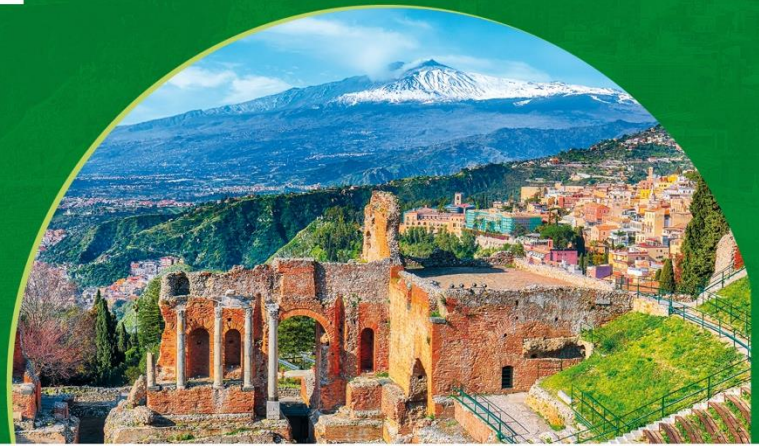
CORSO EDUCAZIONALE COMMISSIONE ANZIANI

XIII EDIZIONE

Giardini Naxos - Marriott Delta Hotels
17-18 aprile 2026

FONDAZIONE ITALIANA LINFOMI



Debate: Pro bispecifici

Guido Gini

AOU delle Marche-Università Politecnica delle Marche

Ancona

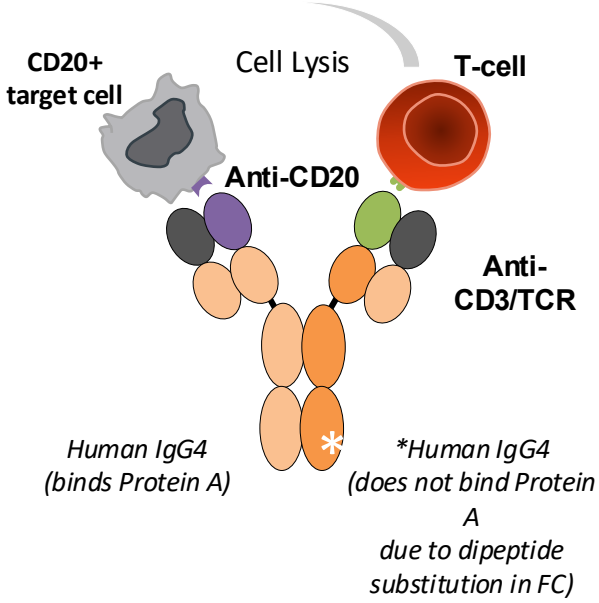
Disclosures (1) – Guido Gini

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Roche					X	X	Educational activity
Incyte					X	X	Educational activity
Kiowa Kirin						x	Educational activity
Janssen						X	Educational activity
Takeda					x	X	Educational activity
Astrazeneca						X	Educational activity
Gilead					X		Educational activity
Gentili					x	x	Educational Activity

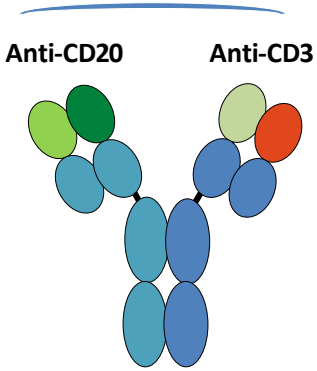
Disclosures (2) – Guido Gini

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Sobi					X	X	Educational activity
Lilly					X	X	Educational activity
GSK						x	Educational activity
Abbvie						X	Educational activity

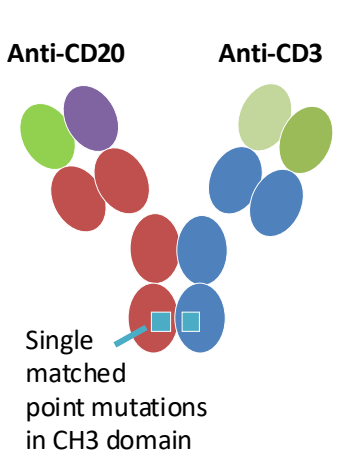
CD20/CD3 Bispecific Antibodies in B-Cell Lymphomas



