Advancing DLBCL Treatment with Bi-specifics

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Disclosures

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- Speaker fees: AbbVie, Adaptive Biotechnologies, AstraZeneca, Janssen, Merck, Roche
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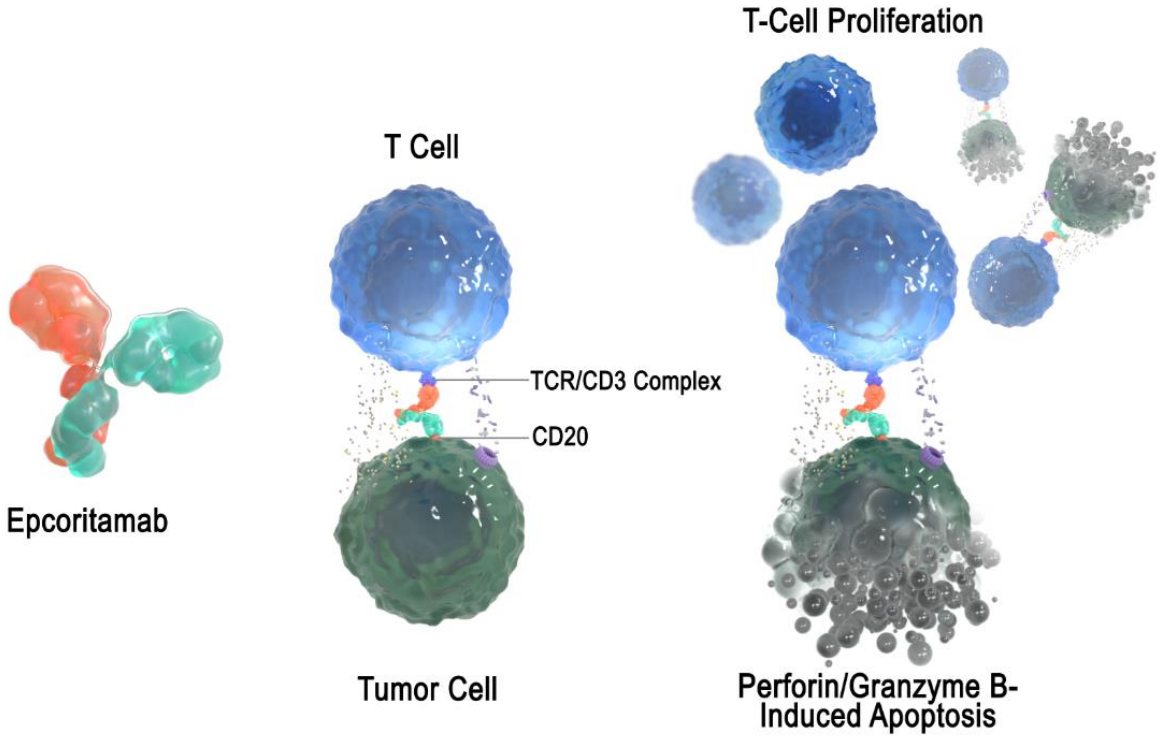
3L+ treatment of diffuse large B cell lymphoma

Mechanism of Action of Epcoritamab (DuoBody®-CD3xCD20)

Epcoritamab (DuoBody®-CD3×CD20) is a subcutaneously administered bispecific antibody that induces T-cell–mediated killing of CD20-expressing tumors[1,2]

- **Induces T-cell activation** by binding to CD3 on T cells and CD20 on malignant B cells
- **Promotes immunological synapse** between bound cells, resulting in apoptosis of B cells
- **Binds to a distinct epitope on CD20**, different from the epitopes of rituximab and obinutuzumab
- **Retains activity** in the presence of CD20 mAbs



1. Engelberts PJ, et al. EBioMedicine. 2020;52:102625. 2. Chiu C, et al. Presented at EHA 2020. [Abstract #EP1330].

Study Design: EPCORE NHL-1 LBCL Expansion

Dose escalation

Dose expansion data cutoff: November 18, 2022
Median follow-up: 20.0 mo

B-NHL:

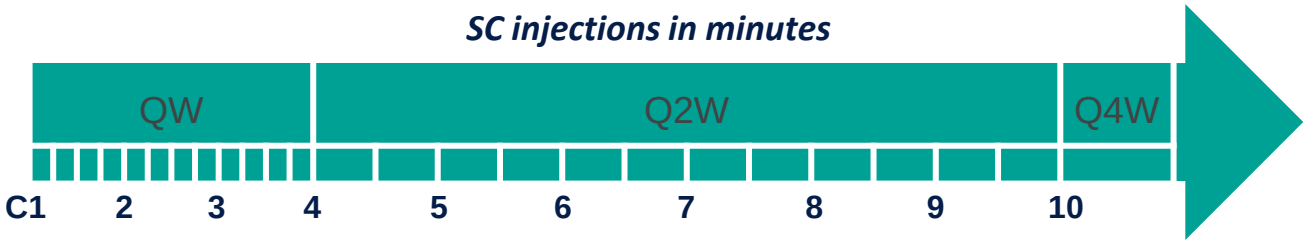
- ✓ No DLTs
- ✓ MTD not reached
- ✓ RP2D identified
- ✓ Manageable safety profile
- ✓ Encouraging antitumor activity

Key inclusion criteria:

- R/R CD20^{+} mature B-cell neoplasm
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- FDG PET–avid and measurable disease by CT/MRI
- **Prior CAR T allowed**

Step-up dosing[a]

Epcoritamab SC RP2D 48 mg
Treatment until PD[b,c] or unacceptable toxicity
LBCL cohort, N=157
DLBCL & HGBL, n=148; PMBCL, n=4; FL G3B, n=5



- **Primary endpoint:** ORR by IRC
- **Key secondary endpoints:** DOR, TTR, PFS, OS, CR rate, and safety/tolerability

[a]Step-up dosing (SUD; priming [SUD 1] 0.16 mg and intermediate [SUD 2] 0.8 mg dosing before first full dose) and corticosteroid prophylaxis were used to mitigate CRS. [b]Radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. [c]≥2 measurable (by CT/MRI) and FDG PET–positive lesions. C, cycle; CAR T, chimeric antigen receptor; CR, complete response; CT/MRI, computed tomography/magnetic resonance imaging; DLBCL, diffuse large B-cell lymphoma; DLTs, dose-limiting toxicities; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG-PET, 18F-fluorodeoxyglucose-positron emission tomography; FL, follicular lymphoma; G, grade; HGBL, high-grade B-cell lymphoma; IRC, independent review committee; LBCL, large B-cell lymphoma; mo, months; mAb, monoclonal antibody; MTD, maximum tolerated dose; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; RP2D, recommended phase 2 dose; R/R, relapsed or refractory; SC, subcutaneous; TTR, time to response; Wk, week.

ClinicalTrials.gov: NCT03625037. EudraCT: 2017-001748-36.

Karimi Y, et al. Poster presentation at: American Society of Clinical Oncology; June 2-6, 2023; Chicago, IL, USA/Virtual.

Patient Population in EPCORE NHL-1 LBCL Expansion

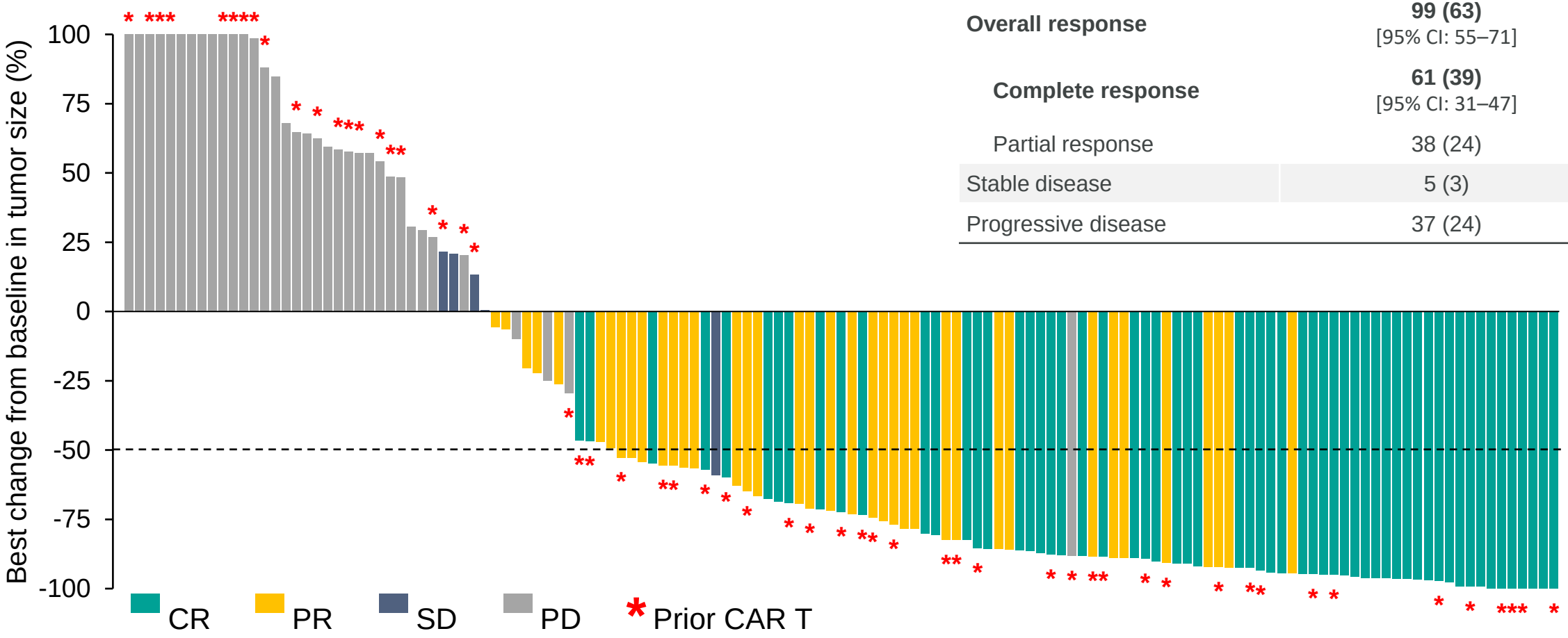
Demographics	DLBCL & HGBL, n=148	LBCL, N=157
Median age (range), y	65 (22–83)	64 (20–83)
≥75 y, n (%)	29 (20)	29 (18)
ECOG PS, n (%)		
0	71 (48)	74 (47)
1	72 (49)	78 (50)
2	5 (3)	5 (3)
Disease Type, n (%)	**DLBCL & HGBL, n=148**	**LBCL, N=157**
DLBCL[a]	127 (86)	127 (81)
De novo	92/127 (72)	92/127 (72)
Transformed	33/127 (26)	33/127 (26)
HGBL	21 (14)	21 (13)
PMBCL	0	4 (3)
FL G3B	0	5 (3)

Prior Treatments	**DLBCL & HGBL, n=148**	**LBCL, N=157**
Median time from initial diagnosis to first dose, mo	19	19
Median time from end of last therapy to first dose, mo	2.4	2.4
Median prior lines of therapy (range)	3 (2–11)	3 (2–11)
≥3 Lines of therapy, n (%)	104 (70)	110 (70)
Primary refractory[b] disease, n (%)	88 (59)	95 (61)
Refractory[b] to last systemic therapy, n (%)	122 (82)	130 (83)
Refractory[b] to ≥2 consecutive lines of therapy, n (%)	112 (76)	118 (75)
Prior ASCT, n (%)	27 (18)	31 (20)
Prior CAR T therapy, n (%)	58 (39)	61 (39)
Refractory[b] to CAR T therapy	43/58 (74)	46/61 (75)

[a]De novo versus transformed status of 2 patients with DLBCL was unknown. [b]Refractory disease is defined as disease that either progressed during therapy or progressed within <6 mo of completion of therapy.
ASCT, autologous stem cell transplant; CAR T, chimeric antigen receptor; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; G, grade; HGBL, high-grade B-cell lymphoma; LBCL, large B-cell lymphoma; mo, months; PMBCL, primary mediastinal large B-cell lymphoma; y, years.
Karimi Y, et al. Poster presentation at: American Society of Clinical Oncology; June 2-6, 2023; Chicago, IL, USA/Virtual.

