ER Congressi

9th Postgraduate Lymphoma Conference
Florence, Hotel Brunelleschi, March 20-21, 2025
Responsabile Scientifico: Pier Luigi Zinzani

Session III : Large B-cells lymphoma

Bispecifics and beyond

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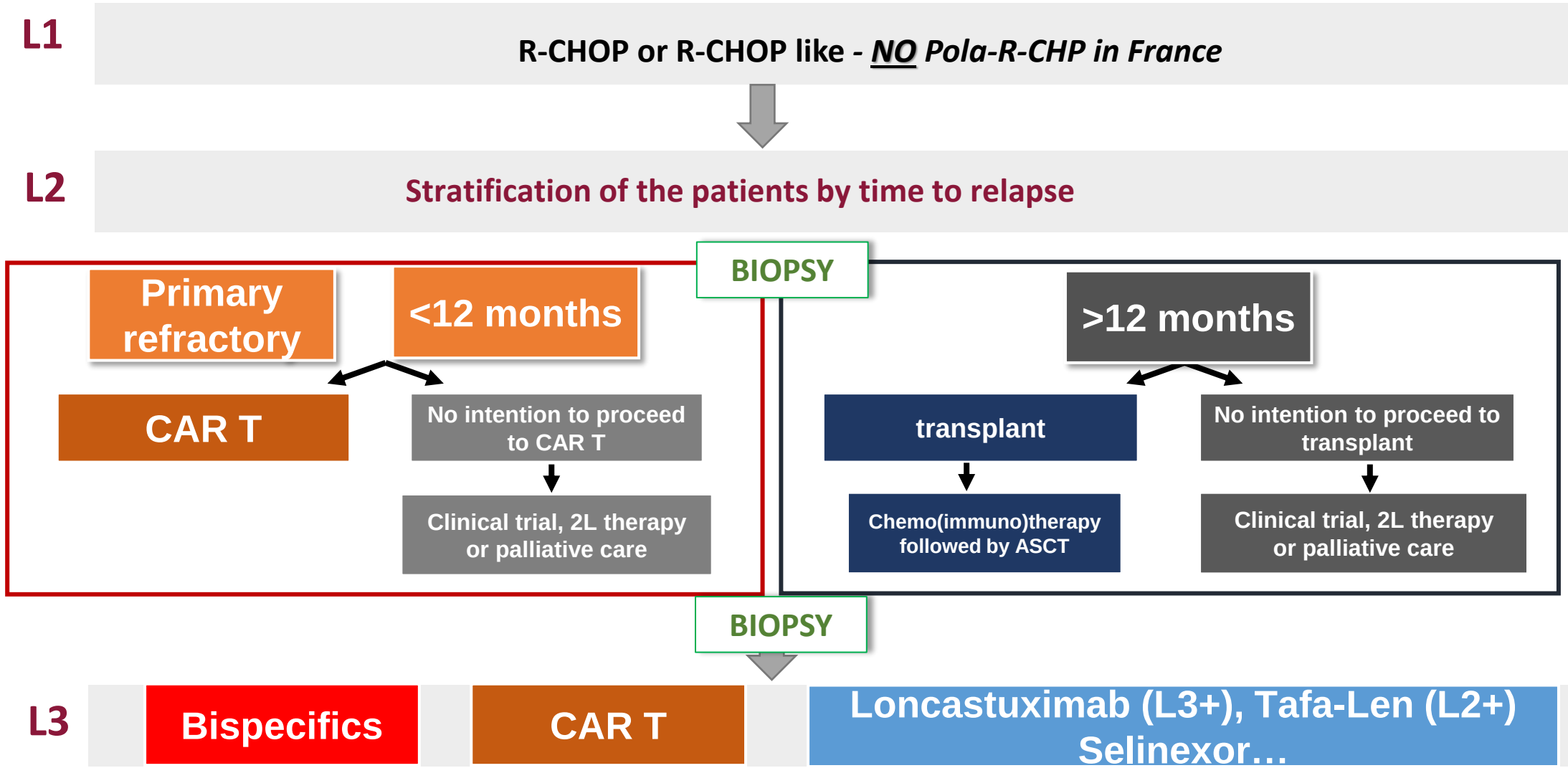
Large B-cell lymphomas : new treatment algorithm

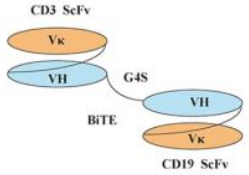


Pola=Polatuzumab Vedotin

- NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas. Version 5.2023 (May 2023; available at www.nccn.org).
- **EU recommendations**, EHA and ESMO guidelines, on this topic are currently under process of publication

Bispecific antibodies: novel class of off-the-shelf T-cell redirecting drugs

CD3 x CD19

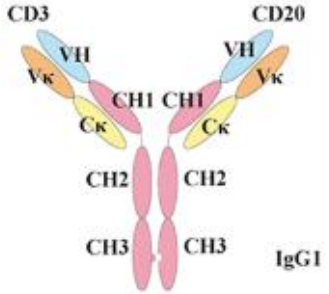


Blinatumomab

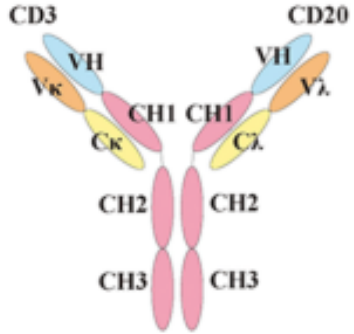
AZD0486

CD3 x CD20

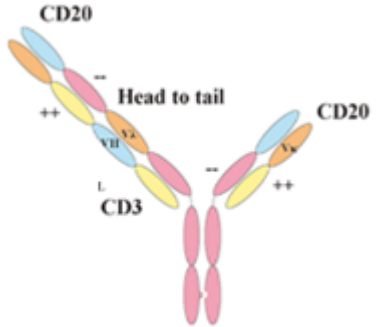
Ig G-based



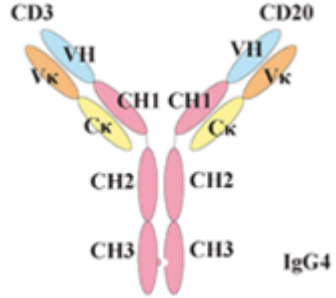
Mosunetuzumab



Epcoritamab

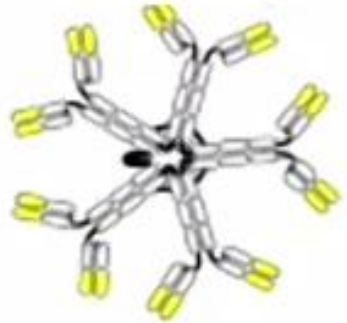


Glofitamab



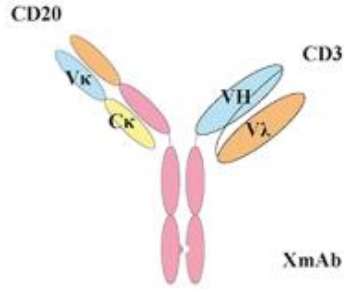
Odronextamab

Ig M-based



Imvotamab

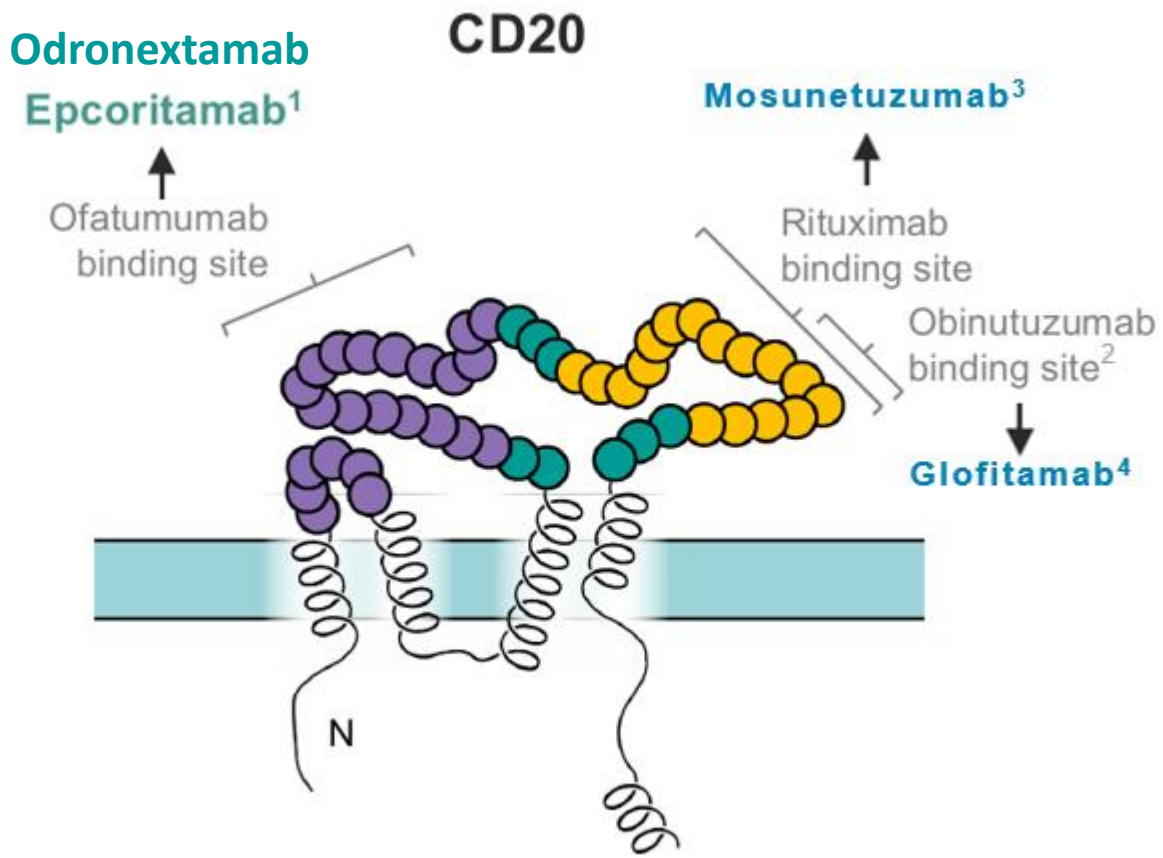
Under development



Plamotamab

Adapted Ma et al. Frontiers in Immunology 2021

CD20 Binding sites of CD20xCD3 BsAbs



Adapted from: 1. Engelberts PJ, et al. EBioMedicine. 2020;52:102625.; 2. Klein C, et al. MAbs. 2013;5(1):22-33; 3. Liping L. Sun et al. Sci. Transl. Med. (2015); 4. Bacac M, et al. Clin Cancer Res 1 October 2018; 24 (19): 4785–4797

Updates from LBCL phase 2 expansion cohorts

- Epcoritamab
- Glofitamab
- Odronextamab

Epcoritamab in aggressive LBCL

Dose escalation

Dose expansion data cutoff: April 21, 2023
Median follow-up: 25.1 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

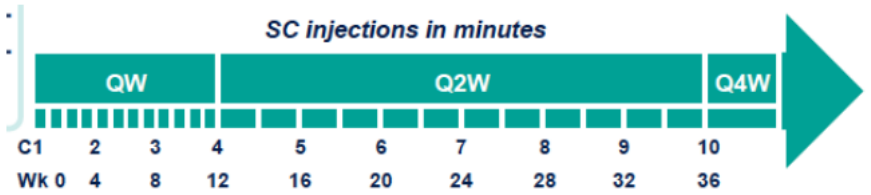
Step-up dosing[a]

Epcoritamab SC RP2D 48 mg
QW C1–3,
Q2W C4–9,
Q4W C10+

→ **Treatment until PD or unacceptable toxicity**

→ **LBCL Cohort N=157**
DLBCL, HGBCL, PMBCL, and FL Gr3B

- To ensure patient safety and better characterize CRS, inpatient monitoring was required at first full dose for 24 h in this part of the study
- **Primary endpoint:** ORR by Investigator Review Committee (IRC)
- **Key secondary endpoints:** DOR, TTR, PFS, OS, CR rate, and safety/tolerability



[a] C1D1 0.16 mg, C1D8 0.8 mg, C1D15 48 mg

Thieblemont C., J Clin Oncol, 2022, 41:2238-2247.