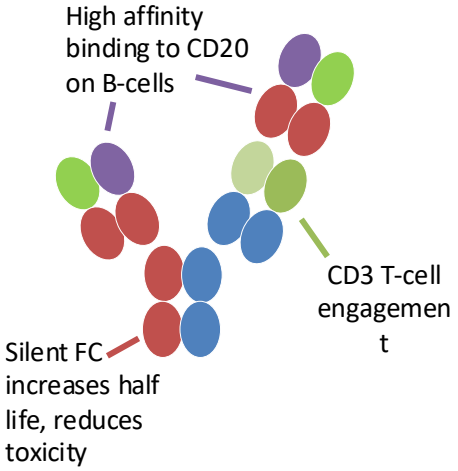
Odronextamab
(IV)



Mosunetuzumab
(IV/SC)



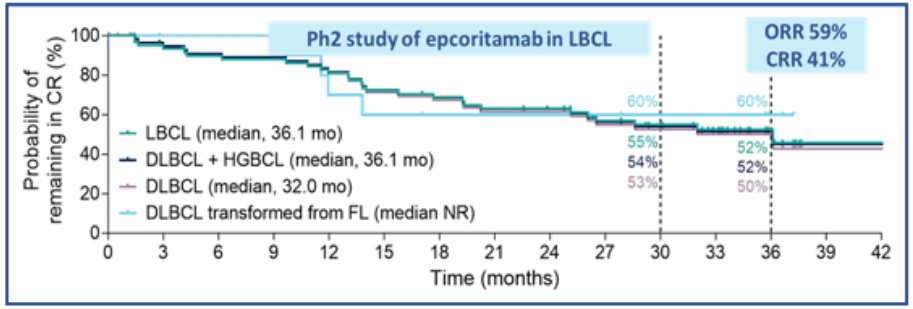
Epcoritamab
(SC)



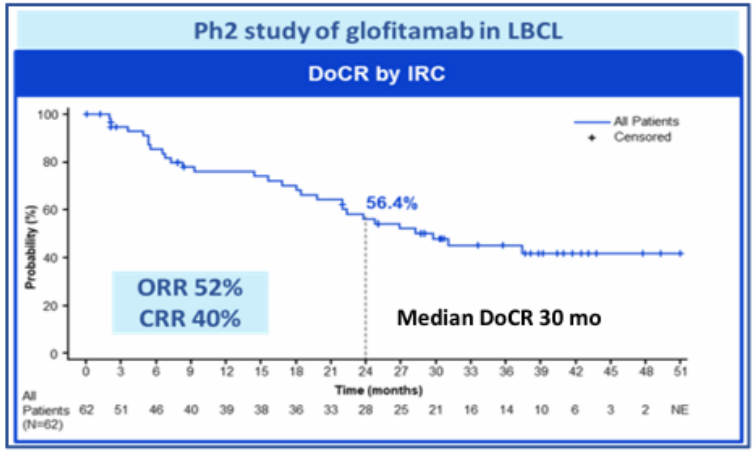
Glofitamab
(IV)

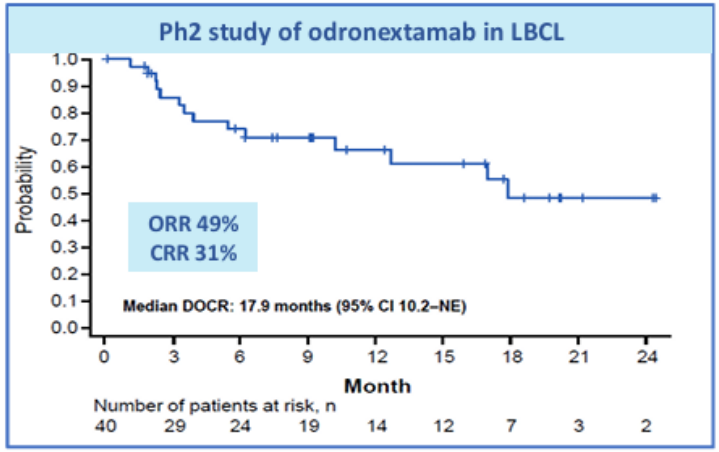
Castaneda-Puglianni. Drugs Context. 2021;10:2021. Bannerji. ASH 2020. Abstr 42. Budde. ASH 2018. Abstr 399. Hutchings. Lancet. 2021;398:1157. Engelberts. eBioMedicine. 2020;52:102625. Hutching. ASH 2020. Abstr 403.

