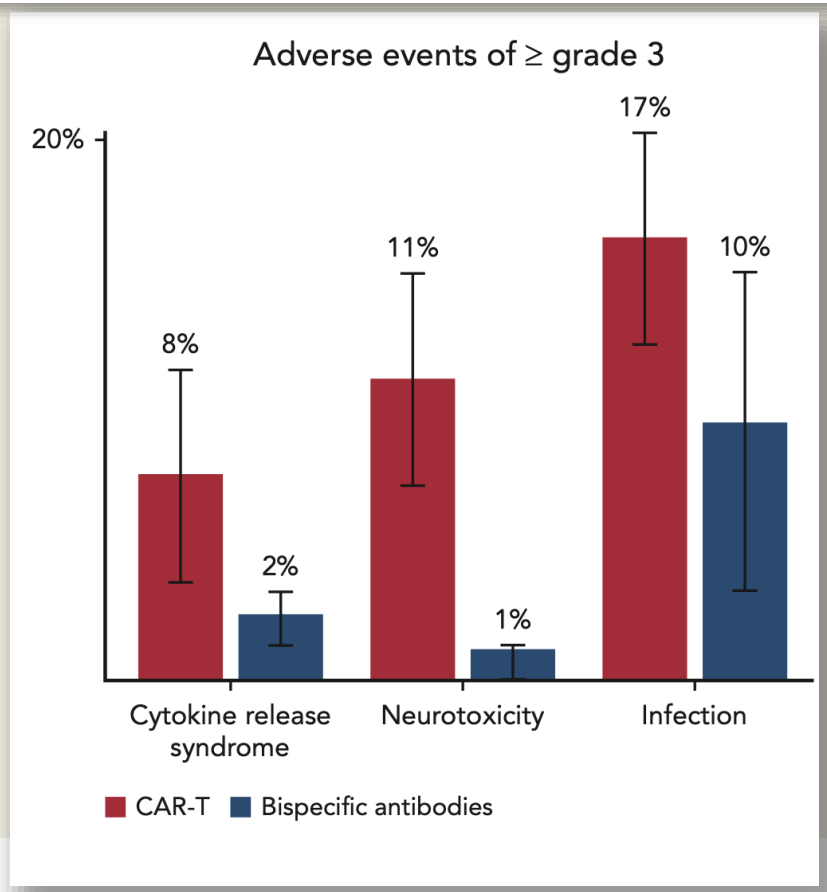


Thieblemont et al, Leukemia 2024

Vergleich CD19-CAR-T-Therapie versus CD20/CD3-BiTE
Metaanalyse – 3L+

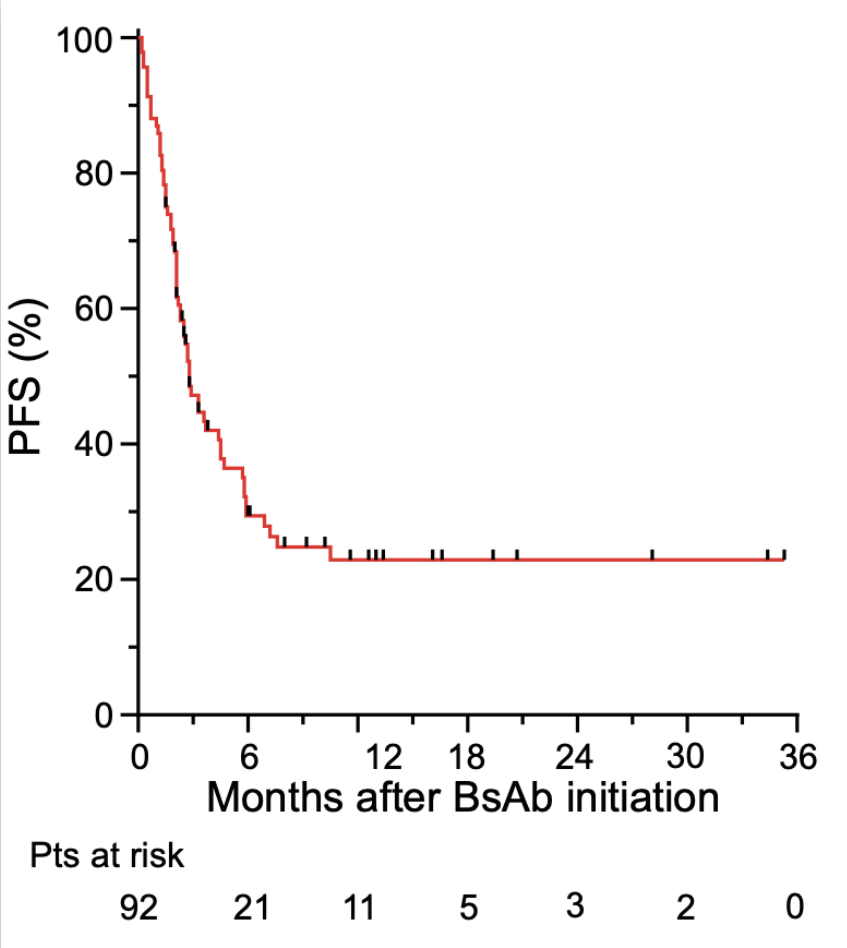
CAR-T cell therapy: 10 studies including 742 patients
Bispecific antibodies: 6 studies including 605 patients