Patients were challenging to treat and highly refractory

Demographics	LBCL, N=157
Median age (range), y	64 (20–83)
<65 y, n (%)	80 (51)
65 to <75 y, n (%)	48 (31)
≥75 y, n (%)	29 (18)
ECOG PS, n (%)	
0	74 (47)
1	78 (50)
2	5 (3)
Disease Characteristics[a]	**LBCL, N=157**
Disease type, n (%)	
DLBCL	139 (89)
De novo	97/139 (70)
Transformed	40/139 (29)
Unknown	2/139 (1)
HGBCL	9 (6)
PMBCL	4 (3)
FL Gr3B	5 (3)

Prior Treatments	LBCL, N=157
Median time from initial diagnosis to first dose, y	1.6
Median time from end of last therapy to first dose, mo	2.4
Median prior lines of therapy (range)	3 (2–11)
≥3 Lines of therapy, n (%)	111 (71)
Primary refractory[b] disease, n (%)	96 (61)
Refractory[b] to last systemic therapy, n (%)	130 (83)
Refractory[b] to ≥2 consecutive lines of therapy, n (%)	119 (76)
Prior ASCT, n (%)	31 (20)
Prior CAR T therapy, n (%)	**61 (39)**
Progressed within 6 mo of CAR T therapy	46/61 (75)

[a]Double/triple-hit patients included, many with responses. [b]Refractory disease is defined as disease that either progressed during therapy or progressed within <6 months of completion of therapy.

Thieblemont C., J Clin Oncol, 2022, 41:2238-2247.

Response rates

Primary result : median follow-up, 10.7 months

Long-term result : median follow-up, 25.1-month

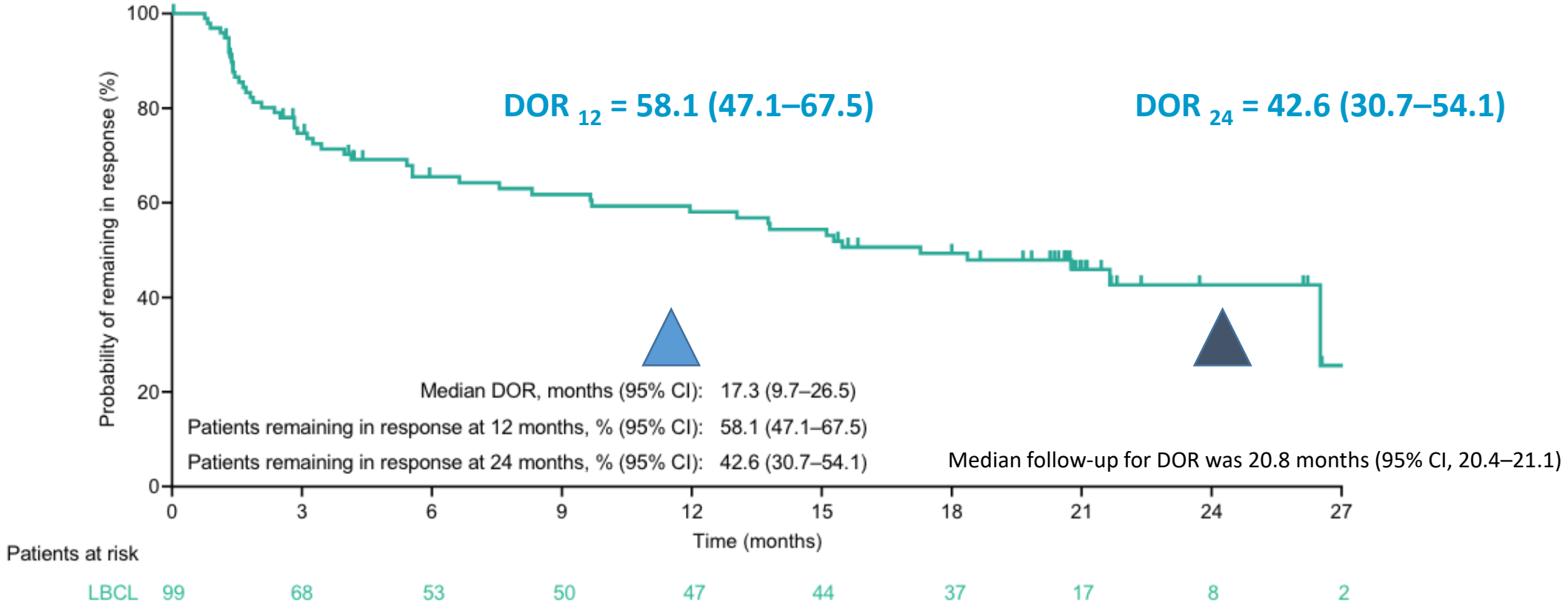
Best Overall Response by IRC, n(%)[a]	LBCL N=157	DLBCL N=139	HGBL N=9	PMBCL N=4	FL G3B N=5
Overall response	**99 (63.1%)**	**86 (62%)**	**4 (44%)**	**4 (100%)**	**5 (100%)**
Complete response	**63 (40.1%)**	**55 (40%)**	**2 (22%)**	**2 (50%)**	**3 (60%)**
Partial response	**36 (22.9%)**	31 (22%)	2 (22%)	2 (50%)	2 (40%)
Stable disease	5 (3%)	4 (3%)	1 (11%)	-	-
Progressive disease	37 (24%)	33 (24%)	4 (44%)	-	-

Median time to response was **1.4 mo** (range, 1.0–8.4); median time to CR was **2.6 months** (range, 1.2–23.2)

Thieblemont C., J Clin Oncol, 2022; 41:2238-2247
Thieblemont, Leukemia, 2024; 8:2653 – 2662

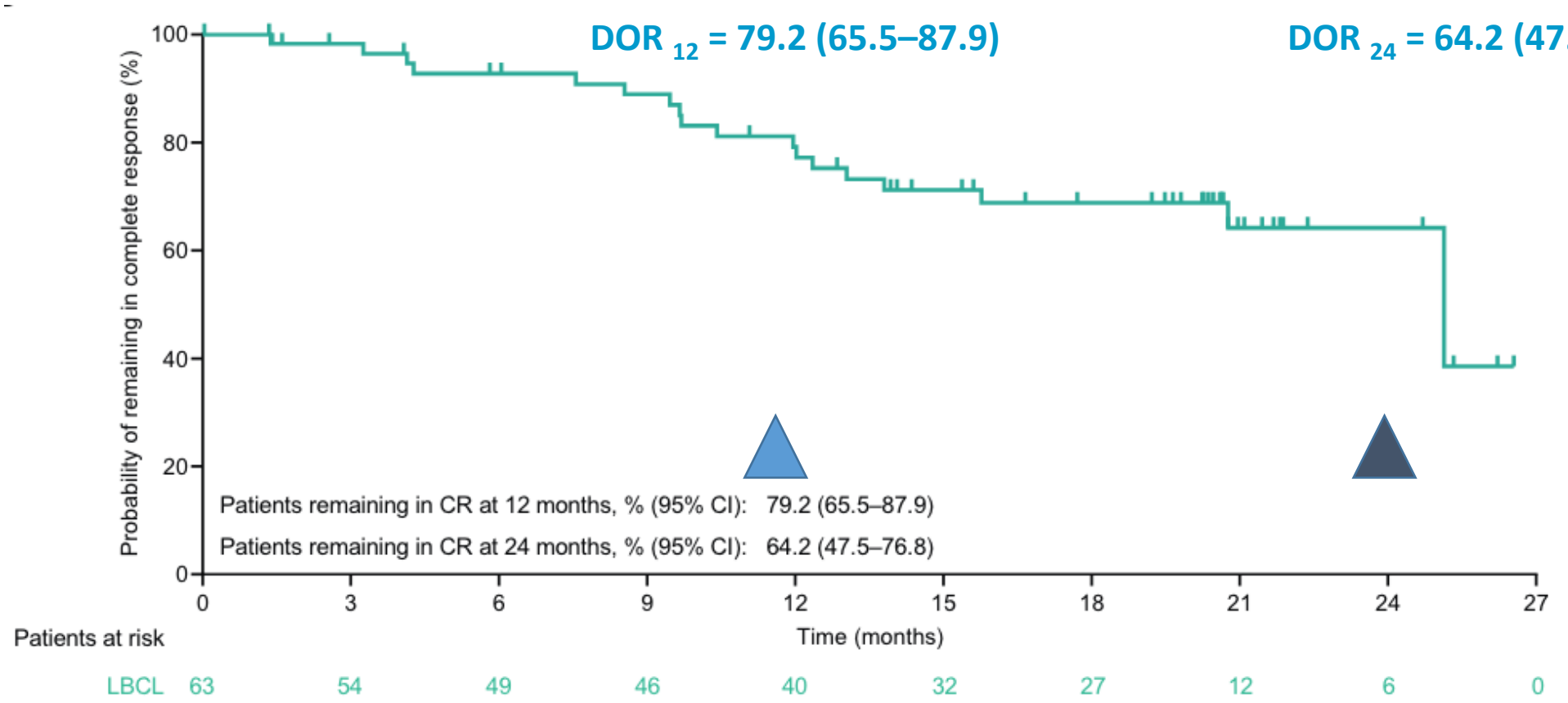
Duration of Response

Median **DOR** was **17.3 months** (95% CI, 9.7–26.5)



