Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

66th ASH Meeting 2024

San Diego & virtuell

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Expert:innen berichten zu Lymphomen & Leukämien

Prof. Dr. med. Peter Borchmann
Uniklinik Köln

Diffuses großzelliges B-Zell-Lymphom (DLBCL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ASH2024 wird in Kooperation mit sieben unterstützenden Firmen durchgeführt.
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Employment, management position	–
Advisory/expert activity	Takeda Oncology, BMS, Roche, Amgen, Novartis, Miltenyi Biotech, Gilead, MSD, Incyte, Beigene
Ownership (shares, stocks, funds)	–
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Honoraria	Takeda Oncology, Novartis, BMS, Roche, MSD, Celgene, Miltenyi Biotech, Gilead, Abbvie
Funding scientific research	Takeda Oncology, MSD, Incyte, Amgen
Other financial relationships	–
Intangible conflicts of interest	–

Kapitel 1 DLBCL Erstlinie

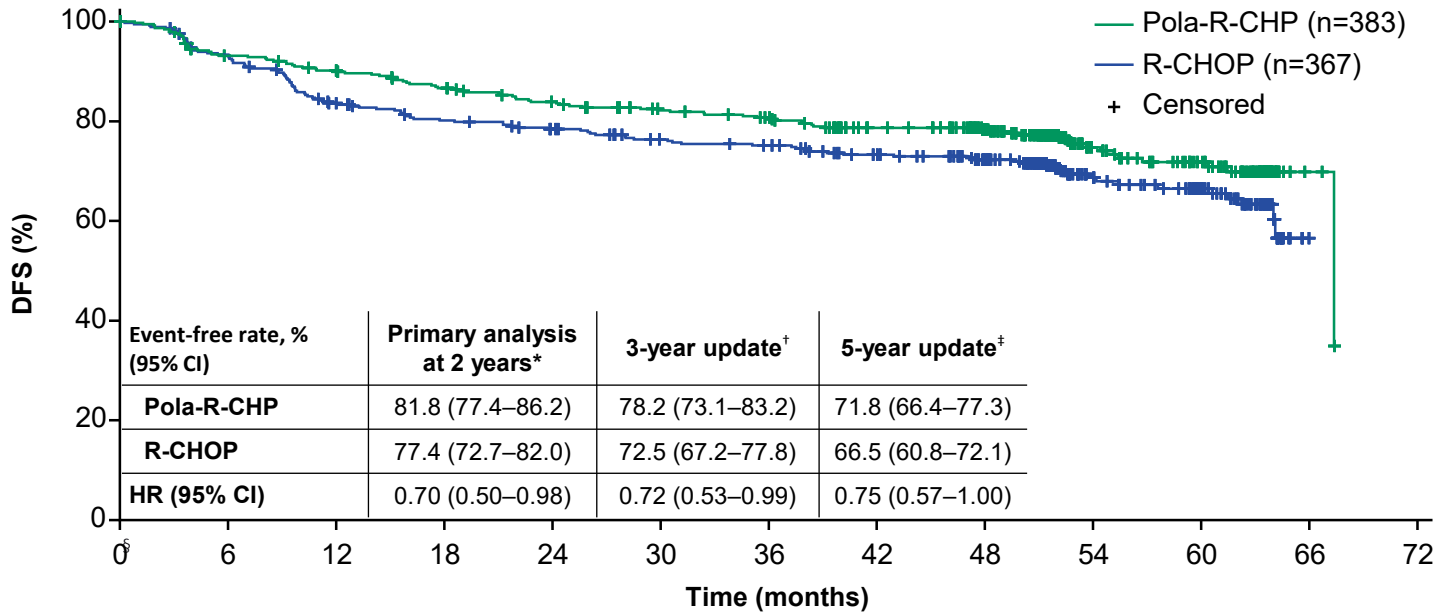
1. Langzeitdaten der POALRIX Zulassungsstudie von Pola-R-CHP versus R-CHOP: Wie sieht das Gesamtüberleben aus?
2. Wie wirksam ist die Kombination von Epcoritamab und R-CHOP in der Erstlinie?

469 Five-year analysis of the POLARIX study: Prolonged follow-up confirms positive impact of polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP) on outcomes

Gilles Salles[1], Franck Morschhauser[2], Laurie H. Sehn[3], Alex F. Herrera[4], Jonathan W. Friedberg[5], Marek Trněný́[6], Georg Lenz[7], Jeff P. Sharman[8], Charles Herbaux[9], John M. Burke[10], Matthew Matasar[11], Graham P. Collins[12], Yuqin Song[13], Antonio Pinto[14], Shinya Rai[15], Koji Izutsu[16], Calvin Lee[17]*, Saibah Chohan[18], Matthew Sugidono[17], Yanwen Jiang[17], Connie Lee Batlevi[17], Mark Yan[18], Jamie Hirata[17]*, Hervé Tilly[19], Christopher R. Flowers[20]

Complete remission obtained after Pola-R-CHP treatment is maintained with 5-year follow-up

DFS (DoCR) in the global ITT population



Event-free rate, % (95% CI)	Primary analysis at 2 years*	3-year update†	5-year update‡
Pola-R-CHP	81.8 (77.4–86.2)	78.2 (73.1–83.2)	71.8 (66.4–77.3)
R-CHOP	77.4 (72.7–82.0)	72.5 (67.2–77.8)	66.5 (60.8–72.1)
HR (95% CI)	0.70 (0.50–0.98)	0.72 (0.53–0.99)	0.75 (0.57–1.00)