Change in Tumor Burden

Best Overall Response by IRC, n (%)[a]	LBCL N=157
Overall response	**99 (63)** [95% CI: 55–71]
Complete response	**61 (39)** [95% CI: 31–47]
Partial response	38 (24)
Stable disease	5 (3)
Progressive disease	37 (24)



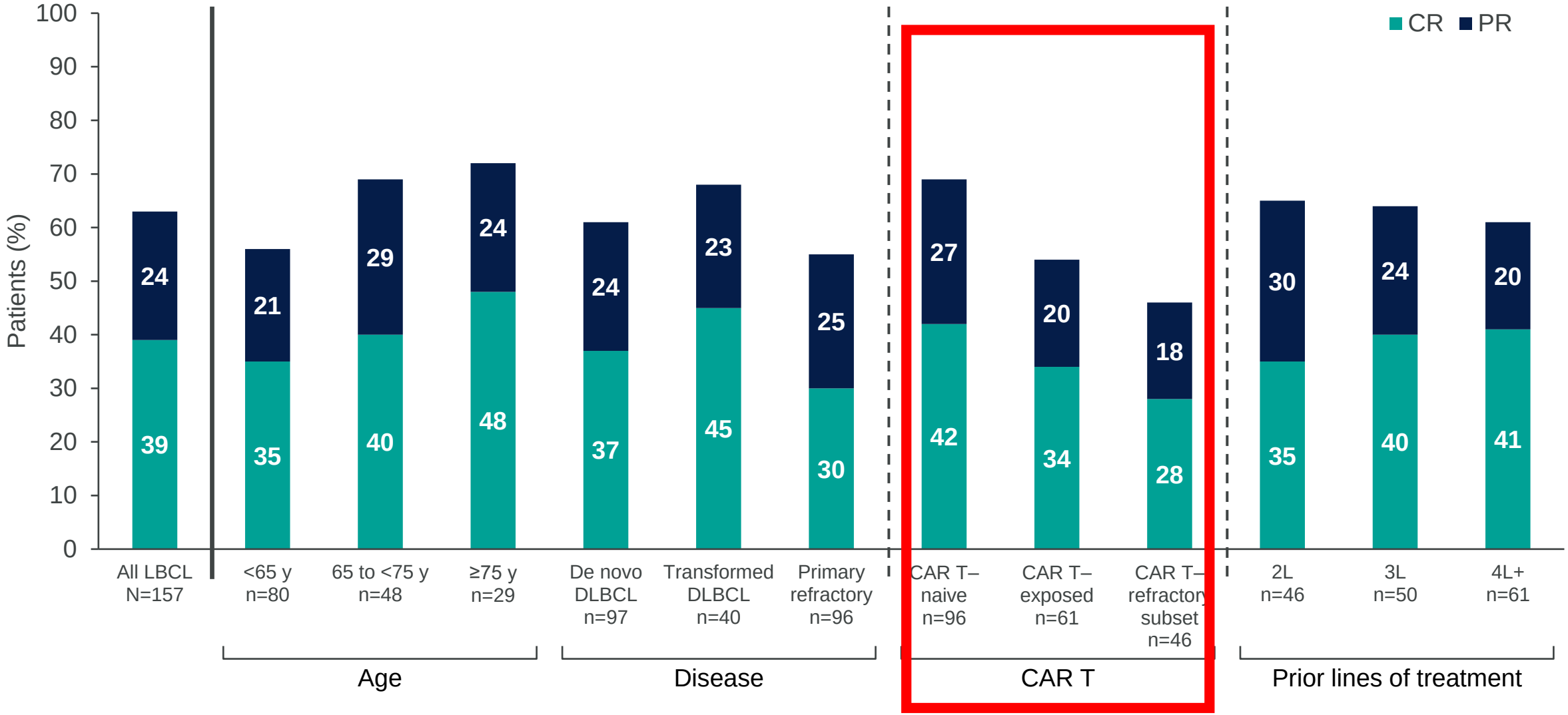
Data cutoff: Jan 31, 2022.
CAR T; chimeric antigen receptor T cell; CR, complete response; LBCL, large B-cell lymphoma; PD, progressive disease; PR, partial response; R/R, relapsed/refractory; SD, stable disease.
Based on IRC assessment and Lugano criteria.
Thieblemont C, et al. *J Clin Oncol.* 2022. doi: 10.1200/JCO.22.01725.

Overall Response to Treatment

Best Overall Response, n (%)	DLBCL & HGBL, n=148[a]	LBCL, N=157[a]
Overall response	90 (61) [95% CI, 53–69]	99 (63) [95% CI, 55–71]
Complete response	57 (39) [95% CI, 31–47]	62 (39) [95% CI, 32–48]
Partial response	33 (22)	37 (24)
Stable disease	5 (3)	5 (3)
Progressive disease	37 (25)	37 (24)

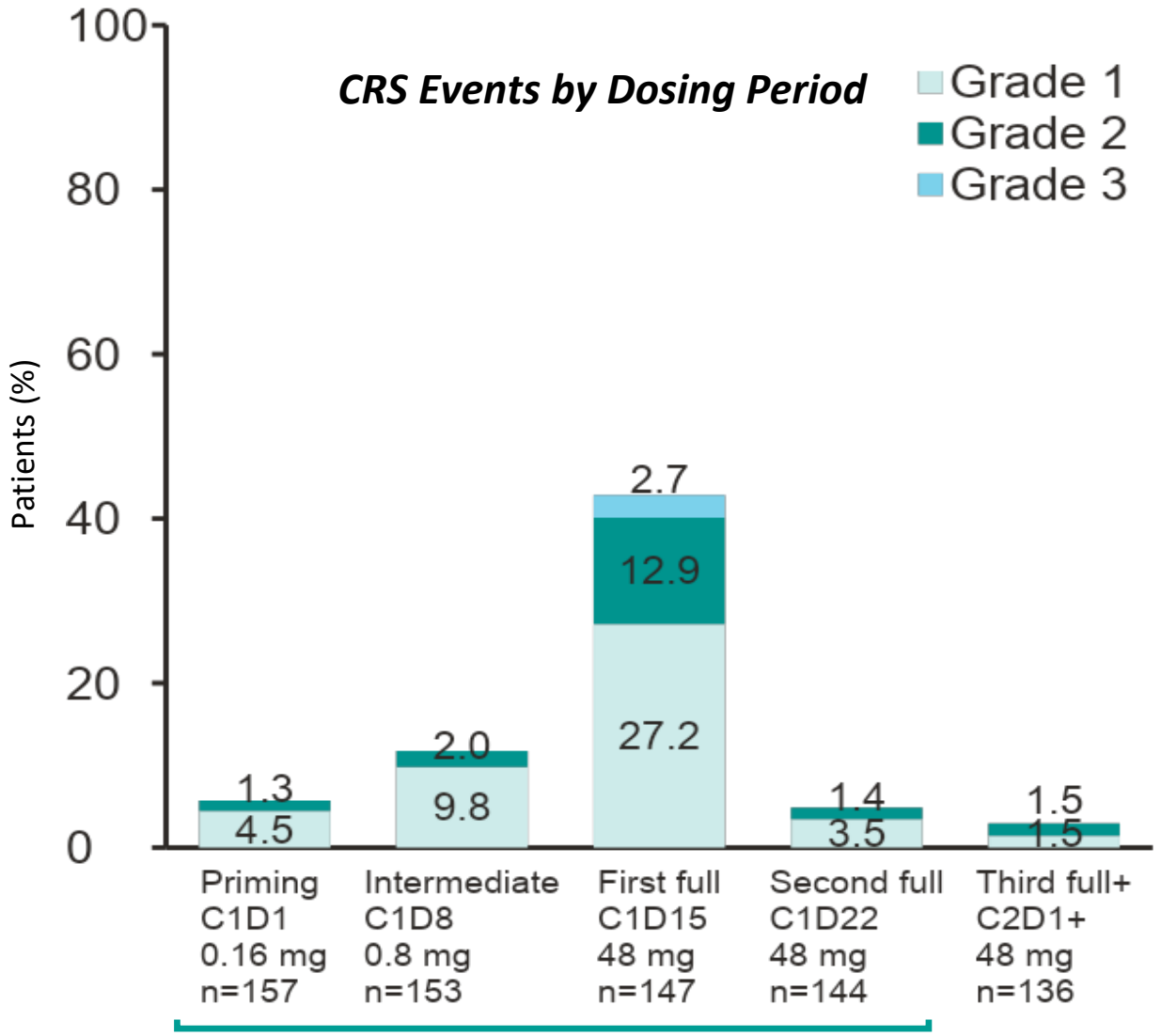
Based on IRC per Lugano criteria. [a]16 patients were not evaluable.
CAR T, chimeric antigen receptor; CI, confidence interval; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; HGBL, high-grade B-cell lymphoma; IRC, independent review committee; LBCL, large B-cell lymphoma; mo, months.
Karimi Y, et al. Poster presentation at: American Society of Clinical Oncology; June 2-6, 2023; Chicago, IL, USA/Virtual.

Responses Across Key Subgroups



Data cutoff: Jan 31, 2022.
Based on IRC assessment and Lugano criteria.
2L, second line; 3L, third line; 4L, fourth line; CAR T, chimeric antigen receptor T cell; CR, complete response; DLBCL, diffuse large B-cell lymphoma; IRC, independent review committee; LBCL, large B-cell lymphoma; PR, partial response; y, years.
Thieblemont C, et al. *J Clin Oncol.* 2022. doi: 10.1200/JCO.22.01725.

Treatment-Emergent Adverse Events: CRS



CRS was primarily low grade and predictable (most occurred following first full dose)

Median time to CRS onset from **most recent dose**

2 days
(range: 1-11 days)

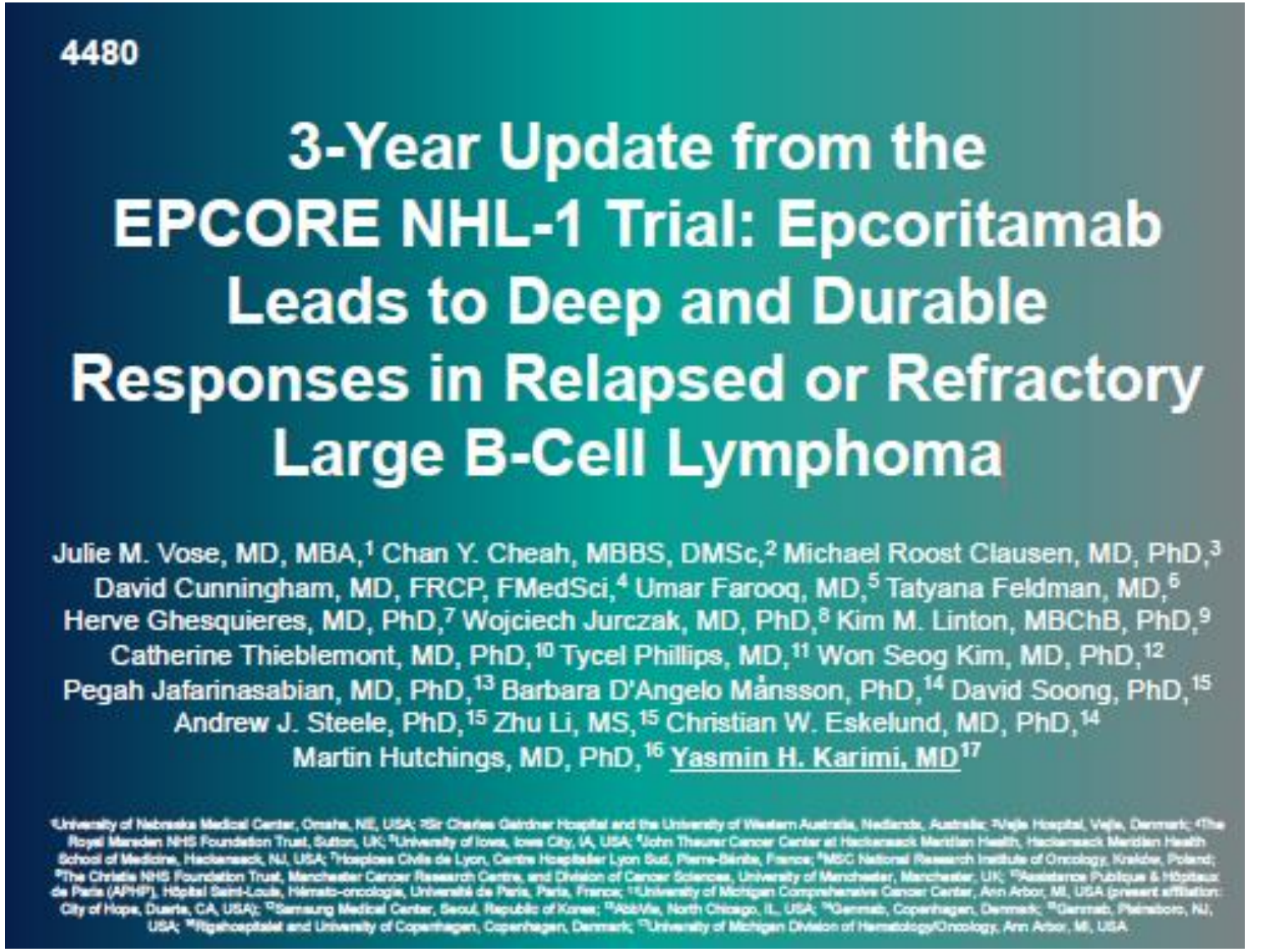
Median time to CRS onset from **first full dose**

20.2 hours
(range: 0.2-7 days)

Data cutoff: Jan 31, 2022.