Thieblemont C., Leukemia 2024; 8:2653 – 2662

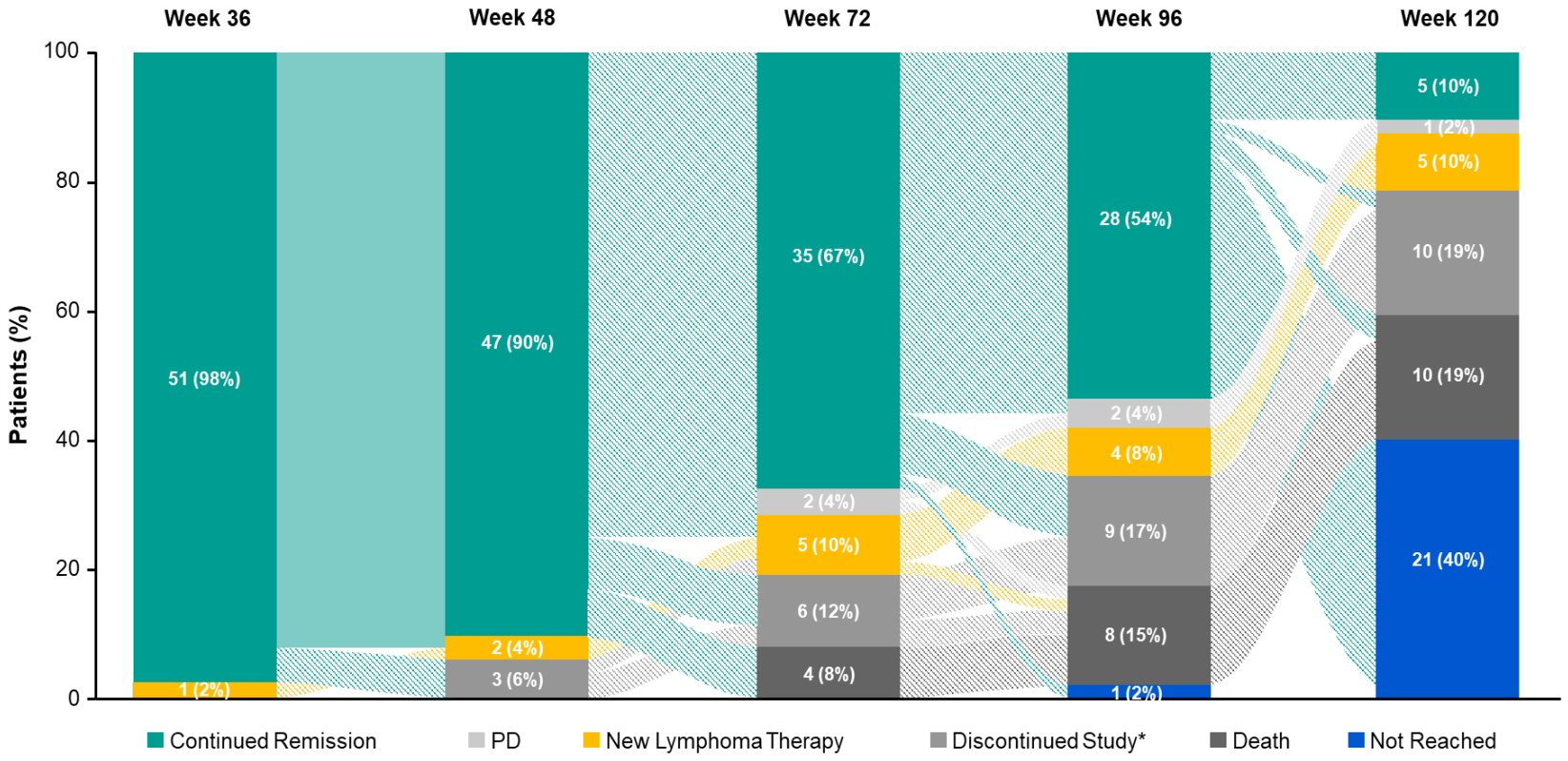
Duration of Complete Response



An estimated **64.2%** of complete responders remained in **CR at 24 months**

Thieblemont, *Leukemia 2024*

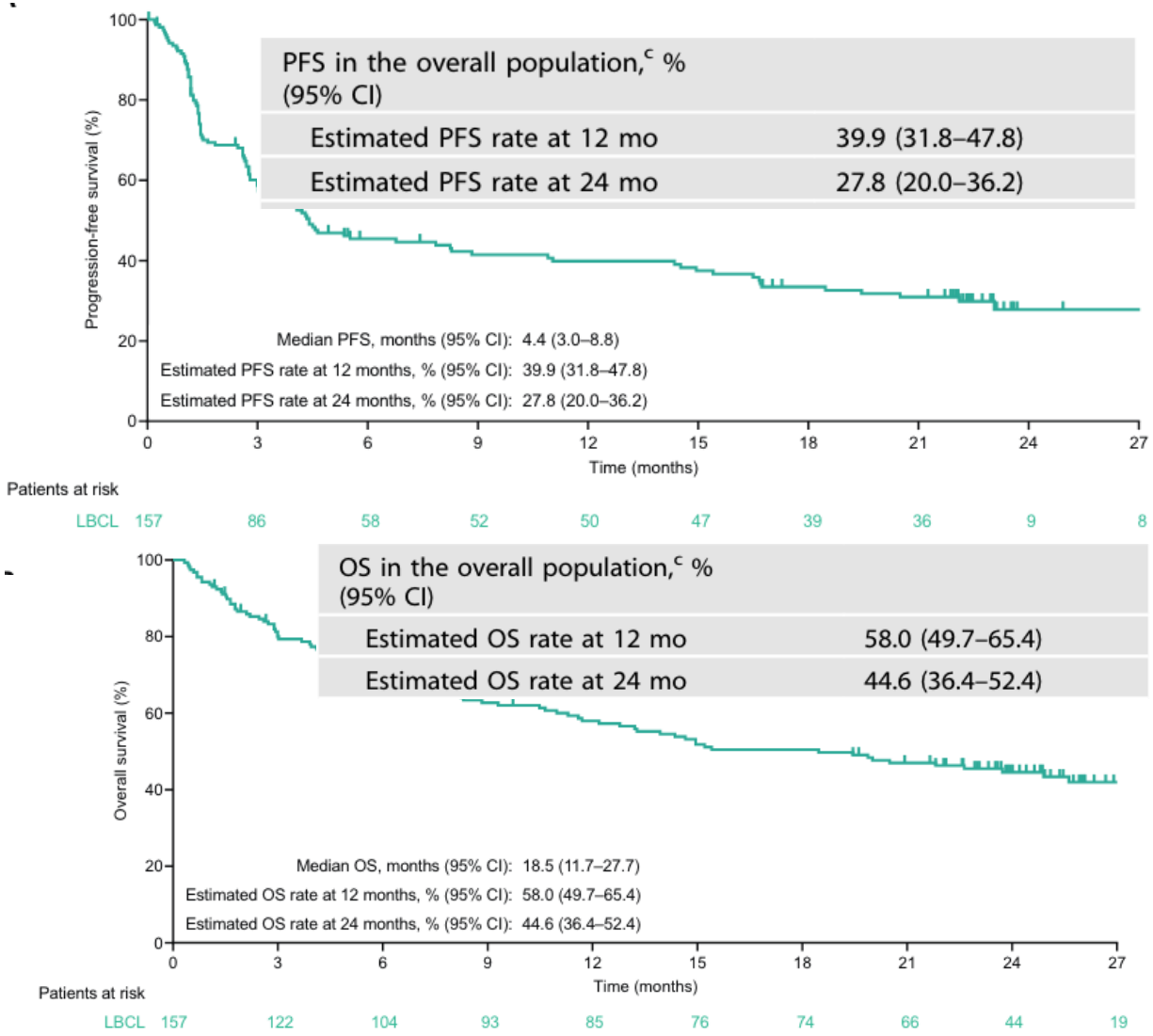
Response Status after week 36

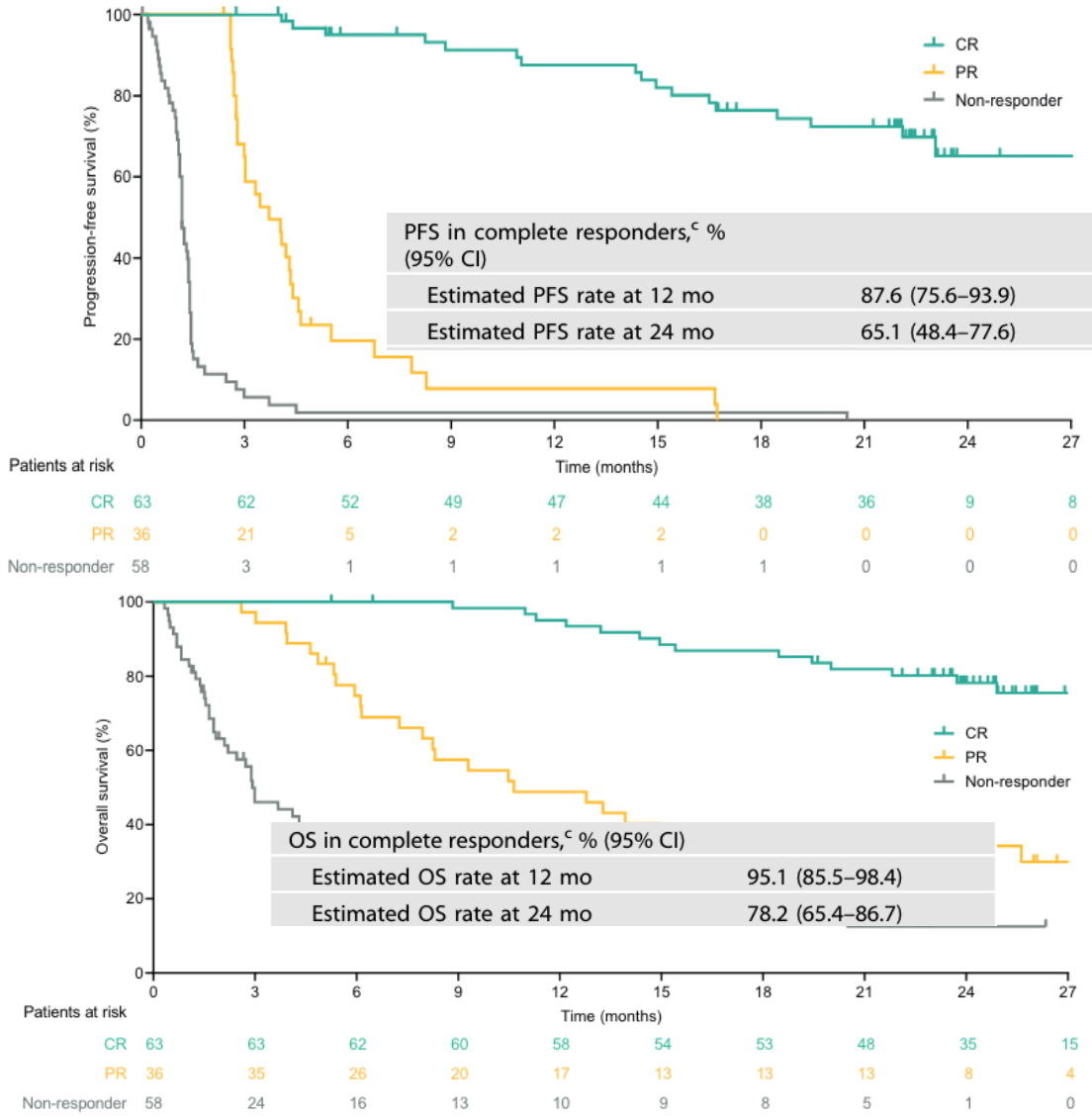


Among 51 patients with a response at 8.4 months (week 36),
47 (90%) remained in response at 11.2 months (week 48)
and 28 (54%) remained in response at 22.3 months (week 96)