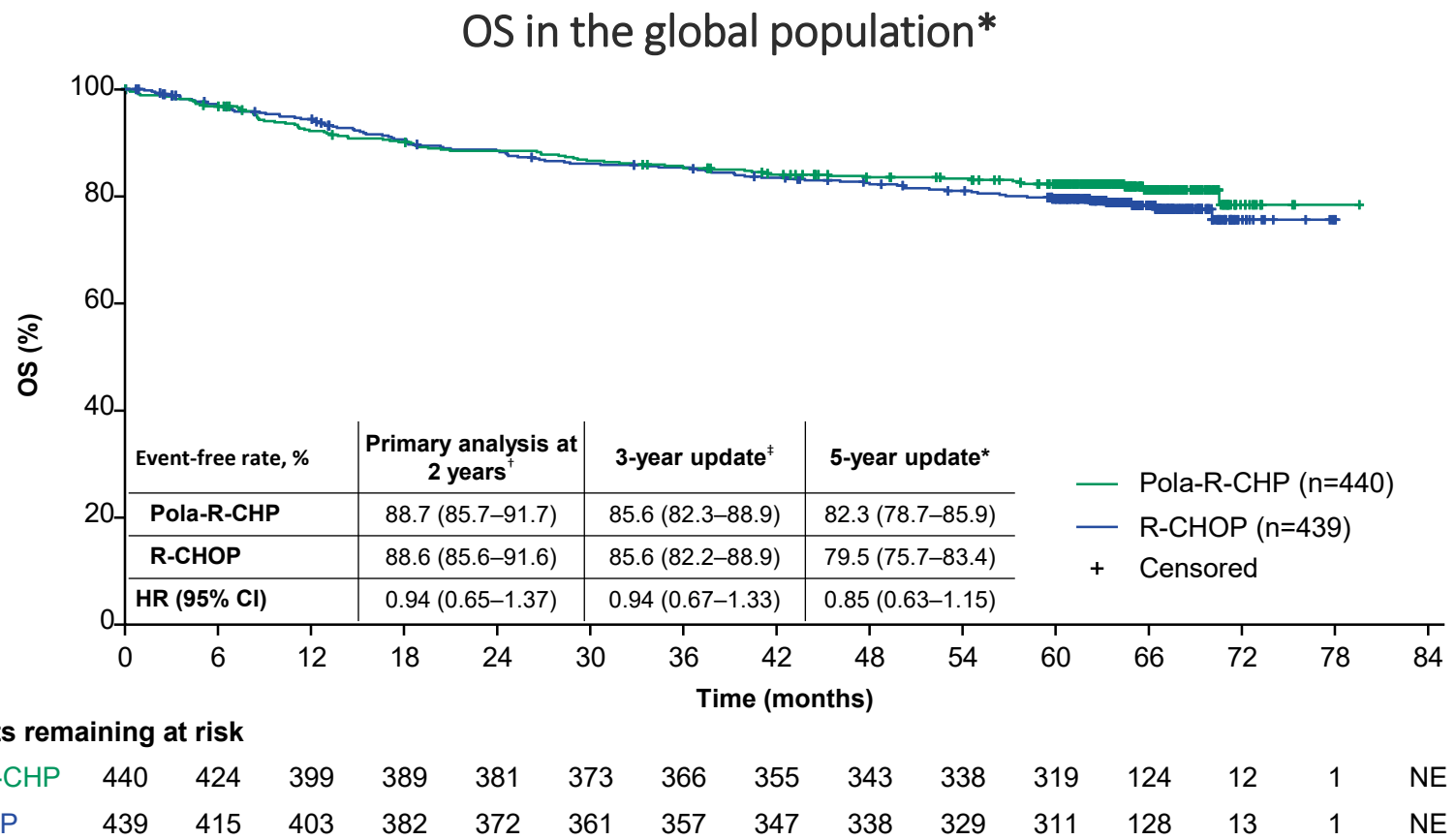
Patients remaining at risk

Pola-R-CHP	383	347	333	317	301	286	277	251	222	105	79	3	NE
R-CHOP	367	336	295	279	268	253	247	230	206	98	72	NE	NE

Complete remissions are durable and sustained with longer follow-up.

*Data cut-off: June 28, 2021; †Data cut-off: June 15, 2022; ‡Data cut-off: July 5, 2024; §CR assessment occurred at the 0-month timepoint.
CR, complete remission; DFS, disease-free survival; DoCR, duration of complete remission.

5-year overall survival shows favorable results for Pola-R-CHP-treated patients



Event-free rate, %	Primary analysis at 2 years†	3-year update‡	5-year update*
Pola-R-CHP	88.7 (85.7–91.7)	85.6 (82.3–88.9)	82.3 (78.7–85.9)
R-CHOP	88.6 (85.6–91.6)	85.6 (82.2–88.9)	79.5 (75.7–83.4)
HR (95% CI)	0.94 (0.65–1.37)	0.94 (0.67–1.33)	0.85 (0.63–1.15)

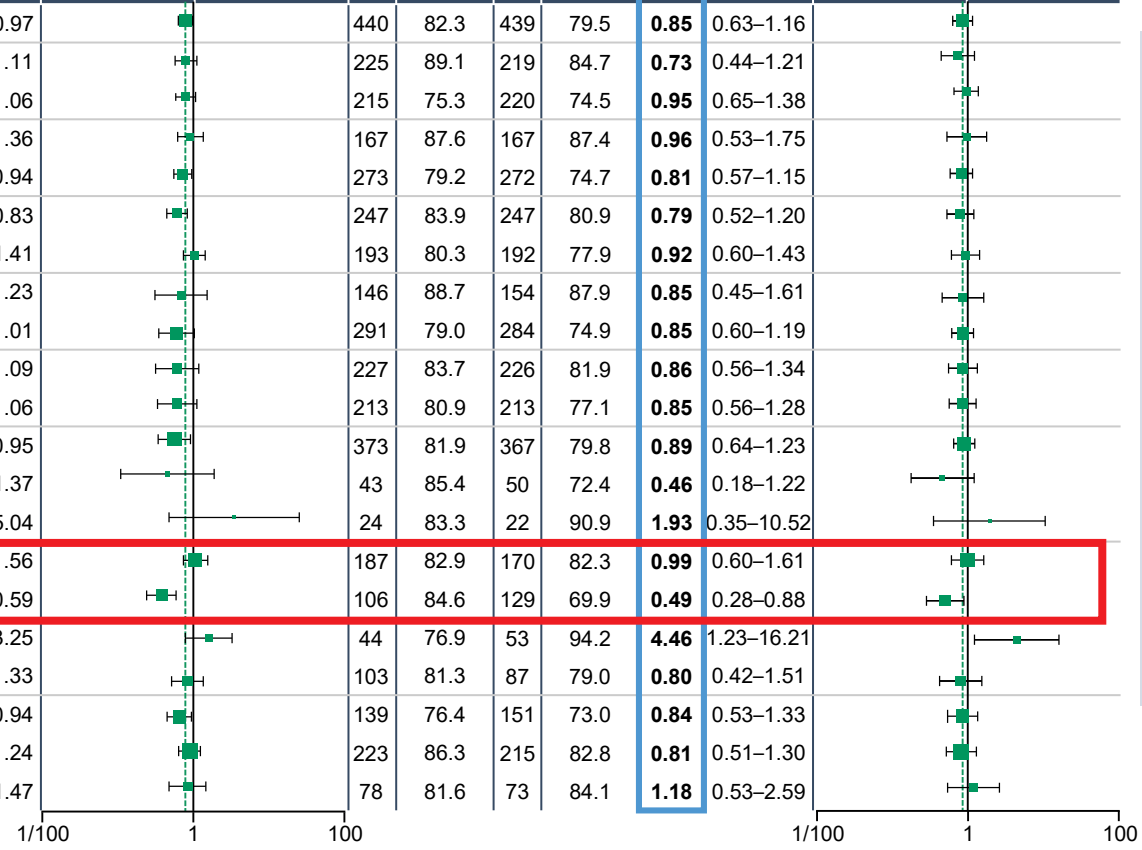
Deaths, n§	Pola-R-CHP (n=440)	R-CHOP (n=439)
Primary analysis at 2 years†	53	57
5-year update*	79	91
Progressive disease	40 (9.1)	51 (11.6)
Not disease related	23 (5.2)	28 (6.8)

After 5 years of follow-up, numerically fewer deaths were observed in the Pola-R-CHP versus R-CHOP arm, with an associated HR of 0.85 (0.63–1.15).

*Data cut-off: July 5, 2024; †Data cut-off: June 28, 2021; ‡Data cut-off: June 15, 2022; §In addition to the known deaths, there were two patients (one in the Pola-R-CHP arm and one in the R-CHOP arm) who died due to an unknown cause and an unknown death date and were not counted as death events in the OS analysis.

5-year PFS and OS outcomes show consistent treatment effect of Pola-R-CHP across subgroups in the global population