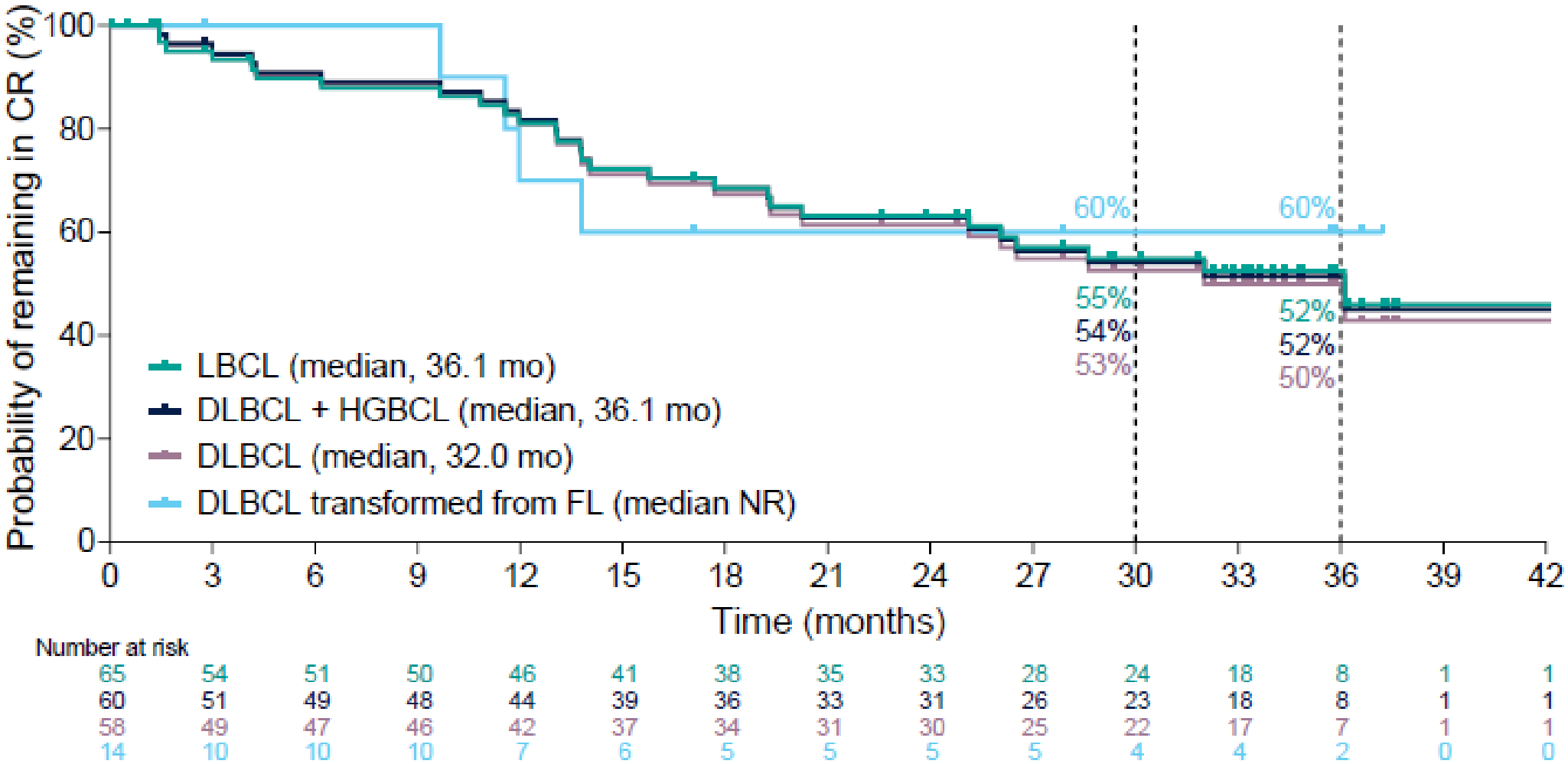
C, cycle; CRS, cytokine release syndrome; d, days; D, day; h, hours; LBCL, large B-cell lymphoma; SC, subcutaneous.

Thieblemont C, et al. J Clin Oncol. 2022. doi: 10.1200/JCO.22.01725. TEPKINLY EMA SmPC Sep2023



Vose et al. ASH 2024, Abstract 4480

Durable Complete Responses: Overall Median DOCR of 36.1 mo (95% CI, 20.2–NR)



Vose et al. ASH 2024, Abstract 4480

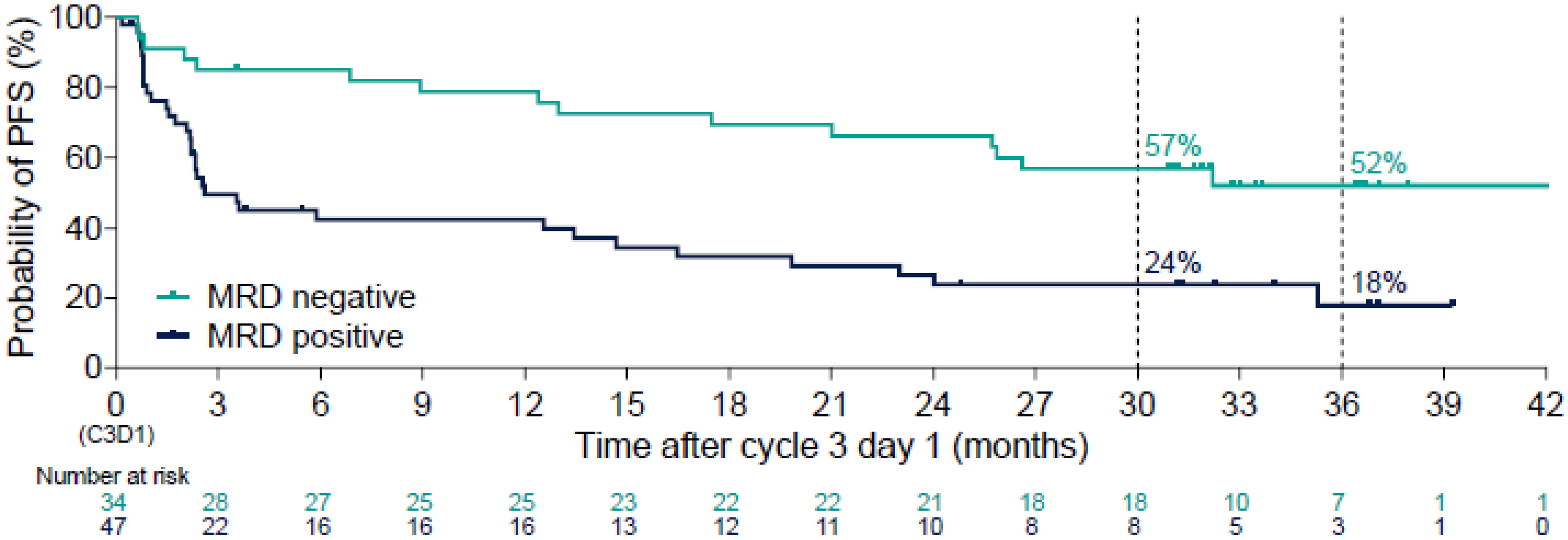
Interpretation of early PET results

- Eleven patients with indeterminate response (by LYRIC criteria) or progressive disease (by Lugano criteria) had subsequent response by Lugano criteria, as assessed by IRC
- 6 had durable CR and 5 of the 6 had MRD negativity in plasma preceding the Lugano CR.
- Take care not to abandon potentially useful treatment too early.
- If in doubt, consider short interval repeat scan, biopsy (or ctDNA analysis, if available).

Thieblemont et al. Leukemia. 2024 Sep 25;38(12):2653–2662

MRD Analysis

Cycle 3 Day 1 MRD Negativity Correlated With Improved PFS



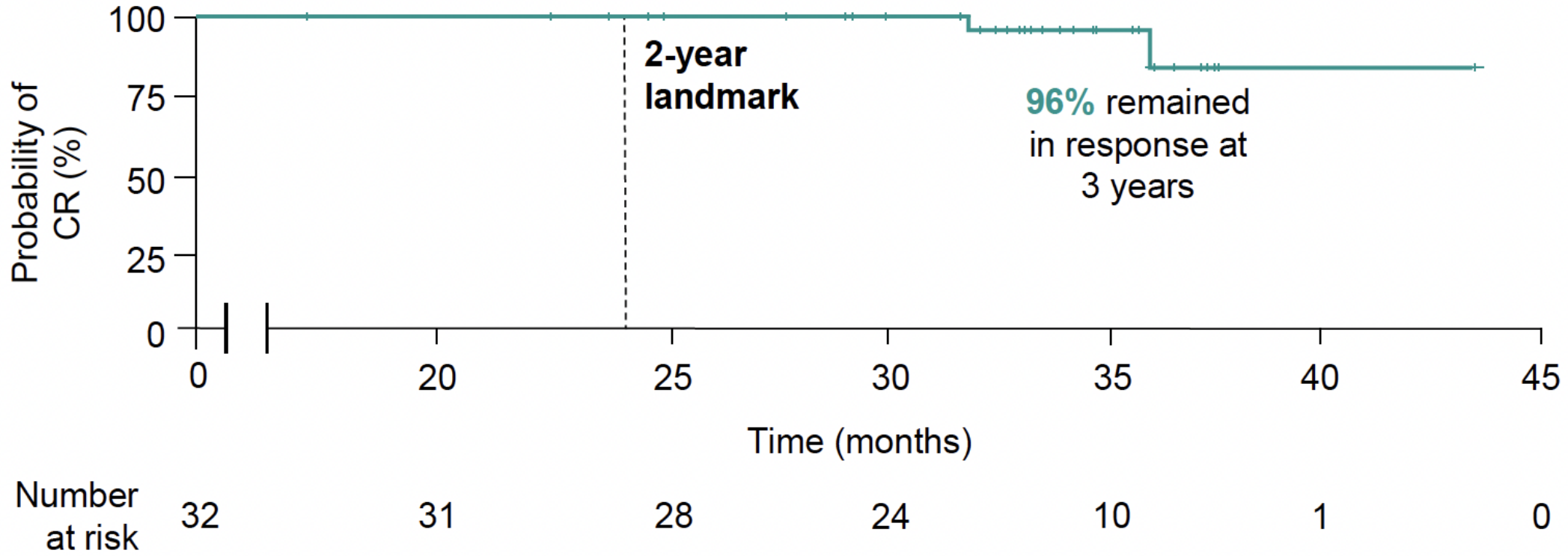
- Of 119 MRD-evaluable patients, 54 (45%) were MRD negative at any time
- In an exploratory landmark analysis, 98% (40/41) of MRD-evaluable patients were MRD negative at C13D1

ctDNA by Clonoseq

Vose et al. ASH 2024, Abstract 4480

Long-term follow-up from EPCORE-NHL-1

Landmark Analysis for Disease-Free Survival in Patients With CR at 2 Years



Cheah et al. EHA 2025

Outcomes after cessation of epcoritamab

- In the 12 patients with CR at 2 years who discontinued treatment for reasons other than PD, median follow-up after discontinuation was 14 months (range, 2–28). During this time, none of the 12 patients relapsed

Cheah et al. EHA 2025

Long-term safety profile

Incidence of TEAEs After 2 Years

	Patients with CR at 2 years (n=32)
TEAEs, n (%)	25 (78)
G3 and higher TEAEs	11 (34)
Serious TEAEs, n (%)	7 (22)
TEAEs leading to treatment discontinuation, n (%)	3 (9)
TEAEs leading to dose delay, n (%)	16 (50)
Fatal TEAEs, n (%)	2 (6)
Most common TEAEs of any grade, n (%)	
COVID-19	11 (34)
Diarrhea	5 (16)
Upper respiratory tract infection	5 (16)
Neutrophil count decreased	4 (13)
Pneumonia	4 (13)

Cheah et al. EHA 2025

Fixed-duration glofitamab monotherapy continues to demonstrate durable responses in patients with relapsed or refractory large B-cell lymphoma: 3-year follow-up from a pivotal Phase II study

Michael Dickinson,[1] Carmelo Carlo-Stella,[2] Franck Morschhauser,[3] Emmanuel Bachy,[4] Guillaume Cartron,[5] Paolo Corradini,[6] Nancy L. Bartlett,[7] Gloria Iacoboni,[8] Cyrus Khan,[9] Mark Hertzberg,[10] Lorenzo Falchi,[11] Joshua Brody,[12] Marek Trněný,[13] Estefania Mulvihill,[14] Aurelien Berthier,[14] Alessia Bottos,[14] James Relf,[15] Fabiola Bene Tchaleu,[16] Linda Lundberg,[14] Martin Hutchings[17]

[1]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and The University of Melbourne, Melbourne, Australia; [2]Humanitas University and IRCCS Humanitas Research Hospital, Milan, Italy; [3]Hôpital Claude Huriez and CHU de Lille, Lille, France; [4]Centre Hospitalier Lyon Sud, Lyon, France; [5]CHU de Montpellier, Montpellier, France; [6]University of Milan and Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [7]Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA; [8]Vall d'Hebron University Hospital, Barcelona, Spain; [9]Allegheny Health Network, Pittsburgh, PA, USA; [10]Prince of Wales Hospital and University of New South Wales, Sydney, Australia; [11]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [12]Tisch Cancer Institute, New York, NY, USA; [13]Charles University, Prague, Czech Republic; [14]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [15]Roche Products Ltd, Welwyn Garden City, UK; [16]Genentech, Inc., South San Francisco, CA, USA; [17]Rigshospitalet, Copenhagen, Denmark