Thieblemont, *Leukemia 2024*

Survival Outcomes



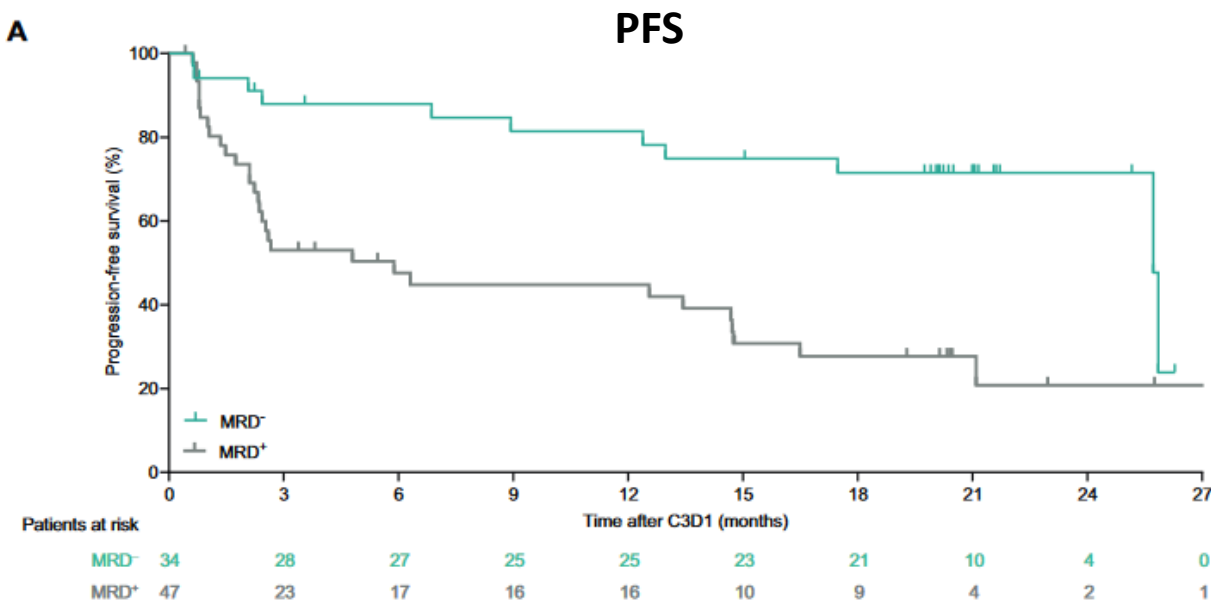


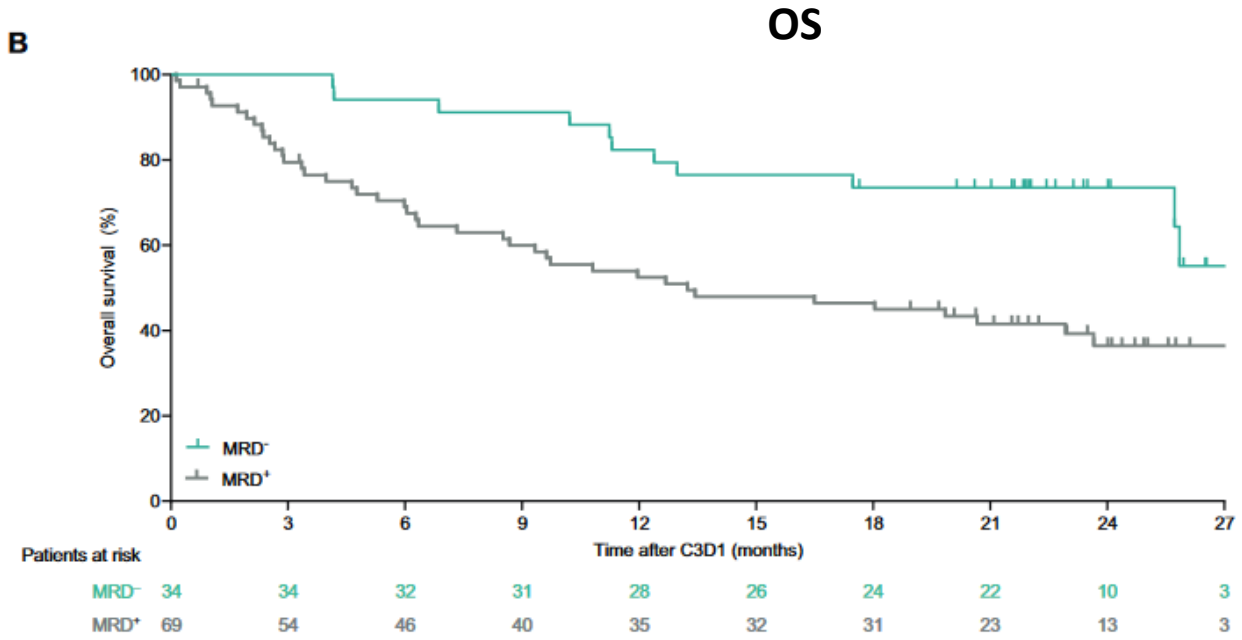
Thieblemont, *Leukemia 2024*

Landmark progression-free and overall survival analyses for patients with LBCL

Analysis by MRD assessment up to cycle 3 day 1

CR at C3 is an early predictor of long-term outcomes





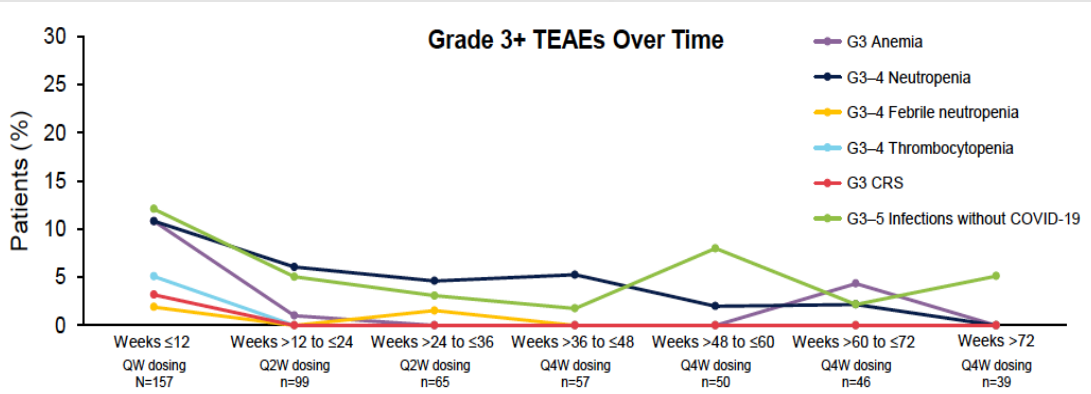
Landmark analyses excluded patients who had an event or were censored before cycle 3 day 1.

Thieblemont, *Leukemia 2024*

Treatment-Emergent Adverse Events (TEAEs) > 5%

Adverse events[a]	Any grade (*N* = 157) No. (%)	Grade ≥ 3 (*N* = 157) No. (%)
Any treatment-emergent AE	156 (99.4)	108 (68.8)
Any treatment-related AE	133 (84.7)	53 (33.8)
Serious AE	105 (66.9)	71 (45.2)
Serious treatment-related AE	59 (37.6)	18 (11.5)
Treatment-emergent AE leading to treatment discontinuation	23 (14.6)	21 (13.4)
Treatment-emergent AE in ≥10% of patients		
CRS[b,c]	80 (51.0)	5 (3.2)
Pyrexia[d]	39 (24.8)	1 (0.6)
Fatigue	38 (24.2)	3 (1.9)
Neutropenia	37 (23.6)	26 (16.6)
Nausea	34 (21.7)	2 (1.3)
Anemia	33 (21.0)	19 (12.1)
Diarrhea	33 (21.0)	0
Injection-site reaction	31 (19.7)	0
COVID-19[e]	30 (19.1)	13 (8.3)
Abdominal pain	25 (15.9)	3 (1.9)
Constipation	23 (14.6)	0
Decreased appetite	23 (14.6)	2 (1.3)
Vomiting	23 (14.6)	1 (0.6)
Headache	22 (14.0)	1 (0.6)
Thrombocytopenia	19 (12.1)	8 (5.1)
Insomnia	18 (11.5)	1 (0.6)
Peripheral edema	18 (11.5)	0
Back pain	17 (10.8)	1 (0.6)

Adverse events[a]	Any grade (*N* = 157) No. (%)	Grade ≥ 3 (*N* = 157) No. (%)
Infections (grade 3 or 4 in ≥2.0% of patients)		
COVID-19[e,f]	30 (19.1)	13 (8.3)
Pneumonia	13 (8.3)	5 (3.2)
Sepsis	5 (3.2)	5 (3.2)
COVID-19 pneumonia	9 (5.7)	4 (2.5)
AEs of special interest		
CRS[b,c]	80 (51.0)	5 (3.2)
ICANS[f]	10 (6.4)	1 (0.6)



Thieblemont, Leukemia 2024

Glofitamab – expansion cohort

Pivotal Phase II expansion in patients with R/R DLBCL and ≥2 prior therapies (NP30179)

Key inclusion criteria

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

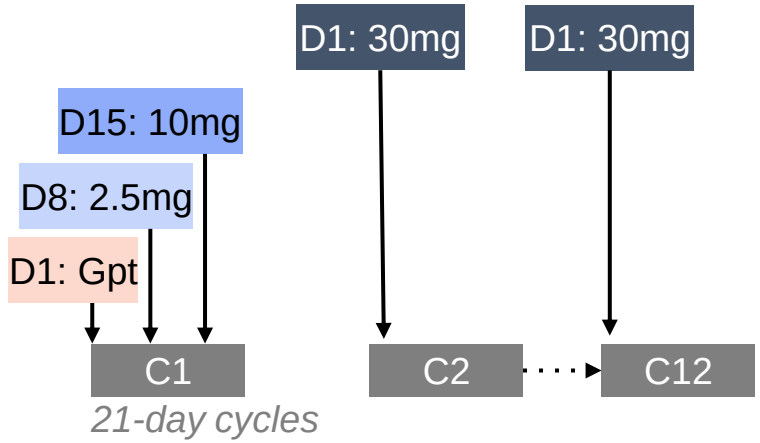
Glofitamab IV administration

Fixed-duration treatment

- max. 12 cycles

CRS mitigation:

- obinutuzumab pretreatment (1 x 1000mg)
- C1 step-up dosing
- monitoring after first dose (2.5mg)



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

Dickinson M. et al., *NEJM 2022 & EHA 2022 oral presentation*

Baseline characteristics: heavily pre-treated, highly refractory population

n (%)*		N=154†
Median age, years (range)		66.0 (21–90)
Male		100 (64.9)
ECOG PS‡	0	69 (44.8)
	1	84 (54.5)
Ann Arbor stage	I	10 (6.5)
	II	25 (16.2)
	III	31 (20.1)
	IV	85 (55.2)
NHL subtype	DLBCL	110 (71.4)
	trFL	27 (17.5)
	HGBCL	11 (7.1)
	PMBCL	6 (3.9)
Bulky disease	>6cm	64 (41.6)
	>10cm	18 (11.7)