Baseline risk factors		PFS								OS							
		Pola-R-CHP (n=440)		R-CHOP (n=439)		HR	95% Wald CI	Pola-R-CHP better	R-CHOP better	Pola-R-CHP (n=440)		R-CHOP (n=439)		HR	95% Wald CI	Pola-R-CHP better	R-CHOP better
		n	60-month (%)	n	60-month (%)					n	60-month (%)	n	60-month (%)				
All patients		440	64.9	439	59.1	**0.78**	0.62–0.97			440	82.3	439	79.5	**0.85**	0.63–1.16		
Age group	≤65	225	69.6	219	64.3	**0.80**	0.57–1.11			225	89.1	219	84.7	**0.73**	0.44–1.21		
	>65	215	60.0	220	54.5	**0.78**	0.58–1.06			215	75.3	220	74.5	**0.95**	0.65–1.38		
Stratification – IPI score	2	167	67.2	167	68.3	**0.91**	0.61–1.36			167	87.6	167	87.4	**0.96**	0.53–1.75		
	3–5	273	63.2	272	53.5	**0.72**	0.55–0.94			273	79.2	272	74.7	**0.81**	0.57–1.15		
Stratification – bulky disease (≥ 7cm)	Absent	247	69.9	247	60.0	**0.61**	0.44–0.83			247	83.9	247	80.9	**0.79**	0.52–1.20		
	Present	193	58.5	192	57.9	**1.02**	0.73–1.41			193	80.3	192	77.9	**0.92**	0.60–1.43		
Baseline LDH	≤1xULN	146	65.3	154	64.8	**0.83**	0.55–1.23			146	88.7	154	87.9	**0.85**	0.45–1.61		
	>1xULN	291	64.3	284	55.7	**0.77**	0.59–1.01			291	79.0	284	74.9	**0.85**	0.60–1.19		
No. of extranodal sites	0–1	227	68.1	226	64.2	**0.78**	0.56–1.09			227	83.7	226	81.9	**0.86**	0.56–1.34		
	≥2	213	61.2	213	53.8	**0.78**	0.58–1.06			213	80.9	213	77.1	**0.85**	0.56–1.28		
NHL subtype	DLBCL	373	65.7	367	58.8	**0.75**	0.59–0.95			373	81.9	367	79.8	**0.89**	0.64–1.23		
	HGBL, DHL/THL	43	66.0	50	57.6	**0.67**	0.33–1.37			43	85.4	50	72.4	**0.46**	0.18–1.22		
	Other LBCL	24	49.7	22	70.3	**1.86**	0.69–5.04			24	83.3	22	90.9	**1.93**	0.35–10.52		
NanoString COO	NanoString GCB	187	65.9	170	65.8	**1.07**	0.74–1.56			187	82.9	170	82.3	**0.99**	0.60–1.61		
	NanoString ABC	106	72.5	129	45.8	**0.38**	0.24–0.59			106	84.6	129	69.9	**0.49**	0.28–0.88		
	NanoString UNC	44	55.2	53	70.8	**1.60**	0.79–3.25			44	76.9	53	94.2	**4.46**	1.23–16.21		
	Unknown	103	60.2	87	59.7	**0.83**	0.51–1.33			103	81.3	87	79.0	**0.80**	0.42–1.51		
Double expressor by IHC	DEL	139	63.1	151	50.0	**0.65**	0.45–0.94			139	76.4	151	73.0	**0.84**	0.53–1.33		
	Non DEL	223	66.6	215	64.7	**0.89**	0.64–1.24			223	86.3	215	82.8	**0.81**	0.51–1.30		
	Unknown	78	63.7	73	63.5	**0.84**	0.48–1.47			78	81.6	73	84.1	**1.18**	0.53–2.59		

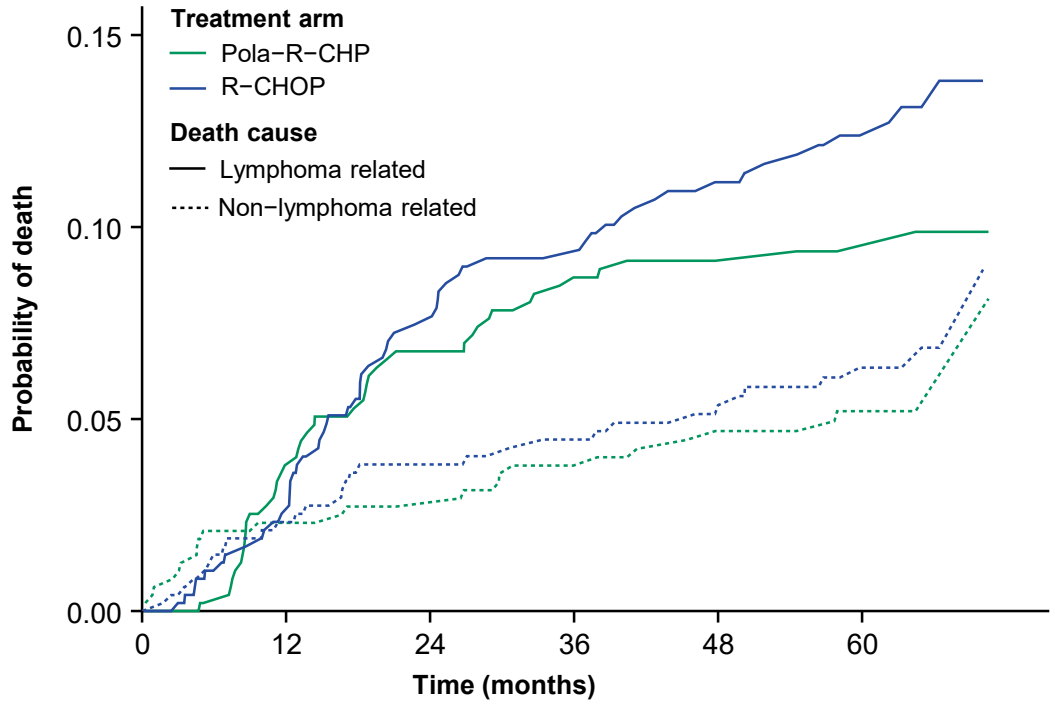


- PFS and OS by subgroups, including high-risk subgroups, generally favor Pola-R-CHP; however, subgroup analyses are exploratory and generally underpowered (especially for OS).
- Patient characteristics are multidimensional; therefore, translating univariate subgroup results into patient care should be applied with caution.

DEL, double-expressor lymphoma; IHC, immunohistochemistry; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; ULN, upper limit of normal; UNC, unclassified.

Competing risk analysis for deaths in the expanded population

Cumulative incidence of deaths due to lymphoma and other causes



	Pola-R-CHP (n=500)	R-CHOP (n=500)
Probability of lymphoma-related deaths, %		
2 years	6.52	7.26
3 years	8.37	8.94
5 years	9.02	12.05
Probability of non-lymphoma-related deaths, %		
2 years	4.44	4.73
3 years	6.09	6.21
5 years	8.56	8.93

Cumulative incidence of lymphoma-related deaths was lower in patients treated with Pola-R-CHP versus R-CHOP (9.02% vs 12.05%).

Data cut-off: July 5, 2024. Competing risks for deaths were defined as deaths due to non-lymphoma related causes that prevent lymphoma-related deaths from occurring.

Fixed-Duration Epcoritamab + R-CHOP Induces High Complete Response Rates in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma with High-Risk Features: Long-Term Results from the EPCORE NHL-2 Trial

Lorenzo Falchi, MD,1 Fritz Offner, MD, PhD,2 Sven de Vos, MD, PhD,3 Joshua D. Brody, MD,4 Raul Cordoba, MD, PhD,5 Kim M. Linton, MBChB, PhD,6 Sylvia Snauwaert, MD, PhD,7 Michael Roost Clausen, MD, PhD,8 Toshihiko Oki, MD, PhD,9 Andrew J. Steele, PhD,10 Yi Hao, DrPH,10 Kimberly G. Archer,10 Ali Rana, MD, PhD,10 David Belada, MD, PhD11

Study Design: EPCORE® NHL-2 Arm 1

Key inclusion criteria

- Newly diagnosed CD20+ DLBCL[a]
  - DLBCL, NOS
  - T-cell/histiocyte-rich DLBCL
  - Double-hit or triple-hit DLBCL[b]
  - FL grade 3B
- IPI score ≥3
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: May 15, 2024
Median follow-up: 27.4 mo

