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Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

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Disclosures

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Optimizing the Use of Novel Therapies for Patients with DLBCL

Module 1: Selection of First-Line Therapy for Patients with Diffuse Large B-Cell Lymphoma (DLBCL)

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Module 6: Clinician Survey Results

RTP RESEARCH TO PRACTICE

Key Datasets

- Morschhauser F et al. **Five-year outcomes** of the **POLARIX study** comparing **Pola-R-CHP and RCHOP in patients with diffuse large B-cell lymphoma**. *J Clin Oncol* 2025 December 10;43(35):3698-705.
- Trněný M et al. Analysis of **peripheral neuropathy in the POLARIX** study using **clinician- and patient-reported outcomes**. *Blood Adv* 2025 July 8;9(13):3263-7.
- Vitolo U et al. **frontMIND**: A **phase III,** randomized, double-blind study of **tafasitamab + lenalidomide + R-CHOP** versus R-CHOP alone for **newly diagnosed high-intermediate and high-risk diffuse large B-cell lymphoma**. ASCO 2022;Abstract TPS7590.
- Sehn LH et al. **ESCALADE:** A **phase 3** study of **acalabrutinib in combination** with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) for **patients ≤65y** with **untreated non-germinal center B-cell–like (non-GCB) diffuse large B-cell lymphoma (DLBCL)**. ASCO 2021;Abstract TPS7572.

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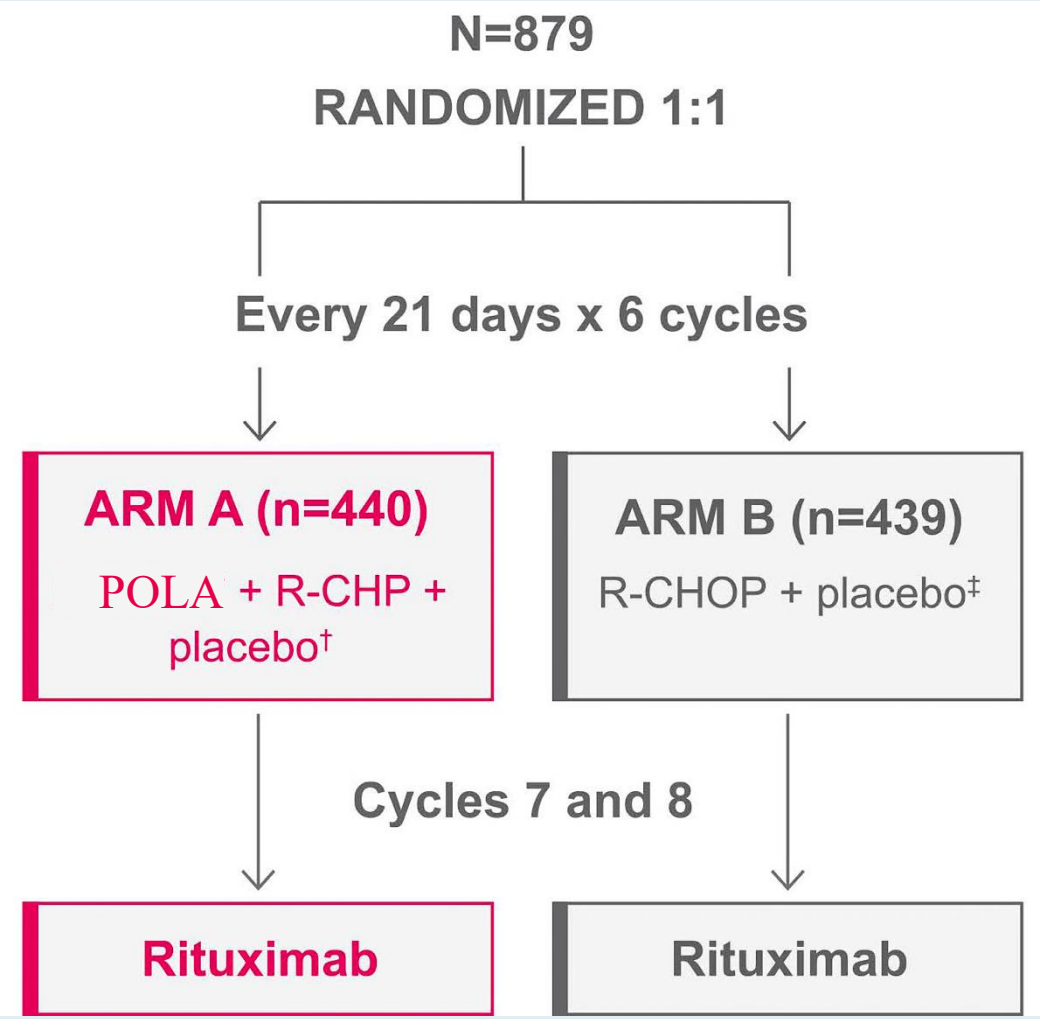
Phase III POLARIX Study Design

Eligibility Criteria:

- Previously untreated LBCL
- Aged 18-80 years
- IPI score 2-5
- ECOG PS 0-2

Primary endpoint:
Investigator-assessed PFS

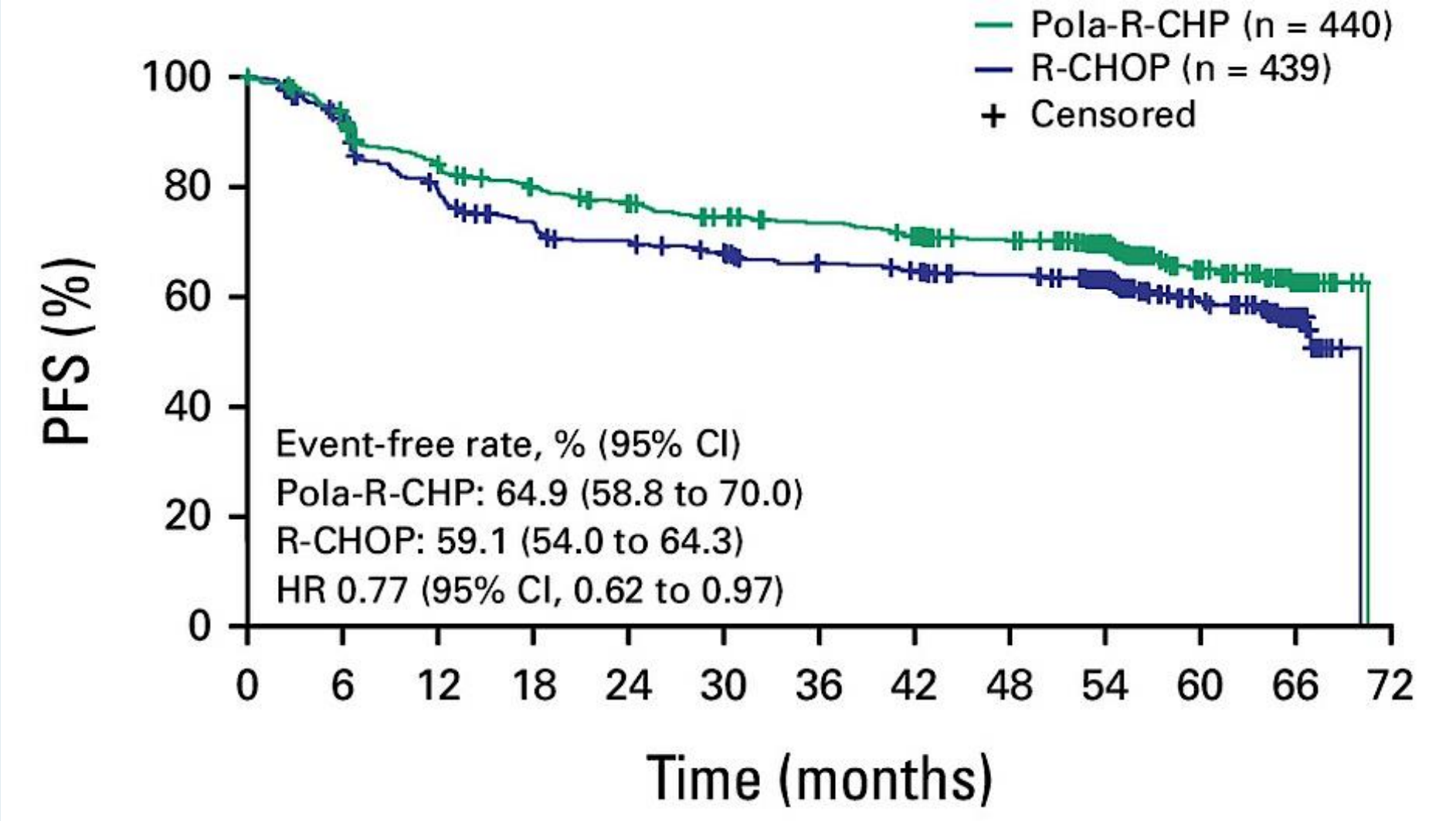
Secondary endpoints:
Investigator-assessed EFS, ORR, OS



LBCL = large B-cell lymphoma; PFS = progression-free survival; EFS = event-free survival; ORR = overall response rate; OS = overall survival

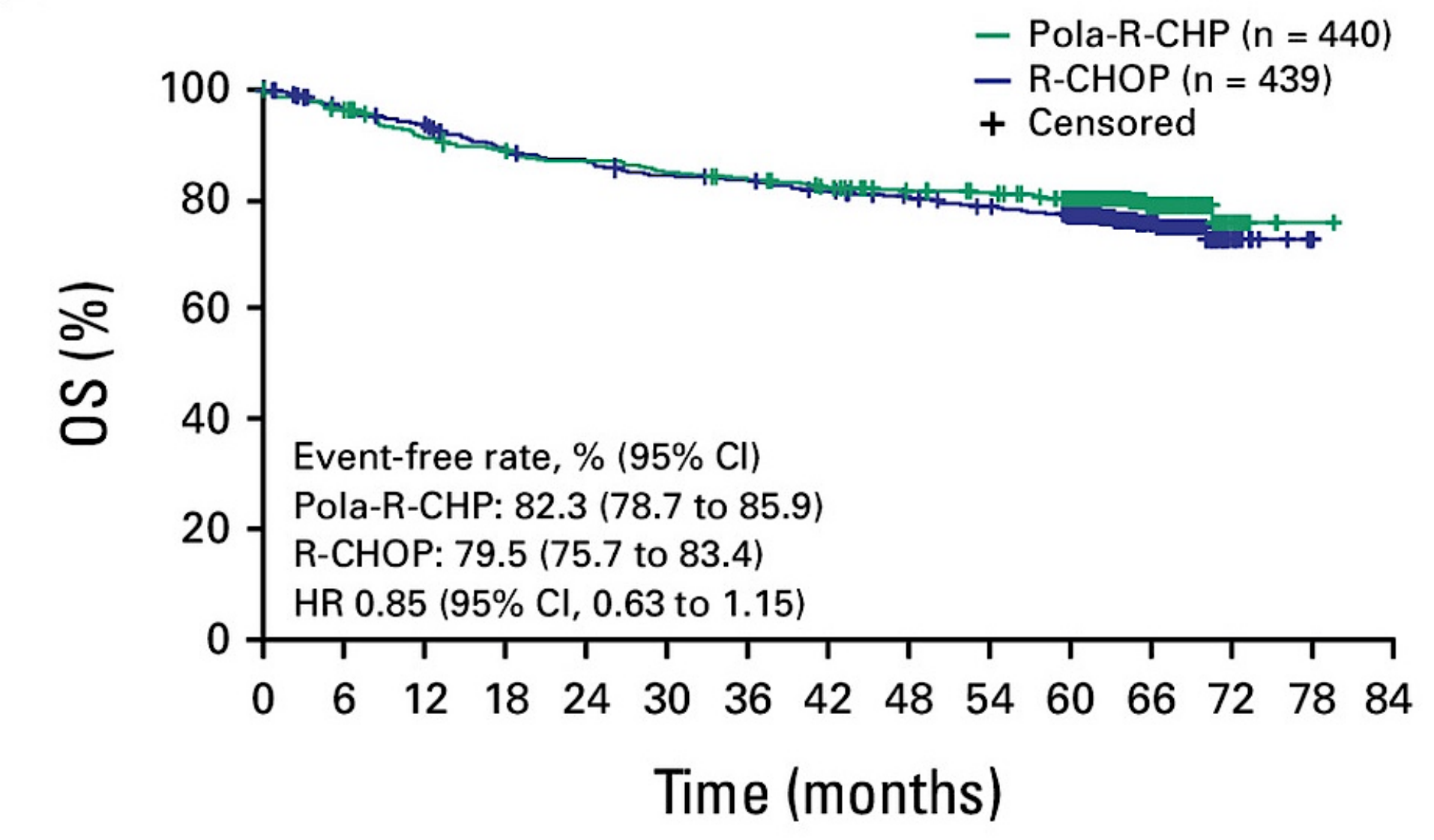
[from the manufacturer's website]

Phase III POLARIX: 5-Year PFS (Global Population)



Morschhauser F et al. *J Clin Oncol* 2025 December 10;43(35):3698-705.

Phase III POLARIX: 5-Year OS (Global Population)



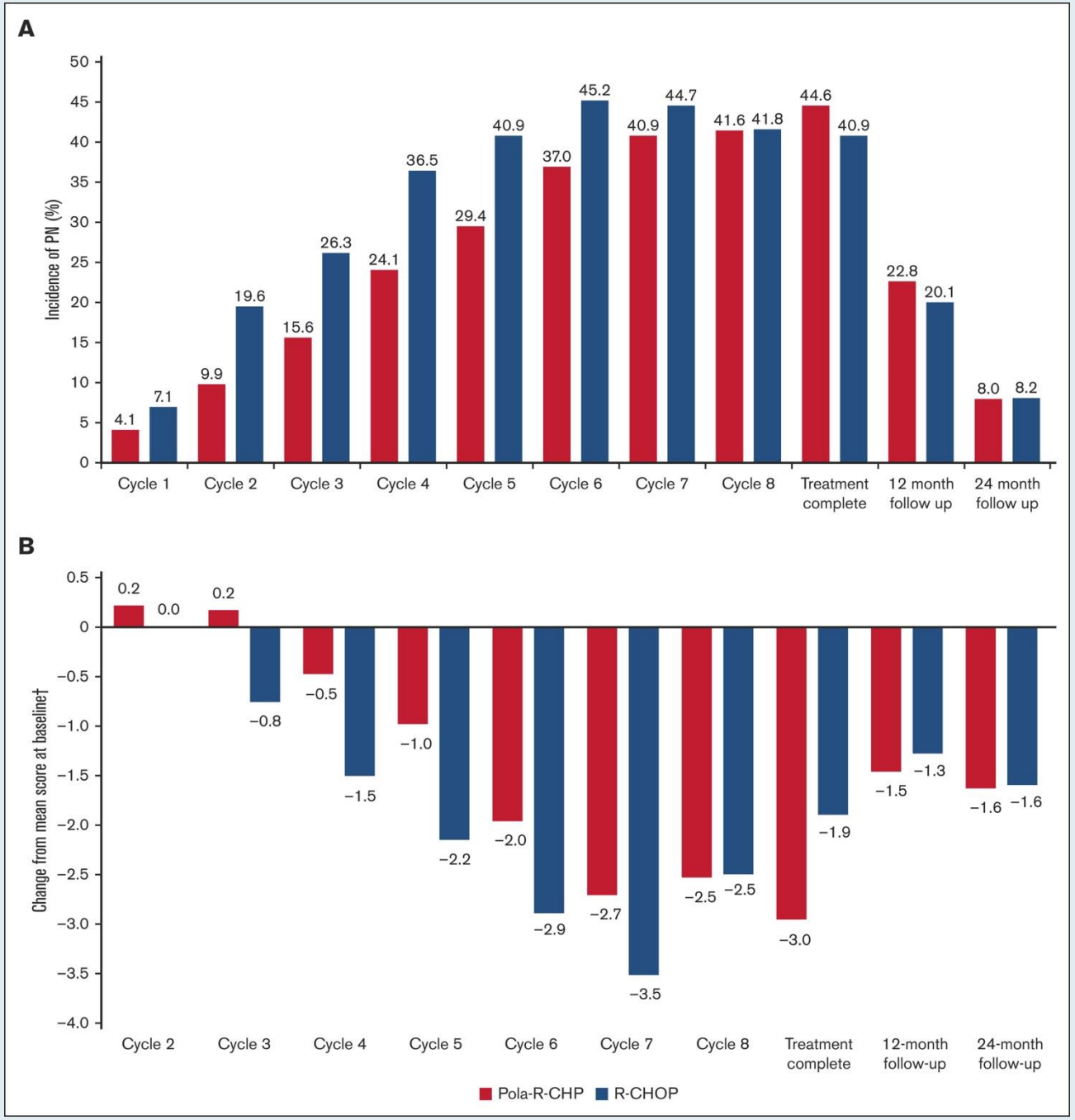
Morschhauser F et al. *J Clin Oncol* 2025 December 10;43(35):3698-705.

Phase III POLARIX: Adverse Events of Interest

Patients, n (%)	Pola-R-CHP (n=495)	R-CHOP (n=498)
Peripheral neuropathy		
All grade	249 (50.3)	261 (52.4)
Grade 3–5	7 (1.4)	5 (1.0)
Resolved[a]	170 (68.3)	195 (74.7)
Ongoing/Unresolved[b]	79 (31.7)	66 (25.3)
Neutropenia		
All grade	240 (48.5)	228 (45.8)
Grade 3–5	216 (43.6)	205 (41.2)
Infections		
All grade	237 (47.9)	219 (44.0)
Grade 3–5	75 (15.2)	66 (13.3)
Anemia		
All grade	165 (33.3)	150 (30.1)
Grade 3–5	56 (11.3)	49 (9.8)
Thrombocytopenia		
All grade	89 (18.0)	86 (17.3)
Grade 3–5	32 (6.5)	31 (6.2)
Cardiac arrhythmias		
All grade	18 (3.6)	26 (5.2)
Grade 3–5	3 (0.6)	5 (1.0)
Secondary malignancies[c]		
All grade	5 (1.0)	12 (2.4)
Grade 3–5	5 (1.0)	9 (1.8)

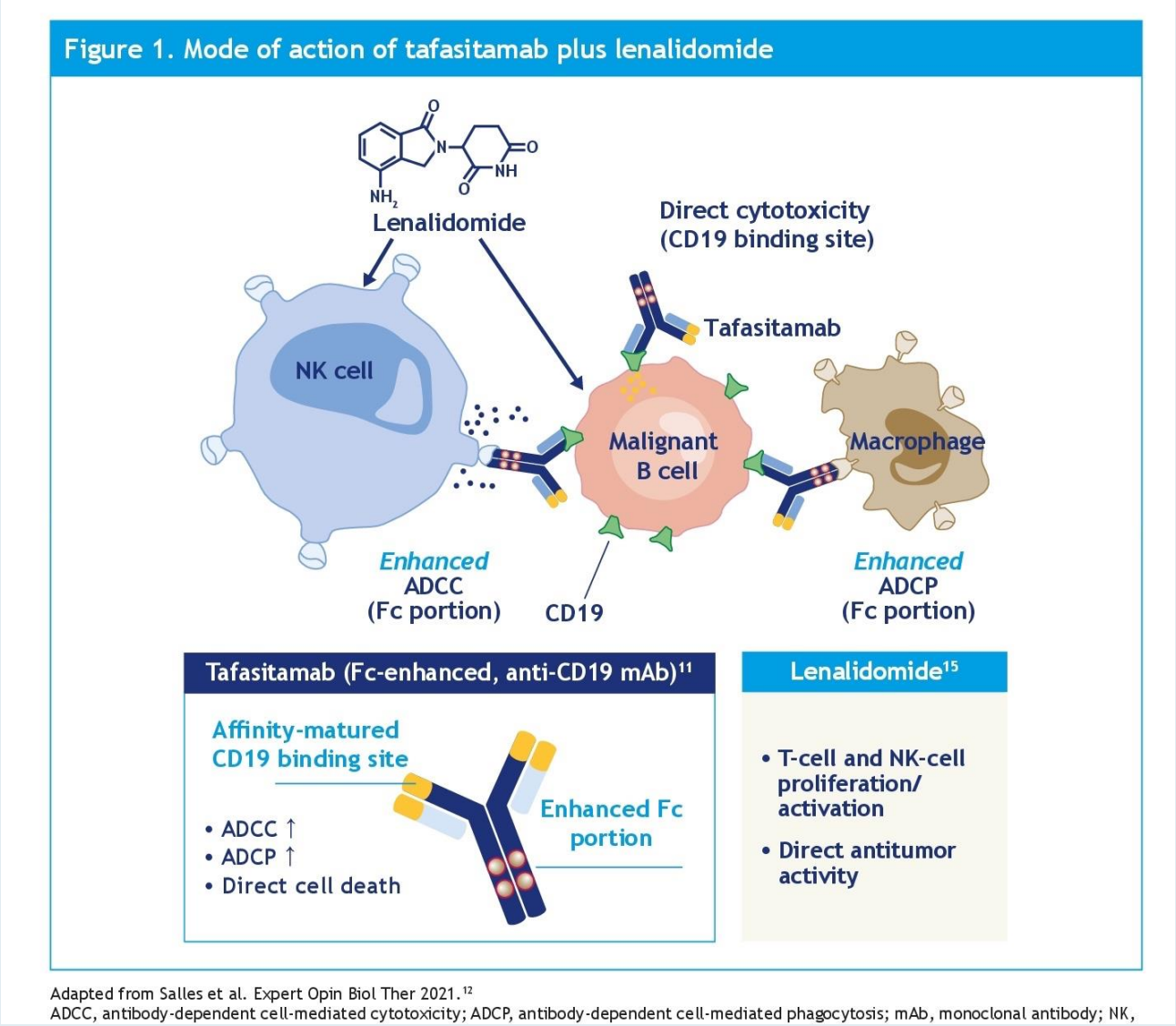
Morschhauser F et al. *J Clin Oncol* 2025 December 10;43(35):3698-705.

Phase III POLARIX: Peripheral Neuropathy



Trněný M et al. *Blood Adv* 2025 March 17;9(13):3263-7.