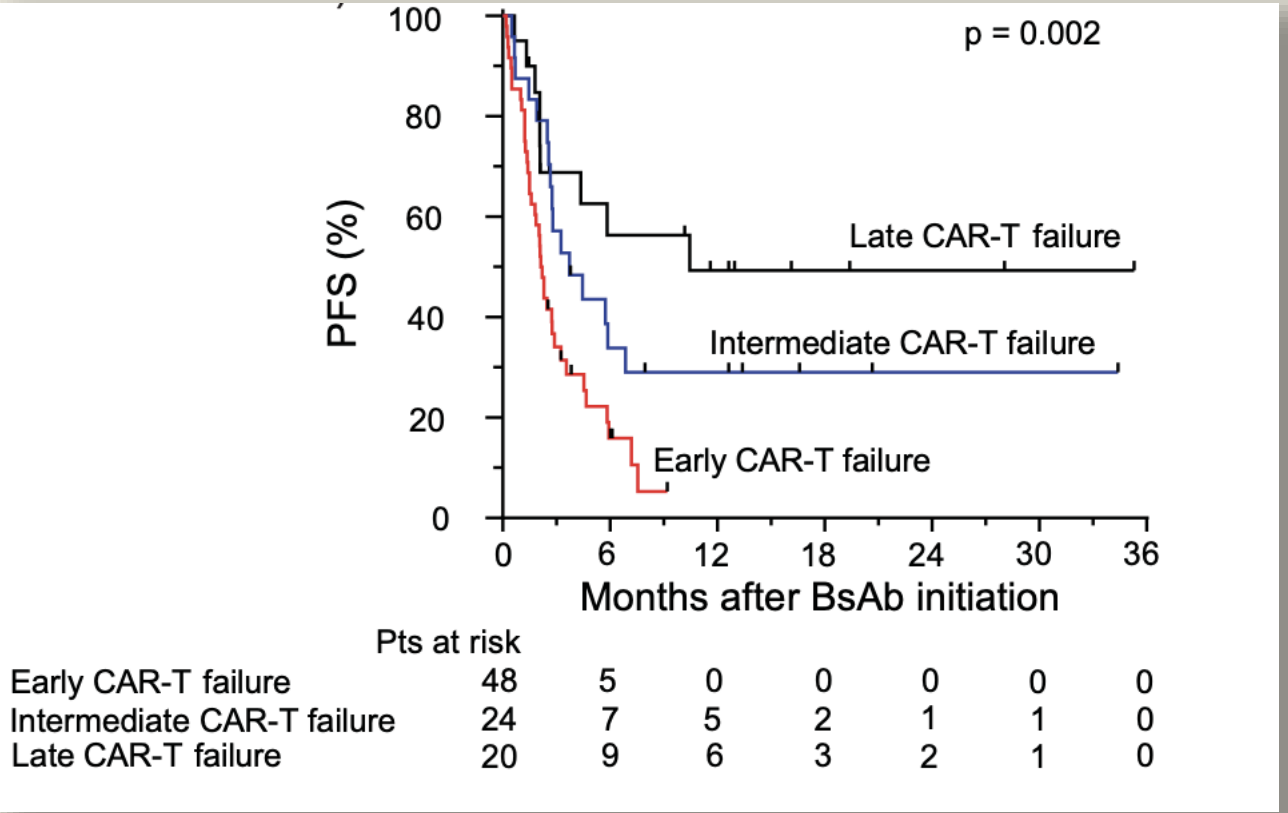




Kim et al, Blood 2024

CD20/CD3-BiTE nach CD19-CAR-T-Zellen
- retrospektive Analyse der GLA

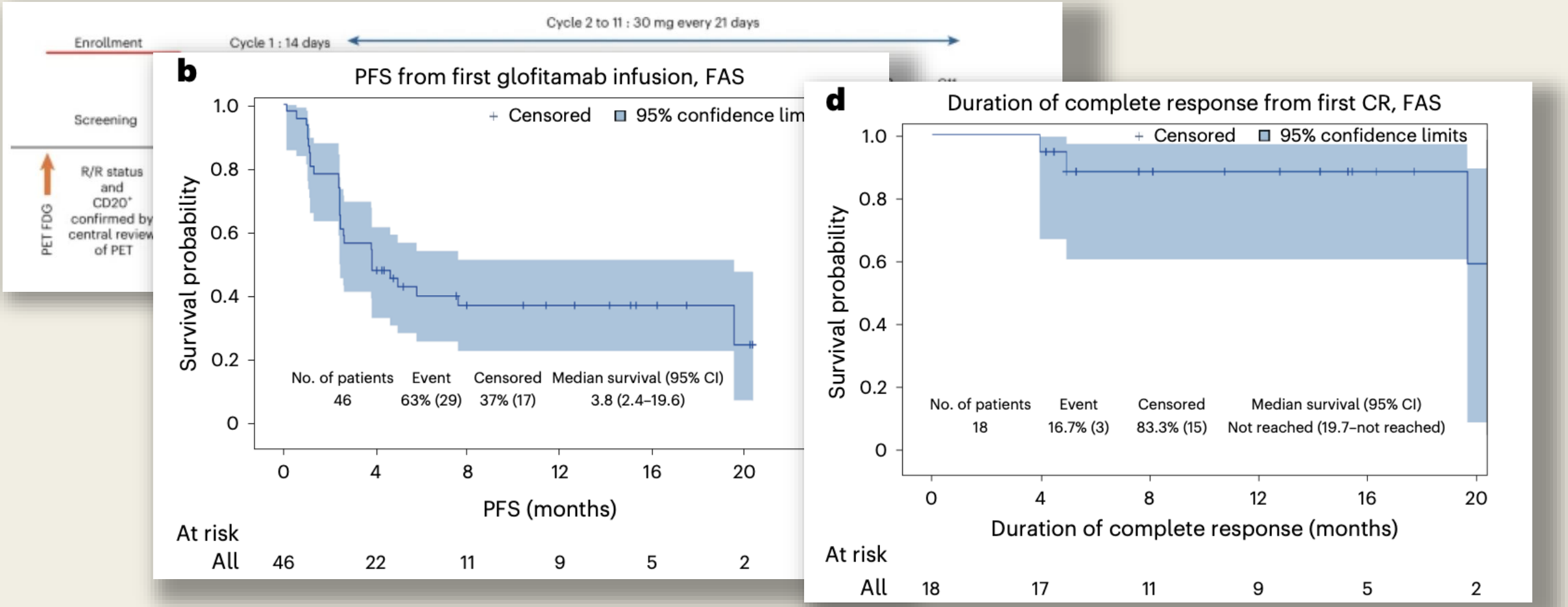




Shunilov et al, Bood adv 2025

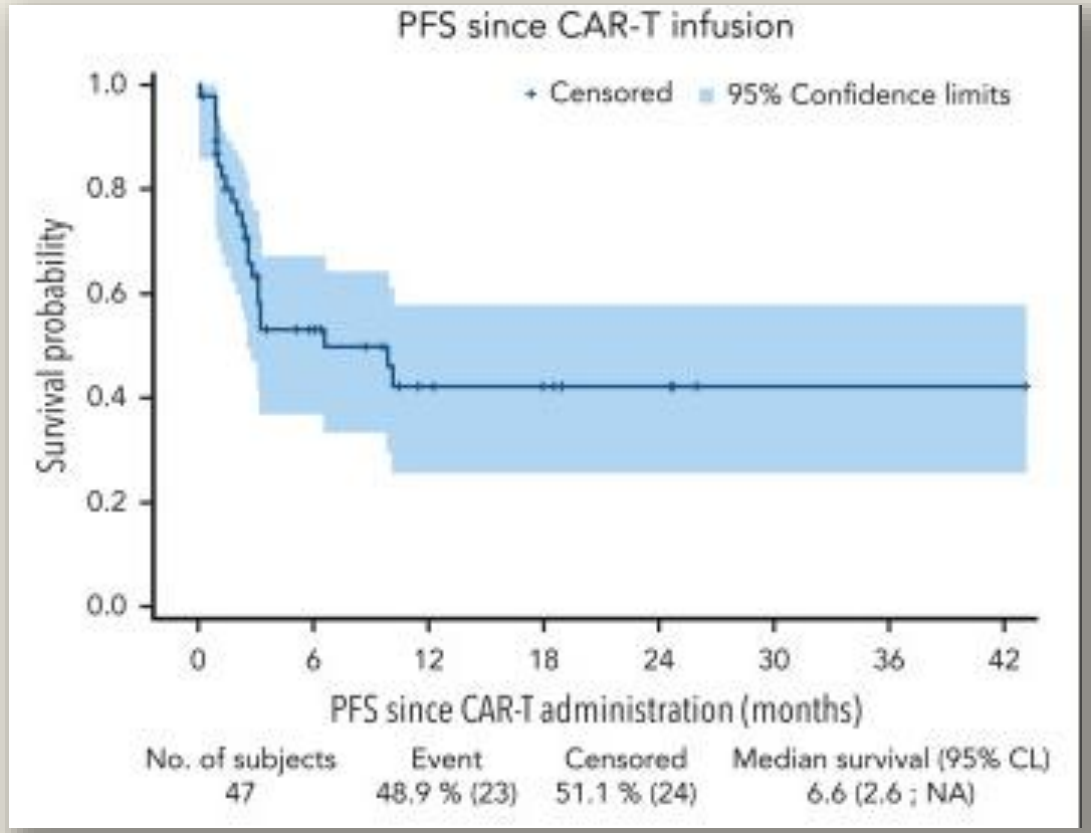
Glofitamab nach CD19-CAR-T – LYSA BiCAR-trial

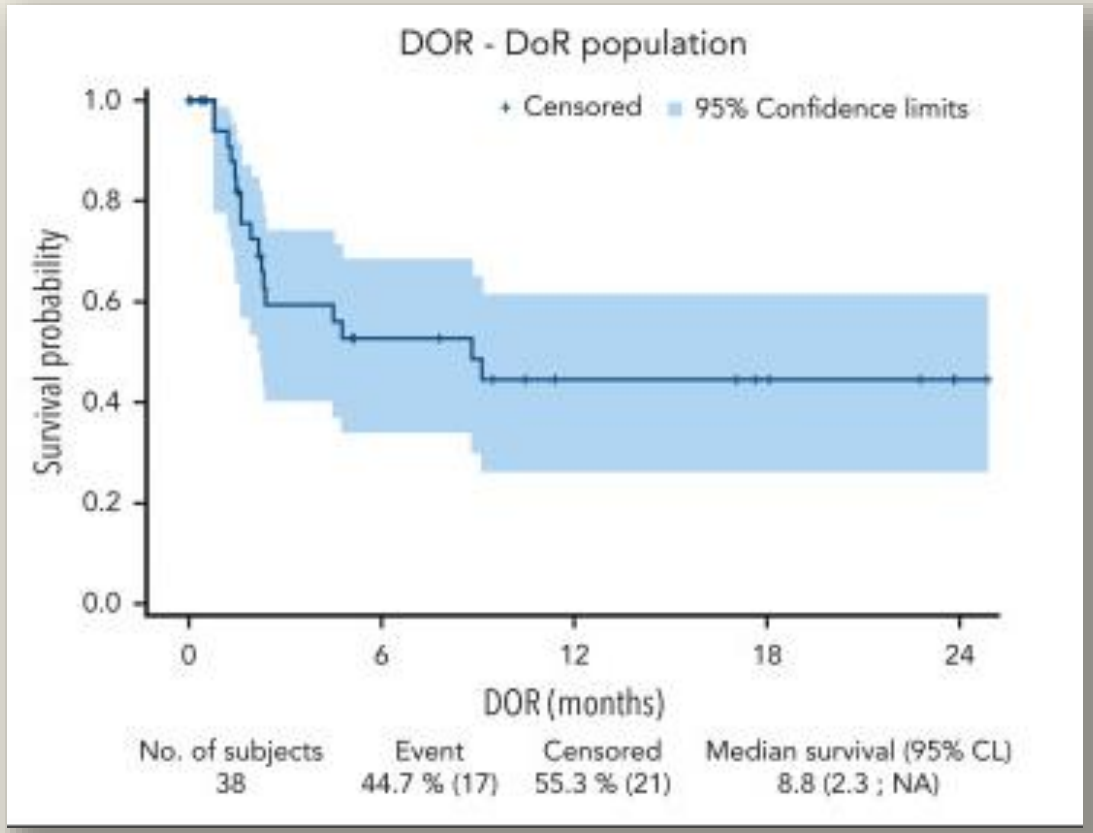
- prospektiv, short ramp-up



Cartron et al, NatCanc 2025

CD19-CAR-T nach CD20/CD3-BiTE
- retrospektive Auswertung





Crochet et al, Blood 2024

CD20/CD3-BiTE in der Kombination

Universitätsklinikum
Tübingen

Glofitamab-GemOx vs R-GemOx - STARGLO
Prospektive Phase III, DLBCL ab 2L – follow-up

Patients R/R DLBCL (N=274)

- R/R DLBCL NOS after ≥1 prior systemic therapy
- Patients with 1 prior line must be transplant ineligible
- ECOG PS 0–2

Stratification factors

- Relapsed vs refractory disease‡
- 1 vs ≥2 prior lines of therapy

Glofit-GemOx (n=183)

Glofitamab plus gemcitabine and oxaliplatin*
Glofitamab step-up dosing in Cycle 1.