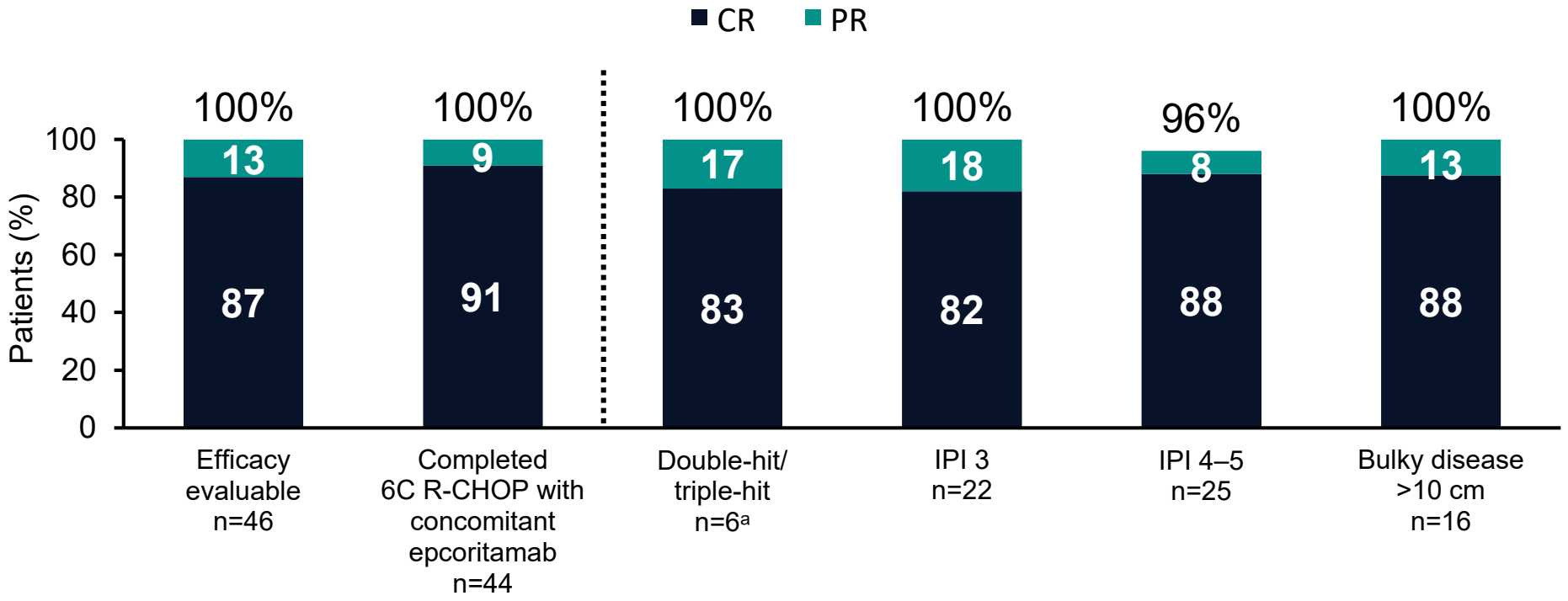
Treatment regimen: concomitant fixed-duration epcoritamab 48 mg + R-CHOP[c]

	Agent	C1–4	C5–6	C7+
	Epcoritamab SC 48 mg	QW	Q3W	Q4W Up to 1 year
R-CHOP	Rituximab IV 375 mg/m^2	Q3W		
	Cyclophosphamide IV 750 mg/m^2			
	Doxorubicin IV 50 mg/m^2			
	Vincristine[d] IV 1.4 mg/m^2			
	Prednisone IV or oral 100 mg/d	D1–5 of each cycle		

- **Primary endpoint:** Overall response rate[e]
- **Key secondary endpoints:** CR rate, time to response, time to CR, DOR, DOCR, PFS, OS, MRD negativity, and safety/tolerability
  - MRD was assessed using the exploratory AVENIO ctDNA method

NCT04663347. C, cycle(s). [a]De novo or histologically transformed from FL or nodal marginal zone lymphoma. [b]Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. [c]Patients received epcoritamab with 2 step-up doses (0.16 mg and 0.8 mg) before the first full dose and corticosteroid prophylaxis to mitigate CRS. Cycles 1–6 were 21 d (epcoritamab + R-CHOP). Subsequent cycles of epcoritamab were 28 d. [d]Recommended maximum 2 mg. [e]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until PD.

High Complete Response Rates Including Across High-Risk Subgroups

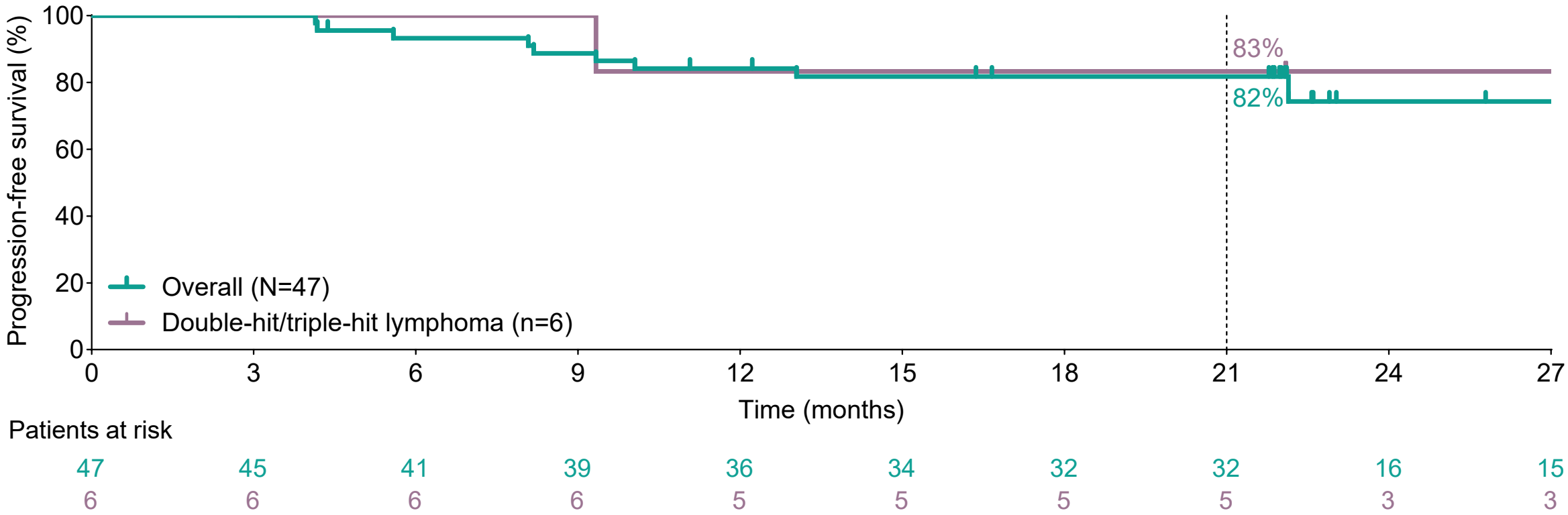


Exposure:

- Median duration of 11.5 mo of epcoritamab (range, 0.6–13.2)
- Median relative dose intensity of R-CHOP 95%–98% for all individual components
  - Three patients did not complete 6C due to withdrawal of consent, PD, and an AE (grade 5 COVID-19)