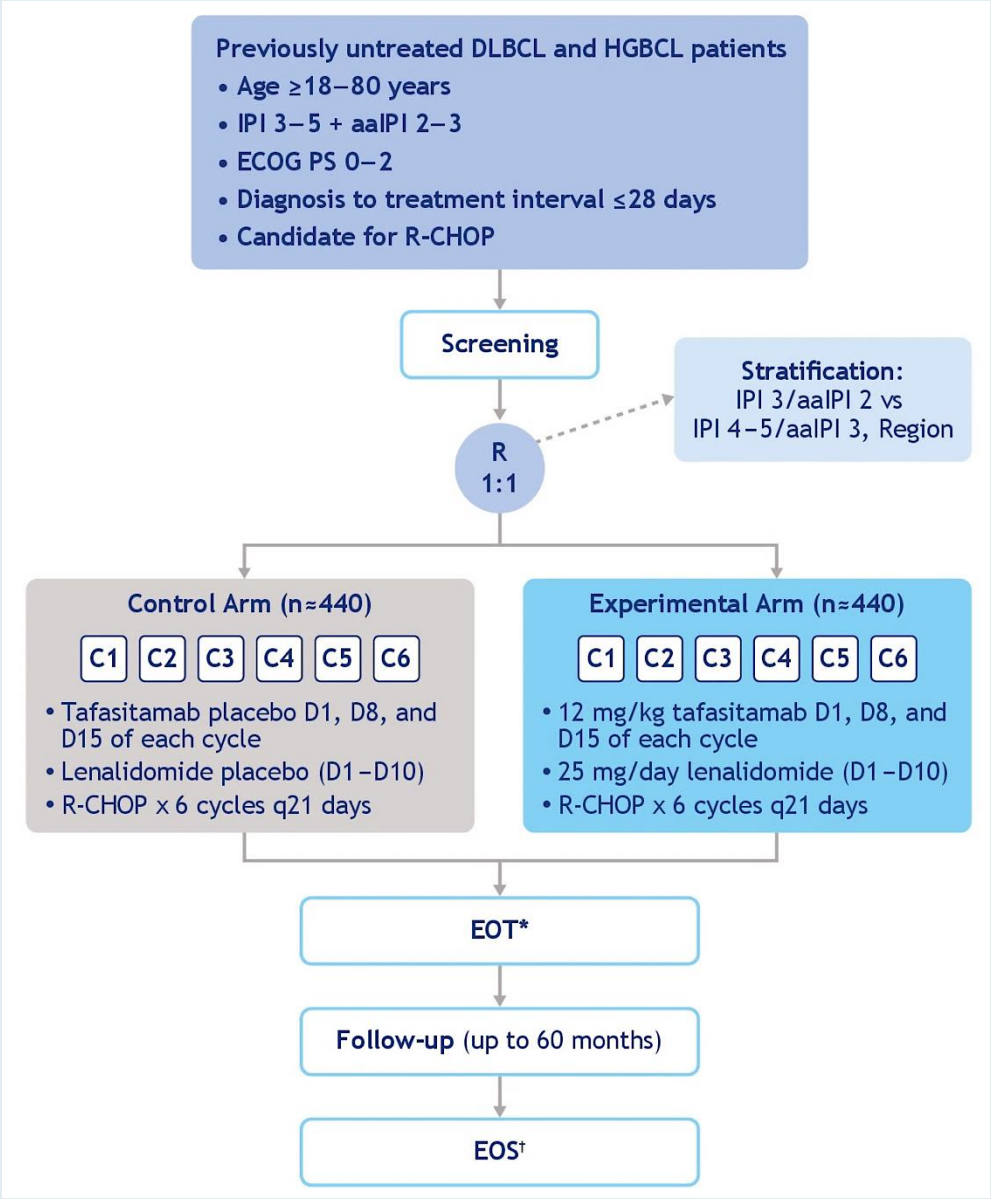
Rationale for Tafasitamab and Lenalidomide Combination Therapy



Adapted from Salles et al. Expert Opin Biol Ther 2021.[12]
ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent cell-mediated phagocytosis; mAb, monoclonal antibody; NK,

Vitolo U et al. ASCO 2022;Abstract TPS7590.

Phase III frontMIND Study Design



Vitolo U et al. ASCO 2022;Abstract TPS7590.

The Manufacturer Announces Positive Topline Results from Pivotal Study of Tafasitamab As a First-Line Treatment for DLBCL

Press Release: January 5, 2026

"[The manufacturer] today announced positive topline results from the pivotal Phase 3 frontMIND trial evaluating the efficacy and safety of tafasitamab, a humanized Fc-modified cytolytic CD19 targeting monoclonal antibody, and lenalidomide in addition to R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) compared to R-CHOP alone as a first-line treatment for adults with newly diagnosed diffuse large B-cell lymphoma (DLBCL) with an International Prognostic Index (IPI) score of three to five (3-5) for patients >60 years of age, or age-adjusted IPI (aaIPI) of two to three (2-3) for patients ≤60 years of age.

The trial met its primary endpoint of progression-free survival (PFS) by investigator assessment (Hazard Ratio 0.75 [0.59,0.96]; *p*-value 0.019), according to Lugano 2014 criteria. The trial also met its key secondary endpoint of event-free survival (EFS) by investigator assessment. No new safety signals were observed.

Based on these positive results, [the manufacturer] expects to file a supplemental Biologics License Application (sBLA) for tafasitamab for the first-line treatment of adults with newly diagnosed DLBCL in the first half of 2026. The frontMIND data will be submitted for presentation at an upcoming scientific meeting."

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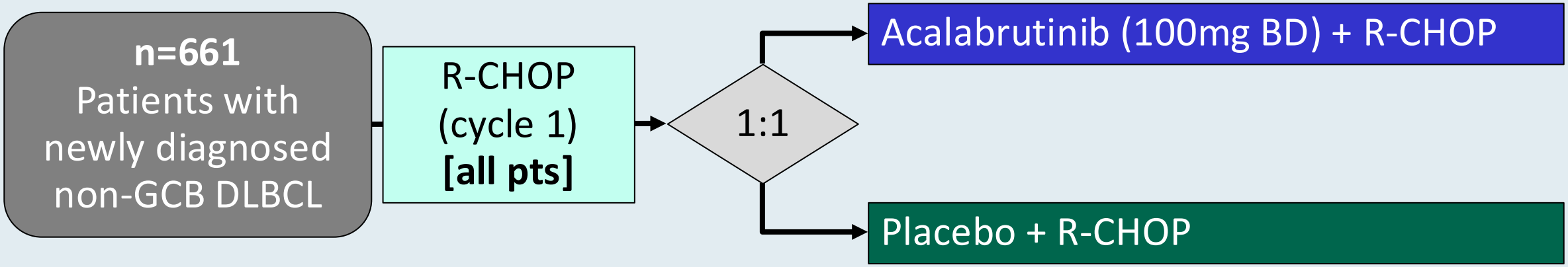
https://incytecorp.gcs-web.com/news-releases/news-release-details/incyte-announces-positive-topline-results-pivotal-study-0

Studies Supporting the ESCALADE Study

- **ACCEPT — Davies et al. ASH 2020**
  - "There is a strong rationale for combining A with R-CHOP in pts with untreated DLBCL, and safety of A + R-CHOP has been shown in a phase 1b/2 study"
- **PHOENIX — Younes et al. *J Clin Oncol* 2019;37:1285-9.**
  - "In untreated non-GCB DLBCL pts, [PHOENIX] showed that addition of the BTKi ibrutinib to R-CHOP (R-CHOP-I) did not improve outcomes in the intent-to-treat population. However, pts age <60y treated with R-CHOP-I had significantly improved progression-free survival (PFS) and overall survival (OS) compared with those receiving R-CHOP alone."

Sehn LH et al. ASCO 2021;Abstract TPS7572.

Phase III ESCALADE (ACE-LY-312) Study Design



***All patients will receive primary prophylaxis with G-CSF accompanying all R-CHOP cycles.**

Primary endpoint:
PFS

Secondary endpoints:
EFS, CR rate, OS, pharmacokinetics, safety

GCB = germinal center B-cell-like; CR = complete response; G-CSF = granulocyte-colony stimulating factor

Sehn LH et al. ASCO 2021;Abstract TPS7572.

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Which first-line therapy would you generally recommend for an otherwise healthy patient with Stage IV germinal center B-cell (GCB)-type diffuse large B-cell lymphoma (DLBCL) with an International Prognostic Index (IPI) score of 3?

	65-year-old	80-year-old
 Dr Abramson	R-CHP + polatuzumab vedotin	Dose-reduced R-CHP + polatuzumab vedotin
 Dr Kahl	R-CHOP	R-mini-CHOP
 Dr Kamdar	R-CHP + polatuzumab vedotin	R-mini-CHOP
 Dr LaCasce	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Matasar	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Phillips	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Prof Salles	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Westin	R-CHOP	R-mini-CHOP

R-CHP = rituximab/cyclophosphamide/doxorubicin/prednisone; R-mini-CHOP = rituximab/cyclophosphamide/doxorubicin/vincristine/prednisone (attenuated)

Which first-line therapy would you generally recommend for an otherwise healthy patient with Stage IV activated B-cell (ABC)-type DLBCL with an IPI score of 3?

	65-year-old	80-year-old
 Dr Abramson	R-CHP + polatuzumab vedotin	Dose-reduced R-CHP + polatuzumab vedotin
 Dr Kahl	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Kamdar	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr LaCasce	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Matasar	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Phillips	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Prof Salles	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin
 Dr Westin	R-CHP + polatuzumab vedotin	R-mini-CHP + polatuzumab vedotin

A 75-year-old woman with a history of congestive heart failure and a LVEF of 45% presents with Stage IV DLBCL with an IPI of 3. Which initial therapy would you most likely recommend if she had the DLBCL molecular subtype below?

	GCB-type	ABC-type, high-risk
 Dr Abramson	R-CHOP + dexrazoxane	Pola-R-CHP + dexrazoxane
 Dr Kahl	R-CEOP	R-mini-CHP + polatuzumab vedotin
 Dr Kamdar	Dose-adjusted R-EPOCH	Pola-R-CHP + dexrazoxane
 Dr LaCasce	R-GCVP	Pola-R-CGP
 Dr Matasar	R-GCVP	R-GCVP
 Dr Phillips	Dose-adjusted R-EPOCH	R-CP + Pola + infusional doxorubicin
 Prof Salles	R-GCVP	R-mini-CGemP-Pola
 Dr Westin	R-CEOP	RCEP-Pola

R = rituximab; C = cyclophosphamide; E = etoposide; O = vincristine; P = prednisone; G = gemcitabine; V = vincristine; Pola = polatuzumab vedotin

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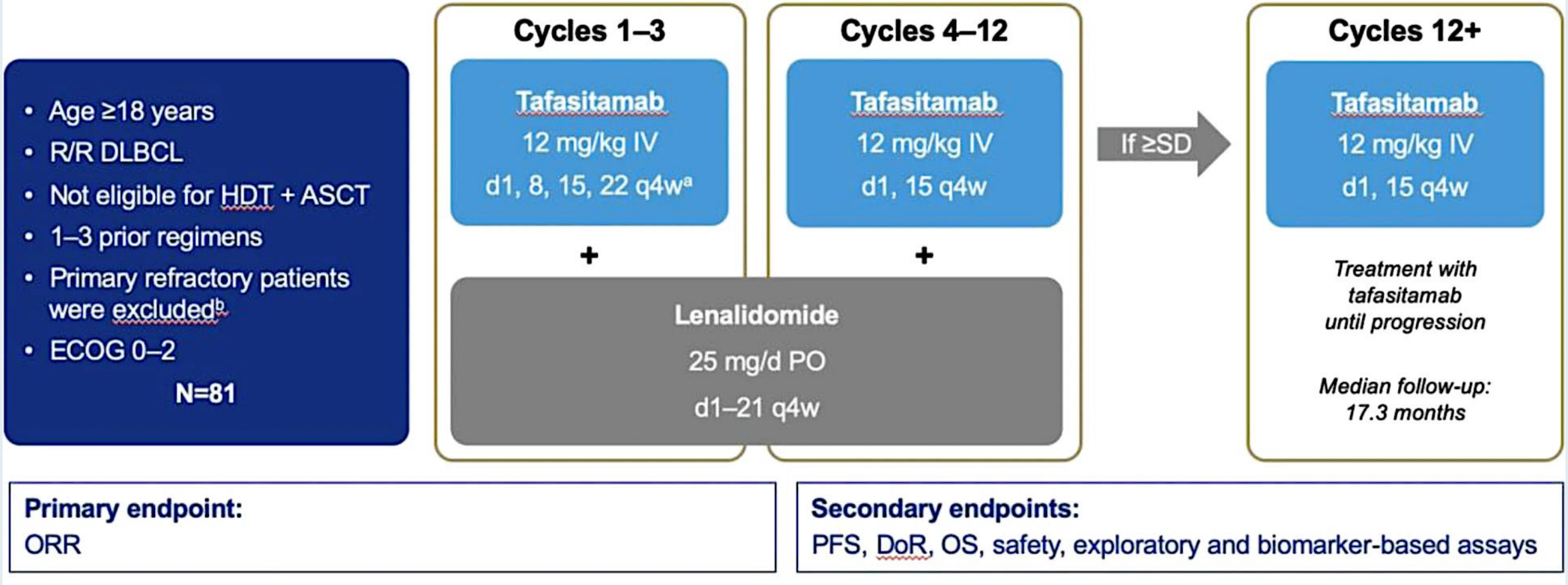
Module 6: Clinician Survey Results

RTP RESEARCH TO PRACTICE

Key Datasets

- Duell J et al. **Tafasitamab** for patients with **relapsed or refractory diffuse large B-cell lymphoma: Final 5-year efficacy and safety findings** in the phase II **L-MIND** study. *Haematologica* 2024 February 1;109(2):553-66.
- Arias DA et al. **CD19 expression** persists in **diffuse large B-cell lymphoma** patient biopsies after treatment with **tafasitamab**. EHA 2024;Abstract P1234.
- Kim TM et al. **Safety and efficacy** of **AZD0486**, a **CD19xCD3 T-cell engager**, in **relapsed or refractory diffuse large B-cell lymphoma**. ASCO 2025;Abstract 7046.
- Dickinson MJ et al. **Glofitamab** for **relapsed or refractory diffuse large B-cell lymphoma**. *N Engl J Med* 2022 December 15;387(24):2220-31.
- Karimi YH et al. **3-year update** from the **Epcore NHL-1 trial**: **Epcoritamab** leads to deep and durable responses in **relapsed or refractory large B-cell lymphoma.**. ASH 2024;Abstract 4480.
- Abramson JS et al. **Glofitamab plus gemcitabine and oxaliplatin (GemOx)** versus rituximab-GemOx for **relapsed or refractory diffuse large B-cell lymphoma (STARGLO):** A global **phase 3**, randomised, **open-label** trial. *Lancet* 2024 November 16;404(10466):1940-54.

Phase II L-MIND Study Design



HDT = high-dose therapy; ASCT = autologous stem cell transplant; SD = stable disease; DoR = duration of response

Duell J et al. *Haematologica* 2024 February 1;109(2):553-66.

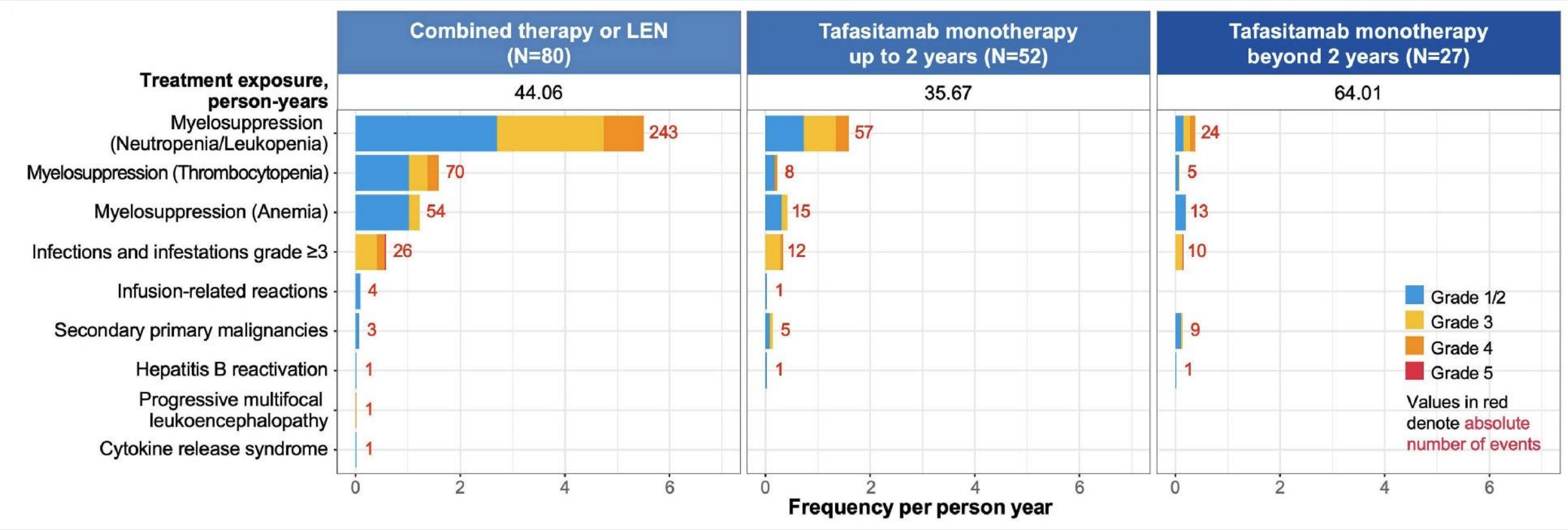
Phase II L-MIND: Efficacy Outcomes (Primary, 3-Year, 5-Year Analyses)

Characteristics	Primary analysis	3-year follow-up	Final 5-year data	5-year data for patients with 1 prior line of therapy, N=40	5-year data for patients with ≥2 prior lines of therapy, N=40
Data cut-off date	Nov 30, 2018	Oct 30, 2020	Nov 14, 2022	Nov 14, 2022	Nov 14, 2022
Best ORR, N (%) [95% CI]	48 (60.0) [48.4-70.9]	46 (57.5) [45.9-68.5]	46 (57.5) [45.9-68.5]	27 (67.5) [50.9-81.4]	19 (47.5) [31.5-63.9]
CR rate, N (%) [95% CI]	34 (42.5) [32.0-54.0]	32 (40.0) [29.2-51.6]	33 (41.3) [30.4-52.8]	21 (52.5) [36.1-68.5]	12 (30.0) [16.6-46.5]
PR rate, N (%) [95% CI]	14 (17.5) [10.0-28.0]	14 (17.5) [9.9-27.6]	13 (16.3) [8.9-26.2]	6 (15.0) [5.7-29.8]	7 (17.5) [7.3-32.8]
Median DoR in months [95% CI]	21.7 [21.7-NR]	43.9 [26.1-NR]	NR [33.8-NR]	NR [9.1-NR]	NR [26.1-NR]
Median PFS in months [95% CI]	12.1 [5.7-NR]	11.6 [6.3-45.7]	11.6 [5.7-45.7]	23.5 [7.4-NR]	7.6 [2.7-45.5]
Median OS in months [95% CI]	NR [18.3-NR]	33.5 [18.3-NR]	33.5 [18.3-NR]	NR [24.6-NR]	15.5 [8.6-45.5]

ORR: objective response rate; 95% CI: 95% confidence interval; CR: complete response; PR: partial response; DoR: duration of response; NR: not reached; PFS: progression-free survival; OS: overall survival.

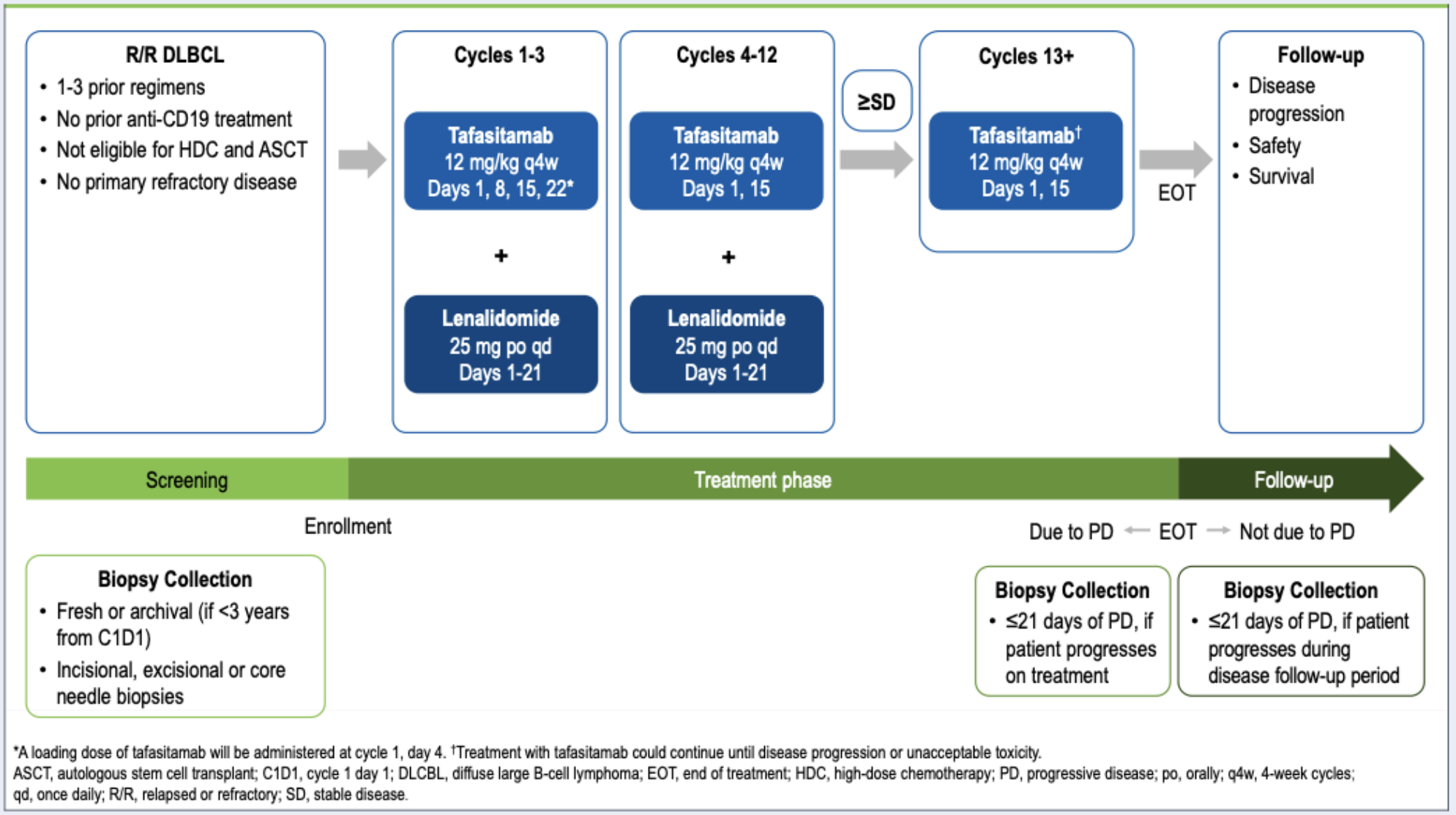
Duell J et al. *Haematologica* 2024 February 1;109(2):553-66.

Phase II L-MIND: Adverse Events of Special Interest



Duell J et al. *Haematologica* 2024 February 1;109(2):553-66.