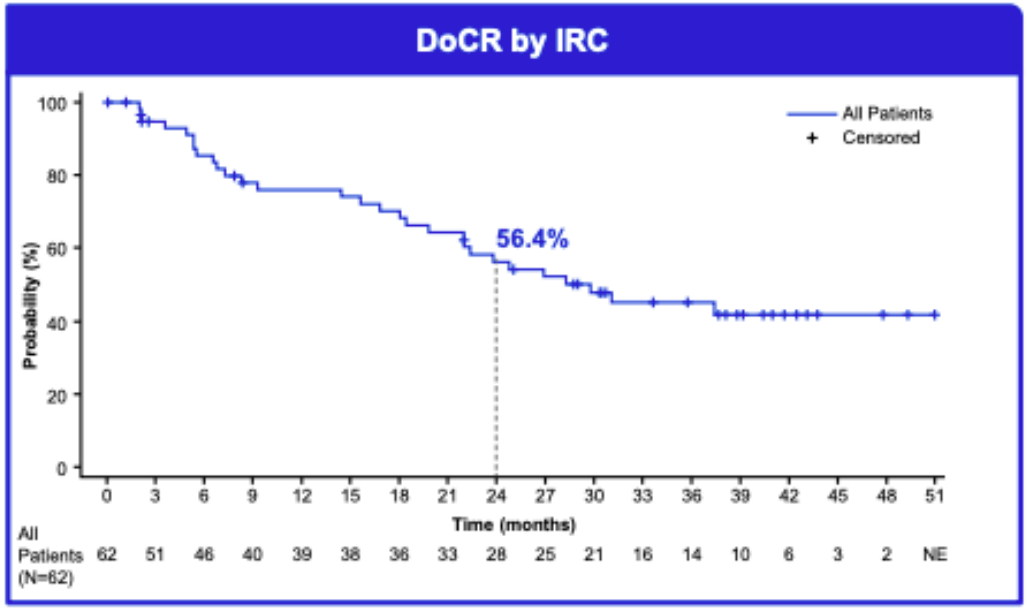
n (%)*	N=154
Median no. of prior lines, n (range)	3 (2–7)
2 prior lines	62 (40.3)
≥3 prior lines	92 (59.7)
Prior anti-CD20 Ab	154 (100.0)
Prior anthracycline	149 (96.8)
Prior CAR-T	51 (33.1)
Prior ASCT	28 (18.2)
Refractory to any prior therapy	139 (90.3)
Refractory to last prior therapy	132 (85.7)
Primary refractory	90 (58.4)
Refractory to prior CAR-T	**46 (29.9)**
Refractory to any prior anti-CD20	128 (83.1)

•Clinical cut-off date: March 14, 2022; *unless otherwise specified; †safety-evaluable population (all treated patients);
‡ECOG PS 2, n=1 (0.6%); Ab, antibody; ASCT, autologous stem cell transplant; trFL, transformed follicular lymphoma.

Dickinson M. et al., *NEJM 2022 & EHA 2022 oral presentation*

Responses and duration of response

	All patients (N=155)*	R/R DLBCL/ trFL (N=132)[1†‡]	Prior CAR-T (N=52)†
ORR, n (%) [95% CI]	80 (52) {43.5-59.7}	74 (56) [47.2–64.7]	26 (50) [35.8–64.2]
CR rate, n (%) [95% CI]	62 (40) {32.2-48.2}	58 (44) [35.3–52.8]	19 (37) [23.6–51.0]
Median DoCR, months (95% CI)	29.8 (22.0-NE)	28.3 (19.8–NR)	22.0 (6.7–NR)
24-month DoCR, % (95% CI)	56.4 (42.9-69.8}	56.2 (41.9–70.4)	33.1 (7.2–59.0)
Median CR follow-up, months (range)	37.7 (0-51)	29.6 (0–39)	23.0 (0–33)
Ongoing CRs, n/N (%)	33/62 (0-51)	32/58 (55)	10/19 (53)



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

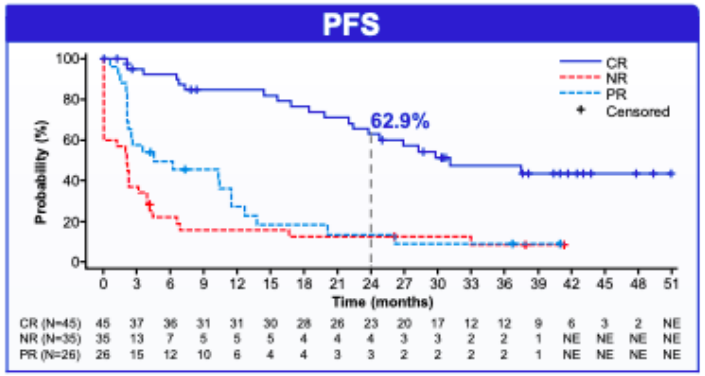
Median time on study: 41.0 months (range: 0–52)

Dickinson M. et al., *NEJM 2022*
Dickinson ASH 2024 oral presentation

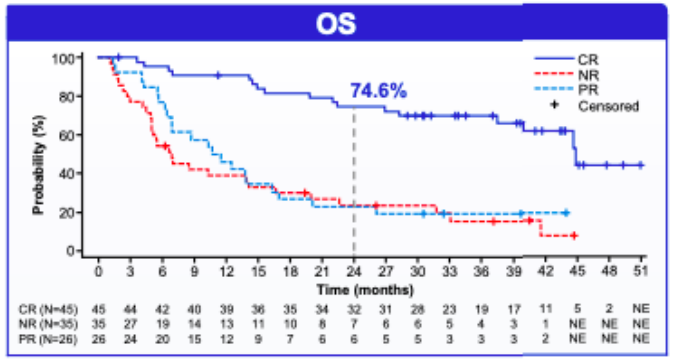
Landmark analysis

CR at C3 is an early predictor of long-term outcomes

by response at C3



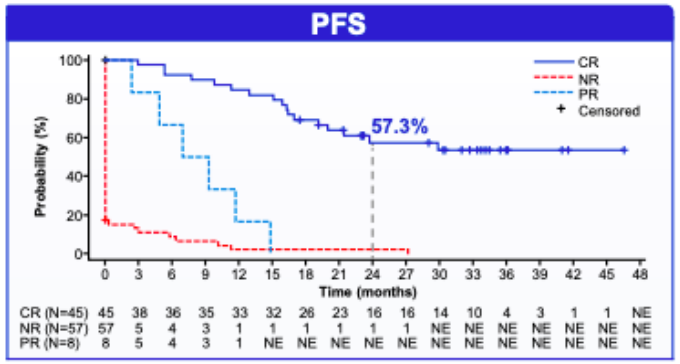
Landmark PFS from C3 in patients with CR at C3*	N=45
Median PFS, months (95% CI)	31.1 (23.8–NE)
24-month PFS rate, % (95% CI)	62.9 (47.5–78.4)



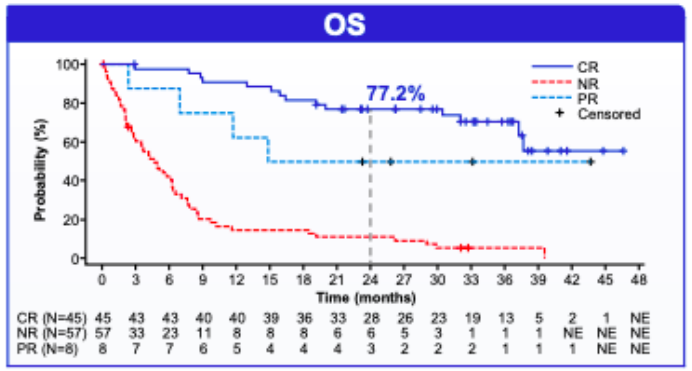
Landmark OS from C3 in patients with CR at C3*	N=45
Median OS, months (95% CI)	44.8 (40.0–NE)
24-month OS rate, % (95% CI)	74.6 (61.6–87.6)

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

by response at EOT



Landmark PFS from EOT in patients with CR at EOT*	N=45
Median PFS, months (95% CI)	NE (20.0–NE)
24-month PFS rate, % (95% CI)	57.3 (41.2–73.4)



Landmark OS from EOT in patients with CR at EOT*	N=45
Median OS, months (95% CI)	NE (37.2–NE)
24-month OS rate, % (95% CI)	77.2 (64.8–89.6)

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

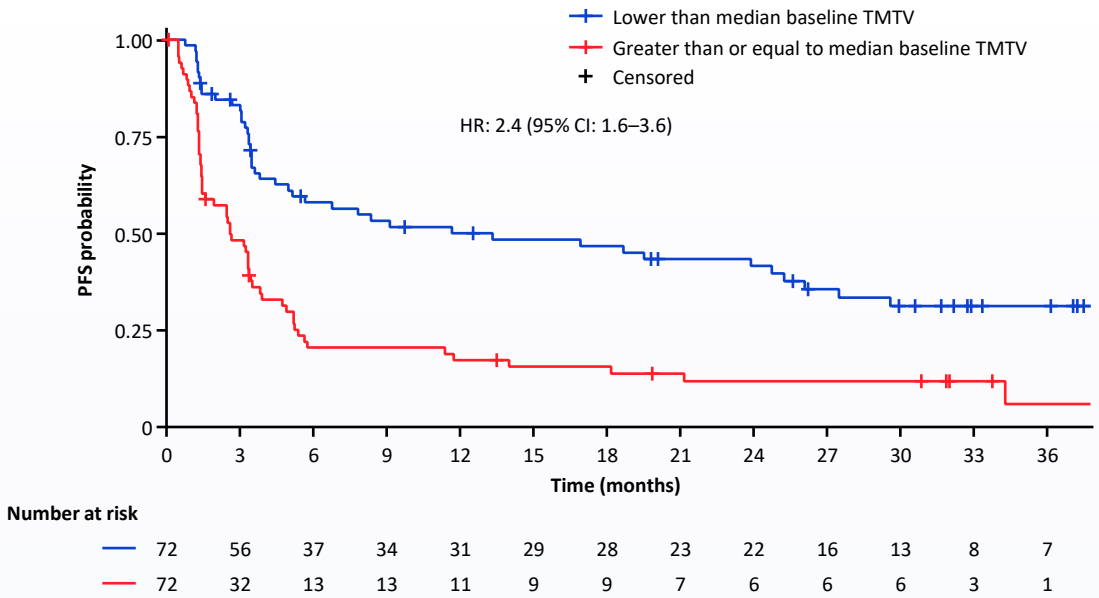
Dickinson M. et al., ASH 2024 oral presentation

TMTV as prognostic factor for PFS / association with CRS

- Baseline TMTV was **derived** using a semi-automated method with a threshold for **TMTV of 2x the SUV_{mean} of the liver**
- Median baseline TMTV was 128.7mL (range: 0–3820; n=144*)
- Higher baseline TMTV was associated with an increased risk of grade ≥2 CRS event and baseline TMTV may be prognostic for PFS

	Baseline TMTV ≥ median (n=72)	Baseline TMTV < median (n=72)
24-month PFS rate, % (95% CI)	11.8 (6.0–23.5)	41.6 (31.1–55.6)

PFS by TMTV at baseline



Hutchings et al., ASH 2023

Safety Summary

- **CRS remained the most common AE**
  - Occurred in **64.3%** of patients
  - Mostly Grade 1 (48.1%) or Grade 2 (12.3%); Grade 3 (2.6%) and Grade 4 (1.3%) events were uncommon
- The incidences of AEs and SAEs have previously been reported
- No new ICANS or cytopenia events were reported from June 17, 2022†–May 17, 2024
- Two new fatal AEs were reported : COVID-19 and acute myeloid leukemia

n (%)	N=154§
AE	152 (98.7)
Grade ≥3 AE	102 (66.2)
SAE	76 (49.4)
Grade 5 (fatal) AE	11 (7.1)
AE leading to treatment discontinuation	14 (9.1)
AE leading to glofitamab dose modification/interruption	30 (19.5)