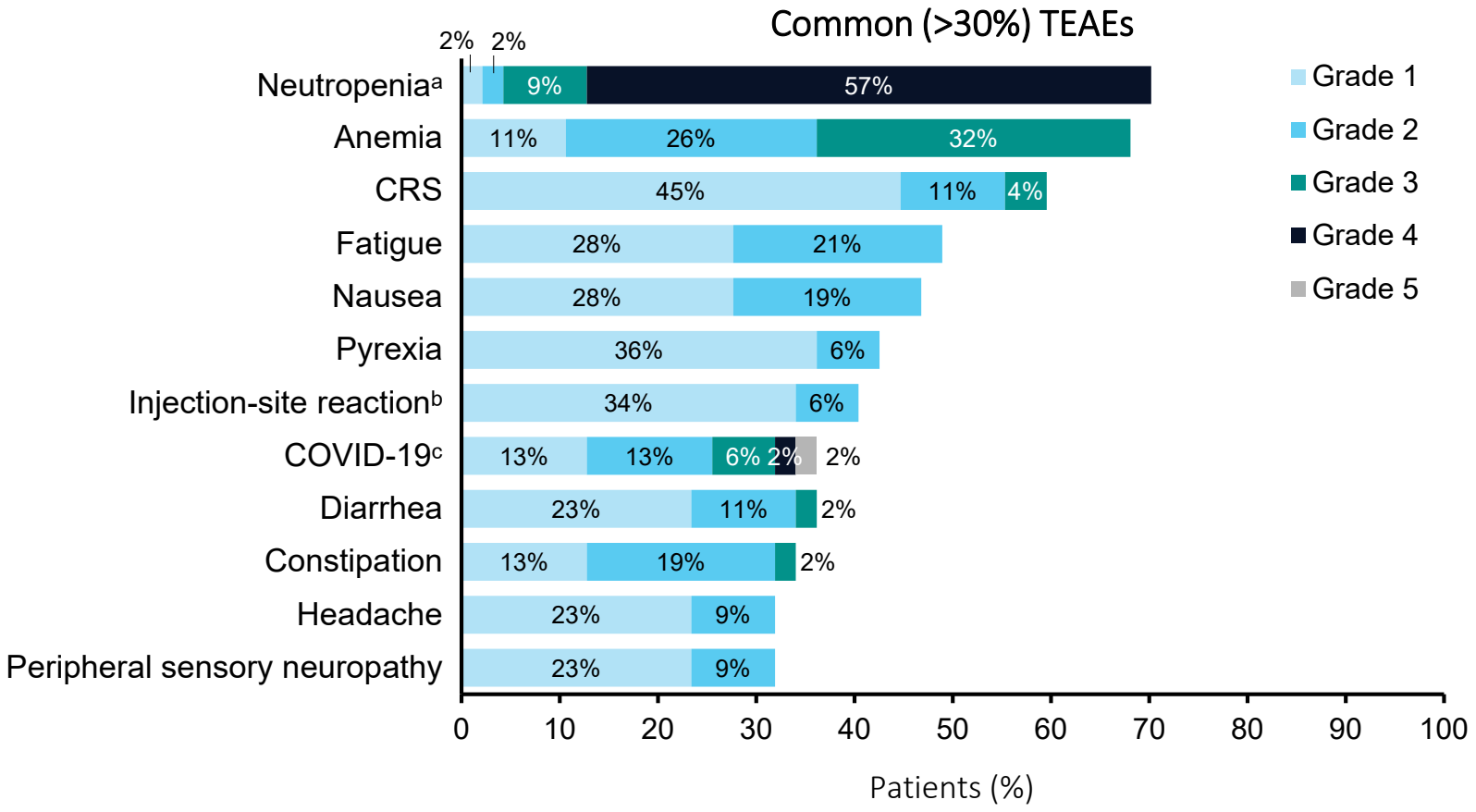
Median follow-up: 27.4 mo. Response rates based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and who had ≥1 postbaseline response evaluation or died within 60 d of first trial treatment. [a]**Double-hit/triple-hit status by central lab was not evaluable in 19 patients**.

High Rates of Progression-Free Survival



Median follow-up for PFS: 22.9 months. Kaplan–Meier estimated probability of remaining progression free.

Manageable Safety Profile



- Febrile neutropenia occurred in 5 patients
- 17 patients (36%) received G-CSF
- Two grade 5 TEAEs (COVID-19 and septic shock)
- Four patients discontinued epcoritamab due to TEAEs (2 due to COVID-19[c] and 1 each due to septic shock and upper respiratory tract infection)
- No clinical tumor lysis syndrome events

[a]Combined term includes neutropenia and decreased neutrophil count. [b]Combined term includes injection-site reaction, pruritus, rash, discoloration, erythema, hematoma, and pain. [c]Combined term includes COVID-19 and COVID-19 pneumonia.

Kapitel 1 DLBCL Zweitlinie

1. Versorgungsdaten mit Liso-cel?

Real-World Outcomes of Lisocabtagene Maraleucel as Second-Line Therapy in Patients with Relapsed or Refractory Large B-Cell Lymphoma: First Results from the Center for International Blood and Marrow Transplant Research Registry

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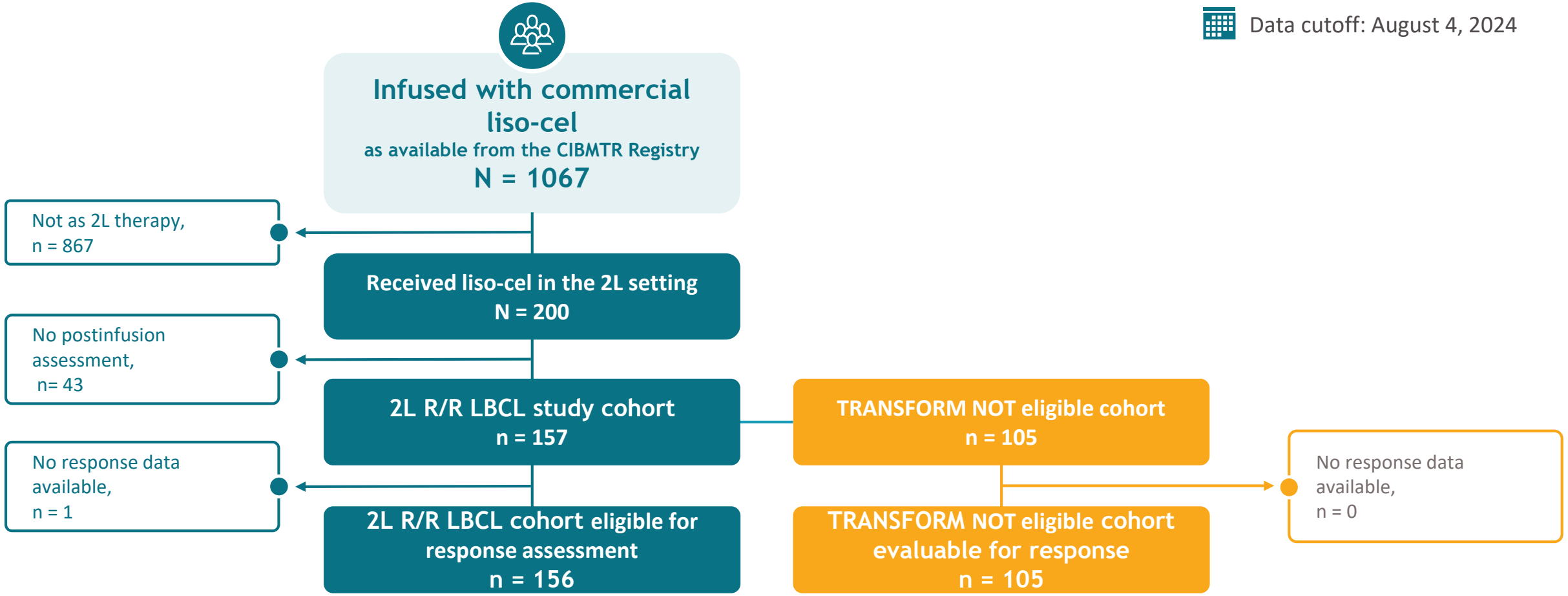
Jennifer L. Crombie, MD,12 Saurabh Dahiya, MD,13 Mehdi Hamadani, MD,14 Catherine J. Lee, MD, MS,15 Marcelo C. Pasquini, MD, MS,9 Mazyar Shadman, MD, MPH,15 Alex F. Herrera, MD,2 Matthew Frigault, MD16