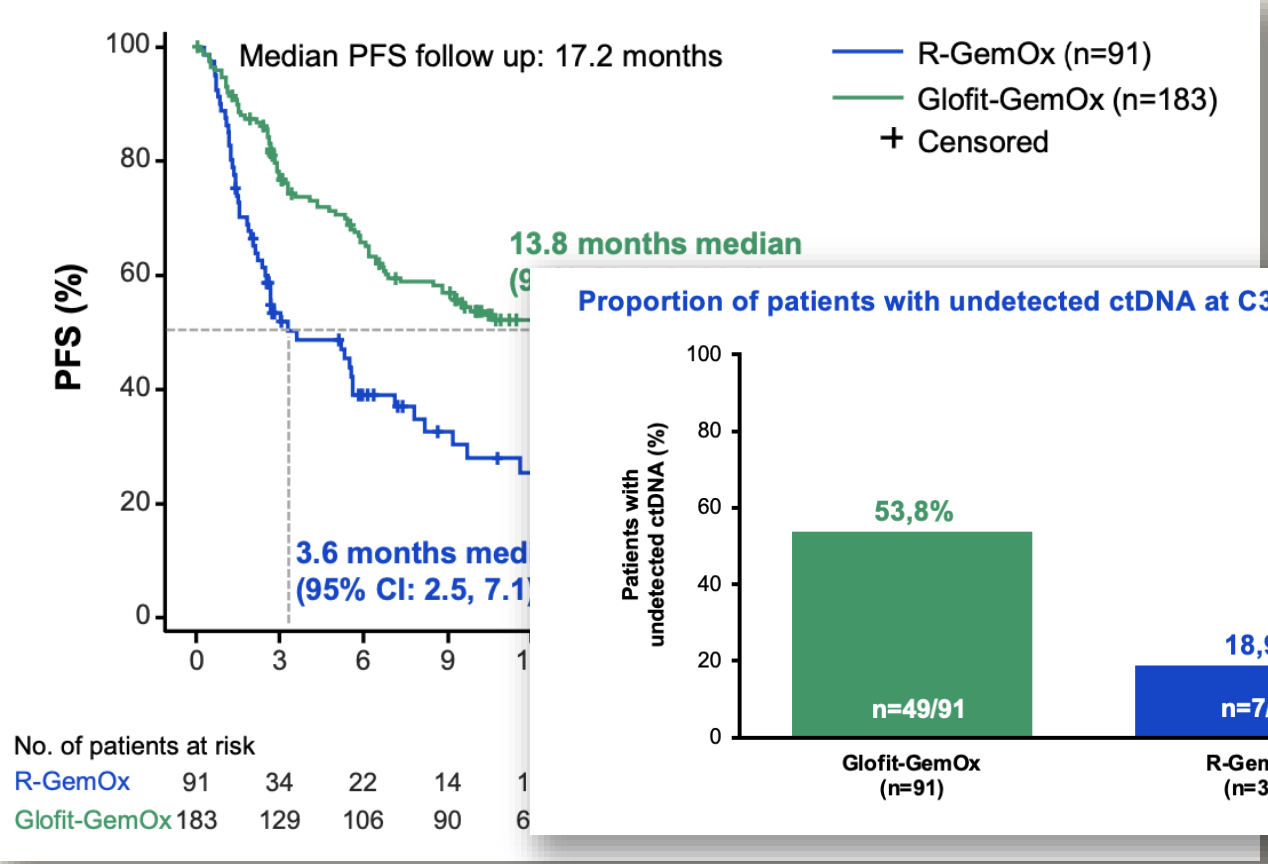
Glofitamab
30 mg administered on Day 1 of each cycle

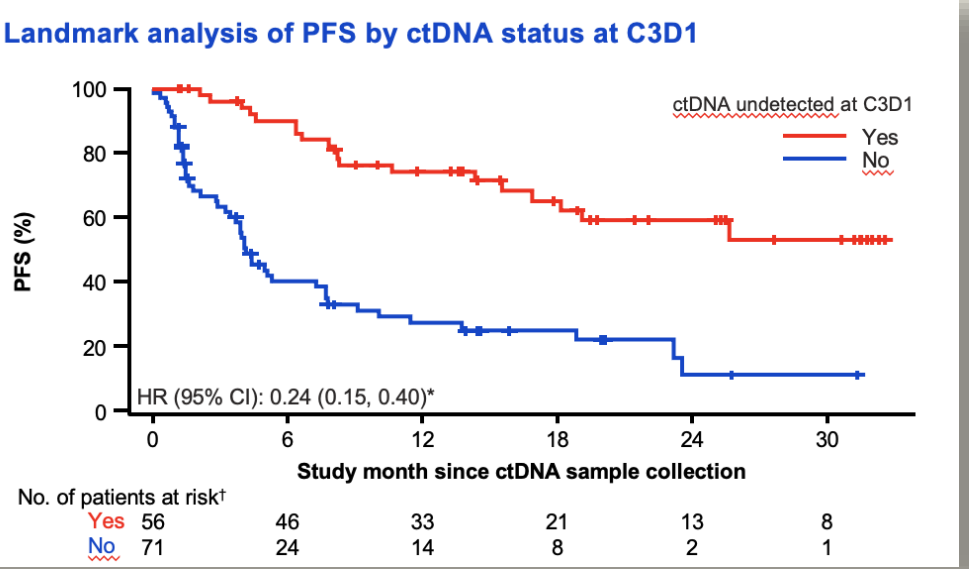
n (%), unless otherwise stated	R-GemOx (n=91)	Glofit-GemOx (n=183)
Age, years; median (range)	69.0 (20–84)	68.0 (22–88)
≥65 years	57 (62.6)	116 (63.4)
Sex, male	53 (58.2)	105 (57.4)
Race		
Asian	51 (56.0)	86 (47.0)
White	33 (36.3)	82 (44.8)
Black or African American	1 (1.1)	2 (1.1)
Unknown	6 (6.6)	13 (7.1)
Number of prior lines of therapy; 1 / ≥2	57 (62.6) / 34 (37.4)	115 (62.8) / 68 (37.2)
R/R status to last therapy; relapsed / refractory	37 (40.7) / 54 (59.3)	71 (38.8) / 112 (61.2)
Primary refractory*	47 (51.6)	106 (57.9)
ECOG PS	(n=88)	(n=180)
0–1 / 2	80 (90.9) / 8 (9.1)	160 (88.9) / 20 (11.1)
Ann Arbor staging	(n=90)	(n=183)
III–IV	70 (77.8)	122 (66.7)
Bulky disease	(n=90)	(n=183)
≥10 cm	14 (15.6)	23 (12.6)
Prior CAR T-cell therapy	8 (8.8)	14 (7.7)