Odronextamab in R/R DLBCL (ELM-2 trial)

Response by ICR	All DLBCL (N = 127)
ORR, % (primary endpoint)	52.0
▪ CR	**31.5**
Survival	**All DLBCL (N = 127)**
PFS	
▪ Median, mo (95% CI)	4.4 (3.6-5.9)
▪ 12 mo, % (95% CI)	29.6 (21.5-38.2)
▪ 24 mo, % (95% CI)	**21.1 (13.7-29.7)**
OS	
▪ Median, mo (95% CI)	9.2 (6.5-12.7)
▪ 12 mo, % (95% CI)	42.9 (33.7-51.8)
▪ 24 mo, % (95% CI)	**31.6 (22.4-41.1)**

Parameter by Best Objective Response	CR (n = 40)	PR (n = 26)
PFS by best response		
▪ Median, mo (95% CI)	**20.4 (12.7-NE)**	**5.8 (4.4-7.8)**
▪ 12 mo, % (95% CI)	67.2 (50.3-79.5)	25.2 (9.5-44.7)
▪ 24 mo, % (95% CI)	47.5 (29.9-63.1)	18.9 (5.4-38.6)
OS by best response		
▪ Median, mo (95% CI)	**NR (17.2-NE)**	**17.0 (9.6-27.3)**
▪ 12 mo, % (95% CI)	75.0 (58.5-85.7)	60.2 (37.2-77.0)
▪ 24 mo, % (95% CI)	59.6 (41.7-73.7)	30.5 (9.3-55.3)

Median duration follow-up for efficacy: **29.9 mo** (95% CI: 20.4-32.6)

EZB subtype of DLBCL was associated with improved PFS compared with the MCD DLBCL subtype

PFS was similar regardless of the DLBCL cell of origin or the presence of *MYC, BCL2, and BCL6* rearrangements

Ayyappan. ASH 2023. Abstr 436.
Arnason. ASH 2023. Abstr 427.

Odronextamab in R/R DLBCL (ELM-2 trial)

CRS	Cycle 1 LD 0.7/4/20 mg Step-up Dosing (n = 60)
CRS, n (%)	32 (53.3)
▪ Grade 1	24 (40.0)
▪ Grade 2	7 (11.7)
▪ Grade 3	1 (1.7)*
▪ Grade ≥ 4	0
Median time to onset CRS, hr (range)	18.00 (1-3.4 to 221.0)
Median CRS duration, days (range)	2.00 (1.0-7.0)
Systemic steroid for CRS management, n (%)	13 (21.7)
Tocilizumab for CRS management, n (%)	15 (25.0)

*At Wk 6 in patient with pancreatitis.

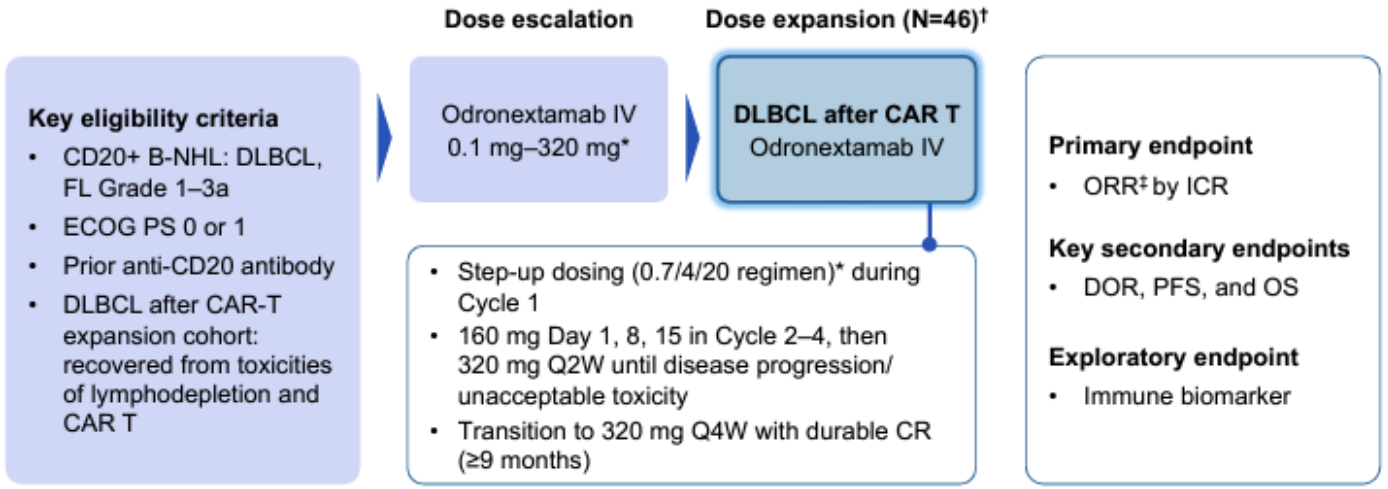
- No ICANS reported

Infections, n (%)	All DLBCL (N = 127)	
	Any TEAE	COVID-19
Any grade	82 (64.6)	23 (18.1)
Grade 1	4 (3.1)	2 (1.6)
Grade 2	29 (22.8)	5 (3.9)
Grade 3	33 (26.0)	11 (8.7)
Grade 4	1 (0.8)	0
Grade 5	15 (11.8)	5 (3.9)

- Most common infections: COVID-19 (16.5%), pneumonia (14.2%), URTI (8.7%), UTI (8.7%), *Pneumocystis jirovecii* pneumonia (6.3%)
- Treatment-related infections in 4.7% of patients required d/c of odronextamab

Ayyappan. ASH 2023. Abstr 436.

Odronextamab monotherapy in R/R DLBCL after progression with CAR T-cell therapy: Primary analysis of the ELM-1 study



*Revisions to step-up dosing were reported previously.[4] †FL, DLBCL without prior CAR T, MCL, MZL, and other B-NHL cohorts are not shown. ‡According to Lugano criteria.[6]
B-NHL, B-cell non-Hodgkin lymphoma; CAR, chimeric antigen receptor; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; ICR, independent central review; IV, intravenous; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q2W, once every 2 weeks; Q4W, once every 4 weeks.

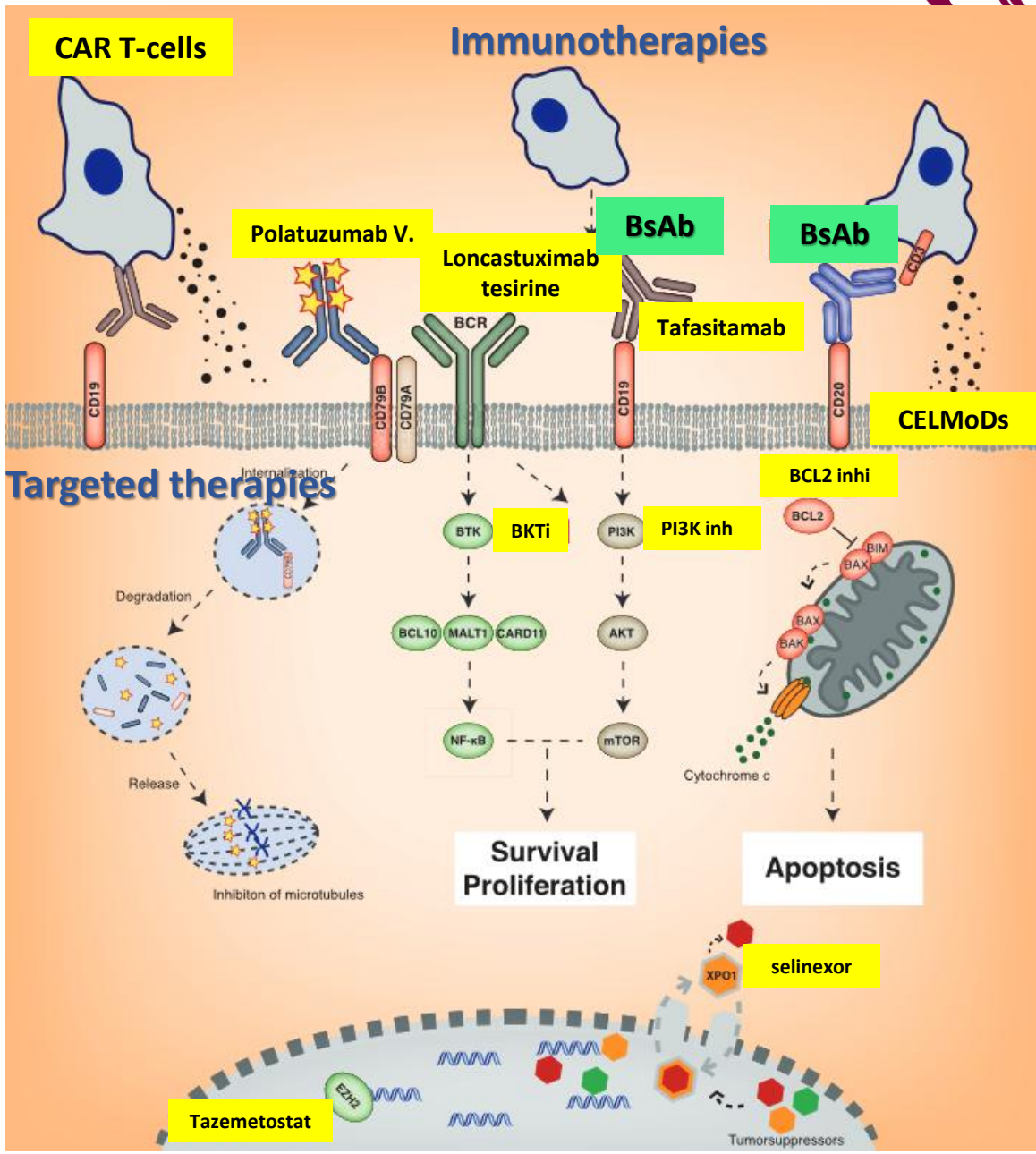
Odronextamab monotherapy demonstrated encouraging efficacy and generally manageable safety, supporting its potential as an off-the-shelf option for post-CAR T patients.