CONSORT diagram

A collaboration of BMS and CIBMTR

Data cutoff: August 4, 2024

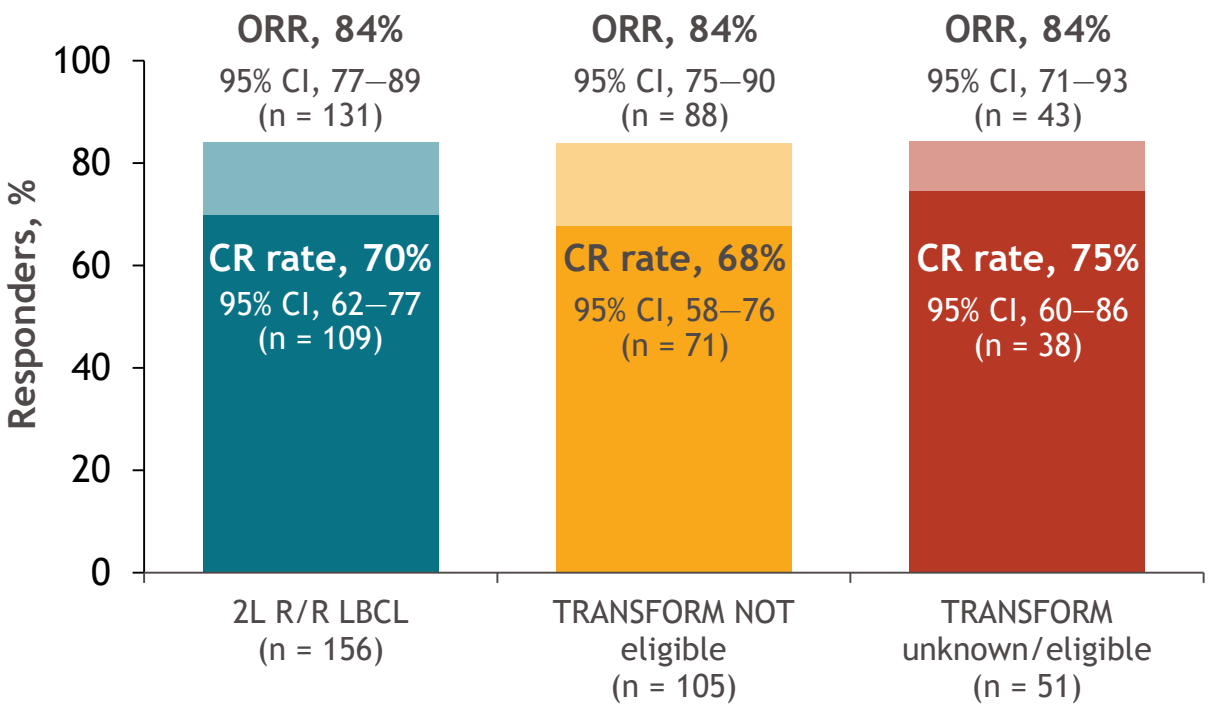


Comparison to PILOT was not feasible due to the lack of granularity around organ function that was used to define the PILOT population.