Abramson et al, ICML 2025

Glofitamab-GemOx vs R-GemOx - STARGLO

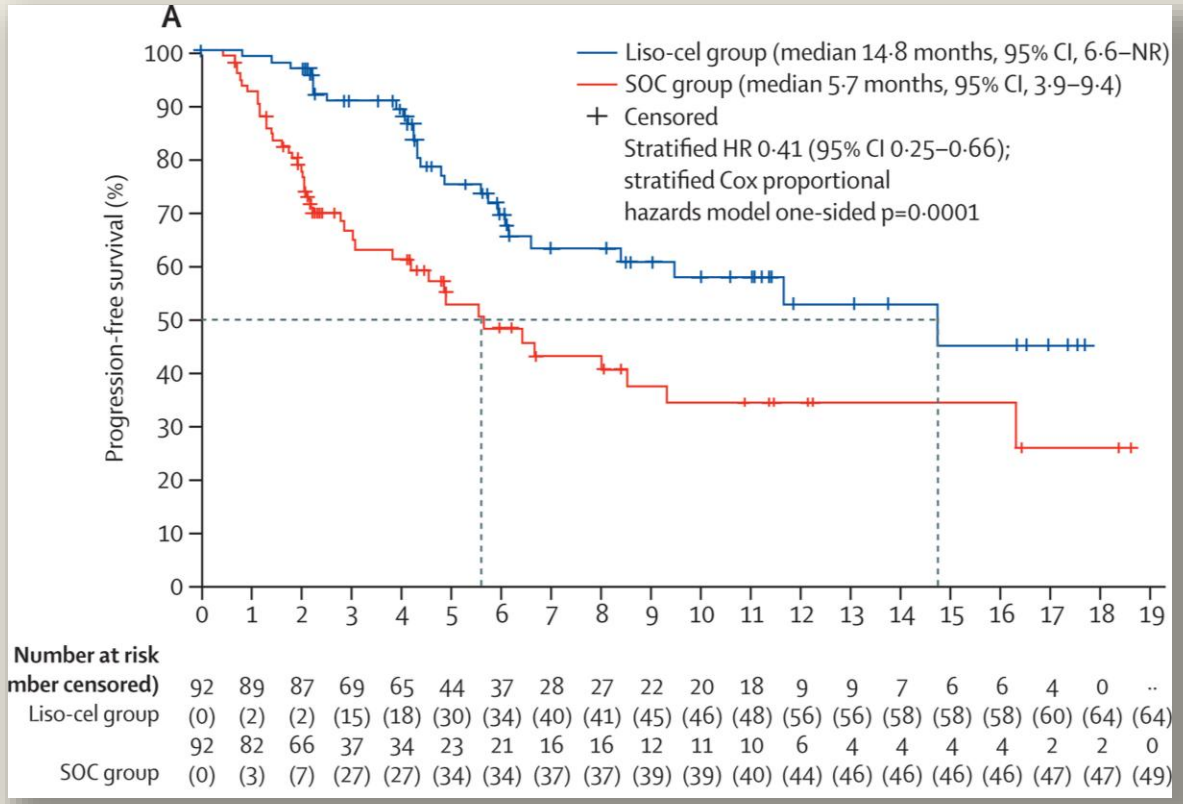
Prospektive Phase III, DLBCL ab 2L – follow-up – frühe ctDNA/MRDneg