- ⇒ N = 60, median number of prior lines = 3
- ⇒ 71.7% were refractory to CAR T, and 48.3% relapsed within 90 days of CAR T.
- ⇒ **ORR 48%, CR 32%**
- ⇒ Median DOR 14.8 mo, median DoCR NR
- ⇒ Median FU of 16.2 months
- ⇒ Median PFS 4.8 months, median PFS for CR NR
- ⇒ Median OS 10.2 months
- ⇒ Safety
  - CRS any grade 48%, 0 grade ≥ 3
  - **Infection grade ≥ 3 20%**
  - No ICANS

Topp, ASH 2024 oral presentation

Novel agents for R/R LBCL

	TARGET	Novel therapeutic approaches
Immunotherapies	**CD19** surface antigen	- CAR T-cells : Axi-cel, Tisa-cel, Liso-cel - Tafasitamab (Ab) - Loncastuximab tesirine (ADC) - AZD0486 : **Bispecific Ab** CD19xCD3
	CD79B associated with the BCR	- Polatuzumab-vedotin (ADC)
	CD20 B- and **CD3** T -cells mediating T-cell activation	- **Bispecific Ab (BsAb)** epcoritamab, glofitamab, odronextamab
Targeted therapies	Targeted small-molecule inhibitors • **BCR** signaling • **CELMoDs** • **PI3K** signaling	- BTK inh, Ibrutinib - Avadomide, Iberdomide, Golcadomide - Copanlisib
	BCL2 inducing apoptosis	- Venetoclax
	EZH2 oncogenic methyltransferase	- Tazemetostat
	XPO1 inhibition	- Selinexor



Adapted from Frontzek F et al. Ther Adv Hematol 2022, Vol. 13: 1–19
and from Gonzalez Barca, J. Clin. Med. 2023, 12, 7376

Bispecific Development in DLBCL

	Epcoritamab	Glofitamab	Mosunetuzumab	Odronextamab
1L	**Ph3 EPCORE-DLBCL-2**[1] Epcor + R-CHOP **Ph2 EPCORE-DLBCL-3**[2] Epcor +/- Len (frail/unfit) **Ph 2 NHL-2**[3] **and NHL-5**[4] Epcor + (R-CHOP, R-mini-CHOP, Pola-R-CHP)	**Ph3 SKYGLO**[7] Glofit + Pola-R-CHP **Ph 2 GO43075**[8] Glofit + R-CHOP (high-risk) **Ph 1 NP40126**[9] Glofit + (R-CHOP, Pola-R-CHP)	**Ph 1/2 GO40554**[13] Mosun +/- Pola (frail/unfit)	**Ph 3 OLYMPIA-3**[17] Odro + CHOP
2L	**Ph3 EPCORE DLBCL-1**[5] Epcor monotherapy **Ph3 EPCORE DLBCL-4**[6] Epcor + Len **Ph 2 NHL-2**[3] **and NHL-5**[4] Epcor + (R-DHAX/C, GemOx, R-ICE, Len, Ibr-Len, golcadomide)	**Ph3 STARGLO**[10] Glofit + GemOx **Ph 1/2 NP39488**[11] Glofit + Pola Glofit + Atezolizumab **Ph 1 BP41072**[12] Glofit + Englumafusp alfa	**Ph3 SUNMO**[14] Mosun + Pola **Ph 2 MorningSun**[15] Mosun (SC) monotherapy **Ph 2 GO40516**[16] Mosun + Pola	**Ph3 OLYMPIA-4**[18] Odro monotherapy **Ph 1 CLIO-1**[19] Odro + cemiplimab **Ph 1 ATHENA-1**[20] Odro + REGN5837
3L				

DLBCL, diffuse large B-cell lymphoma; Epcor, epcoritmab; GemOx, gemcitabine+oxaliplatin; Glofit, glofitamab; Ibr, ibrutinib; Len, lenalidomide; Mosun, mosunetuzumab; Odro, odronextamab; Pola, polatuzumab; R, rituximab; SC, subcutaneous.

1. NCT05578976 2. NCT05660967. 3. NCT04663347. 4. NCT05283720. 5. NCT04628494. 6. epcore-trials.com/dlbcl-4/. 7. NCT06047080. 8. NCT04980222. 9. NCT03467373. 10. NCT04408638. 11. NCT03533283. 12. NCT04077723. 13. NCT03677154. 14. NCT05171647. 15. NCT05207670. 16. NCT03671018. 17. NCT06091865. 18. NCT06230224. 19. NCT02651662. 20. NCT05685173.

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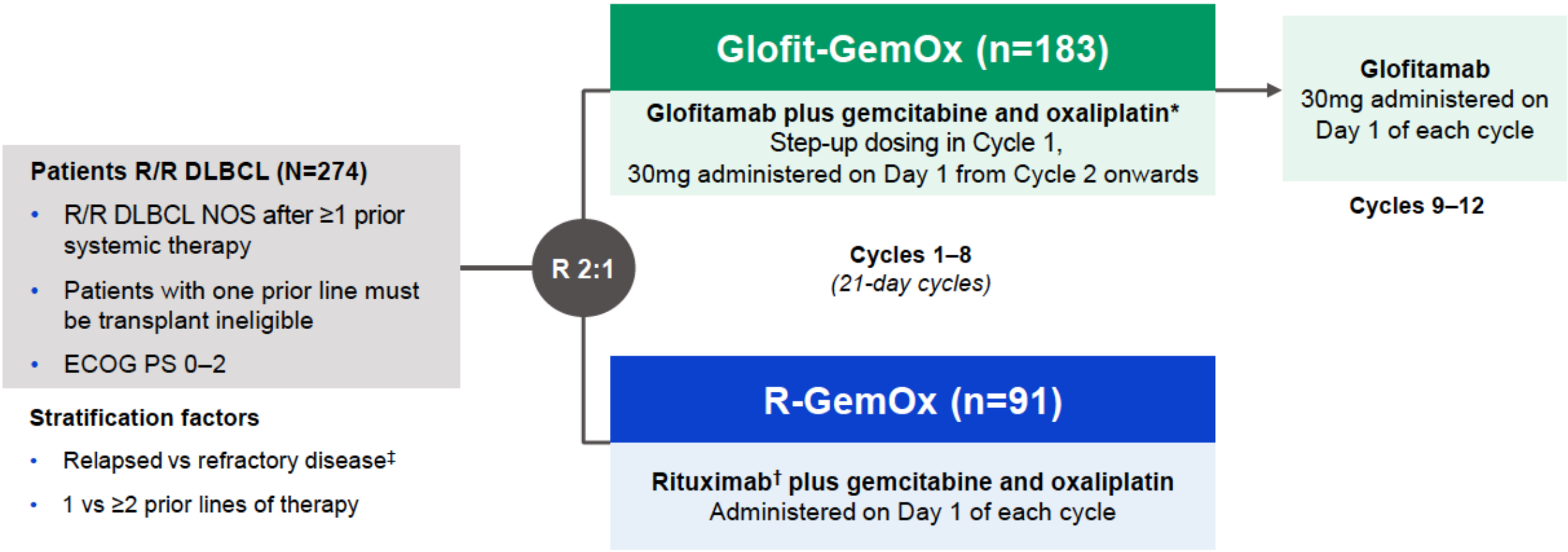
STARGLO: randomized Phase III trial in ASCT-ineligible patients with R/R DLBCL



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Baseline Patients Characteristics

n (%), unless otherwise stated		R-GemOx (n=91)	Glofit-GemOx (n=183)
Age, years	Median (range) ≥65 years	68.0 (20–84) 56 (61.5)	68.0 (22–88) 116 (63.4)
Sex	Male	53 (58.2)	105 (57.4)
Race	Asian Black or African American White Unknown	51 (56.0) 1 (1.1) 33 (36.3) 6 (6.6)	86 (47.0) 2 (1.1) 82 (44.8) 13 (7.1)
ECOG PS	0 1 2	44 (50.0) 36 (40.9) 8 (9.1)	72 (40.0) 89 (49.4) 19 (10.6)
Ann Arbor stage	I–II III–IV	20 (22.0) 70 (76.9)	60 (32.8) 123 (67.2)
Number of prior lines of therapy	1 ≥2	57 (62.6) 34 (37.4)	115 (62.8) 68 (37.2)
Primary refractory	Yes	47 (51.6)	106 (57.9)
R/R to last prior therapy	Relapsed / refractory	37 (40.7) / 54 (59.3)	71 (38.8) / 112 (61.2)
Bulky disease (≥10cm)	Present	14 (15.4)	23 (12.6)
Cell of origin at initial diagnosis	GCB Non-GCB (including ABC) Unknown	29 (31.9) 50 (54.9) 12 (13.2)	60 (32.8) 103 (56.3) 20 (10.9)
Prior CAR T-cell therapy	Received	8 (8.8)	13 (7.1)

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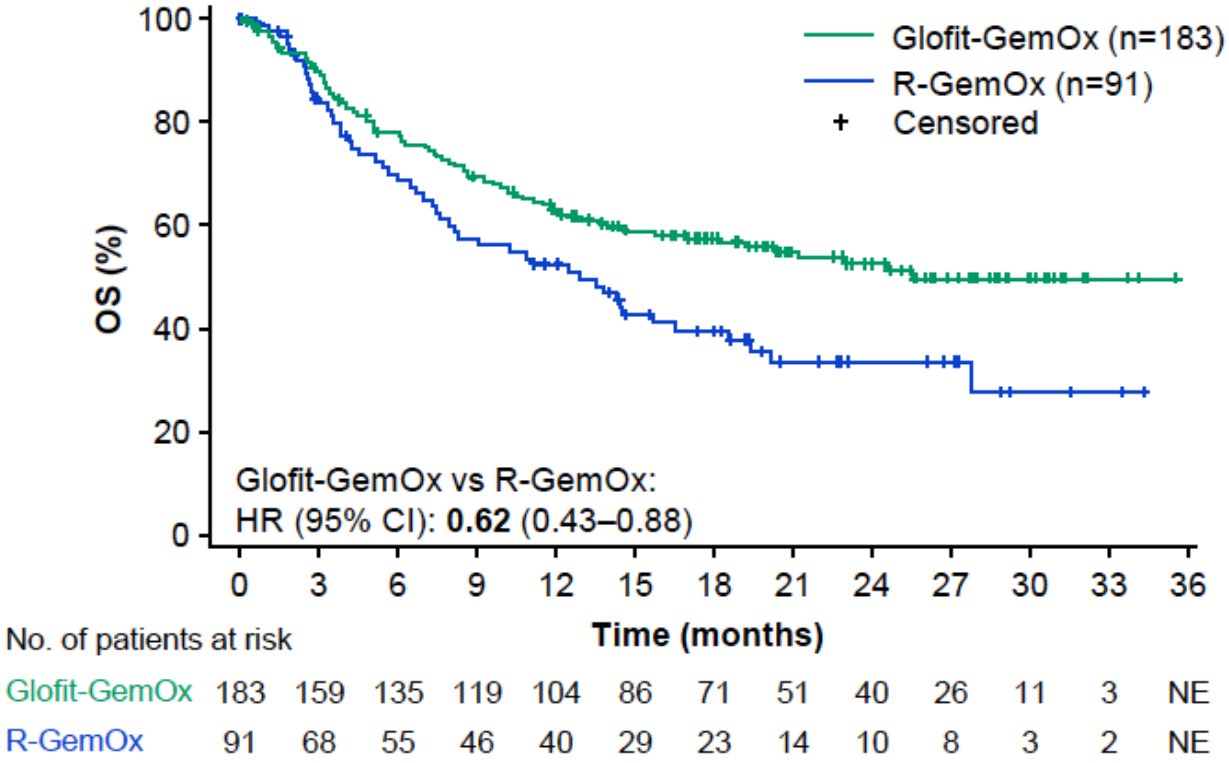
STARGLO : primary endpoint (OS)