Phase III firmMIND Study Design

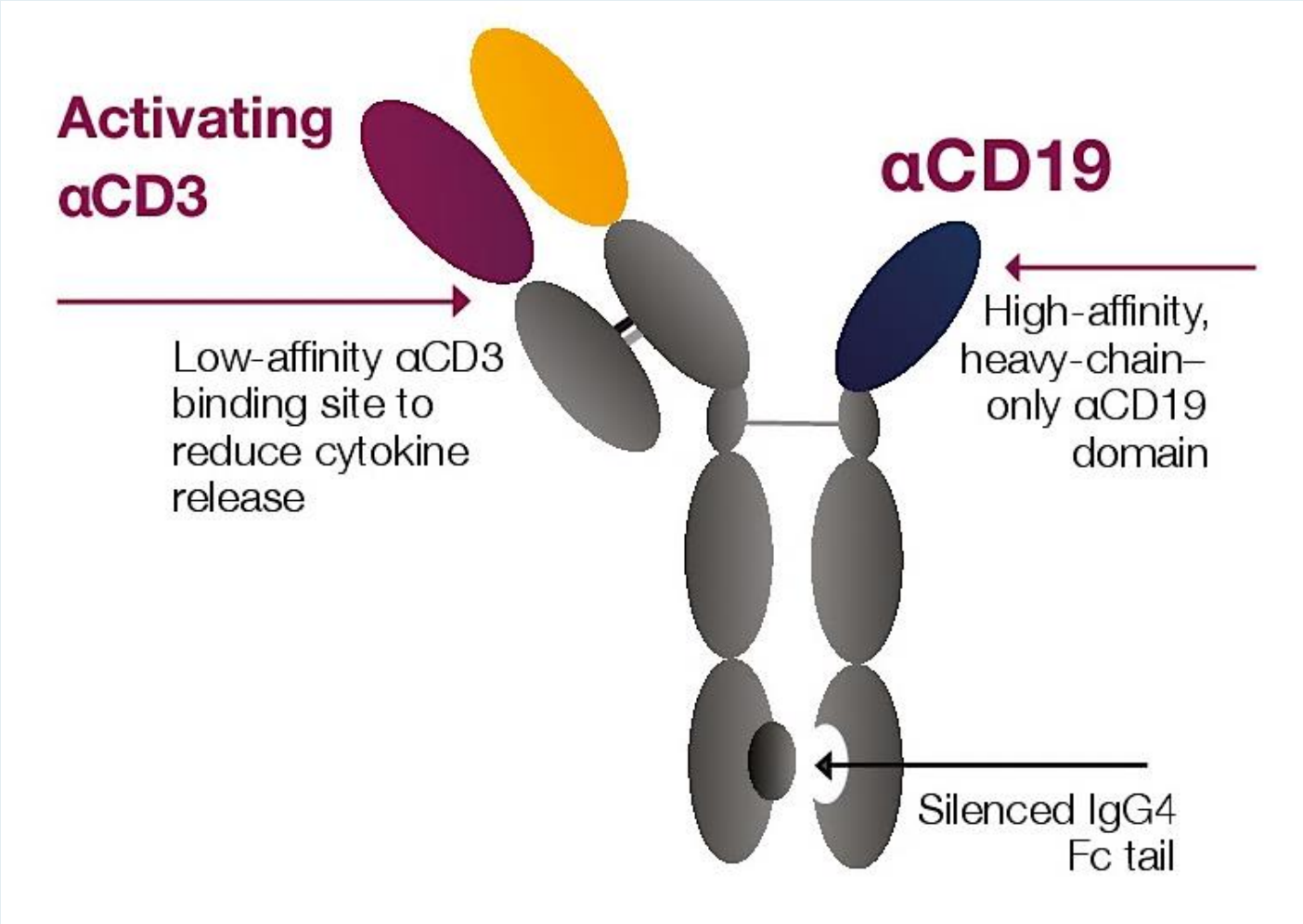


*A loading dose of tafasitamab will be administered at cycle 1, day 4. †Treatment with tafasitamab could continue until disease progression or unacceptable toxicity.
ASCT, autologous stem cell transplant; C1D1, cycle 1 day 1; DLCBL, diffuse large B-cell lymphoma; EOT, end of treatment; HDC, high-dose chemotherapy; PD, progressive disease; po, orally; q4w, 4-week cycles; qd, once daily; R/R, relapsed or refractory; SD, stable disease.

Estimated completion (primary): 2026-04-01

Arias DA et al. EHA 2024;Abstract P1234.

AZD0486: A CD19 x CD3 Bispecific T-Cell Engager



Le Gouill S et al. ASCO 2025;Abstract TPS7083.

Phase I AZD0486 Study: Responses by Target Dose (≥7.2 mg)

	Overall (N=58)			CAR-T Naive (n=31)			CAR-T Exposed (n=27)		
	n	ORR	CR rate	n	ORR	CR rate	n	ORR	CR rate
7.2 mg	24	46%	33%	9	67%	44%	15	33%	27%
15 mg	26	62%	39%	16	75%	38%	10	40%	40%
25 mg	8	75%	63%	6	83%	67%	2	50%	50%

Kim TM et al. ASCO 2025;Abstract 7046.

Phase I AZD0486 Study: Safety

Most common AEs (≥15%)	Any grade	Grade 3	Grade 4
CRS	42 (49)	0	0
Infections and infestations[b]	39 (45)	10 (12)	1 (1)
Neutropenia	29 (34)	9 (10)	15 (17)
Constipation	21 (24)	0	0
Anemia	20 (23)	14 (16)	0
Fatigue	20 (23)	3 (3)	0
ICANS	17 (20)	5 (6)	0
Hypogammaglobulinemia	16 (19)	0	0
Nausea	16 (19)	1 (1)	0
Diarrhea	14 (16)	0	0
Pyrexia	13 (15)	0	0

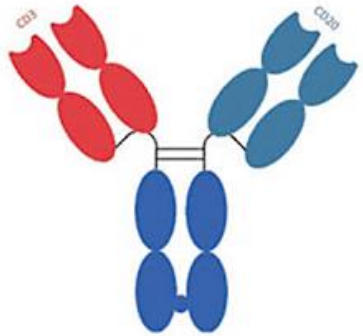
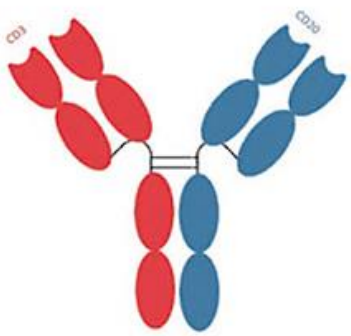
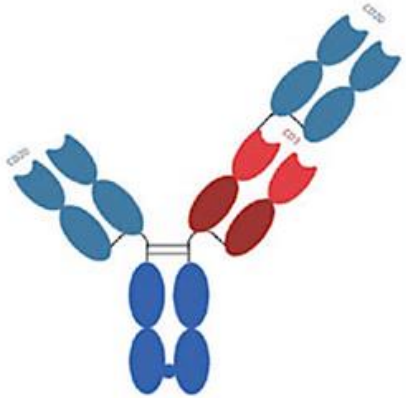
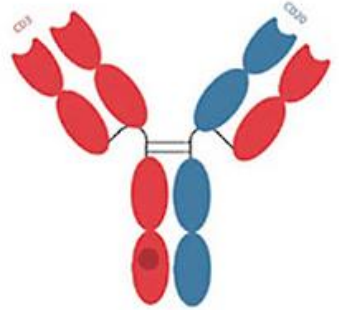
Values are n (%).
[a]All patients eventually received TD.
[b]Grouped by system organ class. One grade 5 event reported (pneumonia). COVID-19 infections reported in 9 (10%) patients (n=3 grade 1; n=6 grade 2).

AEs = adverse events; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome

AZD0486 2SUD cohort (n=70), n (%)	Grade 1	Grade 2	Grade 3	Grade ≥4	Total
CRS	30 (43)	4 (6)	0	0	34 (49)
ICANS	4 (6)	6 (9)	4 (6)	0	14 (20)

Kim TM et al. ASCO 2025;Abstract 7046.

Bispecifics for DLBCL

	BLINATUMOMAB	MOSUNETUZUMAB	EPCORITAMAB	GLOFITAMAB	ODRONEXTAMAB
TARGET	CD3xCD19	CD3xCD20	CD3xCD20	CD3x$(CD20)_2$	CD3xCD20
DESIGN					
	• Monovalent CD3 and monovalent CD19 binding • Two murine scFv-joined by a glycine–serine linker	• Monovalent CD3 and monovalent CD20 binding • Humanized mouse IgG1-based antibody	• Monovalent CD3 and monovalent CD20 binding • Humanized mouse IgG1-based antibody	• Monovalent CD3 and bivalent CD20 binding • Humanized mouse IgG1-based antibody	• Monovalent CD3 and monovalent CD20 binding • Fully human IgG4-based antibody

Brijs J et al. *Belg J Hematol* 2023;14(2):67-72.

Glofitamab for R/R DLBCL Study: Efficacy (IRC- and Investigator-Assessed)

Outcome	Assessment According to Independent Review Committee (N=155)	Assessment According to Investigator (N=155)
Complete response		
No. of patients with response	61	58
Percentage of patients (95% CI)	39 (32–48)	37 (30–46)
Objective response		
No. of patients with response	80	89
Percentage of patients (95% CI)	52 (43–60)	57 (49–65)
Duration of complete response†		
Median (95% CI) — mo	NR (16.8–NR)	19.8 (18.2–NR)
Complete response at 12 mo (95% CI) — %	78 (64–91)	72 (59–86)
Duration of objective response‡		
Median (95% CI) — mo	18.4 (13.7–NR)	10.4 (6.8–NR)
Objective response at 12 mo (95% CI) — %	64 (51–76)	49 (37–61)
Median time to first complete response (range) — days†	42 (31–308)	43 (31–274)
Progression-free survival		
Median (95% CI) — mo	4.9 (3.4–8.1)	3.8 (3.3–5.4)
Alive without progression at 12 mo (95% CI) — %	37 (29–46)	30 (22–38)
Overall survival		
Median (95% CI) — mo	—	11.5 (7.9–15.7)
Alive at 12 mo (95% CI) — %	—	50 (41–58)

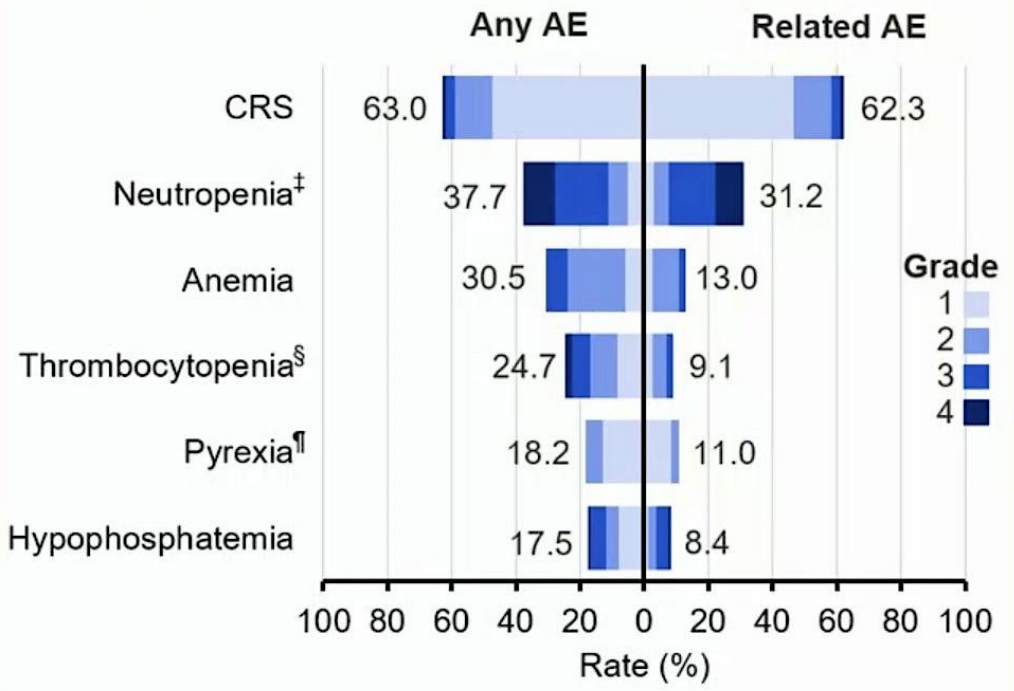
Dickinson MJ et al. *N Engl J Med* 2022 December 15;387(24):2220-31.

IRC = independent review committee

Glofitamab for R/R DLBCL: Safety

n (%)*	N=154
Median no. of cycles received (range)	5 (1–13)
Median relative dose intensity, % (range)	100 (94–100)
AE	152 (98.7)
Related AE	140 (90.9)
Grade 3–4 AE	87 (56.5)
Related AE	64 (41.6)
Serious AE	73 (47.4)
Related AE	46 (29.9)
Grade 5 (fatal AE)	8 (5.2)†
Related AE	0
AE leading to treatment discontinuation	14 (9.1)
Related AE	5 (3.2)

AEs (≥15%) by grade and relationship with glofitamab

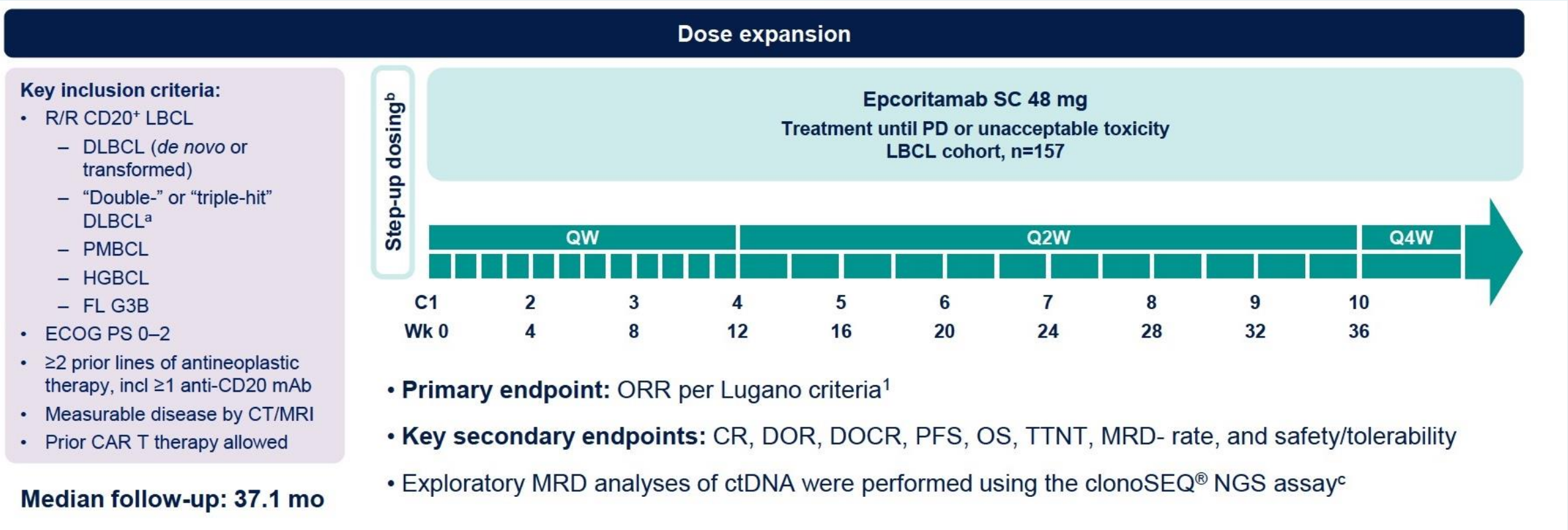


Glofitamab was well tolerated, with a favorable safety profile

*unless otherwise specified; †COVID-19/COVID-19 pneumonia (n=5); sepsis (n=2); delirium (n=1);
‡includes neutrophil count decreased; §includes platelet count decreased; ¶pyrexia events separate from CRS.

Dickinson MJ et al. EHA 2022;Abstract S220.

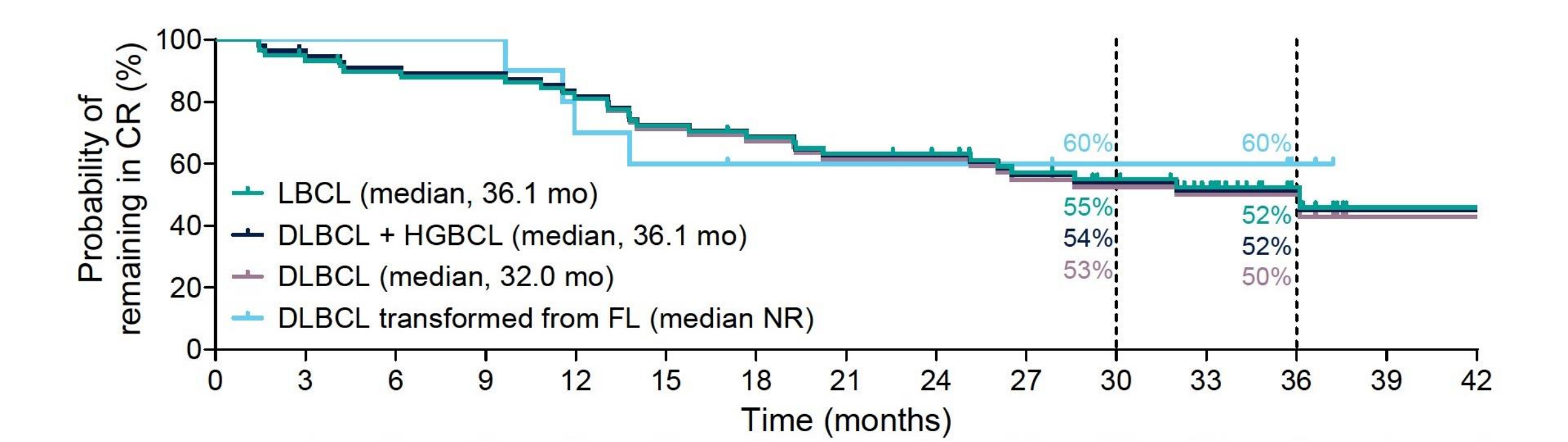
Phase II EPCORE NHL-1 Study Design



PMBCL = primary mediastinal B-cell lymphoma; HGBCL = high-grade B-cell lymphoma; FL = follicular lymphoma; DOCR = duration of complete response; TTNT = time to next treatment; MRD = minimal residual disease; ctDNA = circulating tumor DNA

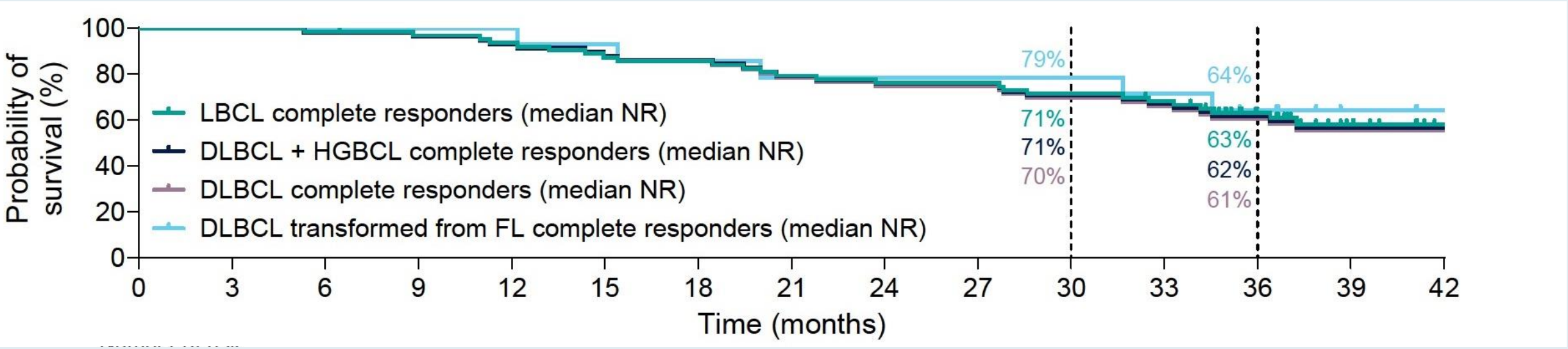
Karimi YH et al. ASH 2024;Abstract 4480.

Phase II EPCORE NHL-1: Responses



Karimi YH et al. ASH 2024;Abstract 4480.

Phase II EPCORE NHL-1: Overall Survival



Karimi YH et al. ASH 2024;Abstract 4480.

The Manufacturer Announces Topline Results for Epcoritamab from Phase III EPCORE DLBCL-1 Trial in Patients with R/R DLBCL

Press Release: January 16, 2026

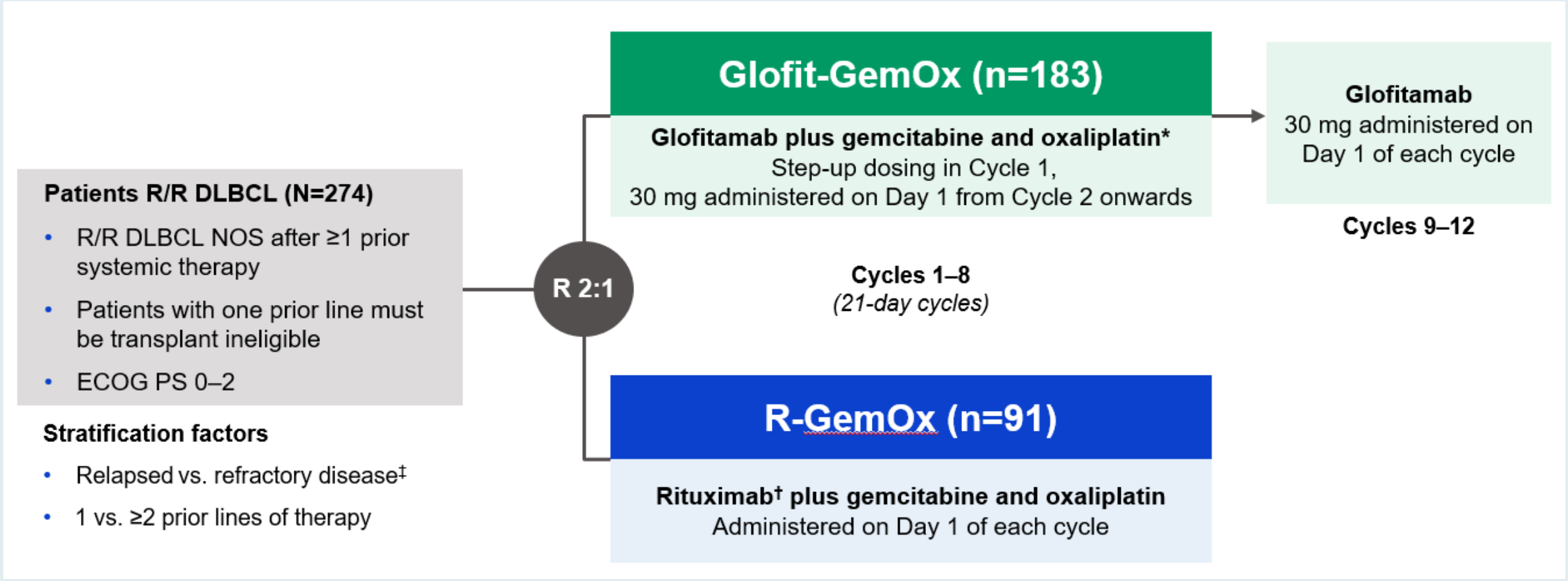
“On January 16, 2026, [the manufacturer] today announced topline results from the Phase 3 EPCORE DLBCL-1 trial evaluating epcoritamab, a T-cell engaging bispecific antibody administered subcutaneously, compared to investigator's choice of chemoimmunotherapy in adult patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). The study demonstrated an improvement in progression-free survival (PFS) (HR: 0.74 [95% CI 0.60 to 0.92]). Improvements were observed in complete response rates (CRR), duration of response (DoR), and time to next treatment among patients treated with epcoritamab. The study did not demonstrate a statistically significant improvement in overall survival (OS) (HR: 0.96 [95% CI 0.77 to 1.20]).