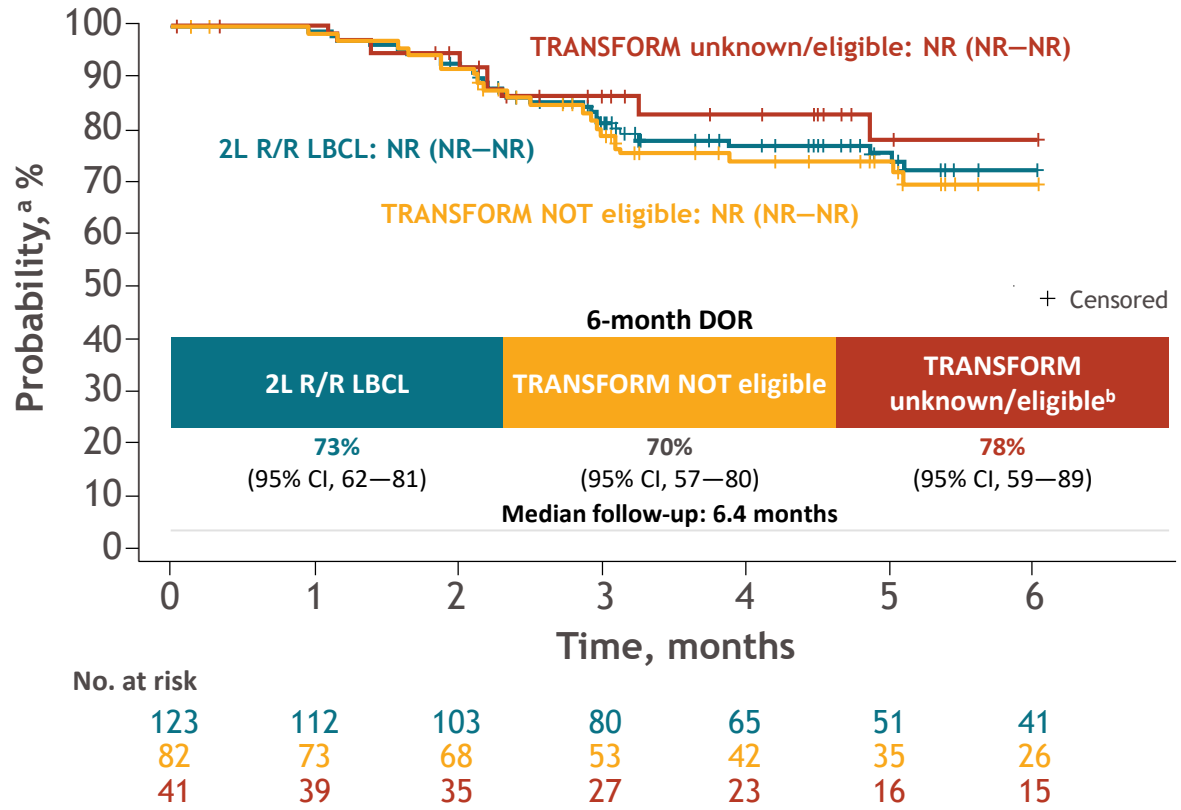
Response rates and duration of response

A collaboration of BMS and CIBMTR

Response rates



DOR

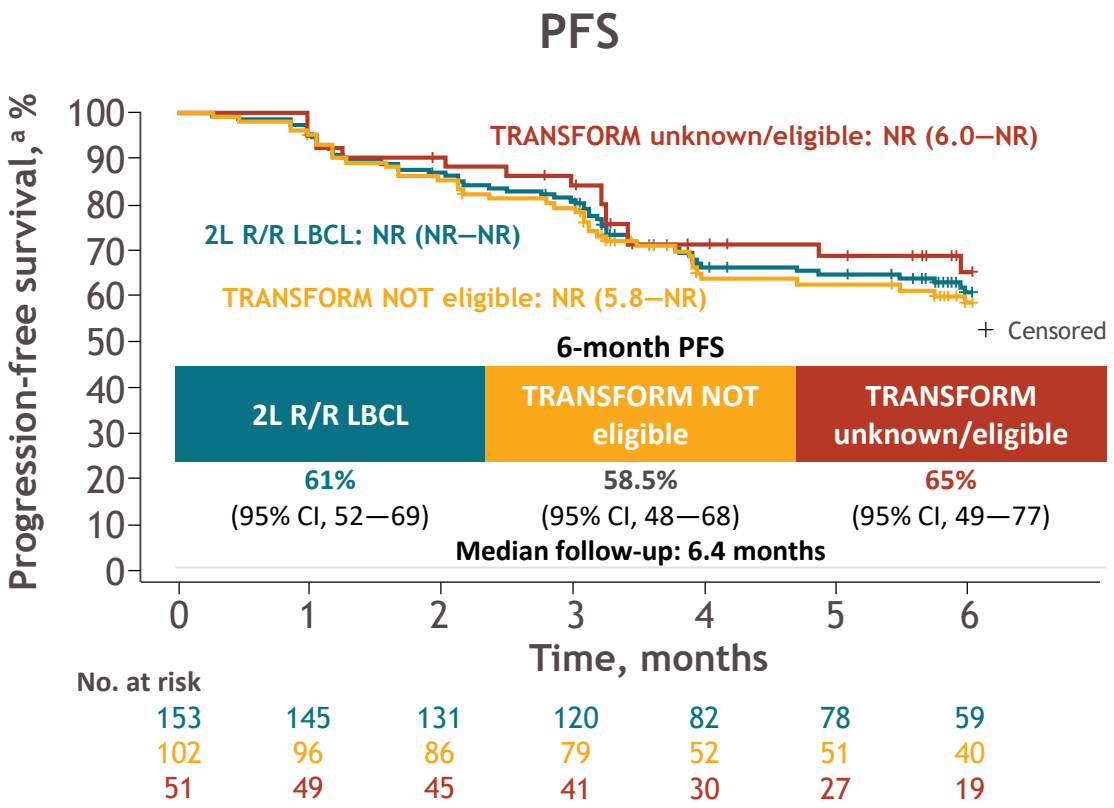


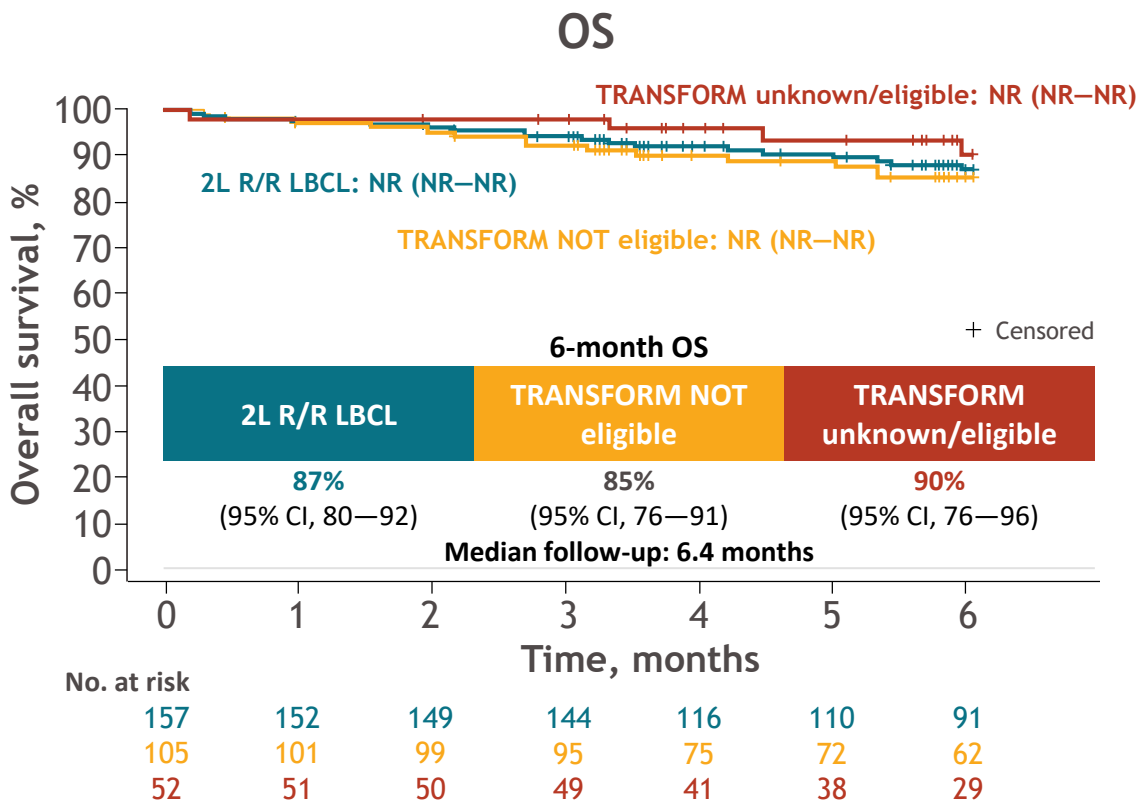
- High response rates were achieved with liso-cel across all eligibility subgroups

[a]Responders with available DOR data; [b]Patients who might have been eligible for TRANSFORM study but could not confirm all eligibility criteria.

Progression-free survival and overall survival

A collaboration of BMS and CIBMTR





- Median PFS and OS were NR with liso-cel
- Patients who achieved CR had similar effectiveness outcomes independent of whether they might have been eligible for TRANSFORM or not, and comparable to the overall cohort

[a]Patients with available PFS data.

Subgroup analysis by disease status in the second-line setting

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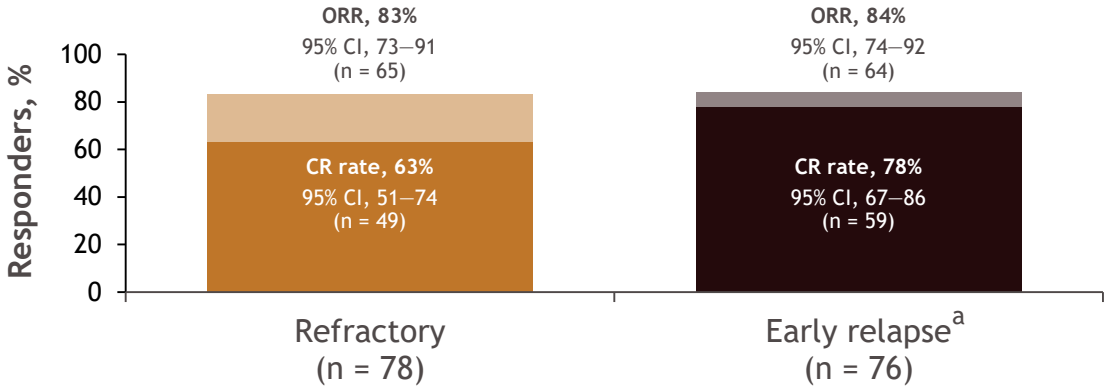
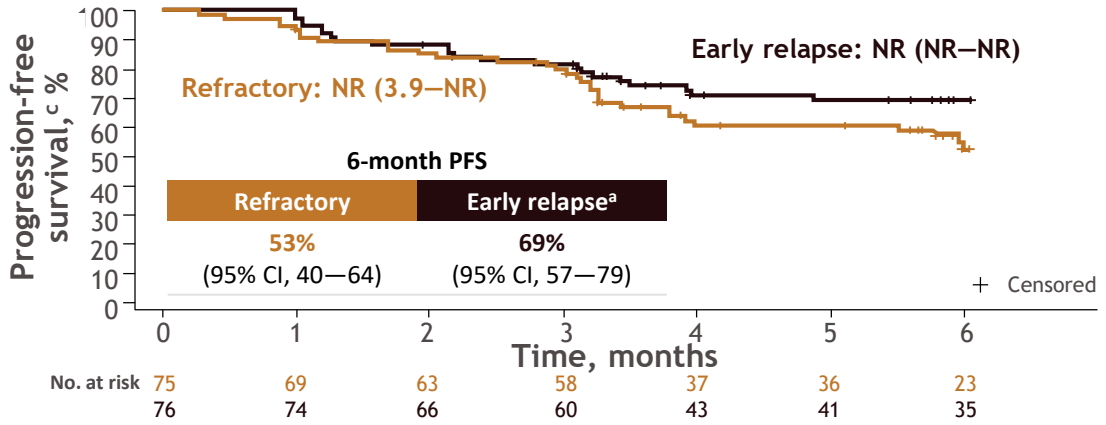
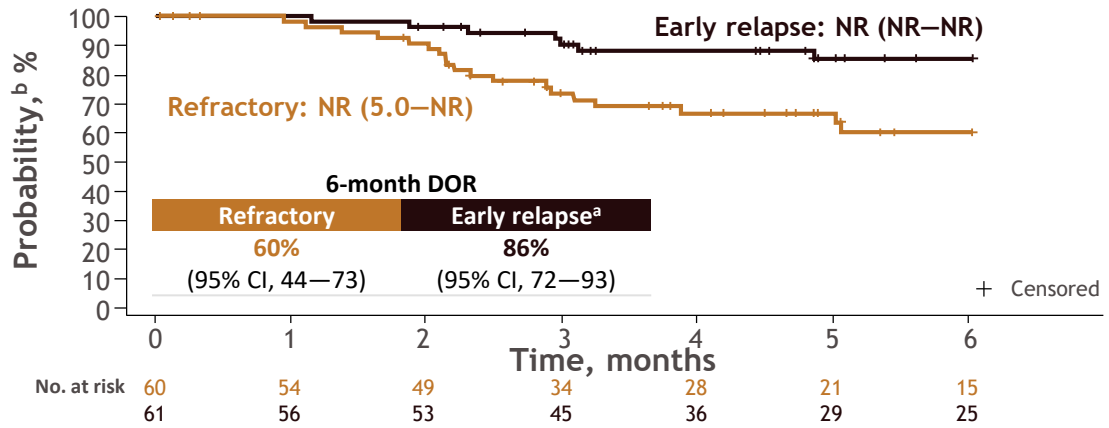
Response rates