Presented at the 66th ASH Annual Meeting | December 7–10, 2024

Study design

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

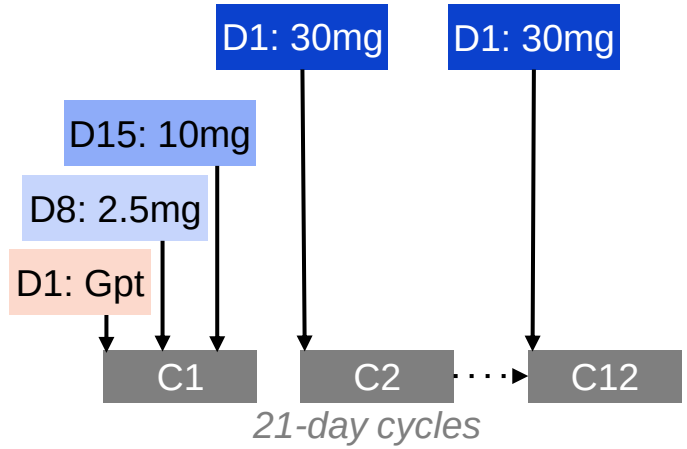
Glofitamab IV administration

Fixed-duration treatment:

- Q3W
- Up to 12 cycles (8.5 months)

CRS mitigation:

- Obinutuzumab IV pre-treatment (1000mg)
- C1 step-up dosing
- Monitoring after first glofitamab dose (2.5mg)



Endpoints

- **Primary**: CR rate (as best response) by IRC*
- **Key secondary**: ORR†, DoR†, DoCR†, PFS, OS

Analyses

- **Landmark**: PFS and OS by response (CR at EOT)
- **Biomarker:** ctDNA kinetics, immune recovery (B-cell, IgG and IgM)

*By PET-CT (Lugano criteria)[1], †By IRC and investigator.

C, cycle; CRS, cytokine release syndrome; ctDNA, circulating tumor DNA; D, day; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; DoCR, duration of complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; FL, follicular lymphoma; Gpt, obinutuzumab pre-treatment; HGBCL, high-grade B-cell lymphoma; IgG, immunoglobulin G; IgM, immunoglobulin M; IRC, independent review committee; IV, intravenous; NOS, not otherwise specified; ORR, overall response rate; OS, overall survival; PET-CT, positron emission tomography-computed tomography;
PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; Q3W, three-weekly.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

Baseline characteristics

n (%)*		All patients (N=154)†
Median age, years (range)		66 (21–90)
Male		100 (64.9)
ECOG PS‡	0	69 (44.8)
	1	84 (54.5)
Ann Arbor stage	I/II	35 (22.7)
	III/IV	116 (75.3)
NHL subtype	DLBCL NOS	110 (71.4)
	trFL	28 (18.2)
	HGBCL	10 (6.5)
	PMBCL	6 (3.9)
Bulky disease	>6cm	64 (41.6)
	>10cm	19 (12.3)

n (%)*	All patients (N=154)†
Median number of prior lines, n (range)	3 (2–7)
2 prior lines	61 (39.6)
≥3 prior lines	93 (60.4)
Prior CAR-T	51 (33.1)
Refractory to prior CAR-T§	46 (29.9)
Prior ASCT	29 (18.8)
Refractory to any prior therapy	138 (89.6)
Refractory to last line of prior therapy	130 (84.4)
Refractory to first line of prior therapy	90 (58.4)
Refractory to any prior anti-CD20	128 (83.1)

The patient population was heavily pre-treated and highly refractory to prior therapy

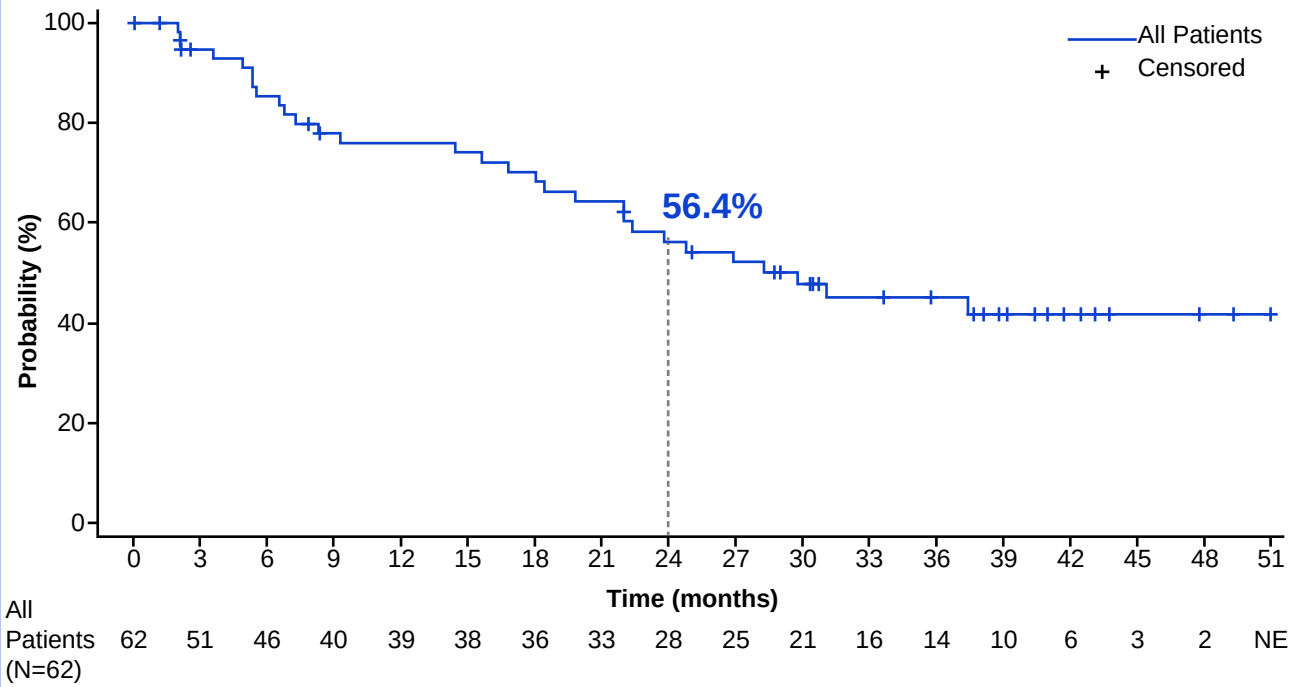
Clinical cut-off date: May 17, 2024. *Unless otherwise specified, †Safety evaluable population (all treated patients, one patient enrolled in the intention-to-treat population did not receive any study drug and was excluded from the safety-evaluable population); ‡ECOG PS 2, n=1 (0.6%); one patient had an ECOG PS of 1 at enrolment, but deteriorated before the receipt of study treatment;[1] §Patients who had no response or relapsed within 6 months.
ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T-cell therapy; NHL, non-Hodgkin lymphoma; trFL, transformed follicular lymphoma.

1. Dickinson M, et al. N Engl J Med 2022;387:2220–31.

Complete responses remained durable following fixed-duration glofitamab treatment

	(N=155)*
CR rate, n (%) [95% CI]	62 (40) [32.2–48.2]
ORR, n (%) [95% CI]	80 (52) [43.5–59.7]
Median DoCR, months (95% CI)	29.8 (22.0–NE)
24-month DoCR, % (95% CI)	56.4 (42.9–69.8)
Ongoing CRs, n/N (%)	33/62 (53.2)
Median CR follow-up, months (range)	37.7 (0–51)

DoCR by IRC



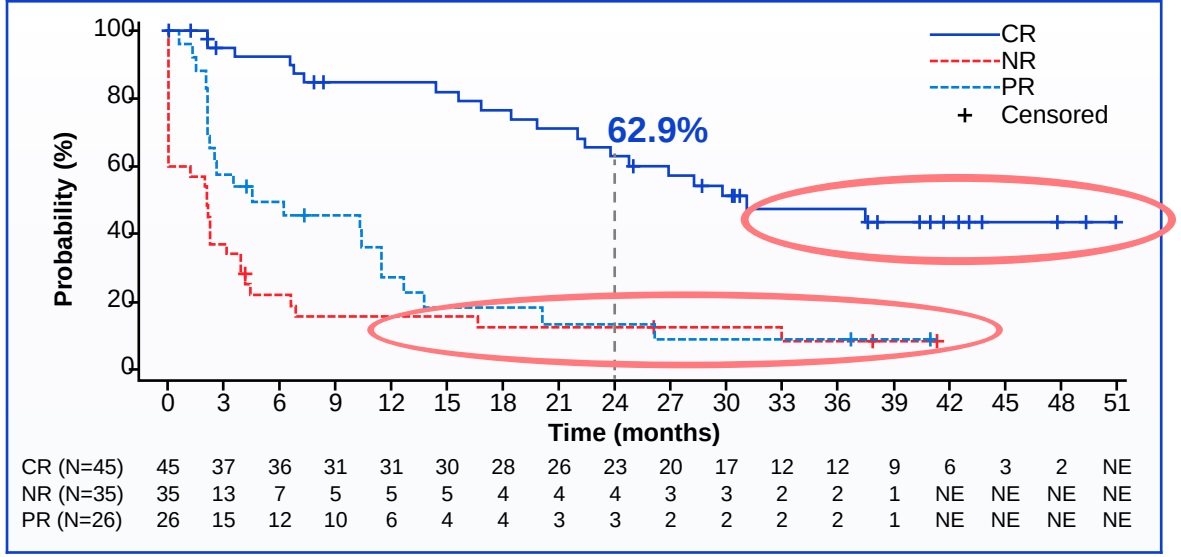
- Median time on study: 41.0 months (range: 0–52)

An estimated 56.4% of patients with a CR at any time remained in remission at 24 months

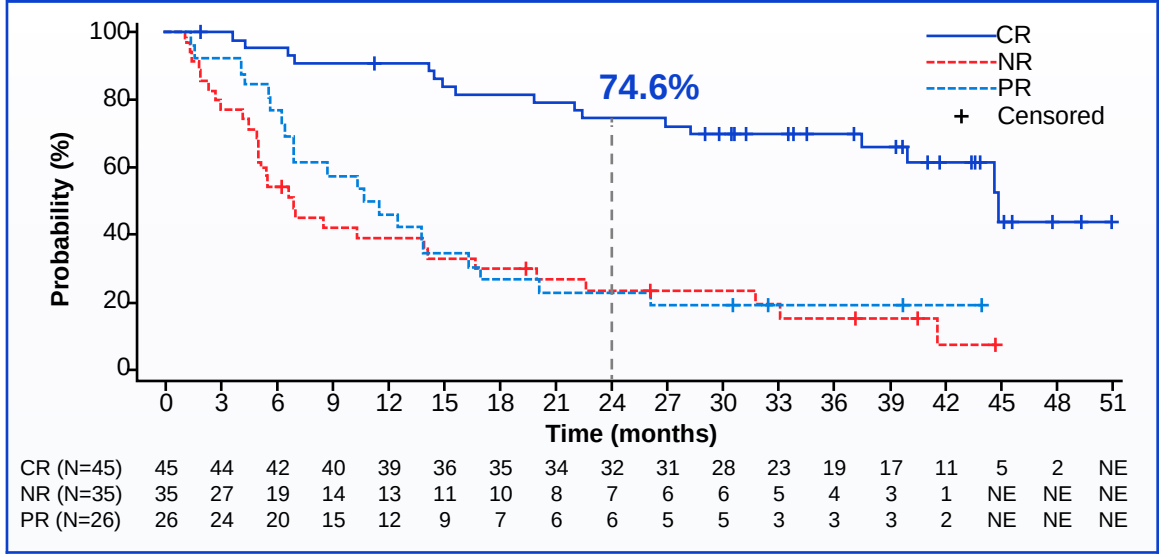
All responses in the table are based on the best overall response; *Intention-to-treat population; CI, confidence interval; NE, not estimable.

Landmark analysis by response at Cycle 3

PFS



OS



Landmark PFS from C3 in patients with CR at C3*	N=45
Median PFS, months (95% CI)	31.1 (23.8–NE)
24-month PFS rate, % (95% CI)	62.9 (47.5–78.4)

Landmark OS from C3 in patients with CR at C3*	N=45
Median OS, months (95% CI)	44.8 (40.0–NE)
24-month OS rate, % (95% CI)	74.6 (61.6–87.6)

Most patients with a CR at C3 remained progression-free and alive after 24 months

*Kaplan-Meier estimates. NR, no response; PR, partial response.