EPCORE DLBCL-1 is the first Phase 3 study to demonstrate improvement in PFS in patients with R/R DLBCL who were treated with a CD3xCD20 T-cell engaging bispecific monotherapy. The global study enrolled 483 patients with R/R DLBCL with at least one prior line of therapy (73% had received two or more prior lines) who were ineligible for high-dose chemotherapy and autologous stem cell transplant (HDT-ASCT).

The data will be submitted for presentation at a future medical meeting, and [the manufacturers] will engage global regulatory authorities to determine next steps.”

https://news.abbvie.com/2026-01-16-AbbVie-Announces-Topline-Results-for-Epcoritamab-DuoBody-R-CD3xCD20-from-Phase-3-EPCORE-R-DLBCL-1-Trial-in-Patients-with-Relapsed-Refractory-Diffuse-Large-B-cell-Lymphoma-DLBCL

Phase III STARGLO Study Design

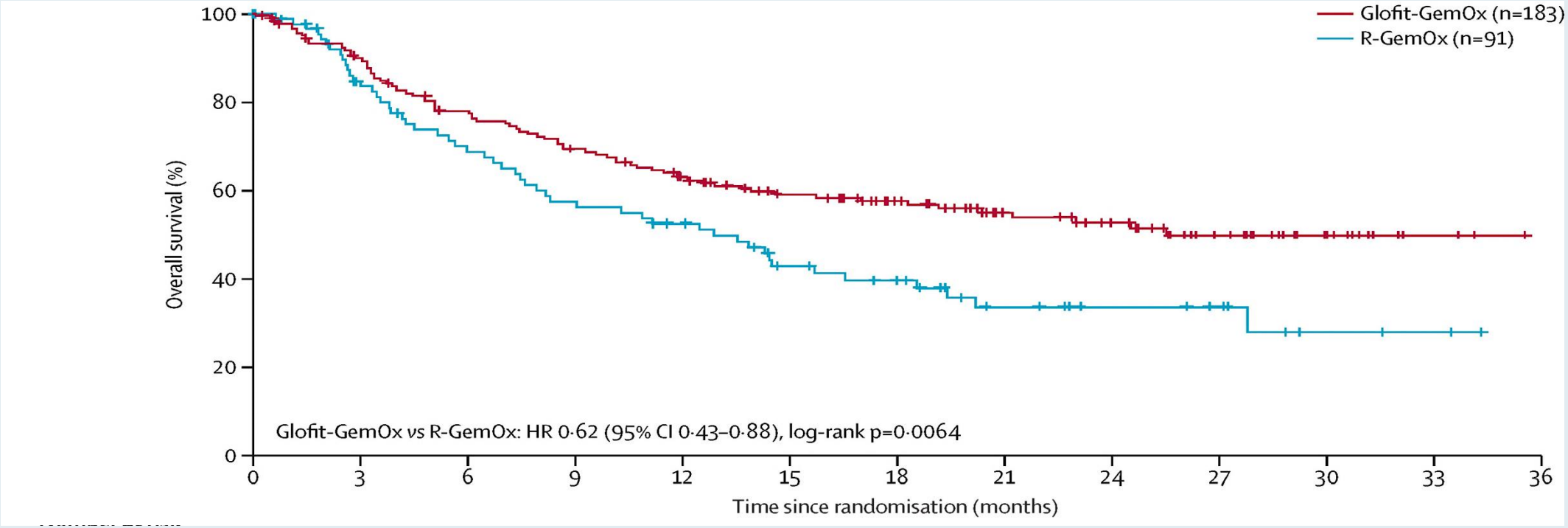


Primary endpoint:
Overall survival

Secondary endpoints:
Progression-free survival, ORR, DoR

Abramson JS et al. *Lancet* 2024 November 16;404(10466):1940-54.

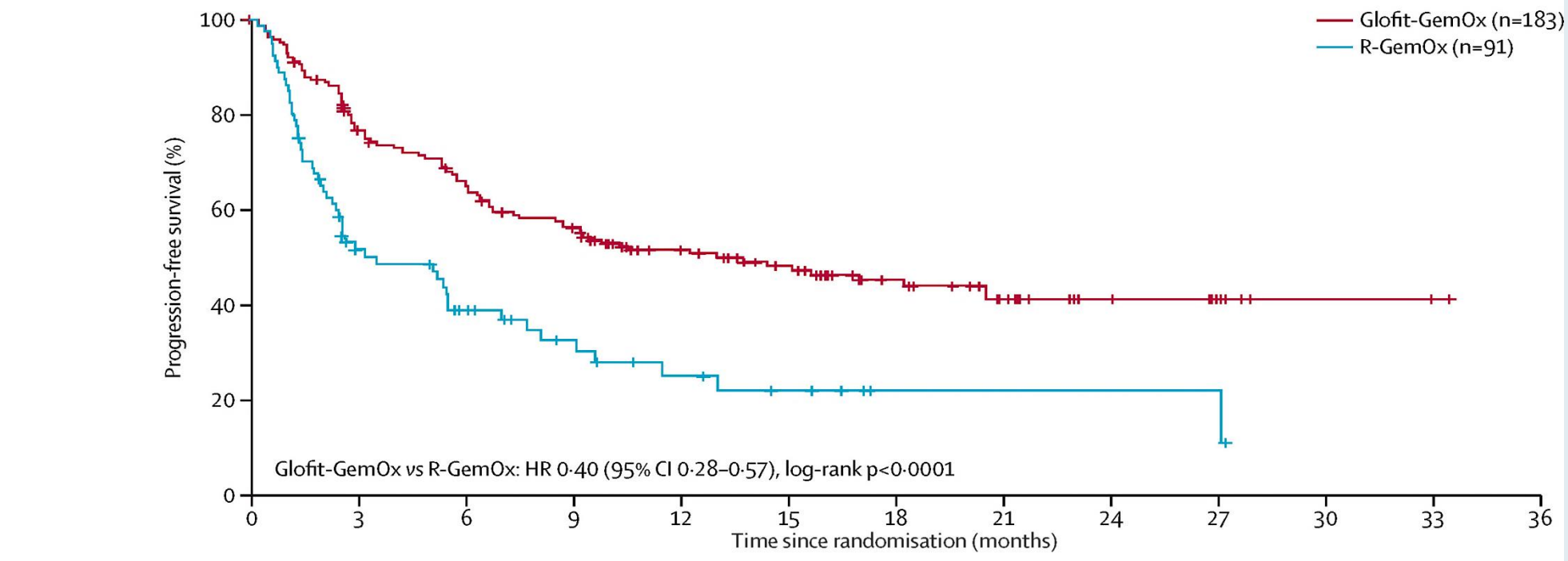
Phase III STARGLO: Overall Survival (Primary Endpoint)



	R-GemOx (n=91)	Glofit-GemOx (n=183)	p value*
Primary endpoint			
Investigator-assessed overall survival	..	..	..
HR	..	0·62 (0·43–0·88)†	p=0·0064†
Median, months	12·9 (7·9–18·5)	25·5 (18·3–NE)	..
24-month rate, %	33·5 (22·2–44·9)	52·8 (44·8–60·7)	..

Abramson JS et al. *Lancet* 2024 November 16;404(10466):1940-54.

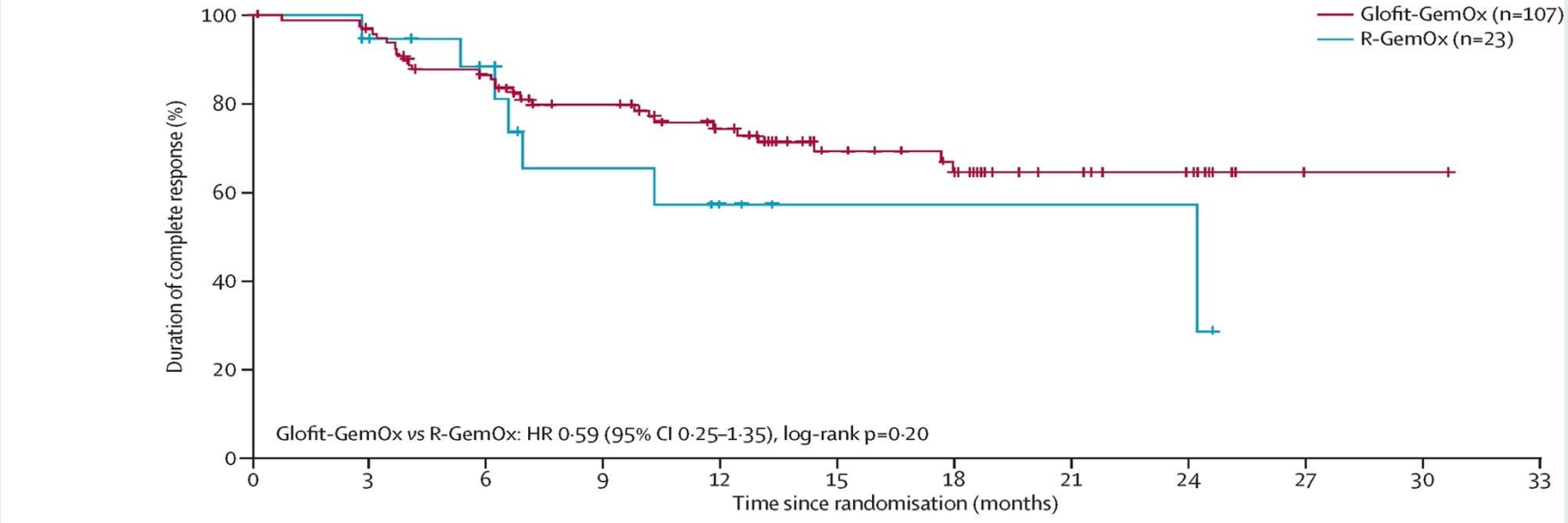
Phase III STARGLO: Progression-Free Survival



	R-GemOx (n=91)	Glofit-GemOx (n=183)	p value*
Secondary endpoints			
IRC-assessed progression-free survival	..	..	..
HR	..	0·40 (0·28–0·57)†	p<0·0001†
Median, months	3·6 (2·5–7·1)	13·8 (8·7–20·5)	..
12-month rate, %	25·2 (13·6–36·9)	51·7 (44·0–59·4)	..
Investigator-assessed progression-free survival	..	..	..
HR	..	0·32 (0·23–0·45)†	p<0·0001†
Median, months	2·7 (2·2–5·3)	14·4 (9·2–24·6)	..
12-month rate, %	20·5 (10·7–30·3)	53·2 (45·5–60·9)	..

Abramson JS et al. *Lancet* 2024 November 16;404(10466):1940-54.

Phase III STARGLO: Responses



	R-GemOx (n=91)	Glofit-GemOx (n=183)	p value*
Secondary endpoints			
IRC-assessed best overall response‡, %	..	..	..
Objective response	40·7 (30·5–51·5)	68·3 (61·0–75·0)	p<0·0001†
Complete response	25·3 (16·8–35·5)	58·5 (51·0–65·7)	p<0·0001†
Investigator-assessed best overall response‡, %	..	..	..
Objective response	37·4 (27·4–48·1)	69·9 (62·7–76·5)	p<0·0001†
Complete response	23·1 (14·9–33·1)	57·4 (49·9–64·6)	p<0·0001†
IRC-assessed duration of complete response	n=23	n=107	..
HR	..	0·59 (0·25–1·35)§	p=0·20§
Median, months	24·2 (6·9–NE)	NE (NE–NE)	..
IRC-assessed duration of objective response	n=37	n=125	..
HR	..	0·57 (0·30–1·10)§	p=0·089§
Median, months	10·3 (6·5–NE)	NE (17·6–NE)	..

Abramson JS et al. *Lancet* 2024 November 16;404(10466):1940-54.

Phase III STARGLO: Safety

	R-GemOx (n=88)	Glofit-GemOx (n=180)
Any adverse event	84 (96%)	180 (100%)
Most common adverse event (≥30% patients in either group)		
Thrombocytopenia*	42 (48%)	87 (48%)
CRS†	NA	76 (44%)†
Neutropenia‡	27 (31%)	76 (42%)
Anaemia	19 (22%)	73 (41%)
Nausea	35 (40%)	71 (39%)
Peripheral neuropathy§	23 (26%)	64 (36%)
Diarrhoea	24 (27%)	62 (34%)
Aspartate transferase increased	17 (19%)	59 (33%)
Alanine transaminase increased	19 (22%)	57 (32%)
Any glofitamab-related or rituximab-related adverse event	58 (66%)	149 (83%)
Any grade ≥3 adverse event	36 (41%)	140 (78%)
Any glofitamab-related or rituximab-related grade ≥3 adverse event	20 (23%)	85 (47%)
Any serious adverse event	15 (17%)	98 (54%)
Any glofitamab-related or rituximab-related serious adverse event	7 (8%)	62 (34%)
Any adverse event of special interest	69 (78%)	176 (98%)
CRS†	NA	76 (44%)†
Grade 1	NA	54 (31%)†
Grade 2	NA	18 (11%)†
Grade 3	NA	4 (2%)†
Neurological adverse event (grade ≥2)	11 (13%)	55 (31%)
Serious infections	11 (13%)	46 (26%)
Febrile neutropenia	1 (1%)	6 (3%)
Tumour flare (grade ≥2)	1 (1%)	1 (1%)
Any grade 5 adverse event	4 (5%)	15 (8%)

Abramson JS et al. *Lancet* 2024 November 16;404(10466):1940-54.

RTP RESEARCH TO PRACTICE

Optimizing the Use of Novel Therapies for Patients with DLBCL

Module 1: Selection of First-Line Therapy for Patients with Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Clinician Survey Results

Module 3: Current and Future Roles of Monoclonal and Bispecific Antibodies in Therapy for Relapsed/Refractory (R/R) DLBCL

Module 4: Clinician Survey Results

Module 5: Evidence-Based Incorporation of Antibody-Drug Conjugates into the Management of R/R DLBCL

Module 6: Clinician Survey Results

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which second-line therapy would you generally recommend for an older (85-year-old) patient with DLBCL who experienced disease relapse 18 months after first-line R-CHOP and who was …

	CAR T eligible but transplant ineligible	Transplant *and* CAR T ineligible
 Dr Abramson	CAR T-cell therapy	Mosunetuzumab/polatuzumab vedotin
 Dr Kahl	CAR T-cell therapy	Mosunetuzumab/polatuzumab vedotin
 Dr Kamdar	CAR T-cell therapy	Tafasitamab/lenalidomide or glofitamab/GemOx
 Dr LaCasce	CAR T-cell therapy	Mosunetuzumab/polatuzumab vedotin
 Dr Matasar	CAR T-cell therapy	Glofitamab/GemOx
 Dr Phillips	Mosunetuzumab/polatuzumab vedotin	Mosunetuzumab/polatuzumab vedotin
 Prof Salles	Glofitamab/GemOx	Glofitamab/GemOx
 Dr Westin	CAR T-cell therapy	Tafasitamab/lenalidomide or mosunetuzumab/polatuzumab vedotin

GemOx = gemcitabine/oxaliplatin

Regulatory and reimbursement issues aside, which third-line therapy would you generally recommend for a 65-year-old patient with DLBCL who received first-line R-CHOP and subsequently experienced disease progression on second-line CAR T-cell therapy?

 Dr Abramson	Glofitamab/GemOx
 Dr Kahl	Glofitamab
 Dr Kamdar	Glofitamab
 Dr LaCasce	Glofitamab
 Dr Matasar	Polatuzumab vedotin/R-GemOx
 Dr Phillips	Glofitamab/polatuzumab vedotin
 Prof Salles	Glofitamab/GemOx or polatuzumab vedotin/glofitamab
 Dr Westin	Glofitamab/GemOx or polatuzumab vedotin/glofitamab

R-GemOx = rituximab/gemcitabine/oxaliplatin

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which third-line therapy would you generally recommend for a 65-year-old patient with DLBCL who received first-line polatuzumab vedotin/R-CHP and subsequently experienced disease progression on second-line CAR T-cell therapy?

 Dr Abramson	Glofitamab/GemOx
 Dr Kahl	Glofitamab
 Dr Kamdar	Glofitamab
 Dr LaCasce	Glofitamab
 Dr Matasar	Loncastuximab tesirine
 Dr Phillips	Glofitamab/GemOx
 Prof Salles	Glofitamab/GemOx
 Dr Westin	Glofitamab/GemOx

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which third-line therapy would you generally recommend for an 85-year-old patient with DLBCL who received first-line R-mini-CHOP and subsequently experienced disease progression on second-line polatuzumab vedotin with bendamustine/rituximab (BR)?

 Dr Abramson	Glofitamab
 Dr Kahl	Glofitamab
 Dr Kamdar	Glofitamab
 Dr LaCasce	Glofitamab
 Dr Matasar	Glofitamab/GemOx
 Dr Phillips	Glofitamab or epcoritamab
 Prof Salles	Glofitamab/GemOx
 Dr Westin	Glofitamab or epcoritamab

Assuming equal access, which bispecific antibody would you prefer to use when administering one of these agents as monotherapy for your patients with R/R DLBCL?

 Dr Abramson	Glofitamab
 Dr Kahl	Glofitamab
 Dr Kamdar	Glofitamab
 Dr LaCasce	Glofitamab
 Dr Matasar	Glofitamab
 Dr Phillips	No preference
 Prof Salles	Glofitamab
 Dr Westin	Glofitamab

RTP RESEARCH TO PRACTICE

Based on the published literature and your clinical experience, would you like to have access to surovatamig for your patients with R/R DLBCL today?

 Dr Abramson	Yes, for patients with CD20-negative disease
 Dr Kahl	Yes, for patients who are ineligible for CAR T or who have lost CD20 expression and are ineligible for glofitamab and epcoritamab
 Dr Kamdar	Yes, for CAR T-ineligible pts in the second-line setting
 Dr LaCasce	Yes, for patients who are ineligible for CD19 CAR T
 Dr Matasar	No
 Dr Phillips	Yes, after CAR T-cell therapy
 Prof Salles	Yes, for patients with PD on CD3 x CD20 combinations or monotherapy, and for those with CD20-negative disease
 Dr Westin	Yes, for patients with CD20 loss and non-CAR T eligible

RTP RESEARCH TO PRACTICE

If surovatamig were granted regulatory approval, would you employ a CD20 x CD3 bispecific antibody and surovatamig in sequence for the same patient with R/R DLBCL?

 Dr Abramson	Yes
 Dr Kahl	Yes
 Dr Kamdar	Yes
 Dr LaCasce	Maybe
 Dr Matasar	Yes
 Dr Phillips	Yes
 Prof Salles	Yes
 Dr Westin	Yes

RTP RESEARCH TO PRACTICE

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Module 5: Evidence-Based Incorporation of Antibody-Drug Conjugates into the Management of R/R DLBCL

Module 6: Clinician Survey Results

RTP RESEARCH TO PRACTICE

Key Datasets

- Sehn LH et al. **Polatuzumab vedotin plus bendamustine and rituximab in relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL): Final results of a phase Ib/II randomized study and single-arm extension (ext) study**. ASH 2022;Abstract 4260.
- Matasar M et al. **Polatuzumab vedotin, rituximab, gemcitabine and oxaliplatin (Pola-R-GemOx) for relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL): Results** from the randomized **phase III POLARGO** trial. EHA 2025;Abstract S101.
- Budde LE et al. **Mosunetuzumab plus polatuzumab vedotin in transplant-ineligible refractory/relapsed large B-cell lymphoma: Primary results** of the **phase III SUNMO trial.** *J Clin Oncol* 2025 December 20;43(36):3799-811.
- Kim JA et al. **Brentuximab vedotin in combination with lenalidomide and rituximab** in patients with **relapsed/refractory diffuse large B-cell lymphoma: Results** from the **phase 3 ECHELON-3** study**.** ASCO 2024;Abstract LBA7005.
- Caimi PF et al. **Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: Long-term efficacy and safety from the phase II LOTIS-2 study.** *Haematologica* 2024 April 1;109(4):1184-93.
- Carlo-Stella C et al. **Updated safety run-in results** from **LOTIS-5:** A **phase 3,** randomized trial of **loncastuximab tesirine with rituximab** versus immunochemotherapy in patients with **R/R DLBCL/HGBL**. EHA 2025;Abstract PS1957.
- Alderuccio JP et al. **Initial results from LOTIS-7: A phase 1b** study of **loncastuximab tesirine plus glofitamab** in patients with **relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL)**. ICML 2025;Abstract 078.

RTP RESEARCH TO PRACTICE

Phase Ib/II GO29365 Study Final Results: Efficacy

Outcome*	Randomized		Extension
	Pola+BR (n=40)	BR (n=40)	Pola+BR (n=106)
ORR, % (95% CI)	42.5 (27.0–59.1)	17.5 (7.3–32.8)	43.4 (33.8–53.4)
CR, % (95% CI)	42.5 (27.0–59.1)	17.5 (7.3–32.8)	39.6 (30.3–49.6)
BOR, % (95% CI)	62.5 (45.8–77.3)	25.0 (12.7–41.2)	57.5 (47.6–67.1)
BCR, % (95% CI)	52.5 (36.1–68.5)	22.5 (10.8–38.5)	53.8 (43.8–63.5)
Median DOR, months (95% CI)	10.9 (5.7–40.7)	10.6 (4.0–19.7)	13.4 (8.6–20.0)
Median PFS, months (95% CI)	9.2 (6.0–13.9)	3.7 (2.1–4.5)	7.0 (5.1–9.8)
Median OS, months (95% CI)	12.4 (9.0–32.0)	4.5 (3.7–6.0)	12.3 (8.3–17.0)

*All endpoints were determined by IRC, except OS, which was INV-determined.
BCR, best complete response; BOR, best overall response; BR, bendamustine + rituximab; CI, confidence interval; CR, complete response; DOR, duration of response; INV, investigator; IRC, independent review committee; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Pola, polatuzumab vedotin.