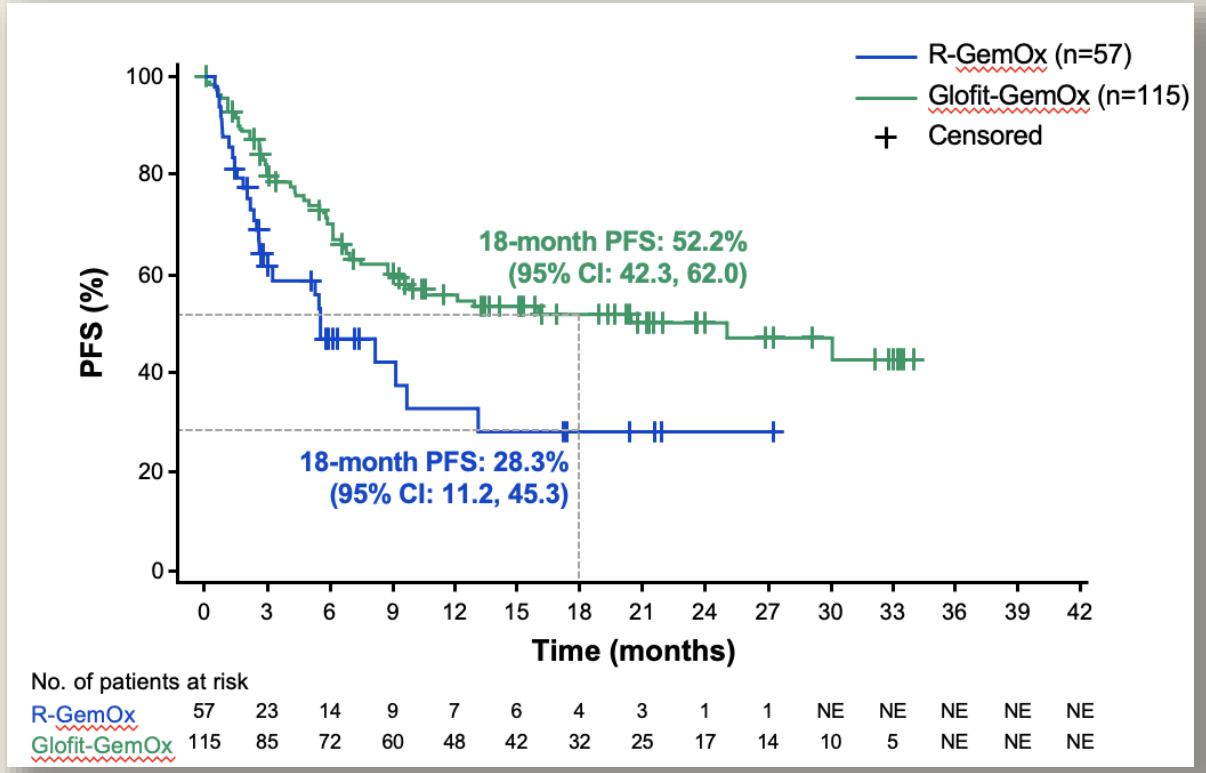
Abramson et al, ICML 2025

PFS LisoCel 2L early relapse
transplant-eligible



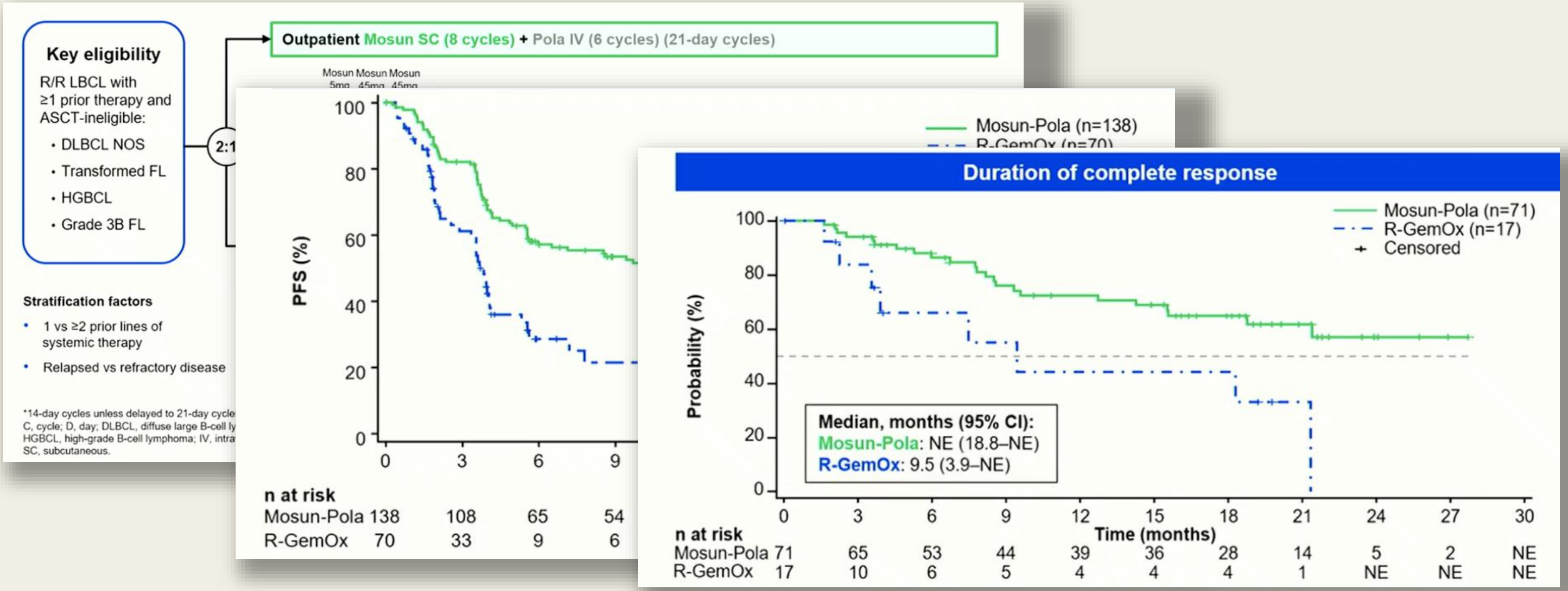
Kamdar et al, Lancet 2022

Glofitamab-GemOx 2L
transplant-ineligible



Abramson et al, ICML 2025

Mosunetuzumab-Pola vs R-GemOx
Phase III – transplant-ineligible



Westin et al, ICML 2025, LBA

CD20/CD3-BiTE in der Erstlinie

Universitätsklinikum
Tübingen

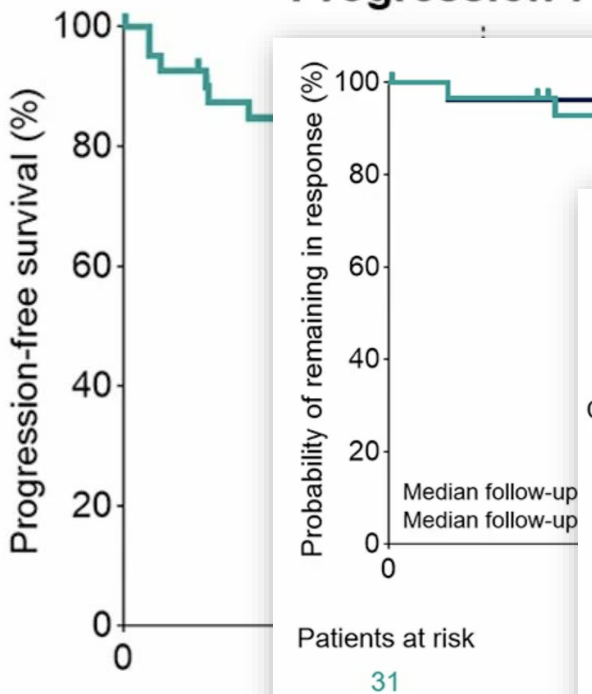
Epcoritamab bei LBCL 1L mono, fixed duration