Bi-specifics in 2L DLBCL – selected trials

- Transplant eligible patients – improving CR rate with chemotherapy - addition of bi-specifics to CIT.
- Non-transplant eligible patients – addition of bi-specifics to SOC CIT (GemOx).
- Won't cover (in the interests of time) – bi-specifics in addition to non-chemoimmunotherapy treatments, eg:

1. Lenalidomide (epcoritamab)
2. Polatuzumab (glofitamab)

First Disclosure of Epcoritamab + R-ICE in Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma Eligible for Autologous Stem Cell Transplantation: EPCORE NHL-2

Raul Cordoba,[1] Marek Trneny,[2] Sven De Vos,[3] Pilar Gomez Prieto,[4] Gerardo Musuraca,[5] Justin Darrah,[6] Eliza Hawkes,[7] Daniel Morillo,[1] Rogier Mous,[8] Anna Sureda,[9] Umberto Vitolo,[10] Reid W. Merryman,[11] Tony Jiang,[12] Jennifer Marek,[13] Liwei Wang,[13] Malene Risum,[14] Catherine Thieblemont,[15] Pau Abrisqueta[16]

[1]Fundacion Jimenez Diaz University Hospital, Madrid, Spain; [2]Charles University and General University Hospital, Prague, Czechia; [3]Ronald Reagan University of California Los Angeles Medical Center, Los Angeles, CA, USA; [4]IdiPaz, La Paz University Hospital, Madrid, Spain; [5]IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, Italy; [6]Cedars-Sinai Medical Center, Los Angeles, CA, USA; [7]Olivia Newton John Cancer Research Centre, Austin Health; Monash University School of Public Health & Preventive Medicine, Melbourne, VIC, Australia; [8]University Medical Center Utrecht, Utrecht, The Netherlands; [9]Institut Català d'Oncologia – L'Hospitalet, IDIBELL; Universitat de Barcelona, Barcelona, Spain; [10]Candiolo Cancer Institute, FPO-IRCCS, Candiolo (Turin), Italy; [11]Dana-Farber Cancer Institute, Boston, MA, USA; [12]AbbVie, North Chicago, IL, USA; [13]Genmab, Plainsboro, NJ, USA; [14]Genmab, Copenhagen, Denmark; [15]Assistance Publique & Hôpitaux de Paris (APHP), Hôpital Saint-Louis; Université de Paris, Paris, France; [16]Hospital Universitario Vall d'Hebron, Barcelona, Spain

Presented at the European Hematology Association Annual Congress; June 12–15, 2025; Milan, Italy

Study Design

Key inclusion criteria:

- R/R CD20+ DLBCL
  - DLBCL, NOS
  - Double-hit or triple-hit DLBCL
  - FL grade 3B
  - T-cell/histiocyte DLBCL
- Relapsed or refractory to ≥1 prior LOT
- Eligible for R-ICE and HDT-ASCT
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Treatment regimen:
Epcoritamab SC 48 mg + R-ICE

R-ICE up to 3 cycles and epcoritamab until ASCT or progression

	Cycle length: 21 days				*Cycle length: 28 days*	
	C1	**C2**	**C3**	**C4**	**C5–9**	**C10+**
Epcoritamab SC 48 mg	QW[a]	QW	QW	QW	Q2W	Q4W
Rituximab[b]	D1	D1	D1			
Ifosfamide IV 5 g/m²/24h	D2	D2	D2			
Carboplatin IV AUC = 5 mg/mL × min	D2	D2	D2			
Etoposide IV 100 mg/m²	D1–3	D1–3	D1–3			

Primary endpoint: Investigator-assessed ORR per Lugano criteria[1,c]
Key secondary endpoints: CR rate, DOR, DOCR, PFS, OS, MRD-negativity rate, and safety/tolerability

Data cutoff: Dec 18, 2024. ClinicalTrials.gov: NCT04663347. 1. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-3068. [a]Patients received epcoritamab in weekly dosing of 2 step-up doses (0.16 mg; 0.8 mg) before the first full dose. Corticosteroid prophylaxis was used to mitigate CRS, and protocol-mandated hospitalization was required for 24 hours after the first full d[illegible]. [b]Dose per local guidelines. [c]Tumor response was evaluated by FDG PET-CT obtained at 9, 18, 24 weeks, and every 24 weeks thereafter until disease progression. AUC, area under the curve; C, cycle; CRS, cytokine release syndrome; CT, computed tomography; D, day; DOCR, duration of complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; IV, intravenous; LOT, line of treatment; MRD, minimal residual disease; MRI, magnetic resonance imaging; NOS, not otherwise specified; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival.

Demographics and Baseline Characteristics

Baseline characteristics	N=31
Median age, years (range)	62 (39–77)
Male sex at birth, n (%)	17 (55)
Race, n (%)	
White	22 (71)
Asian	1 (3)
Black or African American	0
Other	1 (3)
Not reported	7 (23)
ECOG PS, n (%)	
0	14 (45)
1	17 (55)
Ann Arbor stage, n (%)	
I/II	12 (39)
III/IV	19 (61)
Bulky disease (≥7 cm), n (%)[a]	13 (42)
Double hit/triple hit per central lab, n/N[b]	2/10

Treatment history	N=31
Median time from diagnosis to first dose, months (range)	10 (1–75)
Median prior LOTs, n (range)	1 (1–3)
1 prior LOT, n (%)	25 (81)
2 prior LOT, n (%)	5 (16)
3 prior LOT, n (%)	1 (3)
Primary refractory, n (%)[c]	15 (48)
Progressed within 12 months of 1L therapy, n (%)	20 (65)
Progressed >12 months of 1L therapy, n (%)	11 (35)
Refractory to anti-CD20, n (%)	17 (55)

[a]Bulky disease was classified by largest diameter of any lesion. [b]DH/TH status was not assessed in 21 (68%) patients. [c]Primary refractory disease was defined as being refractory to 1L antilymphoma therapy. 1L, first-line.

Most Patients Proceeded to Transplant

	N=31
Median follow-up, months (range)	11 (6–15)
Completed treatment and proceeded to ASCT, n (%)[a]	20 (65)
Remained on epcoritamab, n (%)	3 (10)
Discontinued treatment, n (%)	8 (26)
PD[b]	6 (19)
AE	0
Other[c]	2 (6)

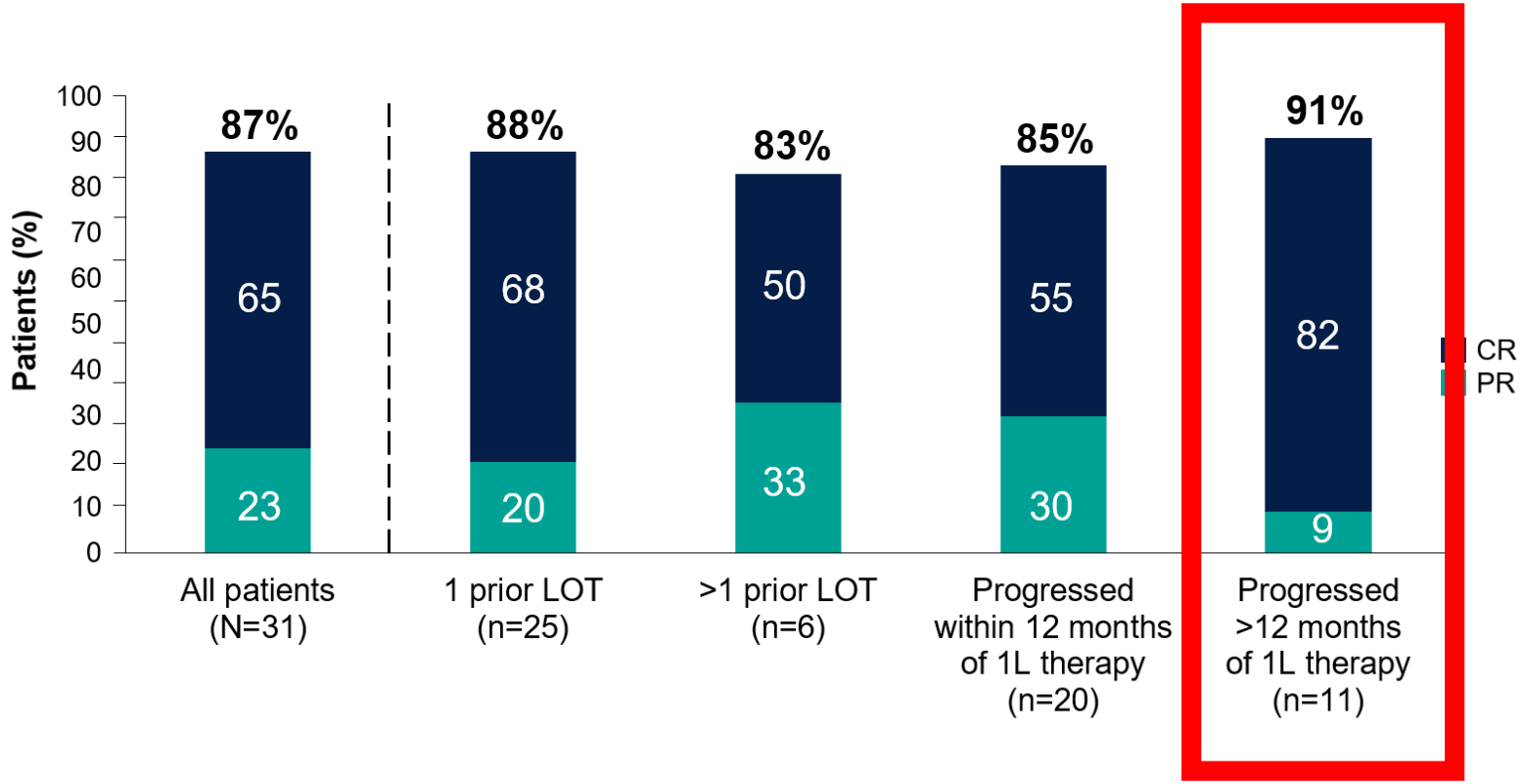
- Median epcoritamab treatment cycles initiated: 4 (range, 2–14)
- Median R-ICE treatment cycles initiated: 3 (range, 2–3)
- Relative dose intensity remained high throughout 3 treatment cycles
  - Median relative dose intensity for epcoritamab was ≥78% and for R-ICE was ≥80%

- Historic CR rate (Gisselbrecht JCO 2010) with RICE (62% rituximab-experienced patients) was 38%.

[a]Completed treatment and move to ASCT indicates that the patient completed epcoritamab + R-ICE and went on to receive transplant. [b]4 patients with PD proceeded to subsequent therapies: 3 to CAR T cell therapy, 1 to a subsequent trial. [c]One patient proceeded to allo SCT and 1 to radiotherapy followed by CAR T cell therapy. AE, adverse event; PD, progressive disease.

Epcoritamab + R-ICE in R/R DLBCL

High Response Rates Overall and Across Subgroups



Similar data exist for glofitamab (Diefenbach ASH 2024)

Use at 2L or in combination is not yet an approved indication of Epcoritamab in Singapore.
For other products, the product and indication registrations may vary by region or country. Please refer to your local prescribing information, which is available on request.

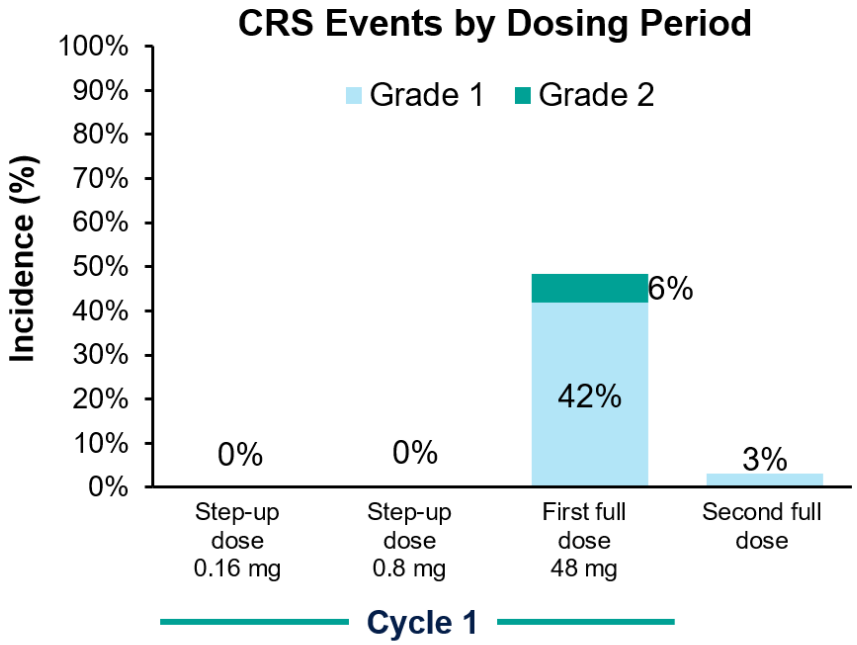
Epcoritamab + R-ICE in R/R DLBCL

CRS Was Low-Grade and Predictable

	N=31
CRS, n (%)[a]	16 (52)
Grade 1	13 (42)
Grade 2	3 (10)
Grade 3/4	0
Median time to first CRS onset, days (range)	17 (15–42)
Treated with tocilizumab, n/n (%)	5/16 (31)
CRS resolution, n/n (%)	16/16 (100)
Median time to resolution, days (range)	2 (1–8)
Leading to epcoritamab discontinuation, n (%)	0

[a]Graded by Lee et al 2019 criteria.[1]

1. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-638.