Sehn LH et al. ASH 2022;Abstract 4260.

Phase Ib/II GO29365 Final Results: Safety

	Randomized		Extension
	Pola+BR (n=39*)	BR (n=39*)	Pola+BR (n=106)
Any-grade AEs, n (%)	39 (100.0)	38 (97.4)	105 (99.1)
Grade 3–4 AEs, n (%)	34 (87.2)	28 (71.8)	83 (78.3)
Neutropenia	18 (46.2)	13 (33.3)	31 (29.2)
Thrombocytopenia	15 (38.5)	9 (23.1)	15 (14.2)
Serious AEs, n (%)	27 (69.2)	24 (61.5)	57 (53.8)
Pyrexia	5 (12.8)	0 (0.0)	7 (6.6)
Pneumonia	4 (10.3)	4 (10.3)	6 (5.7)
Febrile neutropenia	4 (10.3)	4 (10.3)	9 (8.5)
Sepsis	2 (5.1)	2 (5.1)	7 (6.6)
Grade 5 AEs, n (%)	11 (28.2)	10 (25.6)	6 (5.7)
Any-grade PN, n (%)	17 (43.6)	3 (7.7)	29 (27.4)
Grade ≥2 PN	6 (15.4)	2 (5.1)	16 (15.1)
AEs leading to delay of any drug, n (%)	21 (53.8)	14 (35.9)	53 (50.0)
AEs leading to discontinuation of any drug, n (%)	13 (33.3)	5 (12.8)	16 (15.1)

*One patient in each group did not receive study treatment and so was excluded from the safety-evaluable population.

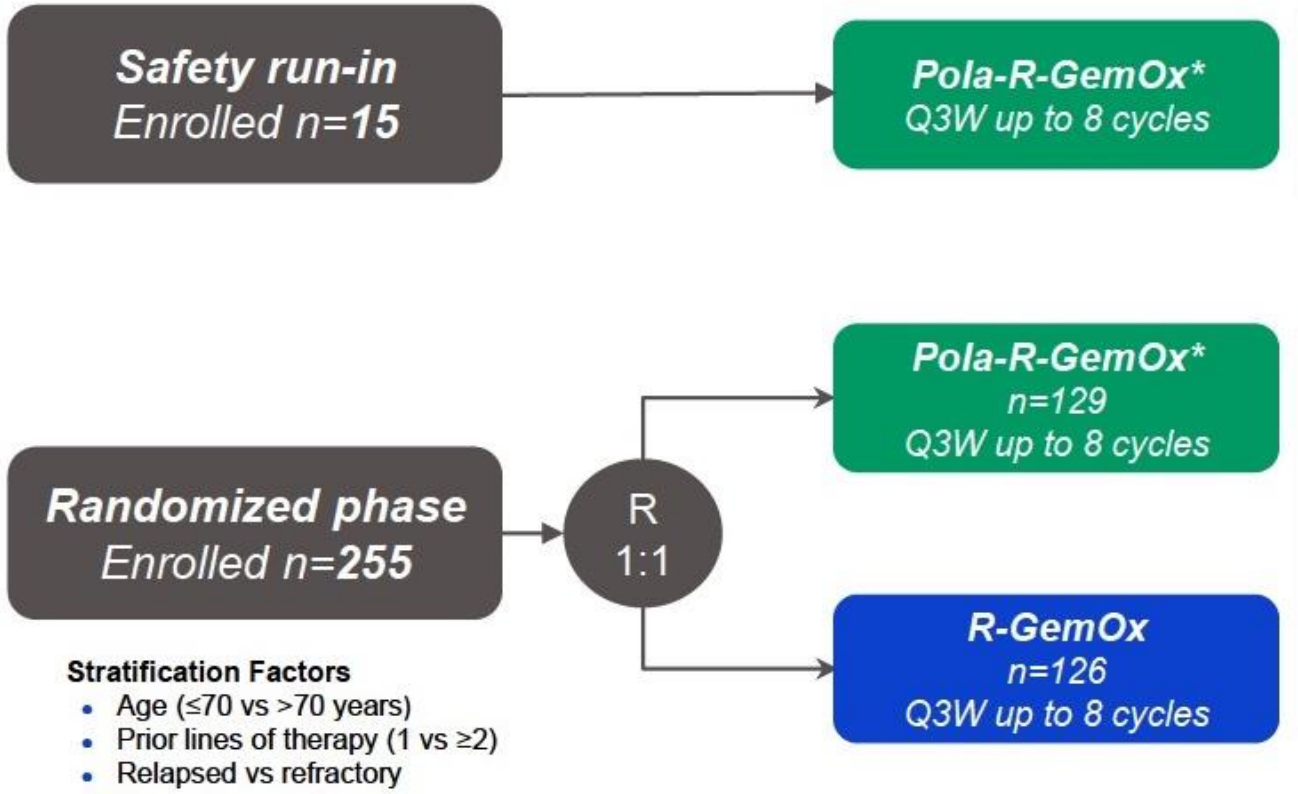
AE, adverse event; BR, bendamustine + rituximab; PN, peripheral neuropathy; Pola, polatuzumab vedotin.

Sehn LH et al. ASH 2022;Abstract 4260.

Phase III POLARGO Study Design

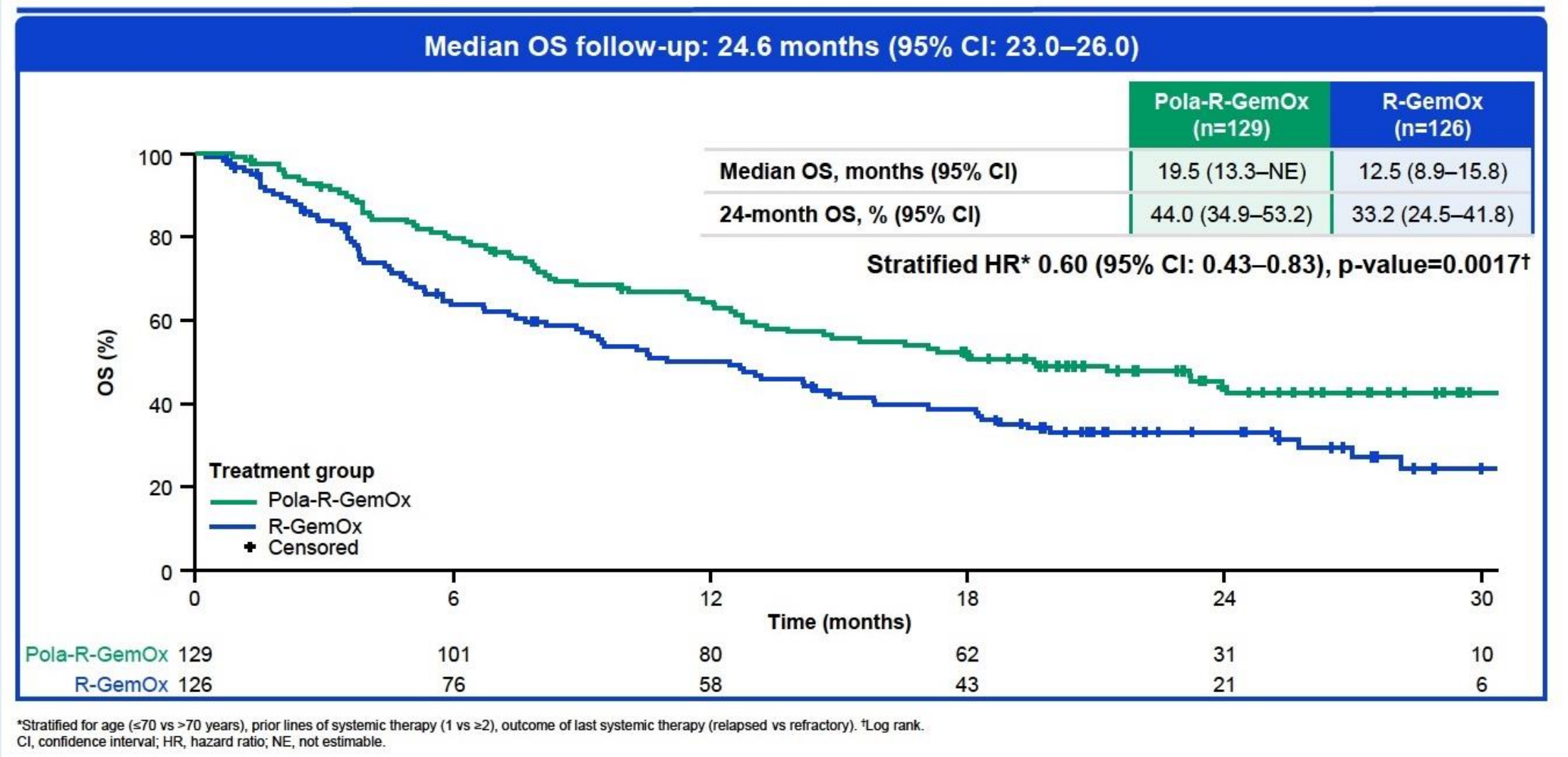
Key eligibility criteria

- DLBCL, NOS or history of transformation of indolent disease to DLBCL
- R/R disease after ≥1 prior line of treatment
- Ineligible for transplant



Matasar M et al. EHA 2025;Abstract S101.

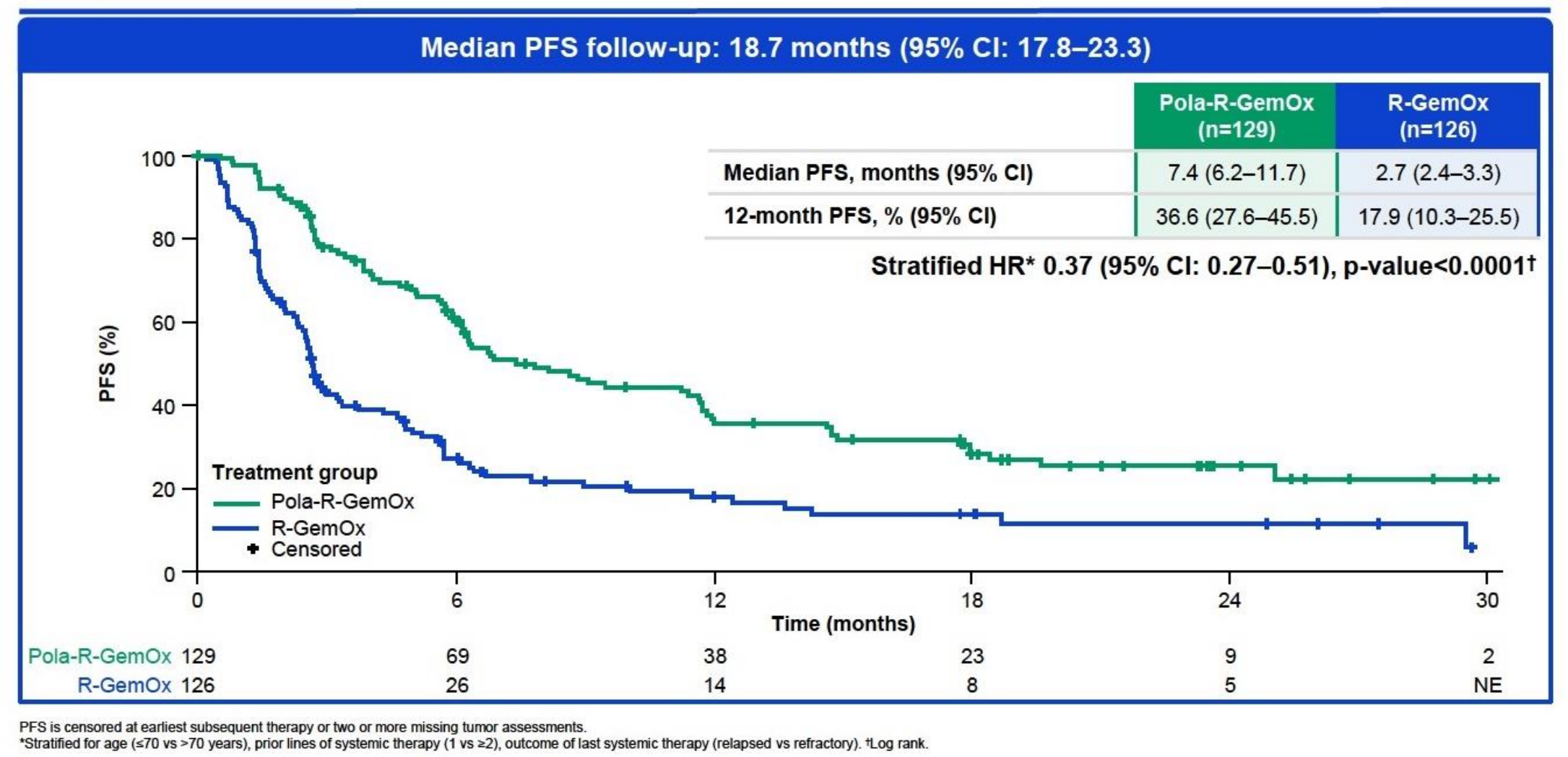
Phase III POLARGO Overall Survival



*Stratified for age (≤70 vs >70 years), prior lines of systemic therapy (1 vs ≥2), outcome of last systemic therapy (relapsed vs refractory). †Log rank.
CI, confidence interval; HR, hazard ratio; NE, not estimable.

Matasar M et al. EHA 2025;Abstract S101.

Phase III POLARGO: Progression-Free Survival



PFS is censored at earliest subsequent therapy or two or more missing tumor assessments.
*Stratified for age (≤70 vs >70 years), prior lines of systemic therapy (1 vs ≥2), outcome of last systemic therapy (relapsed vs refractory). †Log rank.

Matasar M et al. EHA 2025;Abstract S101.

Phase III POLARGO: Select AEs

n (%)	Pola-R-GemOx (n=128)	R-GemOx (n=125)
Thrombocytopenia*	68 (53.1)	51 (40.8)
Grade ≥3	44 (34.4)	33 (26.4)
Neutropenia*	53 (41.4)	52 (41.6)
Grade ≥3	43 (33.6)	38 (30.4)
Febrile neutropenia†	3 (2.3)	3 (2.4)
Grade ≥3	3 (2.3)	3 (2.4)
Anemia*	48 (37.5)	35 (28.0)
Grade ≥3	17 (13.3)	19 (15.2)
Infections*	53 (41.4)	39 (31.2)
Grade ≥3	28 (21.9)	12 (9.6)
Hepatic toxicity*	41 (32.0)	25 (20.0)
Grade ≥ 3	11 (8.6)	2 (1.6)

*Custom grouped terms. †Based on preferred term.

Matasar M et al. EHA 2025;Abstract S101.

RTP RESEARCH TO PRACTICE

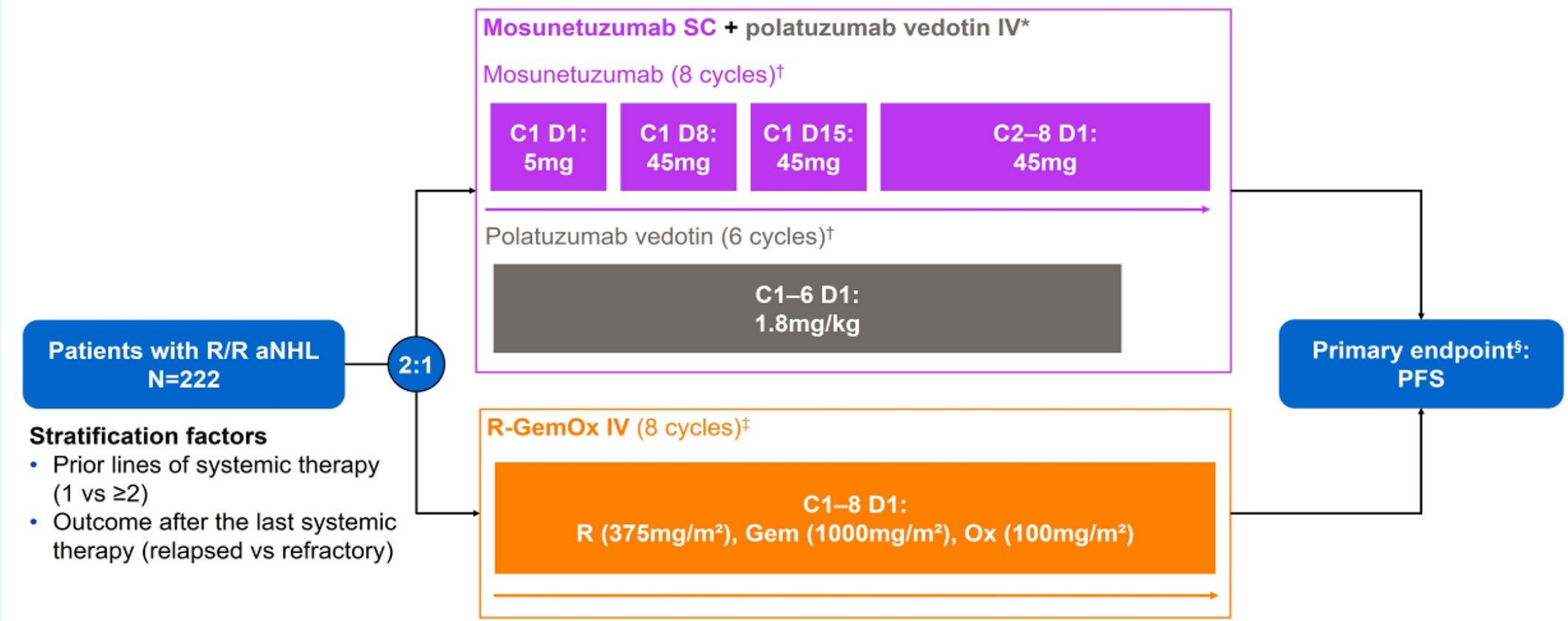
Phase III POLARGO: Peripheral Neuropathy

n (%), unless otherwise specified	Pola-R-GemOx (n=128)	R-GemOx (n=125)
Any Grade PN*	73 (57.0)	36 (28.8)
Grade 1	48 (37.5)	29 (23.2)
Grade 2	20 (15.6)	7 (5.6)
Grade 3	5 (3.9)	0
Median time to onset, months (range)	1.6 (0–8.0)	0.9 (0–4.4)
PN AEs leading to any study drug discontinuation	4 (3.1)	0
Polatuzumab vedotin discontinuation	3 (2.3)	N/A
Number of PN AEs leading to any dose reduction	13 (10.2)	4 (3.2)
Polatuzumab vedotin reduction	13 (10.2)	N/A
Patients with all PN AEs resolved or improved	37 (50.7)	21 (58.3)
Patients with all PN AEs resolved	28 (38.4)	21 (58.3)

*Custom grouped terms.
N/A, not applicable; PN, peripheral neuropathy.

Matasar M et al. EHA 2025;Abstract S101.

Phase III SUNMO Study Design



*Administered as an outpatient regimen. †One cycle is 21 days. ‡One cycle is 14 days and may be adjusted to 21 days. §Secondary endpoints include: OS, investigator-assessed PFS, CR rate, ORR, DoR/CR, and time to deterioration of patient-reported outcomes.
aNHL, aggressive B-cell non-Hodgkin lymphoma; C, cycle; CR, complete response; D, day; DoR, duration of response; Gem, gemcitabine; IV, intravenous; ORR, objective response rate; OS, overall survival; Ox, oxaliplatin; PFS, progression-free survival; R, rituximab; R/R, relapsed/refractory; SC, subcutaneous.

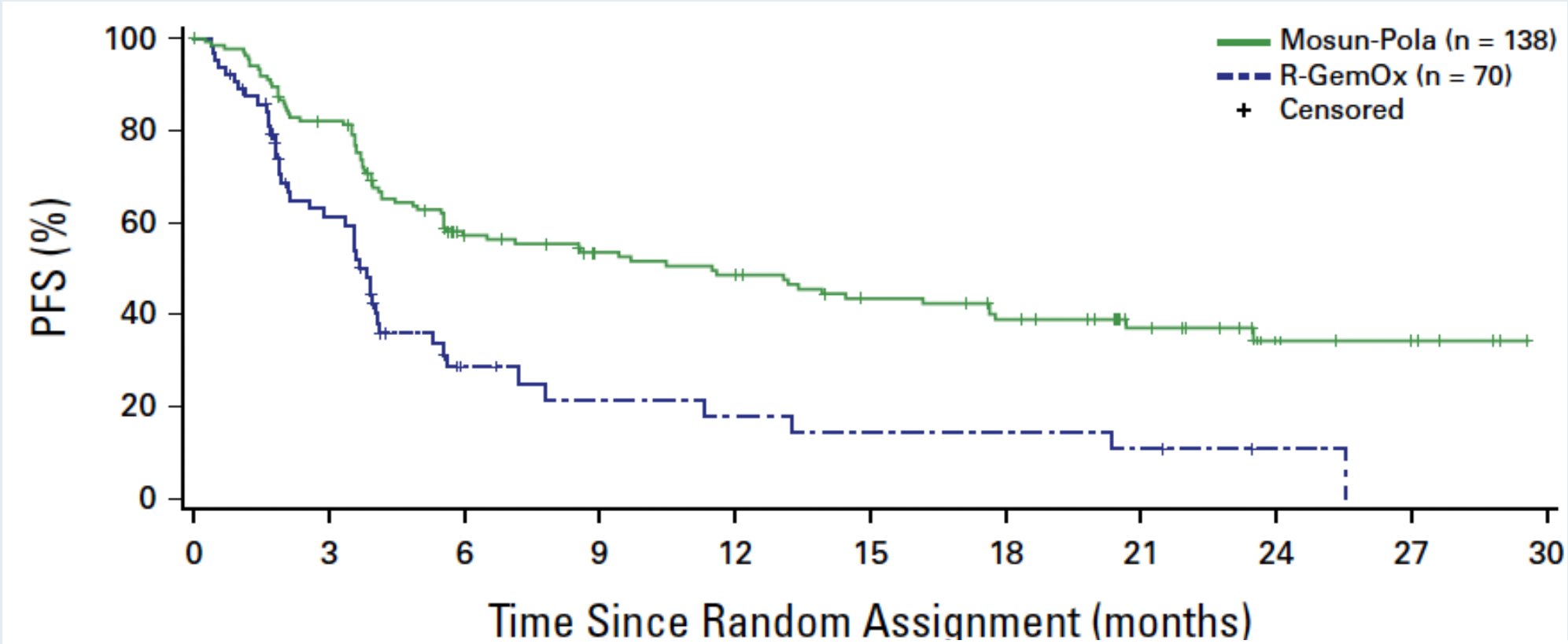
Pavlovsky A et al. ICML 2023.