Bispecific CD20xCD3 antibodies are approved in r/r LBCL



Ph2 study of mosunetuzumab in LBCL	N=88
CR rate, %	**24 (15–34)**
ORR, %	42 (32–53)
Median DOCR, months	NR (9.0–NE)
Median DOR, months	7.0 (4.2–NE)
Median PFS, months	3.2 (2.2–5.3)
Median OS, months	11.5 (9.0–16.4)

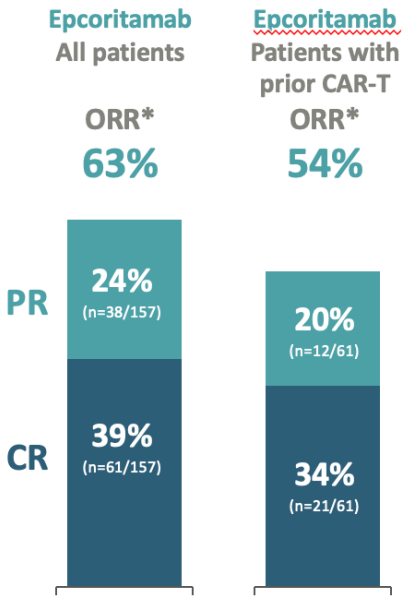


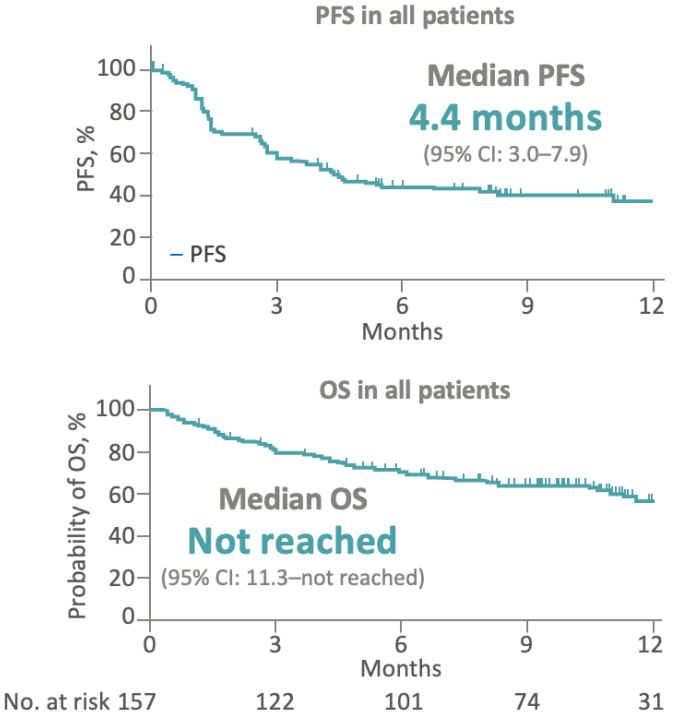


1. Vose JM, et al. ASH 2024. 2. Bartlett NL, et al. Blood Adv 2023;7(17):4926-4935. 3. Dickinson M, et al. ASH 2024. 4. Poon M, et al. ICML 2023, abstract #93.

Epcoritamab in 3rd line + (EPCORE NHL-1 (Phase 2)

Baseline characteristics, n (%)	All patients (N=157)
Median (range) age, years	64 (20–83)
Male, sex	94 (60)
ECOG performance status 0/1	74 (47) / 78 (50)
Ann Arbor Stage III/IV†	21 (13) / 97 (62)
Nr. of previous lines (median, range)	3 (2–11)
Nr. of previous lines	
2 previous lines	46 (29)
3 previous lines	50 (32)
≥4 previous lines	61 (39)
Prior ASCT	31 (20)
Prior CAR T-cell therapy	61 (39)
Refractory to last prior therapy	130 (83)
Primary refractory	96 (61)
Refractory to CAR T-cell therapy, No./n (%)	46/61 (75)
DLBCL histology	139 (88.5)