- CRS occurred predominantly during C1

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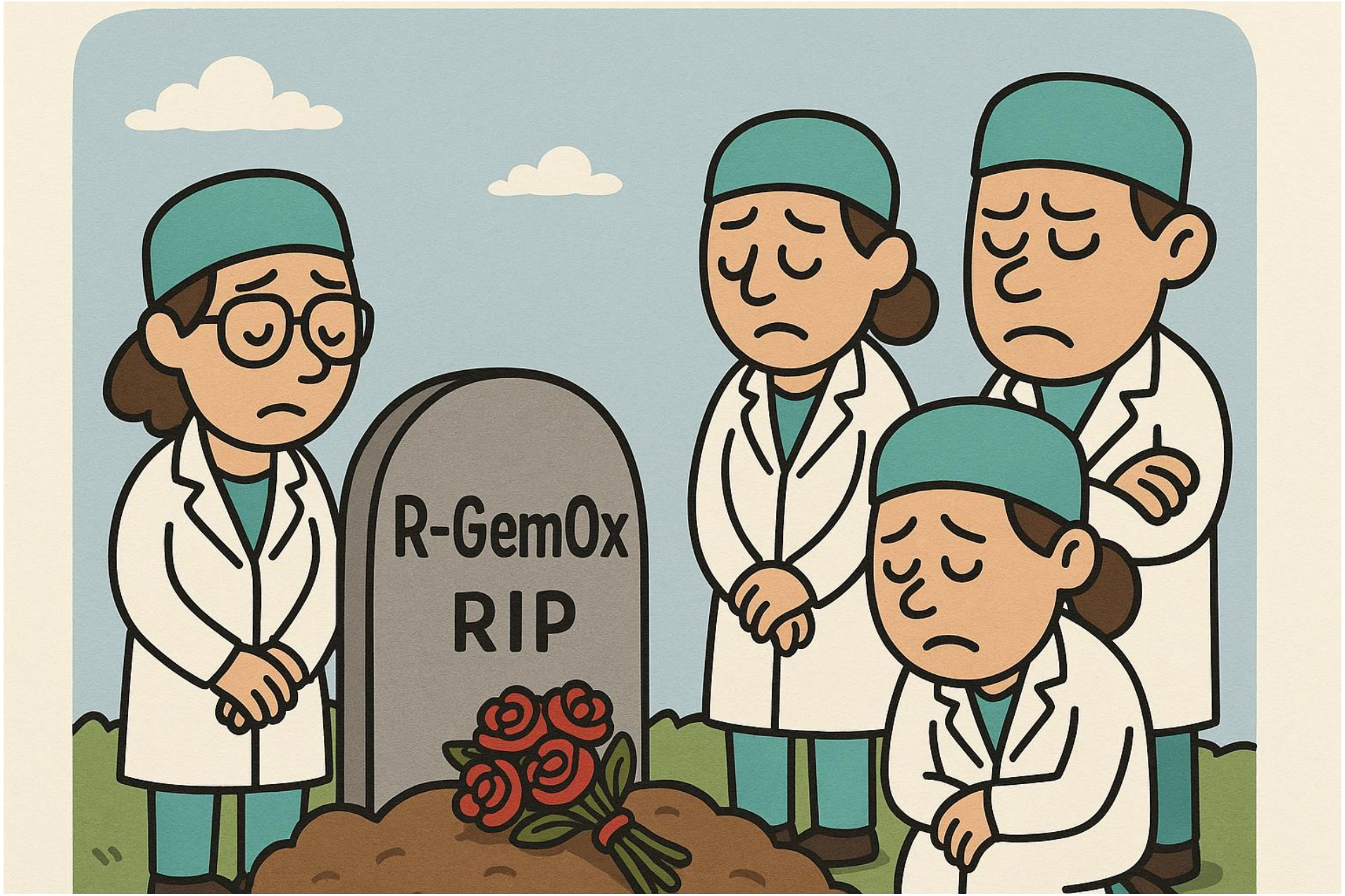
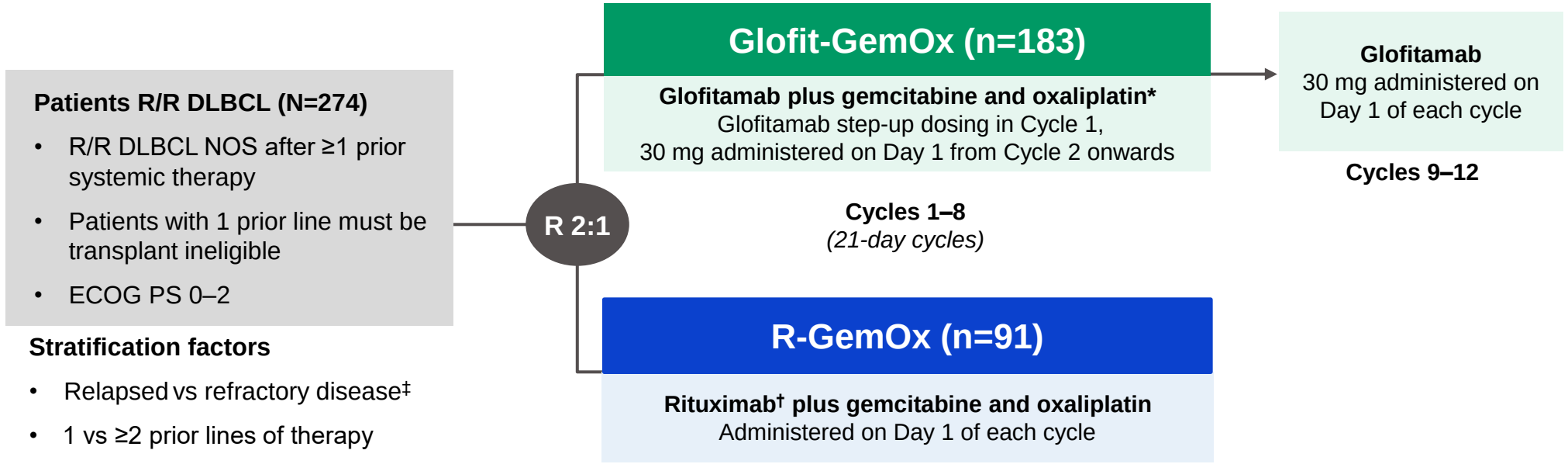
Transplant Ineligible Patients


R-GemOx
RIP

STARGLO: a randomized, global, Phase III trial



Primary endpoint:	Key secondary endpoints:	Safety endpoints:	Additional analyses:
OS	PFS, CR rate, DoCR (all IRC-assessed)	incidence, nature, and severity of AEs	landmark analysis at 1 year of patients in CR at EOT, subgroup analyses in 2L patients, ctDNA analyses, and immune recovery

*Gemcitabine 1000 mg/m^2 and oxaliplatin 100 mg/m^2. In C1, Gpt administered on D1, GemOx on D2, followed by Glofit 2.5 mg on D8 and Glofit 10 mg on D15; in C2–8, Glofit 30 mg and GemOx are administered on D1. †Rituximab 375 mg/m^2. ‡Relapsed disease: recurrence following a response that lasted ≥6 months after completion of the last line of therapy; refractory disease: disease that did not respond to, or that progressed <6 months after completion of the last line of therapy.
2L, second-line; AEs, adverse events; C, cycle; ctDNA, circulating tumor DNA; D, day; DoCR, duration of complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; Gpt, obinutuzumab pre-treatment; IRC, independent review committee; R 2:1, patients randomized in a 2:1 ratio.

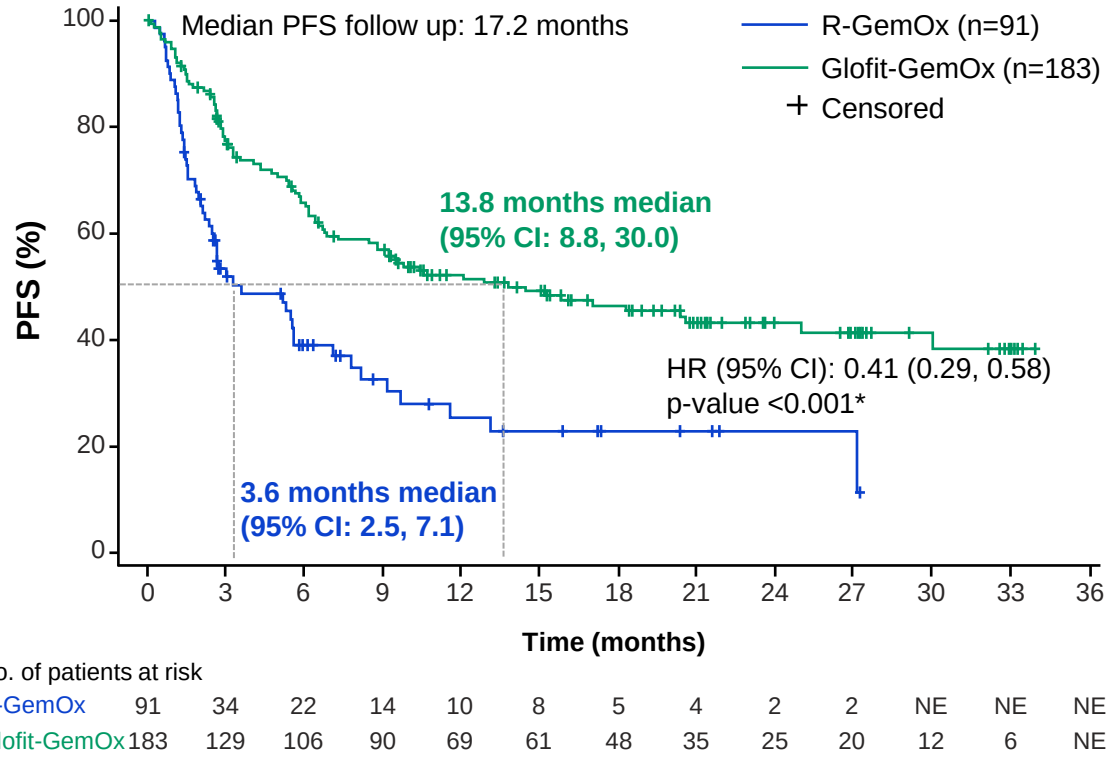
NCT04408638. Available at: https:www.clinicaltrials.gov.

Glofitamab-Gemox is not yet an approved indication of Glofitamab in Singapore.
For other products, the product and indication registrations may vary by region or country. Please refer to your local prescribing information, which is available on request.

Abramson et al. ASH 2024 and Lancet 2024;404:1940–54.

Sustained PFS benefit with Glofit-GemOx

Progression-free survival with extended follow up



Outcome	R-GemOx (n=91)	Glofit-GemOx (n=183)
PFS, median (95% CI); months	**3.6** (2.5, 7.1)	**13.8** (8.8, 30.0)
18-month PFS, % (95% CI)	**23.0** (11.5, 34.4)	**46.5** (38.5, 54.5)
ORR, % (95% CI)	**40.7** (30.5, 51.5)	**68.3** (61.0, 75.0)
CR rate, % (95% CI)	**25.3** (16.8, 35.5)	**58.5** (51.0, 65.7)
DoCR, median (95% CI); months	24.2 (6.9, NE)	NE (27.2, NE)
Ongoing CR, % (n)	**17.6** (16)	**42.1** (77)

Patients treated with Glofit-GemOx showed a sustained PFS benefit versus R-GemOx after 2 years of follow up

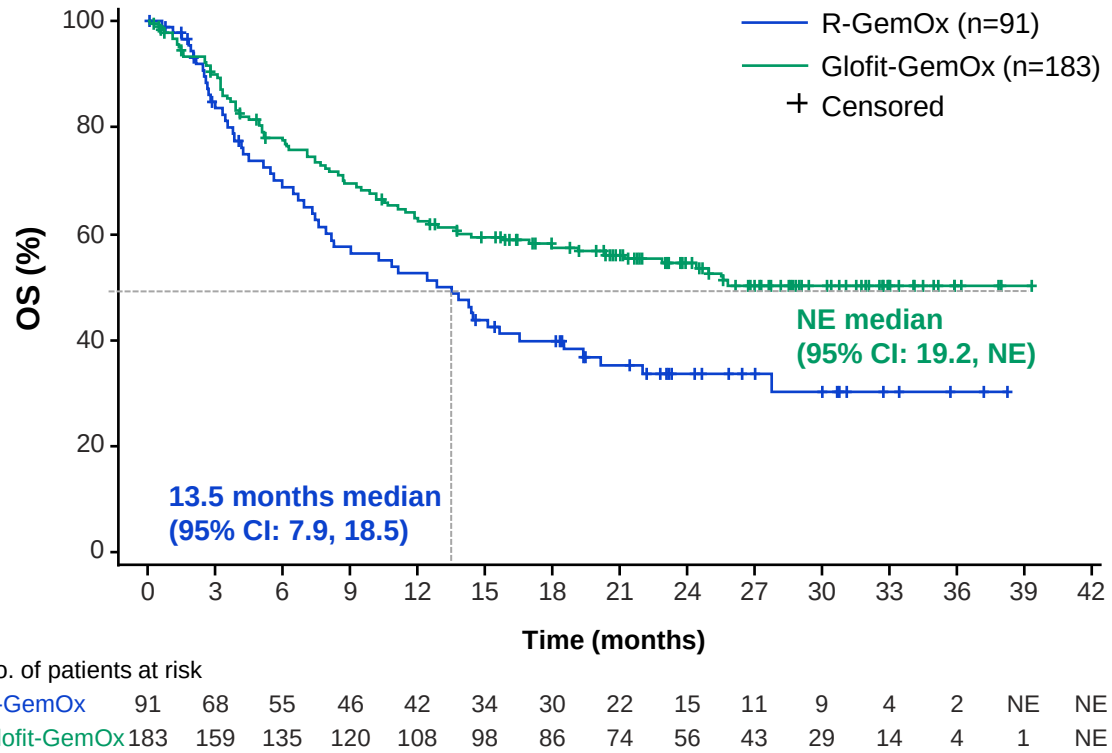
CCOD: June 17, 2024. Median follow up for CR: 17.7 months. Outcomes were IRC-assessed. *p-value is descriptive.
ORR, overall response rate.