Phase III SUNMO Primary Results: Overall Response Rate (Primary Endpoint)

Efficacy Result	Mosun-Pola (n = 138), (95% CI)	R-GemOx (n = 70), (95% CI)
Best overall response		
Overall response rate, %	70 (62 to 78)	40 (28 to 52)
Complete response, %	51 (43 to 60)	24 (15 to 36)
Partial response, %	19 (13 to 26)	16 (8.1 to 26)
Stable disease, %	11 (6.2 to 17)	21 (13 to 33)
Progressive disease, %	14 (8.5 to 21)	27 (17 to 39)
Not evaluable, %	0	1.4
Missing or not done, %	5.1	10

Budde LE et al. *J Clin Oncol* 2025 December 20;43(36):3799-811.

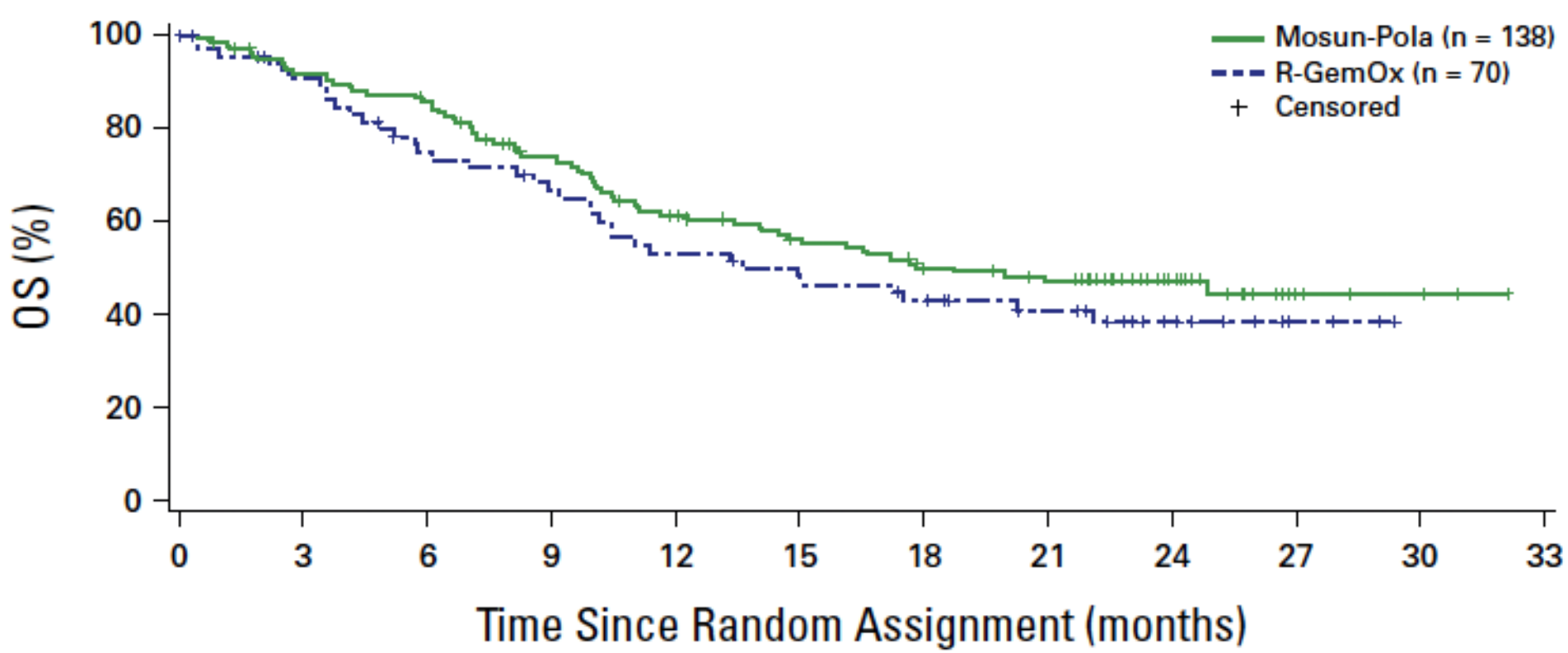
Phase III SUNMO Primary Results: PFS (Primary Endpoint)



Efficacy Result	Mosun-Pola (n = 138), (95% CI)	R-GemOx (n = 70), (95% CI)
Progression-free survival		
Hazard ratio	0.41 (0.3 to 0.6); *P* < .0001	
Median, months	11.5 (5.6 to 18)	3.8 (2.9 to 4.1)
9-month rate, %	53 (45 to 62)	21 (8.6 to 34)
12-month rate, %	48 (40 to 57)	18 (5.4 to 30)
18-month rate, %	39 (30 to 48)	14 (2.5 to 26)

Budde LE et al. *J Clin Oncol* 2025 December 20;43(36):3799-811.

Phase III SUNMO Primary Results: OS



Efficacy Result	Mosun-Pola (n = 138), (95% CI)	R-GemOx (n = 70), (95% CI)
Overall survival		
Hazard ratio	0.80 (0.5 to 1.2); *P* = .28	
Median, months	18.7 (14 to NE)	13.6 (9.9 to NE)
9-month rate, %	74 (67 to 82)	67 (55 to 78)
12-month rate, %	61 (53 to 70)	53 (41 to 66)
18-month rate, %	50 (41 to 59)	43 (31 to 56)

Budde LE et al. *J Clin Oncol* 2025 December 20;43(36):3799-811.

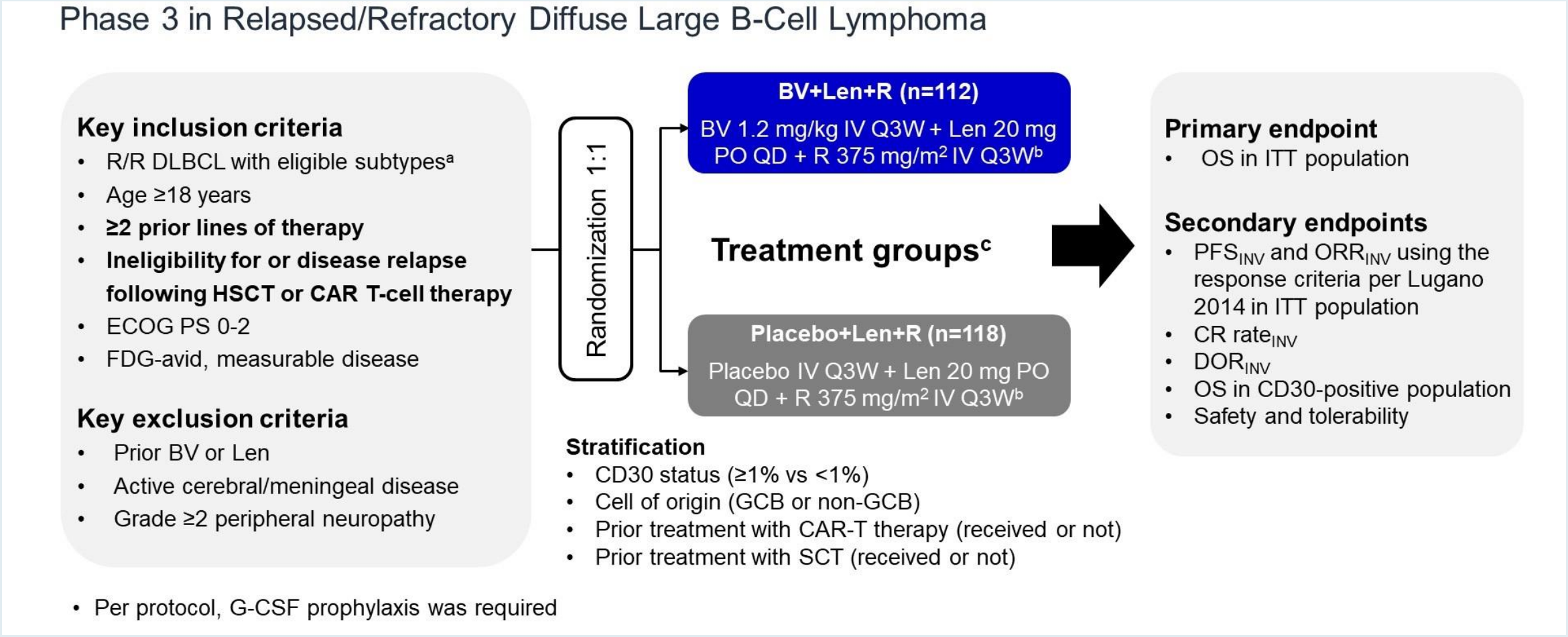
Phase III SUNMO Primary Results: Common AEs

	Mosun-Pola (n = 135), No. (%)		R-GemOx (n = 64), No. (%)	
Adverse Event	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any adverse event	131 (97)	86 (64)	61 (95)	41 (64)
Most common adverse event (≥20%)				
Injection site reaction	71 (53)	0	0	0
Neutropenia[a]	62 (46)	45 (33)	35 (55)	20 (31)
Anemia[a]	41 (30)	8 (5.9)	27 (42)	12 (19)
Cytokine response syndrome	35 (26)	1 (0.7)	0	0
Peripheral neuropathy[b]	33 (24)	0	27 (42)	0
Fatigue	21 (16)	2 (1.5)	13 (20)	1 (1.6)
Nausea	17 (13)	0	17 (27)	1 (1.6)
Diarrhea	14 (10)	0	15 (23)	1 (1.6)
Thrombocytopenia[a]	12 (8.9)	3 (2.2)	42 (66)	23 (36)
Infusion-related reaction	10 (7.4)	2 (1.5)	13 (20)	1 (1.6)
Any treatment-related adverse event	126 (93)	73 (54)	57 (89)	35 (55)

RTP RESEARCH TO PRACTICE

Budde LE et al. *J Clin Oncol* 2025 December 20;43(36):3799-811.

Phase III ECHELON-3 Study Design

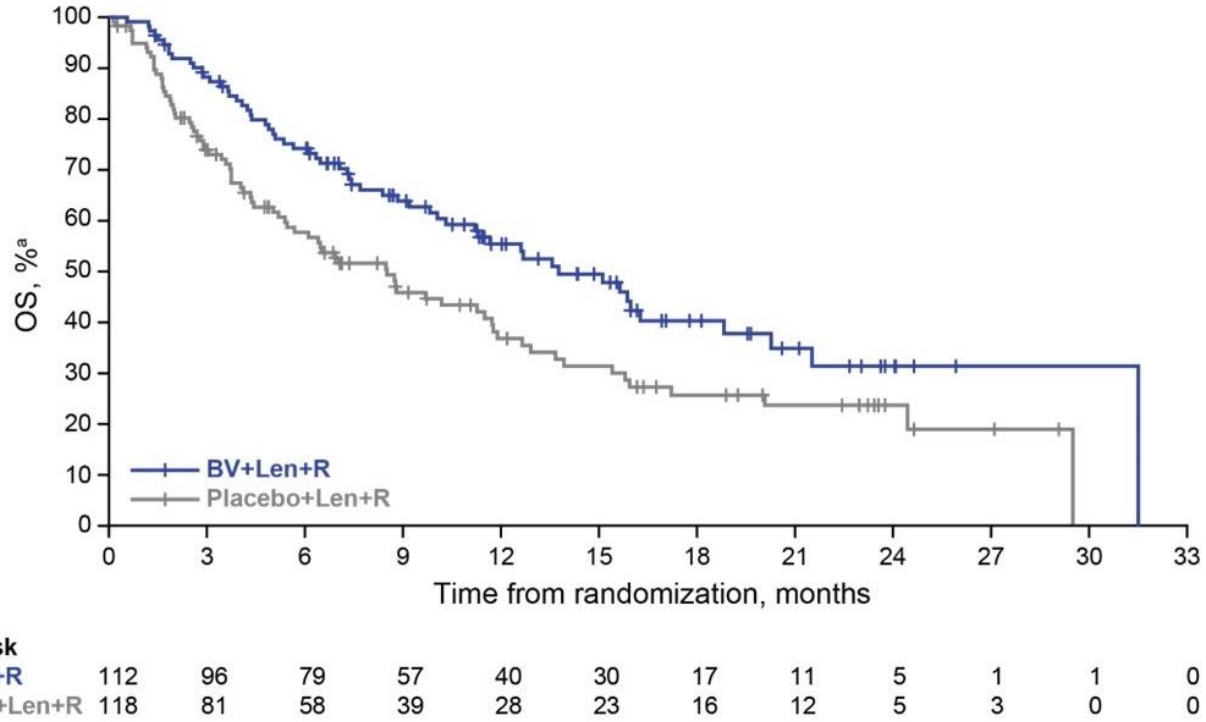


HSCT = hematopoietic stem cell transplantation; FDG = fluorodeoxyglucose; ITT = intent to treat; SCT = stem cell transplant

Kim JA et al. ASCO 2024;Abstract LBA7005.

Phase III ECHELON-3: Overall Survival (Primary Endpoint)

BV+Len+R reduced risk of death by 37% compared with placebo+Len+R



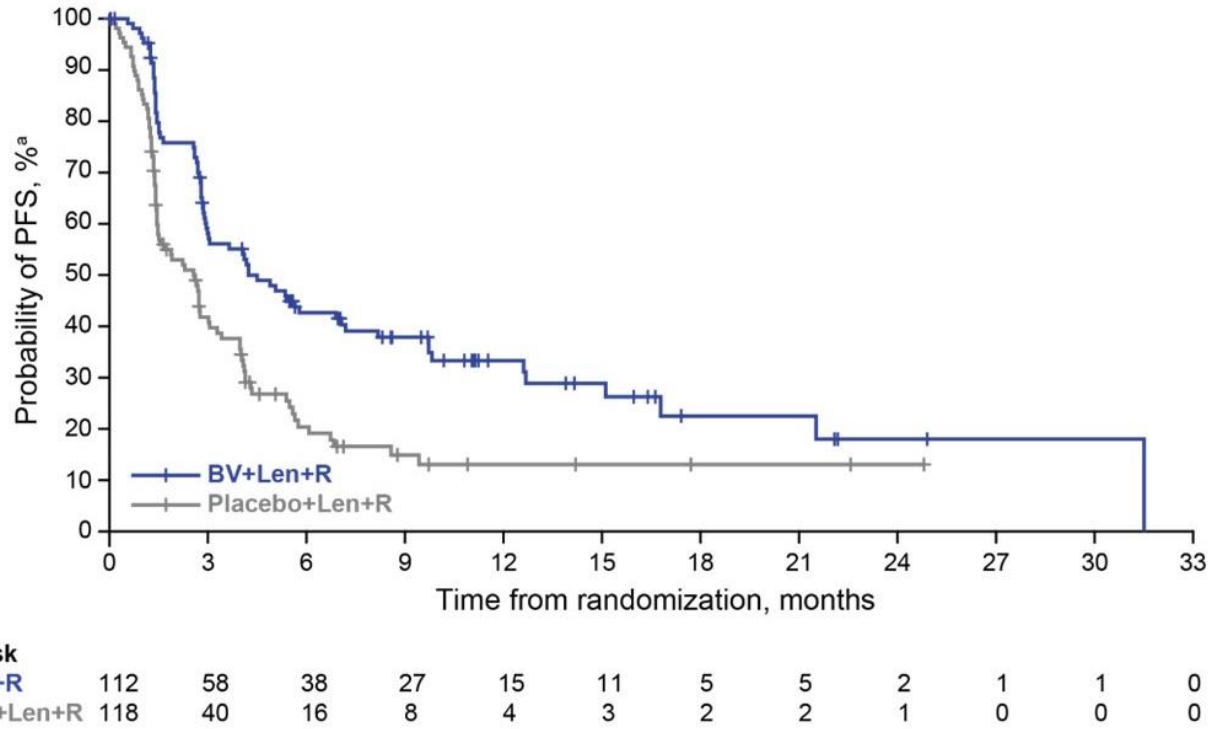
	BV+Len+R (n=112)	Placebo+Len+R (n=118)
OS, median (95% CI), months	**13.8** (10.3-18.8)	**8.5** (5.4-11.7)
Hazard ratio (95% CI)[b]	0.629 (0.445-0.891)	
Log-rank *P* value[c]	.0085	
Events (deaths)	58	76
Follow-up, median (95% CI), months	15.5 (12.2-18.1)	18.9 (12.2-23.2)

- BV+Len+R prolonged median OS by 5.3 months compared with placebo+Len+R
- Prespecified O'Brien-Fleming efficacy boundary was crossed at this interim analysis

Kim JA et al. ASCO 2024;Abstract LBA7005.

Phase III ECHELON-3: PFS (Key Secondary Endpoint)

BV+Len+R reduced risk of disease progression or death by 47% compared with placebo+Len+R



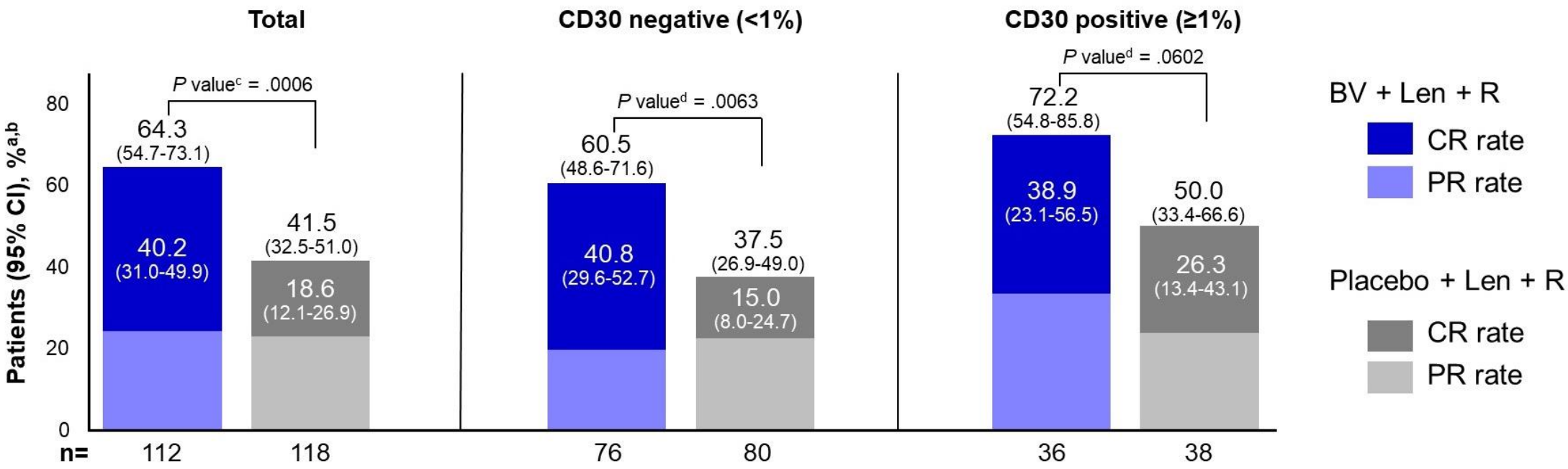
	BV+Len+R (n=112)	Placebo+Len+R (n=118)
PFS, median (95% CI), months	**4.2** (2.9-7.1)	**2.6** (1.4-3.1)
Hazard ratio (95% CI)[b]	0.527 (0.380-0.729)	
Log-rank *P* value[c]	<.0001	
Events	71	85
Follow-up, median (95% CI), months	11.1 (8.6-14.2)	8.8 (6.9-10.9)

- PFS was an alpha controlled key secondary endpoint

Kim JA et al. ASCO 2024;Abstract LBA7005.

Phase III ECHELON-3: Responses

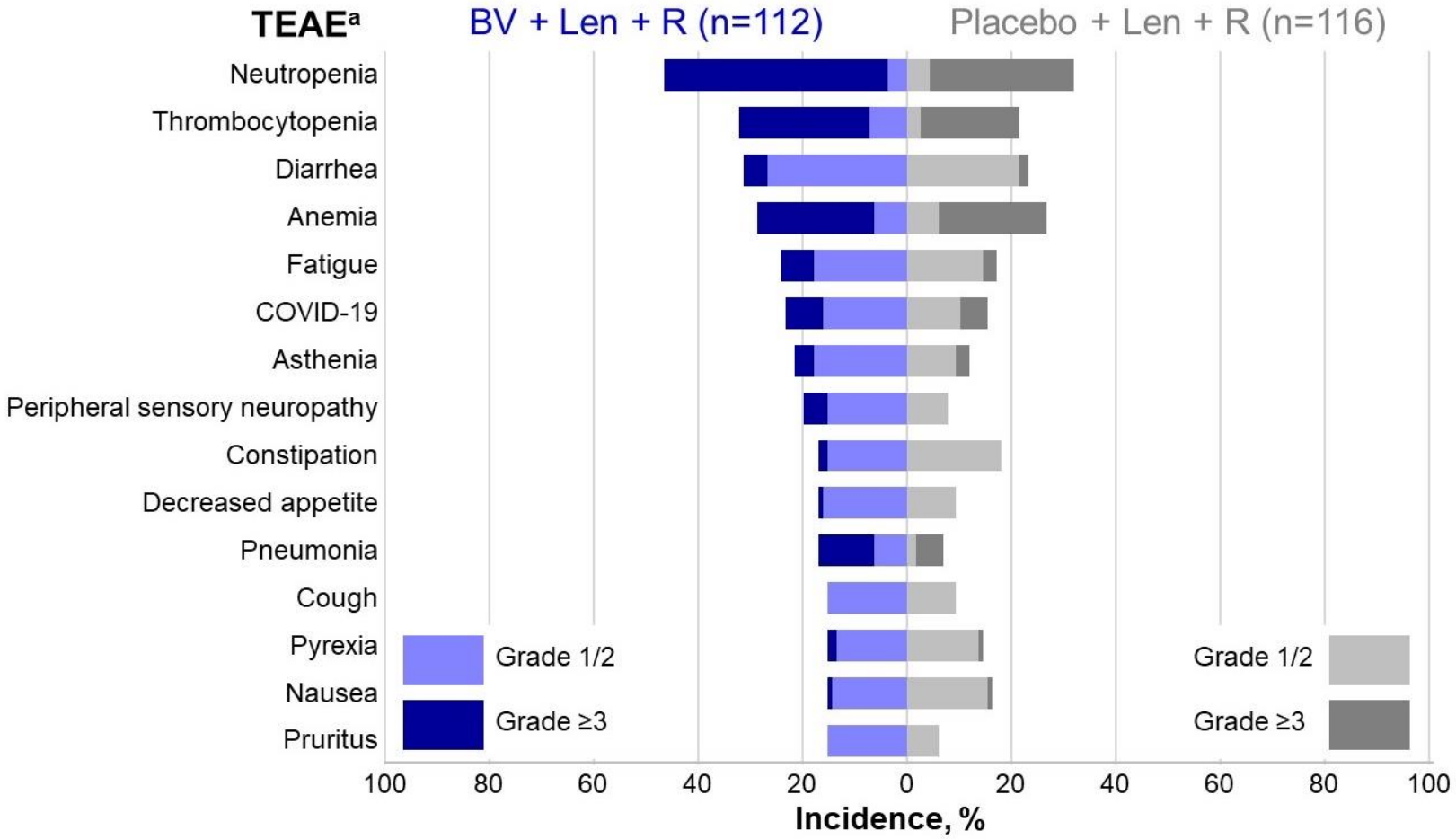
40% CR rate with BV+Len+R and ORR improvement regardless of CD30 expression



- In the total population, the median DOR (95% CI) was longer with BV+Len+R: 8.3 months (4.2-15.3 months) vs 3.0 months (2.8-5.4 months)
  - In patients who had a CR, the median DOR (95% CI) was 18.9 months (11.1 months-NR) with BV+Len+R and NR (2.8 months-NR) with placebo+Len+R
  - The median time to CR onset (range) was 1.58 months (1.2-7.3 months) with BV+Len+R and 1.61 months (0.7-4.6 months) with placebo+Len+R

Kim JA et al. ASCO 2024;Abstract LBA7005.