- Anthracyclin-ineligible, EPCORE DLBCL-3, Phase II

Key inclusion

- Newly diagn
  CD20⁺ LBCL
  - DLBCL, N
  - T-cell/histi
    DLBCL
  - Double-hit
    triple-hit D
  - FL grade 3
- ICE score ≥8

Progression-Free Survival

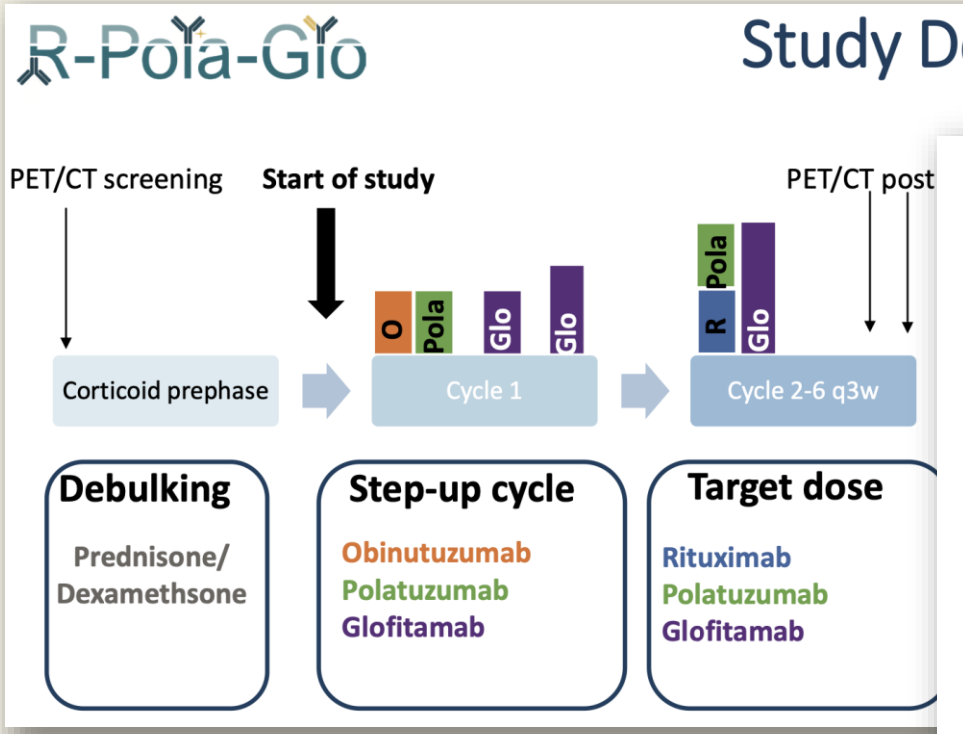


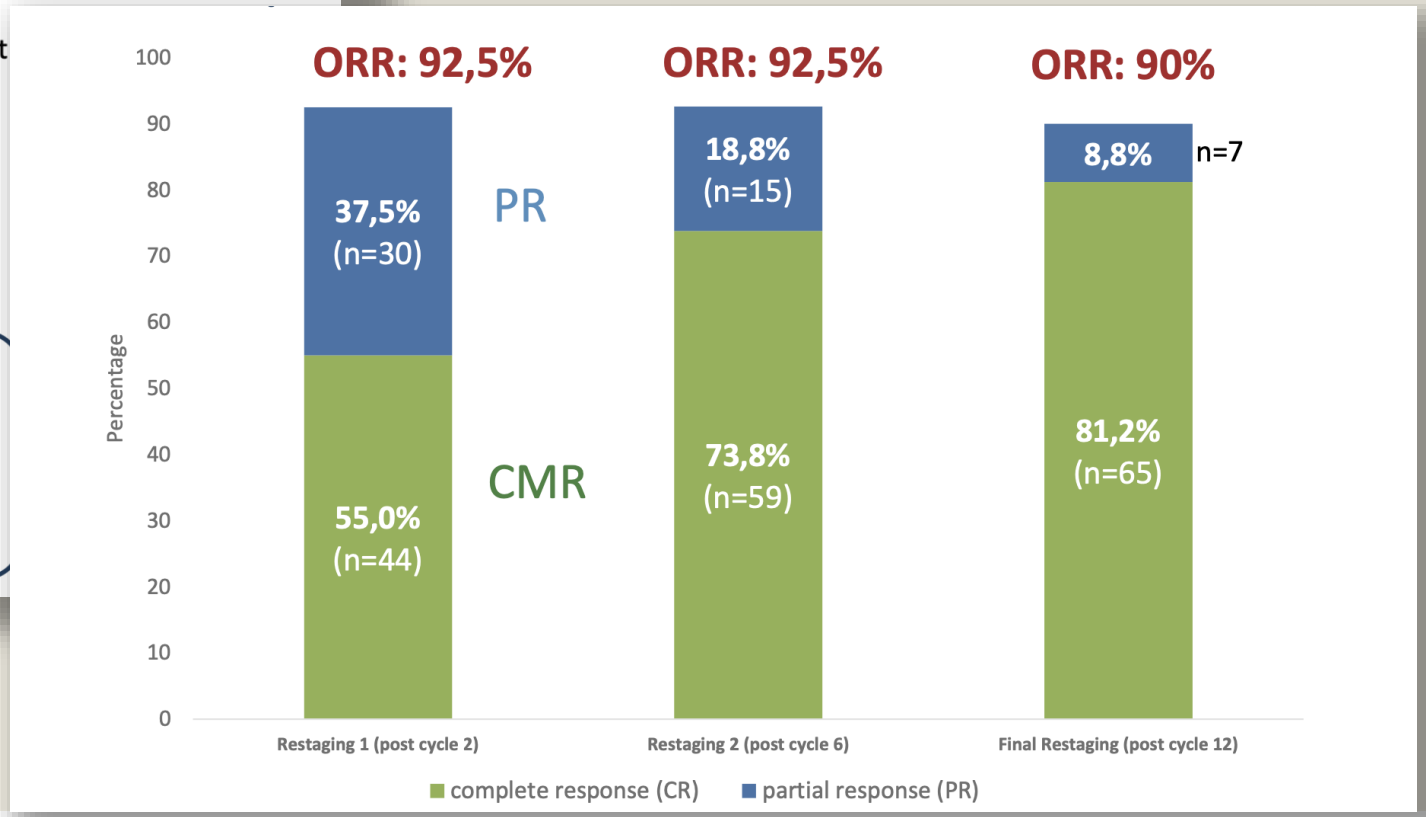
Most Common (≥15%) TEAEs

- 8 patients (18%) experienced a serious infection; 4 (9%) had serious COVID-19
- Neutropenia was reported for 4 patients (9%),[a] with no cases of febrile neutropenia
- 8 patients (18%) experienced TEAEs that led to epcoritamab discontinuation[b]
- 5 patients had fatal TEAEs (COVID-19 [n=2], CMV reactivation, TLS, tumor hemorrhage)

Belada et al, ICML 2025

Rituximab-Polatuzumab-Glofitamab bei LBCL
- Phase II, medical unfit





Melchardt et al, EHA 2025

Glofitamab-Pola-R-CHP als Erstlinientherapie bei LBCL
Phase II

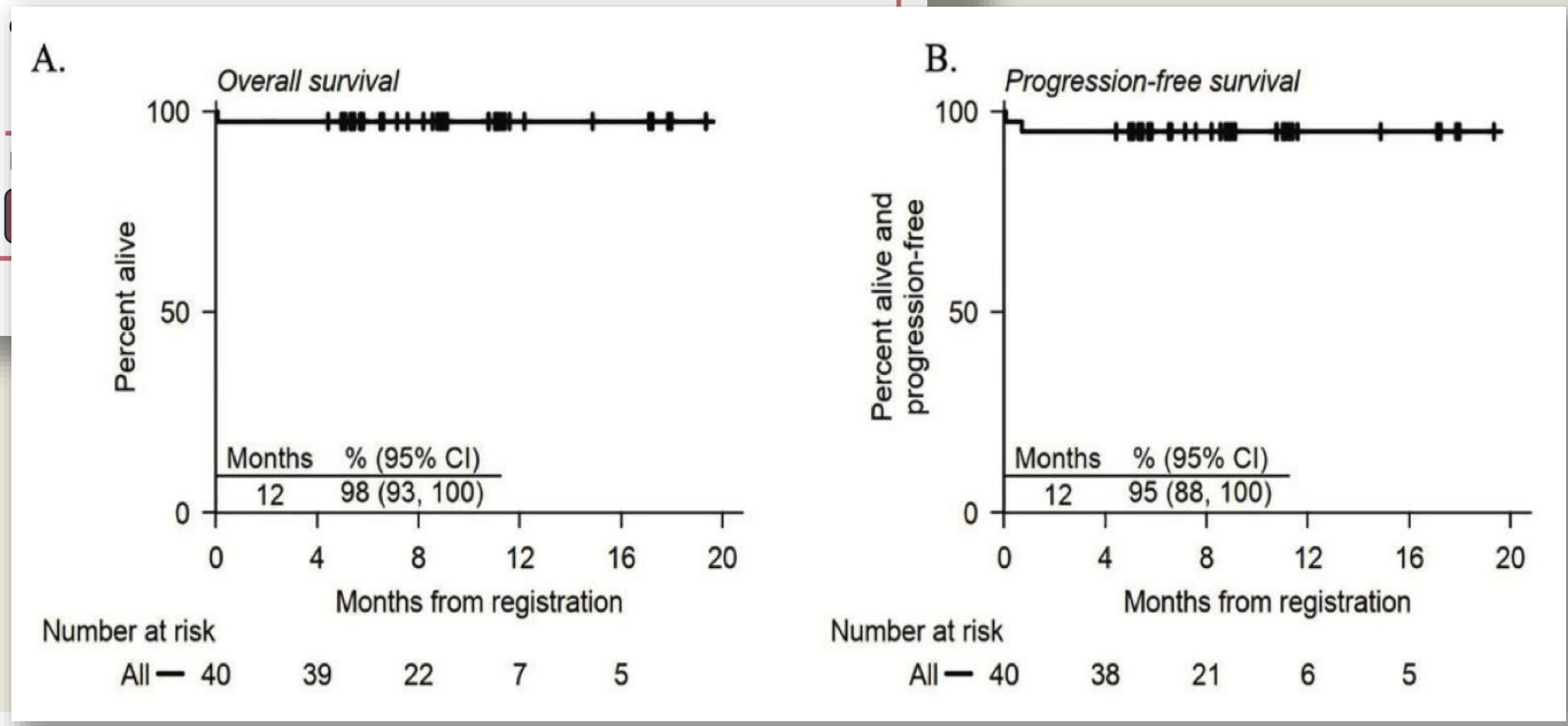
1L aggressive B-NHL

DLBCL NOS
T-cell/histiocyte-rich LBL
Epstein-Barr virus-positive DLBCL, NOS
ALK-positive LBL
HHV8-positive DLBCL, NOS
High-grade B-cell lymphoma (HGBCL)
HGBCL with translocations of MYC and BCL-2, or MYC and BCL-6

IPI 2-5
ECOG 0-2

n = 40

Pola-R-CHP-Glofitamab



Crombie et al, ICML 2025

Zusammenfassung

In Meta-Analysen überlegene Wirksamkeit von CAR-T gegenüber BiTE als Monotherapie

- bei mehr adverse events

BiTE nach CAR-T wirksam – und CAR-T nach BiTE

- keine Evidenz zu vorteilhaften Therapiesequenzen

Kuratives Potential von BiTE als Monotherapie unklar

- sehr günstiges PFS bei Erreichen einer kompletten Remission

BiTE in der Kombination wirksam, auch mit anti-CD20-Antikörper

- Zulassung von Glofitamab-GemOx
- vielversprechende Phase I/II-Studien in der Erstlinie

Unklar, ob eine CAR-T-Therapie bei Erreichen einer CMR nach BiTE vorteilhaft ist

- Glofi-GemOx als Bridging-Option?

Vielen Dank für Ihre Aufmerksamkeit