Updated analysis



	R-GemOx (n=91)	Glofit-GemOx (n=183)
Primary analysis (median follow-up: 11.3 months)		
OS, median (95% CI); months	9 (7.3–14.4)	NE (13.8–NE)
HR (95% CI)	**0.59** (0.40–0.89)	
p-value*	0.011	
Updated analysis (median follow-up: 20.7 months)		
OS, median (95% CI); months	12.9 (7.9–18.5)	25.5 (18.3–NE)
HR (95% CI)	**0.62** (0.43–0.88)	
p-value*	0.006	
24-month OS (95% CI)	33.5% (22.2–44.9)	52.8% (44.8–60.7)

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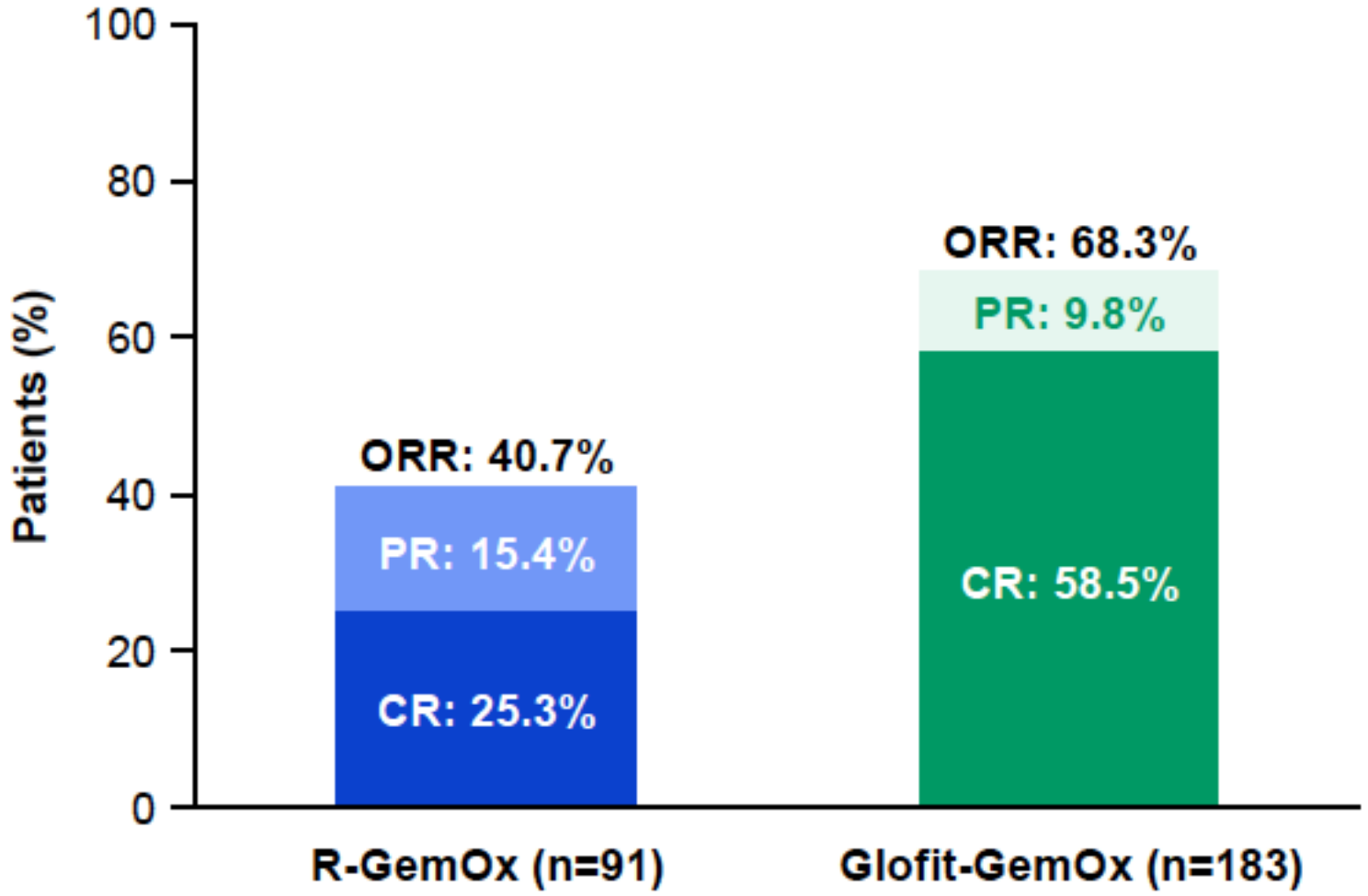
STARGLO : Response rates by IRC assessment



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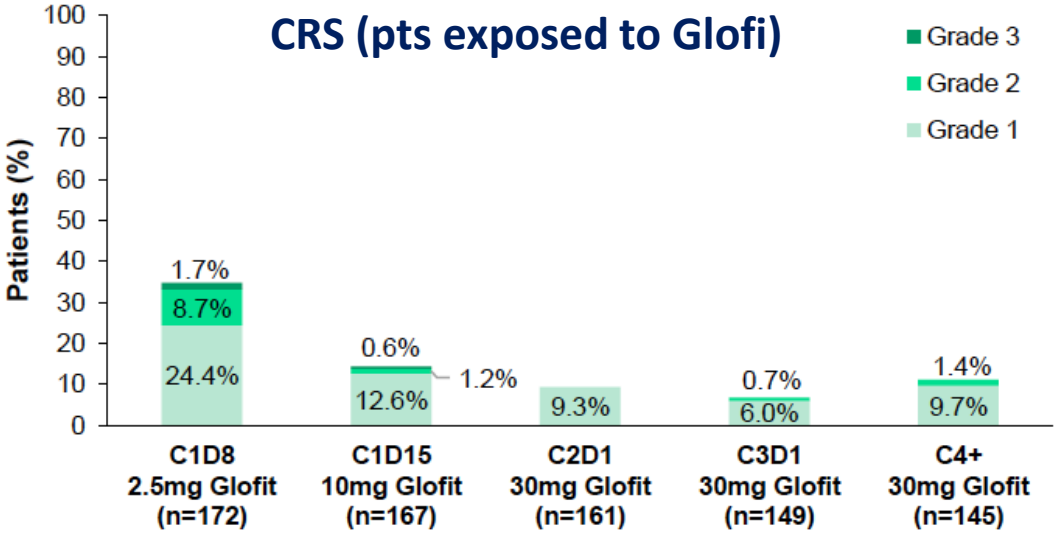
STARGLO : AE of interest



n (%)	R-GemOx (n=88)	Glofit-GemOx (n=180)
Neurological AEs Grade ≥3	35 (39.8) 0	105 (58.3) 12 (6.7)
ICANS Grade ≥3	NA* NA*	4 (2.3)† 1 (0.6)
Tumor flare Grade ≥3	0 0	1 (0.6) 0
Infections Grade ≥3	26 (29.5) 11 (12.5)	103 (57.2) 42 (23.3)
Neutropenia‡ Grade ≥3	27 (30.7) 16 (18.2)	76 (42.2) 61 (33.9)
Febrile neutropenia	1 (1.1)	6 (3.3)

Jeremy S. Abramson EHA 2024 oral presentation

Chemo-free combinations strategies in R/R setting

Glofitamab in combination with Polatuzumab Vedotin in patients with R/R large B-cell lymphoma (LBCL) including high-grade B-cell lymphoma (HGBCL)

Phase Ib/II study in patients with R/R LBCL and ≥1 prior therapy

Key inclusion criteria

- DLBCL, HGBCL, trFL, or PMBCL
- ECOG PS 0–2
- ≥1 prior therapies, including:
  - Anti-CD20 antibody
  - CAR T-cell therapy

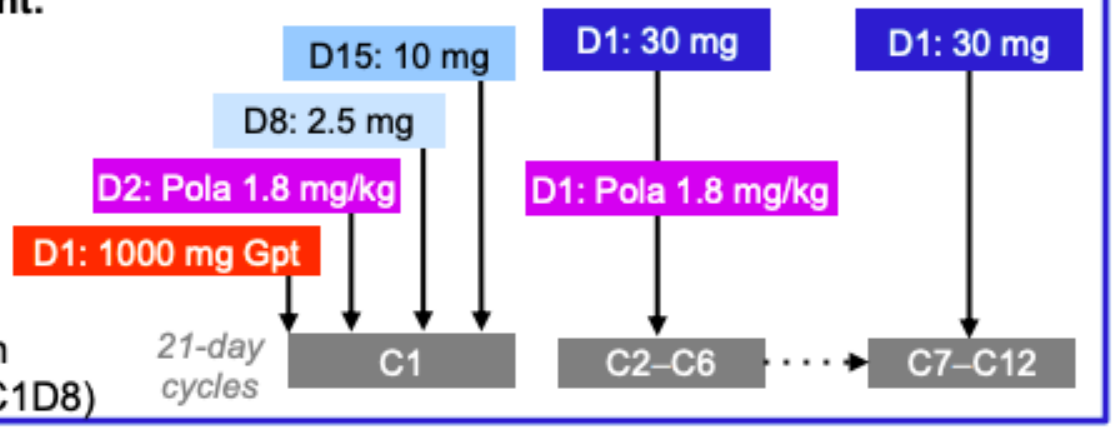
Glofitamab IV administration

Fixed-duration treatment:

- Up to 12 cycles

CRS mitigation:

- Obinutuzumab IV pre-treatment
- C1 step-up dosing
- 24-hour hospitalization with first Glofit dose (C1D8)



Endpoints

- **Primary:** Best ORR* by IRC and MTD and/or RP2D for Glofit
- **Key secondary:** efficacy (best ORR by INV, DoR, DoCR, PFS by IRC and INV, and OS) and safety
- **Exploratory:** ctDNA

Hutchings, ASH 2024 oral presentation

EPCORE DLBCL-3 : Fixed-Duration Epcoritamab Monotherapy in Older (≥75 y), Anthracycline-Ineligible Patients with Previously Untreated Large B-Cell Lymphoma

A phase 2, open-label trial evaluating the efficacy and safety of fixed-duration epcoritamab in older, anthracycline-ineligible adults with newly diagnosed LBCL

Key inclusion criteria

- Newly diagnosed CD20+ LBCL
  - DLBCL, NOS
  - T-cell/histiocyte-rich DLBCL
  - Double-hit or triple-hit DLBCL
  - FL grade 3B
- ICE score ≥8[a]
- ECOG PS 0–2
- Ineligible for anthracycline-based therapy/cytotoxic chemotherapy due to:
  - Age ≥80 y, or
  - Age ≥75 y with a comorbid condition[b]
- Measurable disease by CT or MRI

Data cutoff: September 21, 2024
Median follow-up: 9.5 mo (range, 0.4–17.7+)

1:1 RANDOMIZATION

Agent	C1–3	C4–12
Epcoritamab SC 48 mg[c]	QW	Q4W

Agent	C1–3	C4–12
Epcoritamab SC 48 mg[c]	QW	Q4W
Lenalidomide PO 10–20 mg	QD D1–21	QD D1–21

- **Primary endpoint:** CR rate per Lugano criteria[1]
- **Key secondary endpoints:** ORR, TTR, DOR, DOCR, PFS, OS, MRD negativity,[d] and safety

Morschauser F, ASH 2024 oral presentation

Conclusion

- **T-cell bispecific antibodies (BsAbs) is a breakthrough immunotherapy**
- **BsAb show unprecedented antitumor activity in patients with R/R LBCL**
- **Manageable safety profile**
- **Combined strategies , with chemo or in chemo-free regimens, hold important promises**

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