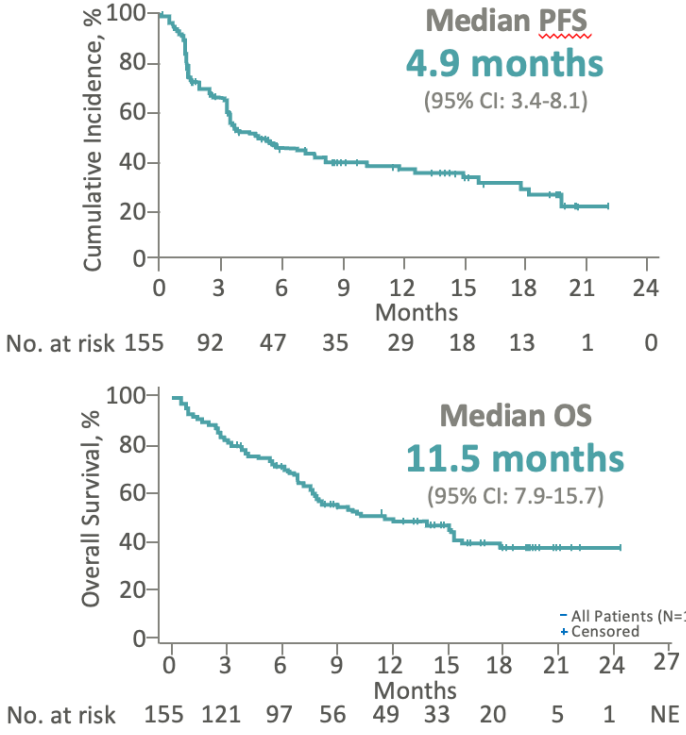




1. Thieblemont et al. *J Clin Oncol* 2022 **2.** Thieblemont et al. *J Clin Oncol* 2022 (Suppl.).

Glofitamab in 3rd line + (NP30179-Phase 1/2)

Baseline characteristics, n (%)	All patients (N=154)
Median (range) age, years	66 (21–90)
Male, sex	100 (65)
ECOG performance status 0/1	69 (45) / 84 (55)
Ann Arbor Stage III/IV†	31 (20) / 85 (55)
Bulky disease	
>6 cm	64 (42)
>10 cm	18 (12)
Nr. of previous lines (median, range)	3 (2–7)
Nr. of previous lines	
Only 2 previous lines	62 (40)
≥3 previous lines	92 (60)
Prior ASCT	28 (18)
Refractory to last prior therapy	132 (86)
Primary refractory‡	90 (58)
DLBCL histology	110 (71)

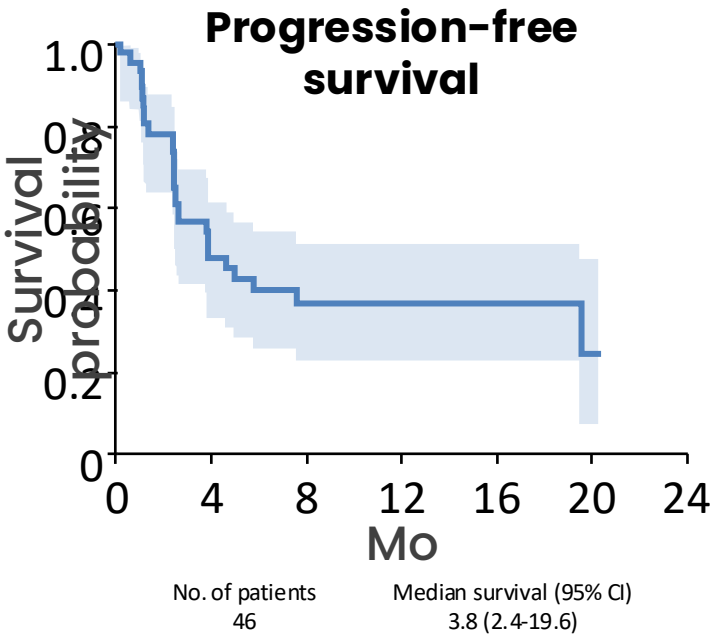


1. Dickinson et al. *N Engl J Med* 2022 **2.** Dickinson et al. *N Engl J Med* 2022 (Suppl.) **3.** Dickinson et al. ASH 2024; Oral presentation #865.