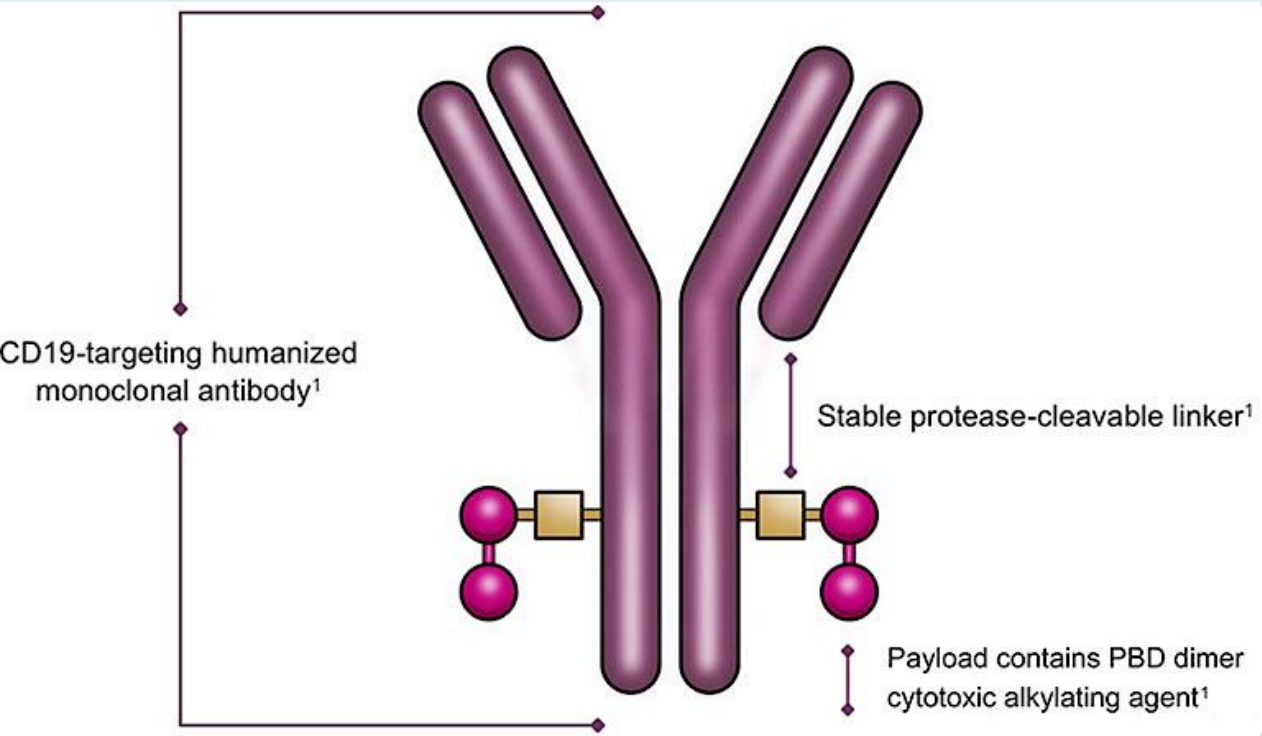
Phase III ECHELON-3: Safety



- TEAEs of any grade occurred in 97% of patients with each treatment
- Grade ≥3 TEAEs:
  - 88% with BV+Len+R
  - 77% with placebo+Len+R
  - 9% febrile neutropenia in each group
- Grade 5 TEAEs:
  - 12% with BV+Len+R
  - 8% with placebo+Len+R
- Any grade peripheral neuropathy TEAEs
  - 31% with BV+Len+R
  - 24% with placebo+Len+R
- Relative dose intensity
  - 94.4% for BV
  - 99.7% for placebo

Kim JA et al. ASCO 2024;Abstract LBA7005.

Loncastuximab Tesirine: A CD19-Directed Antibody-Drug Conjugate



Upon binding to CD19, Loncastuximab tesirine is internalized into the tumor cell and the PBD dimer cytotoxin is released into the cell[1]

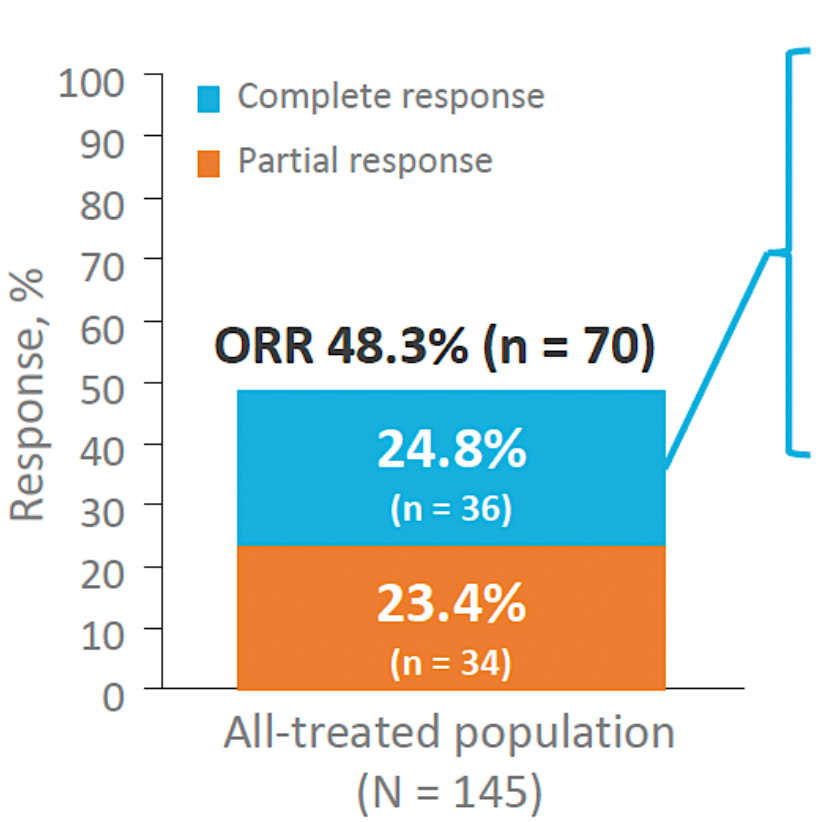
PBD dimer—an alkylating agent—binds to the DNA minor groove and forms highly cytotoxic DNA interstrand crosslinks[1]

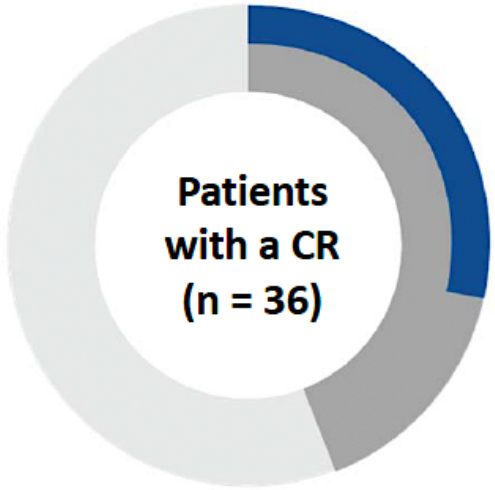
DNA interstrand crosslinks subsequently induce tumor cell death[1]

ADC = antibody-drug conjugate; PBD = pyrrolobenzodiazepine.

[Loncastuximab tesirine manufacturer prescribing information].

Phase II LOTIS-2 Study: Overall Response Rate (ORR) and Long-Term Responses — All-Treated Population





Of the patients with a CR, 44% (16 of 36) were event-free for ≥1 year.

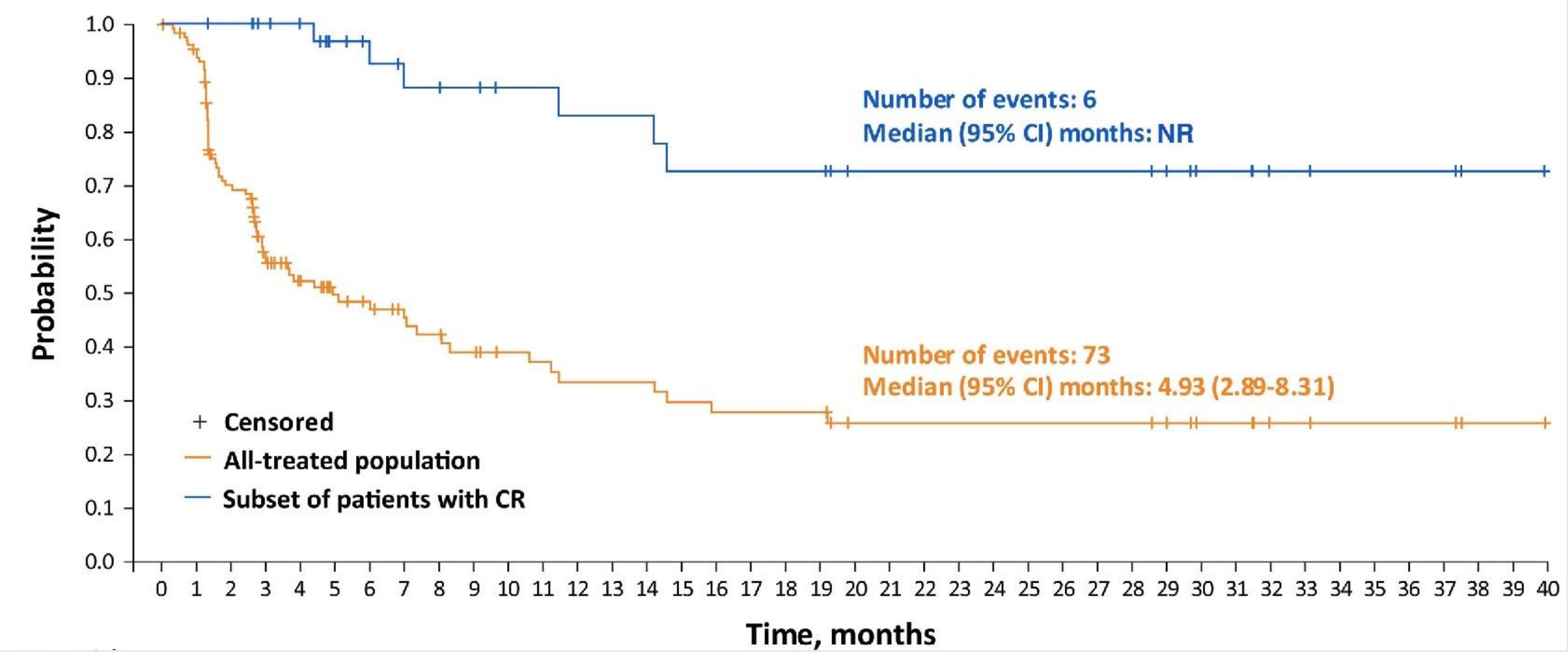
Of the patients with a CR, 31% (11 of 36) were event-free for ≥2 years.

Median (range) number of treatment cycles	
All-treated population	3.0 (1-26)
Pts with a CR	8.0 (1-26)
Pts with a CR, event-free ≥1 year[a]	12.5 (1-26)
Pts with a CR, event-free ≥2 years[a]	13.0 (1-22)

No new safety signals were identified during the long-term follow-up

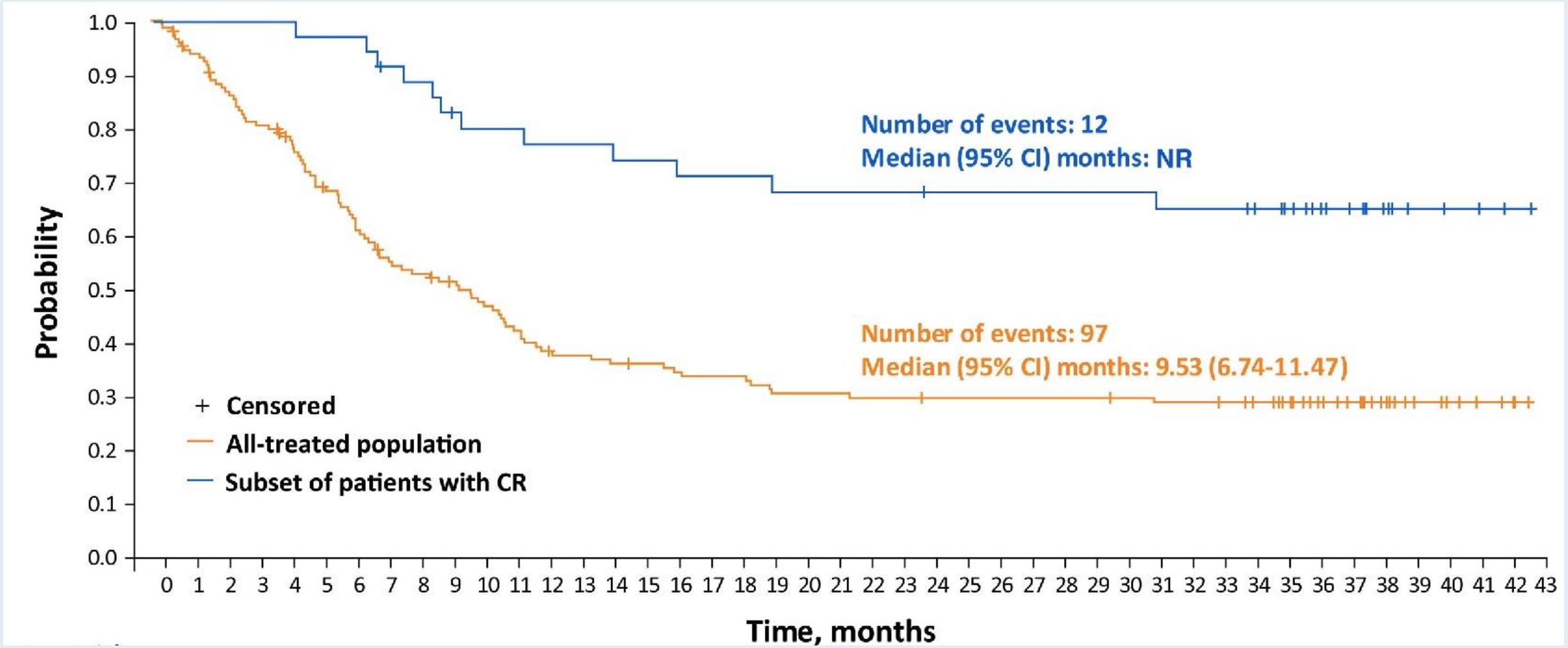
Caimi PF et al. EHA 2023;Abstract P1132.

Phase II LOTIS-2: Progression-Free Survival



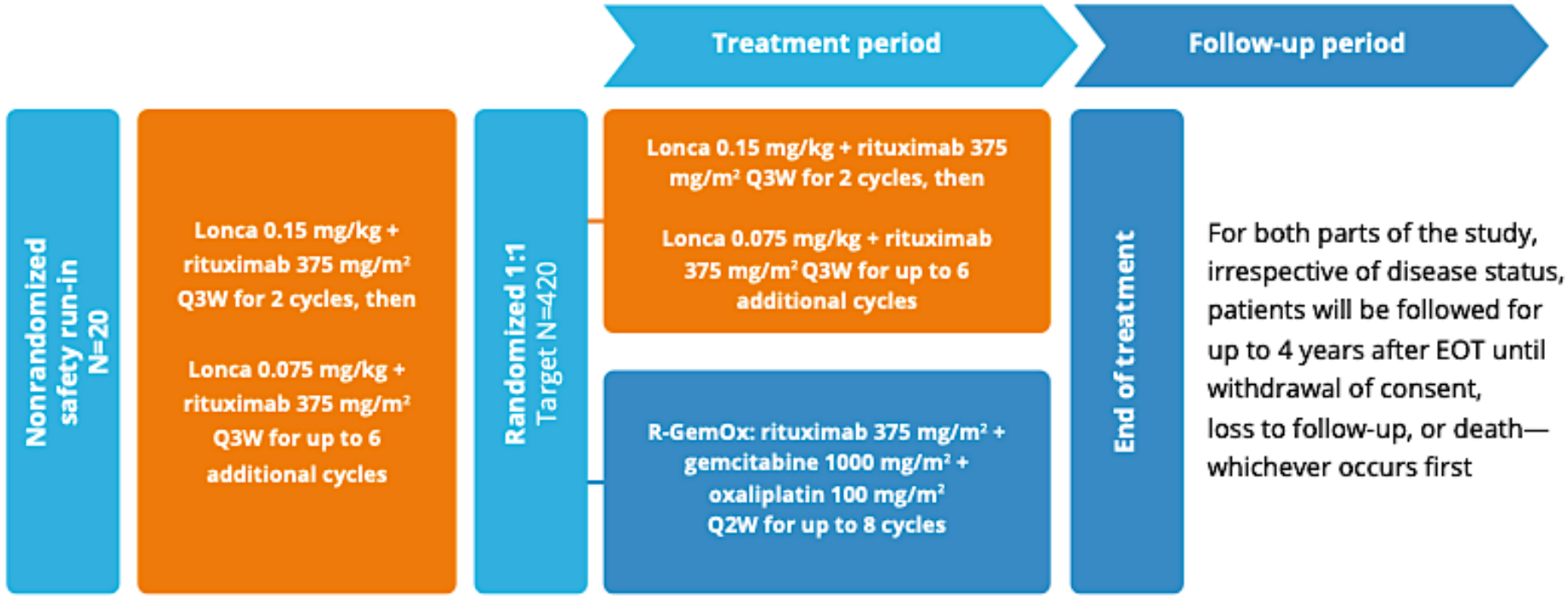
Caimi PF et al. *Haematologica* 2024 April 1;109(4):1184-93.

Phase II LOTIS-2: Overall Survival



Caimi PF et al. *Haematologica* 2024 April 1;109(4):1184-93.

Phase III LOTIS-5 Study Design



EOT, end of treatment; Lonca, loncastuximab tesirine; QXW, every X weeks.

Study Endpoints

- The primary endpoint is progression-free survival (PFS) by independent central review
- Secondary endpoints include OS, overall response rate (ORR), CR rate, duration of response (DOR), safety, PK parameters, Lonca ADAs, and patient-reported outcomes (PROs)
- Exploratory endpoints include correlations between clinical activity and Lonca exposure (ie, Lonca dose and PK metrics) and tumor and/or blood biomarkers

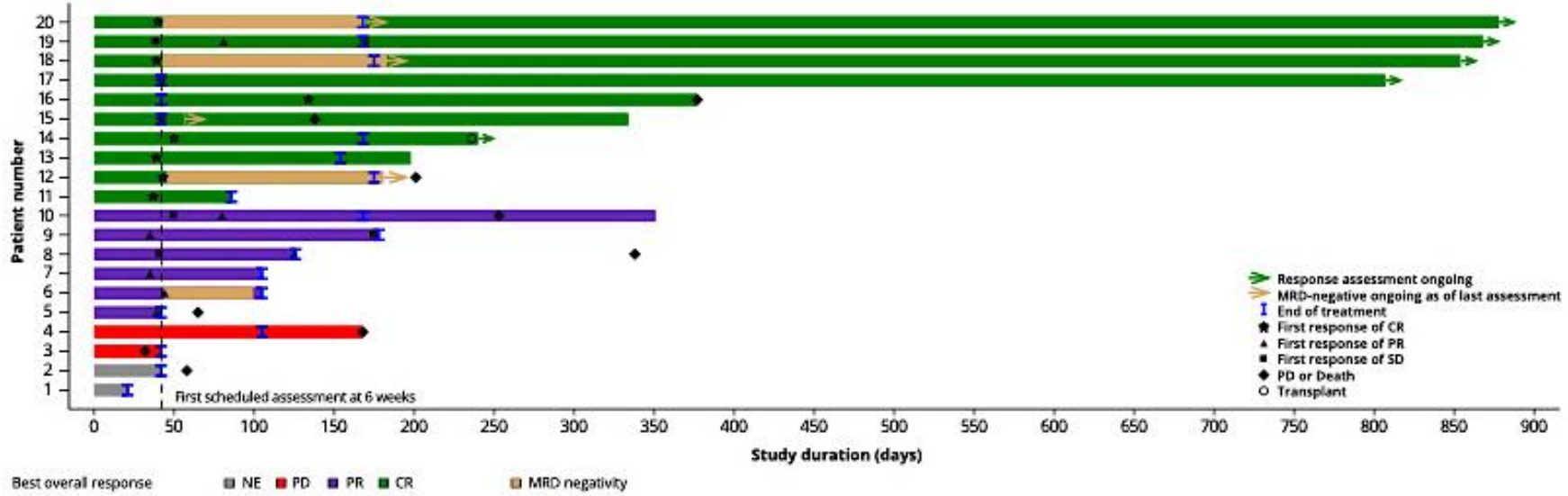
Carlo-Stella C et al. EHA 2025;Abstract PS1957.

Phase III LOTIS-5: Efficacy

Efficacy outcomes in safety run-in population (N=20)	
ORR (95% CI), %	80.0 (56.3-94.3)
CRR (95% CI), %	50.0 (27.2-72.8)
Median PFS (95% CI), months	8.3 (4.5-NE)
Efficacy outcomes in responders (n=16)	
Median DOR (95% CI), months	8.02 (3.19-NE)
Events, n (%)	5 (31.3)
Efficacy outcomes in complete responders (n=10)	
Median DOR, months (95% CI)	NE (3.19-NE)
Events, n (%)	3 (30.0)
MRD results in patients with ctDNA measurements (n=8)	
CR and MRD negative, n (%)	4 (50.0)
MRD negative at end of treatment, n (%)	4 (50.0)

CRR, complete response rate; ctDNA, circulating tumor DNA; DOR, duration of response; MRD, minimal residual disease; NE, not estimable; ORR, overall response rate; PFS, progression-free survival.

Figure 2. Swimmer plot of safety run-in population (N=20)



Each bar represents one patient in the study. Response is determined by independent reviewer.
CR, complete response; MRD, minimal residual disease; NE, not estimable; PD, progressive disease; PR, partial response.

Carlo-Stella C et al. EHA 2025;Abstract PS1957.