Glofitamab-Gemox is not yet an approved indication of Glofitamab in Singapore.
For other products, the product and indication registrations may vary by region or country. Please refer to your local prescribing information, which is available on request.

1. Abramson JS, et al. Lancet 2024;404:1940–54.

Sustained OS benefit with Glofit-GemOx

Overall survival with ~2 years of follow up



Outcome	R-GemOx (n=91)	Glofit-GemOx (n=183)
2-year follow up analysis (median follow up: 24.7 months)		
OS, median (95% CI); months	13.5 (7.9, 18.5)	NE (19.2, NE)
HR (95% CI)	**0.60** (0.42, 0.85)	
p-value*	0.003	
24-month OS, % (95% CI)	**33.6** (22.9, 44.2)	**54.4** (46.8, 62.0)

- 26.9% of Glofit-GemOx-treated patients and 57.1% of R-GemOx-treated patients had received ≥1 NALT

Clinically meaningful OS benefit for Glofit-GemOx versus R-GemOx remains after 2 years of follow up

CCOD: June 17, 2024. *p-value is descriptive.
CI, confidence interval; HR, hazard ratio; NALT, new anti-lymphoma treatment; NE, not evaluable.
Glofitamab-Gemox is not yet an approved indication of Glofitamab in Singapore.
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1. Abramson JS, et al. Lancet 2024;404:1940–54.

Safety profile summary

n (%), unless otherwise stated	R-GemOx n=88	Glofit-GemOx (Glofit-exposed) n=172
Number of infusions, median (range)	4 (1–8)	12 (1–14)
Serious AEs	15 (17.0)	90 (52.3)
Grade ≥3 AEs	36 (40.9)	132 (76.7)
Grade 5 AEs	4 (4.5)	12 (7.0)
AE leading to any treatment discontinuation	11 (12.5)	44 (25.6)
CRS (any grade)	NA	77 (44.8)
Grade 3–4*	NA	4 (2.3)
ICANS (any grade)	NA	4 (2.3)
Grade 3–4*	NA	1 (0.6)
Infections (any grade)	26 (29.5)	95 (55.2)
Grade 3–4	8 (9.1)	29 (16.9)
Grade 5	3 (3.4)	6 (3.5)†

The Glofit-GemOx safety profile is unchanged compared to the primary analysis,[1] and is consistent with the known risk of the individual study drugs

CCOD: June 17, 2024. AEs, including ICANS, are graded by NCI CTCAE v5.0, CRS events are graded by ASTCT 2019. *No grade 4 events reported.
†3 patients had COVID-19, 1 patient had a respiratory tract infection (COVID-19 associated), 1 patient had pneumonia, and 1 patient had septic shock.
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; NA, not applicable.

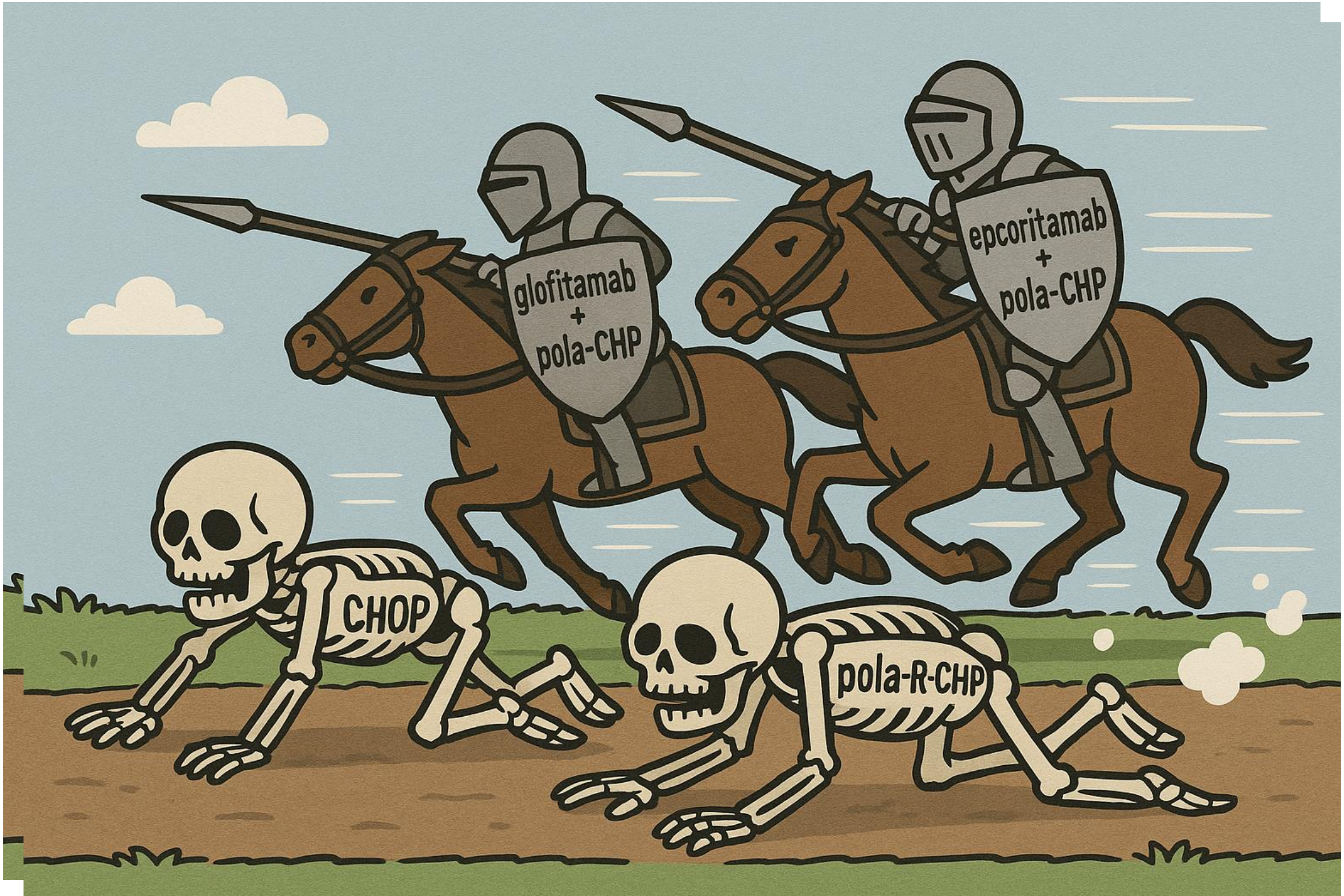
1. Abramson JS, et al. Lancet 2024;404:1940–54.

Glofitamab-Gemox is not yet an approved indication of Glofitamab in Singapore.
For other products, the product and indication registrations may vary by region or country. Please refer to your local prescribing information, which is available on request.

2L Treatment - summary

- Bi-specifics added to CIT lead to high CR rates in both transplant-eligible and transplant ineligible patients.
- In transplant ineligible patients, addition of glofitamab to GemOx resulted in substantial OS benefit *vs* GemOx alone.

1L treatment - How Can we improve on R-CHOP or pola-R-CHP?


glofitamab
+
pola-CHP
epcoritamab
+
pola-CHP
CHOP
pola-R-CHP

581

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, PhD[11]

[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Universitair Ziekenhuis Gent, Ghent, Belgium; [3]Ronald Reagan University of California Los Angeles Medical Center, Los Angeles, CA, USA; [4]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [5]Fundacion Jimenez Diaz University Hospital, Health Research Institute IIS-FJD, Madrid, Spain; [6]The Christie NHS Foundation Trust, Manchester Cancer Research Centre, and Division of Cancer Sciences, University of Manchester, Manchester, UK; [7]Department of Hematology, AZ Sint-Jan Hospital, Bruges, Belgium; [8]Vejle Hospital, Vejle, Denmark; [9]AbbVie, North Chicago, IL, USA; [10]Genmab, Plainsboro, NJ, USA; [11]4th Department of Internal Medicine – Hematology, University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic

Presented at the American Society of Hematology Annual Meeting; December 7–10, 2024; San Diego, CA

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.

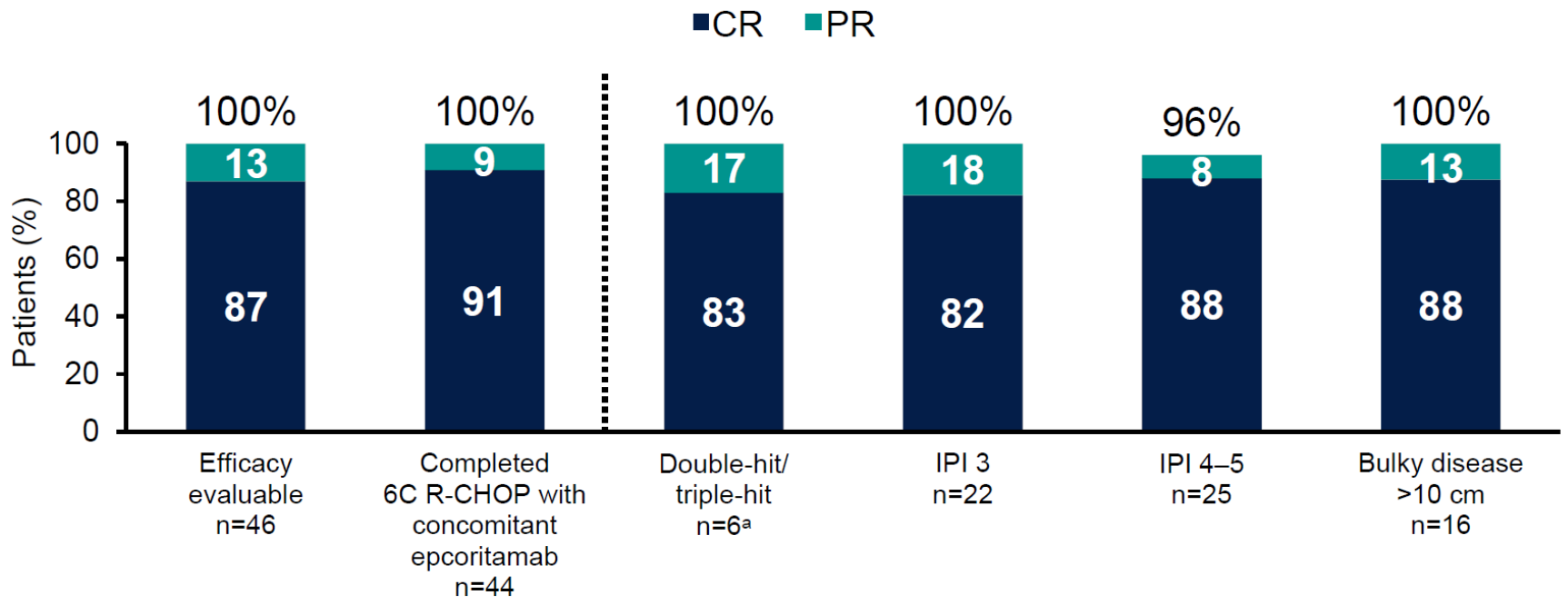
All Patients Were High Risk With IPI 3–5 at Screening

Characteristic	N=47
Median age, y (range)	64 (19–82)
≥75 y, n (%)	7 (15)
Male sex at birth, n (%)	23 (49)
Race, n (%)[a]	
White	37 (79)
Asian	6 (13)
Ethnicity, n (%)[b]	
Not Hispanic or Latino	19 (40)
Hispanic or Latino	1 (2)
ECOG PS, n (%)	
0–1	41 (87)
2	6 (13)
Ann Arbor stage, n (%)	
III	10 (21)
IV	37 (79)
IPI at screening, n (%)	
3	22 (47)
4–5	25 (53)

Characteristic	N=47
DLBCL, n (%)	47 (100)
De novo	39 (83)
Transformed	8 (17)
Double-hit/triple-hit by central lab, n/n (%)[c,d]	6/28 (21)
Bulky disease, n (%)[e]	
>10 cm	16 (34)
LDH, n (%)	
High	32 (68)
Extranodal disease at screening, n (%)	36 (77)
Cell of origin, n (%)	
Germinal center B-cell	28 (60)
Activated/non–germinal center B-cell	15 (32)
Unknown	4 (9)
Median time from initial diagnosis to first dose, wk (range)	4.0 (1.3–60.4)

[a]Race was not reported for 4 patients. [b]Ethnicity was not reported for 1 patient and missing for 26 patients. [c]Double-hit/triple-hit status by central lab was not evaluable in 19 patients. [d]Fourteen of 36 evaluable patients had double-hit/triple-hit lymphoma by local lab; double-hit/triple-hit status by local lab was not evaluable in 11 patients. [e]Lesion measurements per investigator assessment.