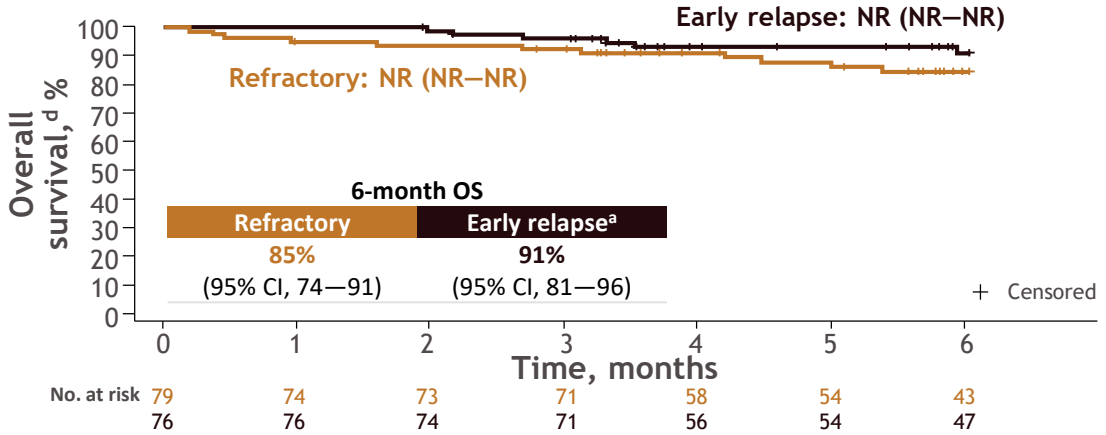
PFS



DOR



OS



- While higher CR rates were reported for patients with early relapsed disease, median DOR, PFS, or OS were NR in either subgroup

[a]Patients whose disease relapsed < 12 months; [b]Responders with available DOR data; [c]Patients with available PFS data; [d]Patients with available OS data.

CRS and ICANS

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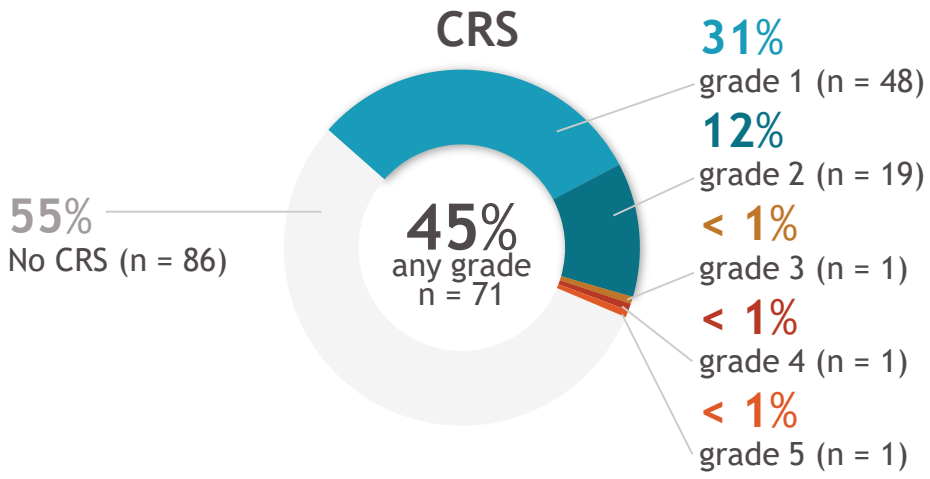

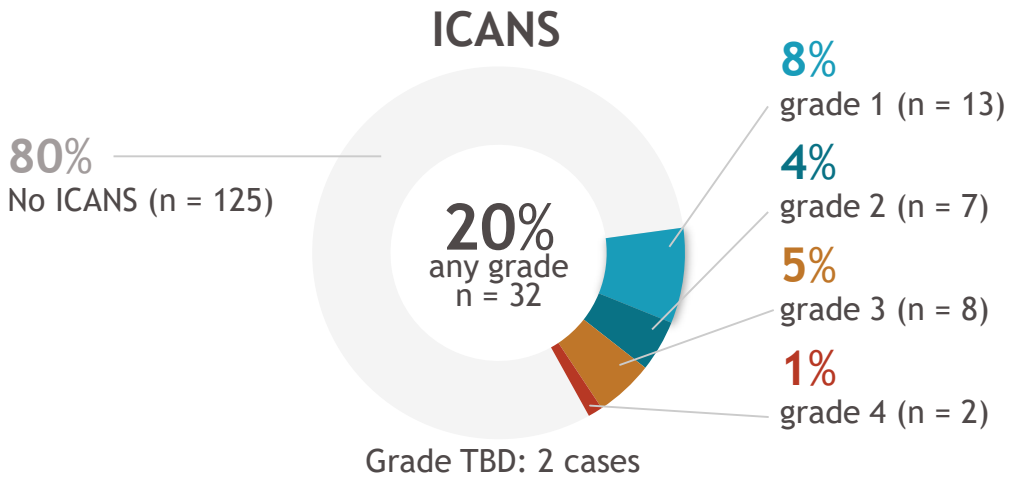

	2L R/R LBCL (n = 157)	
	CRS	ICANS
Median (IQR) time to onset, days	4.0 (3.0—7.0)	8.0 (5.0—9.0)
Median (IQR) duration, days	3.0 (2.0—5.0)	10 (4.0—378.0)
Patients who received treatment, n/N (%)	58/71 (82)	29/32 (91)
Treatments, n (%)		
Tocilizumab alone	34 (59)	1 (3)
Corticosteroids alone	2 (3)	14 (48)
Tocilizumab + corticosteroids	20 (34)	0
Antiepileptics alone or with other agents	0	10 (34)
Other	2 (3)	3 (10)

- Most patients experienced either no or low-grade CRS and ICANS
  - Higher incidence of CRS and ICANS were reported for the TRANSFORM ineligible, refractory disease, or ≥ 70 years cohorts. These differences were not statistically significant, except for incidence of ICANS that was significantly higher in patients ≥ 70 years of age

TBD, to be determined.

Zusammenfassung | Take-Home-Messages

1. Keine „practice changing“ Phase III Studienergebnisse für das DLBCL auf diesem ASH 24
2. Aber Bestätigung unserer aktuellen Standardtherapien in
   - Der Erstlinie mit den 5 Jahresdaten der Polarix Studie
   - Der Zweitlinie mit Registerdaten, die erneut die Zulassungsdaten bestätigen, obwohl etwa die Hälfte der PatientInnen nicht der Studienpopulation entspricht
3. Ausblick auf die Kombination von bispezifischen AK und Chemotherapie in der Erstlinie mit Epcoritamab

Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2024

Für den Inhalt verantwortlich:

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Uniklinik Köln

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

Das Informationsprojekt wird unterstützt von den Firmen:

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Diese hatten keinen Einfluss auf die Inhalte.