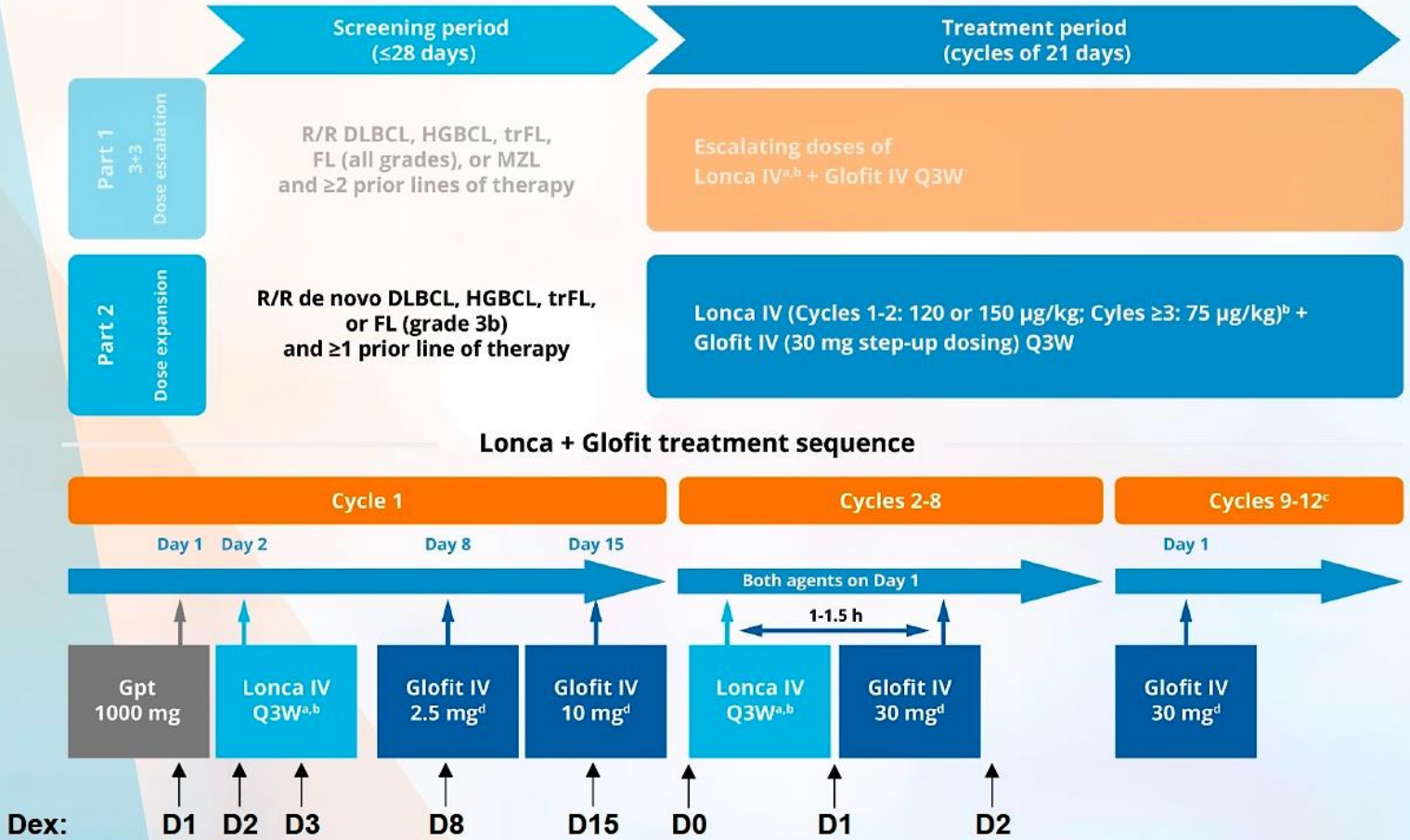
Phase III LOTIS-5: Safety

Safety endpoint, n (%)	N=20
All grade TEAE	20 (100)
Grade ≥3 TEAE	11 (55)
GGT increased	5 (25)
Neutropenia	4 (20)
COVID-19/COVID-19 pneumonia	3 (15)
Alanine aminotransferase increased	1 (5)
Anemia	1 (5)
Aspartate aminotransferase increased	1 (5)
Blood alkaline phosphatase increased	1 (5)
Cataract	1 (5)
Cellulitis gangrenous	1 (5)
Cytomegalovirus infection reactivation	1 (5)
Hyponatremia	1 (5)
Malaise	1 (5)
Neurological decompensation	1 (5)
Photosensitivity reaction	1 (5)
Pleural effusion	1 (5)
Tumor lysis syndrome	1 (5)
Urinary tract infection	1 (5)
Serious adverse events	9 (45)
Infection	6 (30)
Hyponatremia	1 (5)
Anaphylactic reaction	1 (5)
Pleural effusion	1 (5)
Malaise	1 (5)
Neurological decompression	1 (5)
TEAEs leading to any study drug withdrawal	8 (40)

GGT, gamma-glutamyl transferase; TEAE, treatment-emergent adverse event.

Carlo-Stella C et al. EHA 2025;Abstract PS1957.

Phase Ib LOTIS-7 Study Design



Study population

- Patients with 3L+ R/R B-NHL (part 1) and 2L+ R/R LBCL (part 2)
- ECOG PS score of 0-2
- Prior autologous SCT (>100 days) or CAR-T therapy (>100 days) is allowed
- Measurable disease (per 2014 Lugano Classification)
- Excludes patients with clinically significant third-space fluid accumulation

Endpoints

- **Primary**: safety and tolerability; MTD and/or RDE
- **Secondary**: ORR, DOR, CR rate, PFS, RFS, and OS; PK and immunogenicity
- **Exploratory**: Glofit concentration in circulation; biomarker and PK correlations with clinical outcomes

Alderuccio JP et al. ICML 2025;Abstract 078.

Phase Ib LOTIS-7 Initial Results: Safety Outcomes

TREATED POPULATION (N=41)

	120 µg/kg[b] n=20	150 µg/kg[b] n=21	All n = 41
Grade 3/4 TEAEs (> 5% of patients)[a]	**11 (55%)**	**12 (57.1%)**	**23 (56.1%)**
Neutropenia	4 (20%)	6 (28.6%)	10 (24.4%)
Anemia	1 (5%)	3 (14.3%)	4 (9.8%)
AST increased	2 (10%)	1 (4.8%)	3 (7.3%)
GGT increase	1 (5%)	2 (9.5%)	3 (7.3%)
Thrombocytopenia	2 (10%)	1 (4.8%)	3 (7.3%)
Grade 3/4 AESI (all patients)[a]			
Febrile neutropenia	0	1 (4.8%)	1 (2.4%)
Thrombocytopenia	2 (10%)	1 (4.8%)	3 (7.3%)
GGT increase	1 (5%)	2 (9.5%)	3 (7.3%)
Generalized oedema	1 (5%)	1 (4.8%)	2 (4.9%)
Rash	1 (5%)	0	1 (2.4%)
Photosensitivity reaction	0	1 (4.8%)	1 (2.4%)
Sepsis	1 (5%)	0	1 (2.4%)
Upper respiratory infection	1 (5%)	0	1 (2.4%)
Pneumonia	1 (5%)	0	1 (2.4%)
Serious TEAE	**11 (55%)**	**9 (42.9%)**	**20 (48.8%)**
No Grade 5 TEAEs occurred			

[a]As per Investigator reported adverse events. [b]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.
TEAE = treatment emergent adverse event; AESI = adverse event of special interest | Data cutoff: 14 Apr 2025. Data extracted from live clinical database. Data is subject to change.

Alderuccio JP et al. ICML 2025;Abstract 078.

Phase Ib LOTIS-7 Initial Results: CRS and ICANS

TREATED POPULATION (N=41)

	120 µg/kg[b] n=20	150 µg/kg[b] n=21	All n = 41
Cytokine Release Syndrome[a]			
Any grade	11 (55%)	5 (23.8%)	16 (39.0%)
Grade 1	7 (35%)	5 (23.8%)	12 (29.3%)
Grade 2	3 (15%)	0	3 (7.3%)
Grade 3	1 (5%)	0	1 (2.4%)
Grade 4/5	0	0	0
ICANS[a]			
Any grade	2 (10%)	1 (4.8%)	3 (7.3%)
Grade 1	1 (5%)	0	1 (2.4%)
Grade 2	1 (5%)	1 (4.8%)	2 (4.9%)
Grade ≥ 3	0	0	0

Any-grade CRS was less frequent at the Lonca 150 µg/kg starting dose[b] (23.8%) than at 120 µg/kg starting dose[b] (55.0%)

- Grade 1 and 2 CRS cases managed with tocilizumab, corticosteroids, acetaminophen, and/or fluid bolus, without ICU admittance or pressor support
- Grade 3 CRS case managed with tocilizumab, acetaminophen, dexamethasone, norepinephrine. ICU admittance

- All patients with ICANS had complete resolution of symptoms
  - Two patients resumed treatment and ultimately achieved a CR
  - One patient elected to discontinue treatment
- ICANS managed primarily with corticosteroids

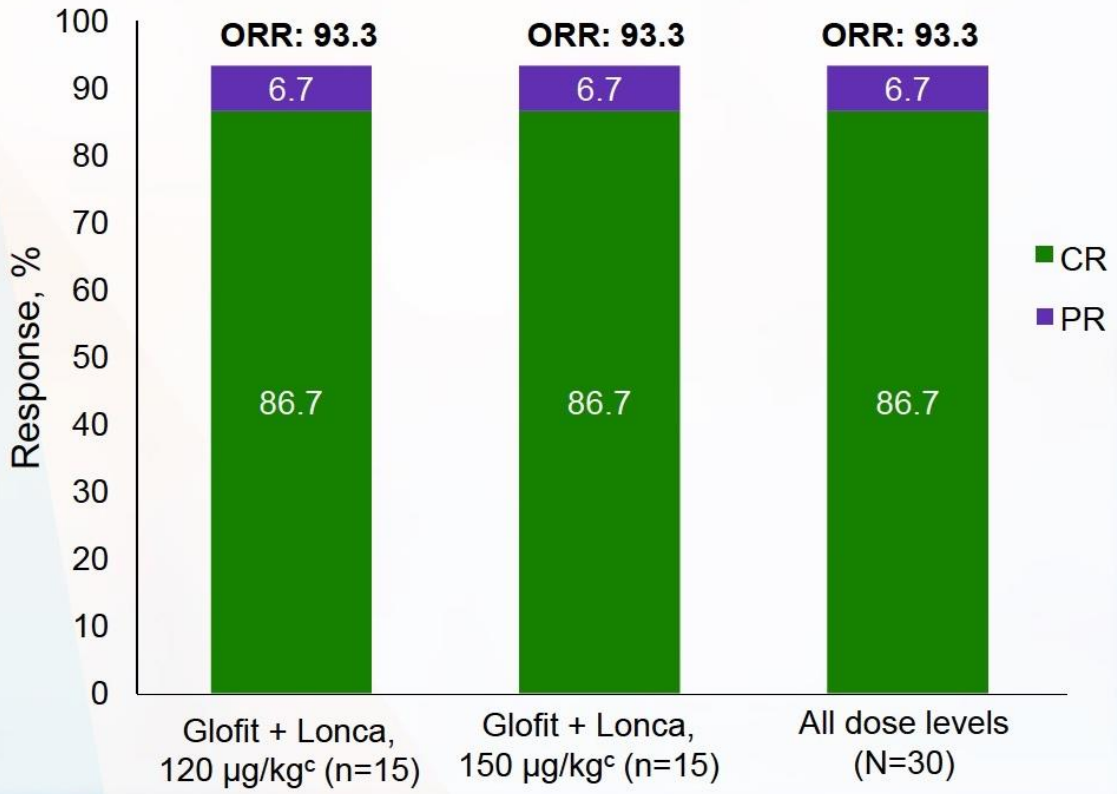
[a]Number of patients who experienced at least 1 event per ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells; worst grade reported if applicable
[b]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.
Data Cutoff 14 Apr 2025. Data extracted from live clinical database. Data is subject to change.

Alderuccio JP et al. ICML 2025;Abstract 078.

Phase Ib LOTIS-7 Initial Results: Best Overall Responses, DoR

EFFICACY EVALUABLE POPULATION (N=30)[a]

Best overall response[b]



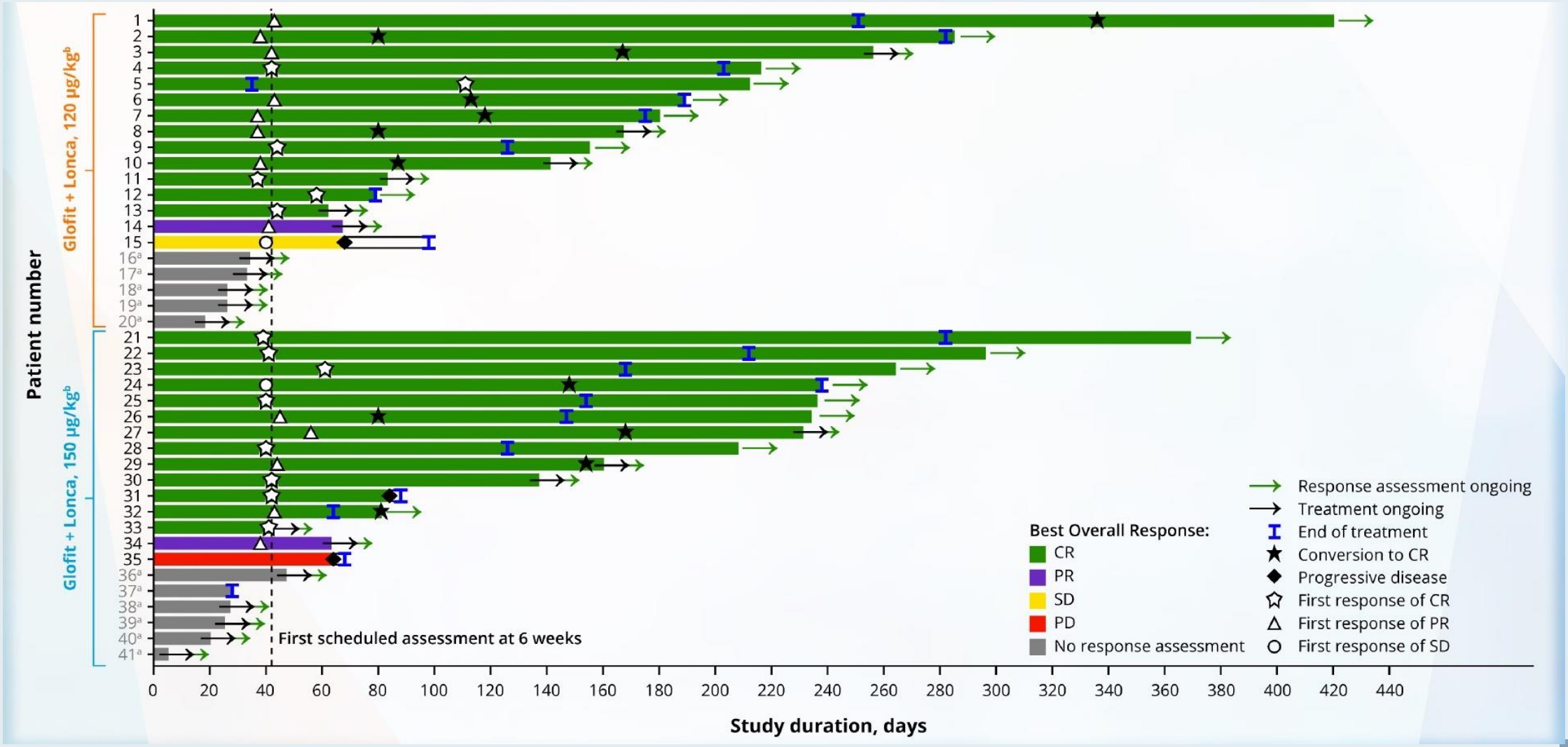
Duration of response

Characteristic, n (%)	Glofit + Lonca, 120 µg/kg[c] (n=15)	Glofit + Lonca, 150 µg/kg[c] (n=15)	All dose levels (N=30)
DOR[d] Median	(n=14) NE	(n=14) NE	(n=28) NE
Time to first response (CR or PR) Median, days	(n=14) 42.0	(n=14) 42.0	(n=28) 42.0
Time to first CR Median, days	(n=13) 80.0	(n=13) 42.0	(n=26) 70.5

Data cutoff: April 14, 2025.
CR, complete response; DOR, duration of response; Glofit, glofitamab; Lonca, loncastuximab tesirine; NE, not estimable; ORR, overall response rate; PR, partial response.
[a]The efficacy evaluable population (N=30) included all patients who received ≥1 dose of the study drug with a valid baseline and ≥1 valid postbaseline disease assessment. Patients who did not have a postbaseline assessment owing to early clinical progression or death were also included. [b]Percentages do not add up to total due to rounding. [c]When the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3. [d]In the efficacy evaluable population, the DOR and probability of maintaining an event-free response were evaluated in responders (n=28), including all patients who had a best response of CR or PR.

Alderuccio JP et al. ICML 2025;Abstract 078.

Phase Ib LOTIS-7 Initial Results: Efficacy over Time



Alderuccio JP et al. ICML 2025;Abstract 078.

Updated Data Announced from LOTIS-7 Phase Ib Trial of Loncastuximab Tesirine in Combination with Bispecific Antibody Supporting Potential Best-in-Class Regimen for R/R DLBCL

Press Release: December 3, 2025

"On December 3, 2025, [the manufacturer] announced updated data from the LOTIS-7 Phase 1b open-label clinical trial evaluating the safety and efficacy of loncastuximab tesirine in combination with the bispecific antibody glofitamab in patients with relapsed or refractory diffuse large B-cell lymphoma (r/r DLBCL). The updated data is based on investigator assessment and reflects the 49 efficacy-evaluable patients with a minimum of 6 months of follow-up from treatment initiation.

Enrollment in the LOTIS-7 clinical trial is ongoing, with complete enrollment of approximately 100 patients at the selected 150 µg/kg dose expected during the first half of 2026. The Company plans to share full data at a medical meeting and submit for publication by the end of 2026. In addition, the Company plans to assess regulatory and compendia strategies."

https://ir.adctherapeutics.com/2025-12-03-ADC-Therapeutics-Announces-Updated-Data-from-LOTIS-7-Phase-1b-Clinical-Trial-of-ZYNLONTA-R-in-Combination-with-Bispecific-Antibody-Supporting-Potential-Best-in-Class-Regimen-in-Patients-with-Relapsed-Refractory-Diffuse-Large-B-cell-Lymphoma

RTP RESEARCH TO PRACTICE

Optimizing the Use of Novel Therapies for Patients with DLBCL

Module 1: Selection of First-Line Therapy for Patients with Diffuse Large B-Cell Lymphoma (DLBCL)

Module 2: Clinician Survey Results

Module 3: Current and Future Roles of Monoclonal and Bispecific Antibodies in Therapy for Relapsed/Refractory (R/R) DLBCL

Module 4: Clinician Survey Results

Module 5: Evidence-Based Incorporation of Antibody-Drug Conjugates into the Management of R/R DLBCL

Module 6: Clinician Survey Results

RTP RESEARCH TO PRACTICE

Outside of a clinical trial, would you partner polatuzumab vedotin with other systemic therapies beyond BR for patients with R/R DLBCL under any circumstances?

 Dr Abramson	Yes, mosunetuzumab and glofitamab
 Dr Kahl	Yes, mosunetuzumab
 Dr Kamdar	Yes, mosunetuzumab and glofitamab
 Dr LaCasce	Yes, mosunetuzumab and glofitamab
 Dr Matasar	Yes, R-GemOx, R-ICE, mosunetuzumab and glofitamab
 Dr Phillips	Yes, mosunetuzumab and glofitamab
 Prof Salles	Yes, mainly glofitamab
 Dr Westin	Yes, mosunetuzumab

R-ICE = rituximab/ifosfamide/carboplatin/etoposide

RTP RESEARCH TO PRACTICE

Where in the treatment course do you typically employ loncastuximab tesirine for your patients with R/R DLBCL? Would you administer it to a patient who has experienced disease progression on one or more other CD19-directed approaches?

	When	After PD on other CD19-directed tx?
 Dr Abramson	After CAR T and BsAb therapies	Yes, but only after assessing CD19 expression
 Dr Kahl	After BsAb failure	Yes, but only after assessing CD19 expression
 Dr Kamdar	After CAR T and BsAb therapies	Yes, but only after assessing CD19 expression
 Dr LaCasce	After CD20 BsAb therapy	Yes, but only after assessing CD19 expression
 Dr Matasar	3L+ especially post-CAR T with residual CD19+	Yes, but only after assessing CD19 expression
 Dr Phillips	3L+, after PD on CAR T (early relapse) or BsAb (late relapse after CAR T)	Yes, but only after assessing CD19 expression
 Prof Salles	When first-line, CAR T and bispecific Ab treatments have failed	Yes, but only after assessing CD19 expression
 Dr Westin	If CAR T ineligible and unable/ unwilling/relapsed after BsAb	Yes, but only after assessing CD19 expression

PD = disease progression; BsAb = bispecific antibody

Approximately what proportion of your patients with R/R DLBCL receiving loncastuximab tesirine derive meaningful clinical benefit? What is the longest duration of response that you have observed with loncastuximab tesirine in your own practice?

	Patients with clinical benefit	Longest duration of response
 Dr Abramson	30%	>1 year
 Dr Kahl	40%	About 1 year
 Dr Kamdar	20%	9 months
 Dr LaCasce	10%	3 months
 Dr Matasar	50%	4 years+
 Dr Phillips	30%	>1 year
 Prof Salles	30%	6 months
 Dr Westin	45%	>1 year

Approximately what proportion of your patients with DLBCL receiving loncastuximab tesirine develop clinically significant peripheral edema? In general, how do you manage peripheral edema in patients who are receiving loncastuximab tesirine?

	Patients with significant peripheral edema	Management
 Dr Abramson	25%	Dexamethasone prophylaxis, diuretics
 Dr Kahl	60%	Stop drug; diuretics
 Dr Kamdar	30%	Dexamethasone prophylaxis, diuretics
 Dr LaCasce	20%	Peri-drug dexamethasone per label, diuretics
 Dr Matasar	25%	Diuretics
 Dr Phillips	50%	Initiate preventative diuretic in most patients, hold/stop drug if AE
 Prof Salles	20%	Diuretic and prophylactic steroids, then diuretic alone
 Dr Westin	33%	Diuretics and steroids

AE = adverse event

Would you administer brentuximab vedotin/R^2 to a patient with CD30-negative R/R DLBCL?

 Dr Abramson	Yes
 Dr Kahl	No
 Dr Kamdar	Yes
 Dr LaCasce	No
 Dr Matasar	No
 Dr Phillips	No
 Prof Salles	No
 Dr Westin	No

R^2 = lenalidomide/rituximab

RTP RESEARCH TO PRACTICE

Questions?