High Complete Response Rates Including Across High-Risk Subgroups

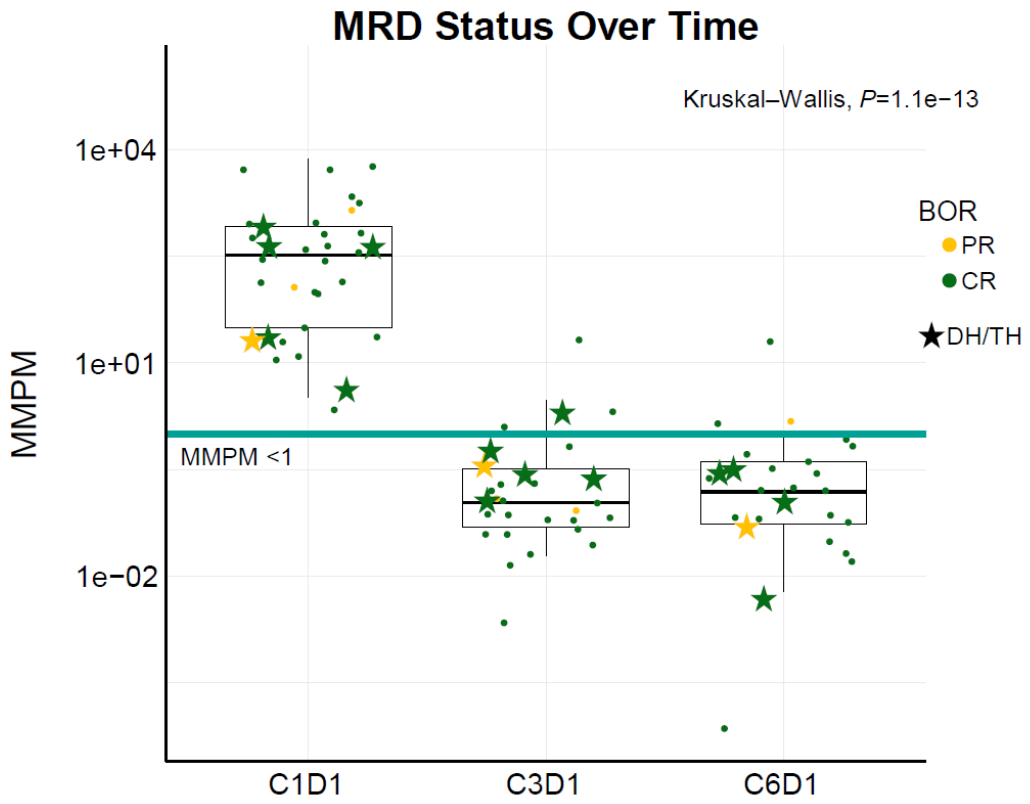


Exposure:

- 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.

Frequent and Sustained MRD Negativity

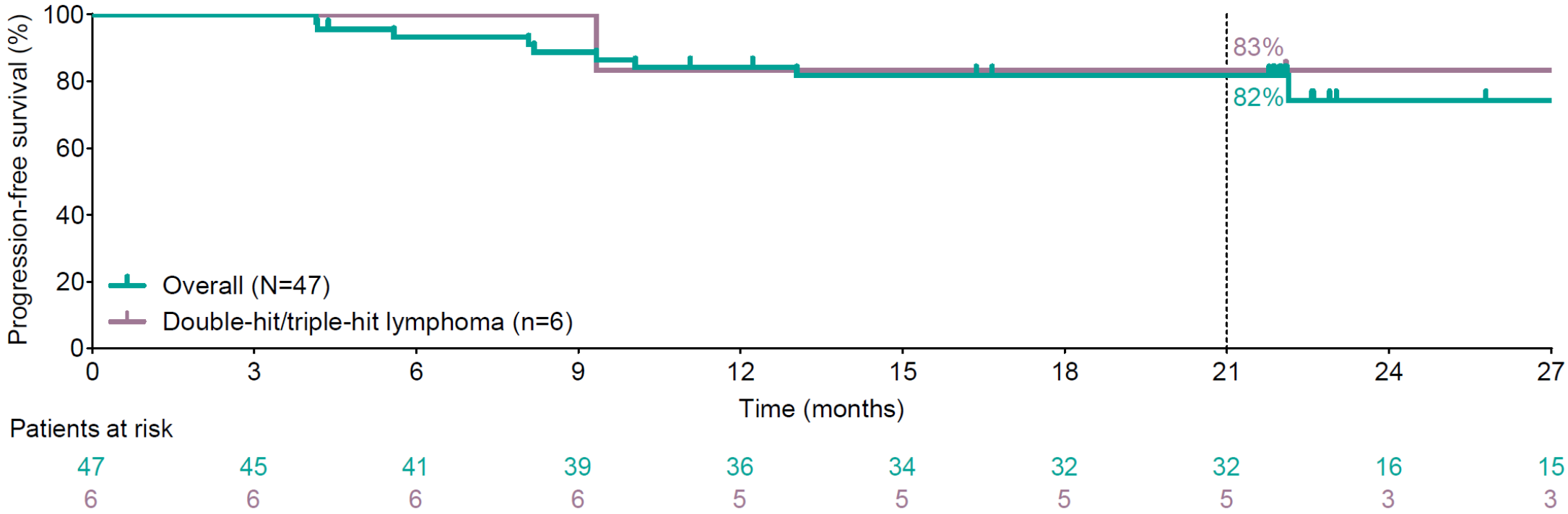


- 91% (30/33) of evaluable patients had MRD negativity
  - 83% (25/30) achieved MRD negativity by C3D1
    - Includes 5 of 6 patients with double-hit/triple-hit lymphoma
- Two patients MRD positive at C3D1 achieved negativity by C6D1

MRD negativity was assessed among patients with ≥1 baseline or on-treatment MRD result and MRD not negative at baseline. MMPM, mutant molecules per milliliter.

Epcoritamab + R-CHOP in 1L DLBCL

High Rates of Progression-Free Survival



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

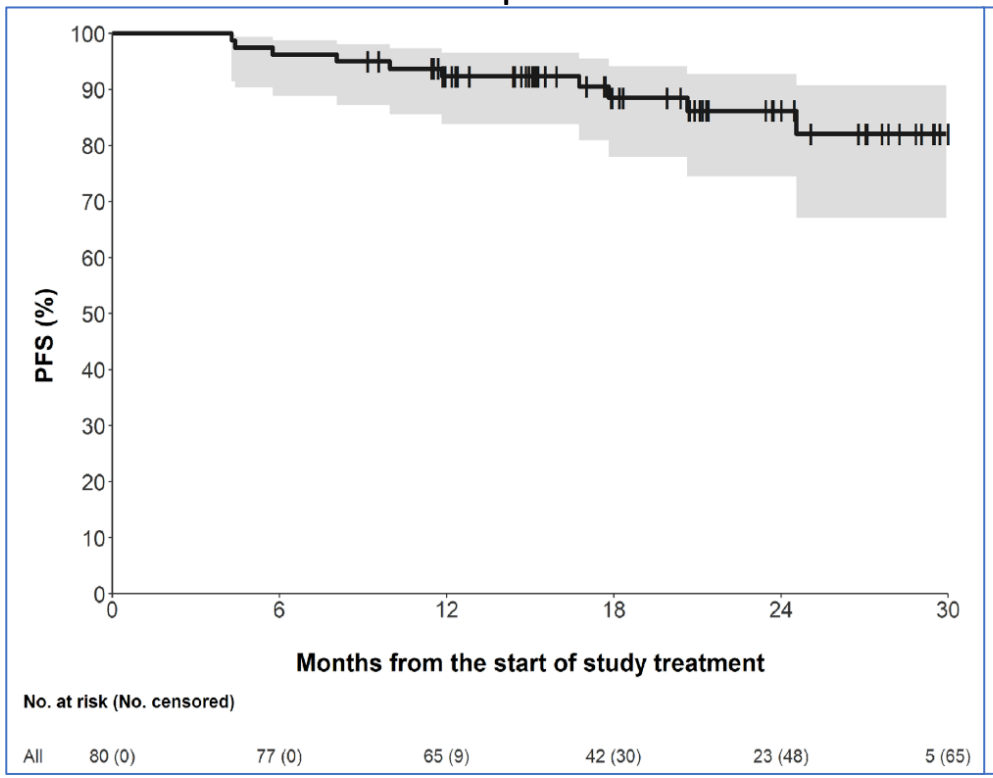
Use at 1L or in combination is not yet an approved indication of Epcoritamab in Singapore.
For other products, the product and indication registrations may vary by region or country. Please refer to your local prescribing information, which is available on request.

“COALITION” Trial in younger patients with high risk 1L DLBCL

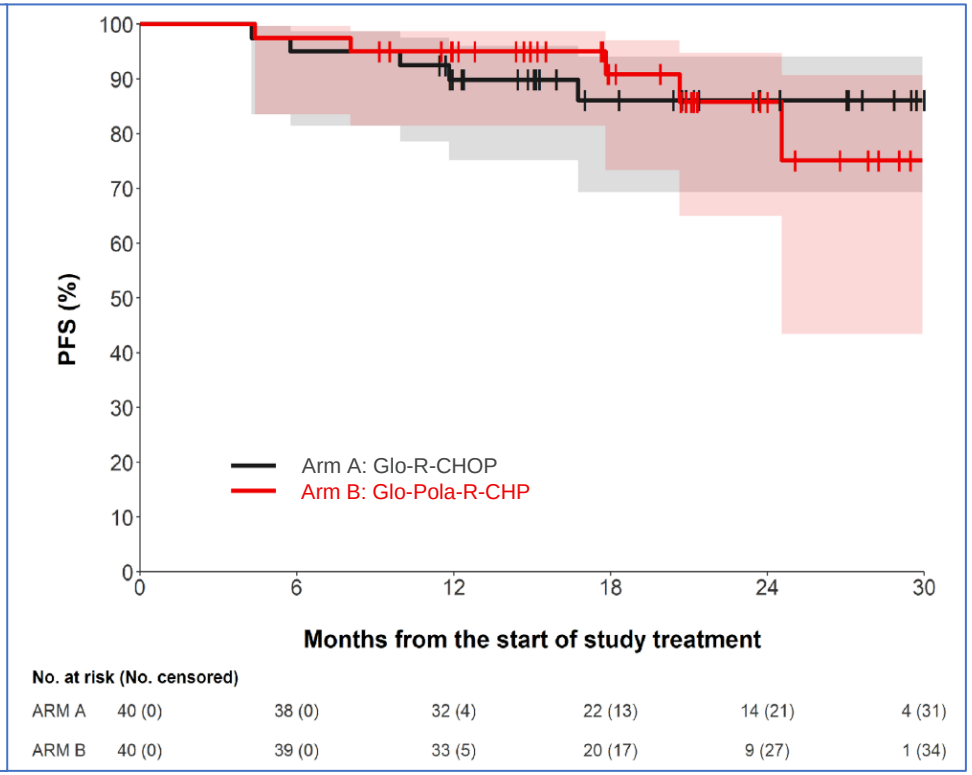
Ultra-high risk patients - <60, with at least one of:

1. IPI >/=3
2. NCCN IPI >/=4
3. Double hit

PFS all patients



PFS by study arm



PFS estimate	Arm A Glo-R-CHOP (n=40)	Arm B Glo-Pola-R-CHP (n=40)	All patients (n=80)
12-month PFS, % (95% CI)	**90%** (75%-96%)	**95%** (81%-99%)	**92%** (84%-97%)
24-month PFS, % (95% CI)	**86%** (69%-94%)	**86%** (65%-95%)	**86%** (75%-93%)

PFS is highly promising in this high-risk patient population – note higher risk than in the Crombie study

Median follow up 20.7 months

Minson et al JCO 2025

Combination at 1L is not yet an approved indication of Glofitamab in Singapore. For other products, the product and indication registrations may vary by region or country. Please refer to your local prescribing information, which is available on request.

Other notable approaches

- Addition of epcoritamab to R-mini-CHOP in elderly patients - Leslie et al. ASH 2024, Abstract 3106 – CRR 82%.
- ”chemo-free” approach in elderly patients with glofitamab added to pola + R – Wurm-Kuzera et al ICML 2025 – CRR 81%.
- Consolidation approaches post-initial chemoimmunotherapy de-bulking (eg. with surovatamig)