Glofitamab Following CAR T-Cell Therapy Failure in DLBCL

- LYSA: phase II study of glofitamab for patients with R/R DLBCL that had progressed/relapsed starting 1 mo after CAR-T cell therapy

Baseline Characteristics	N = 46
Mean age, yr	60
Elevated LDH, %	78%
Median prior tx (range)	3 (2-5)
Prior SCT, %	17
Refractory to last tx, %	33
Median time from CAR, mo (range)	4 (1-16)



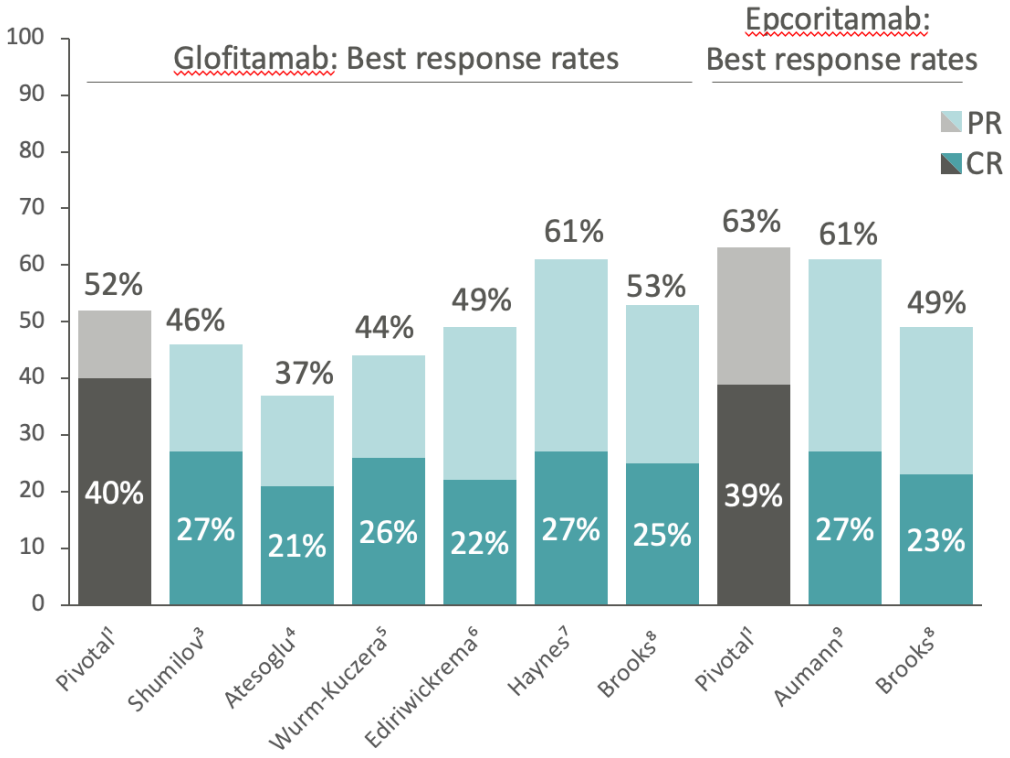
Best Response	
ORR, %	76
CRR, %	46
Median DOR, mo	20
Median DoCR, mo	NE

AESI	
CRS (gr 2), %	9
ICANS (gr 2), %	2
Tumor flare (gr 2), %	9

Cartron. Nat Cancer. 2025;6:1173.

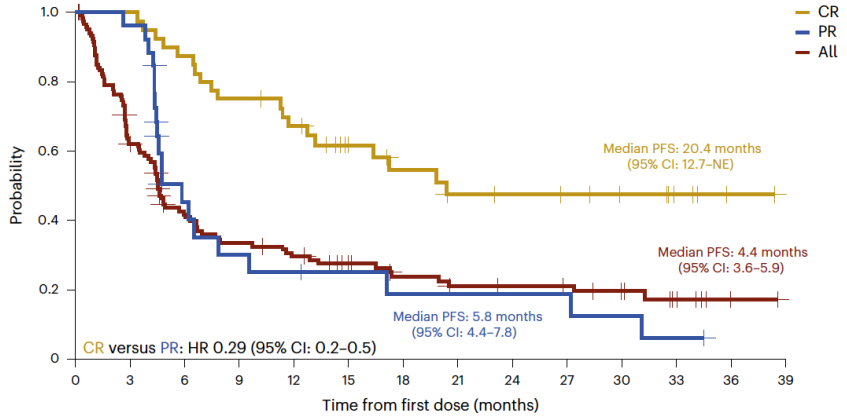
Bispecific Antibodies in the RW

	Pivotal studies[1,2]	RWE[3–9]
ge range, years	20–90	19–94
COG PS ≥2, %	0–3	9–40
ange of prior LoT, n	2–≥4	1–14
efractory to last therapy, %	83–86	54–84
rior CAR-T, %	33–39	60–71
ıPFS, months	4.4–4.9	3.0–10.8
ıOS, months	11.5–Not reached	5.7–Not reached



Odronextamab in 3+ line

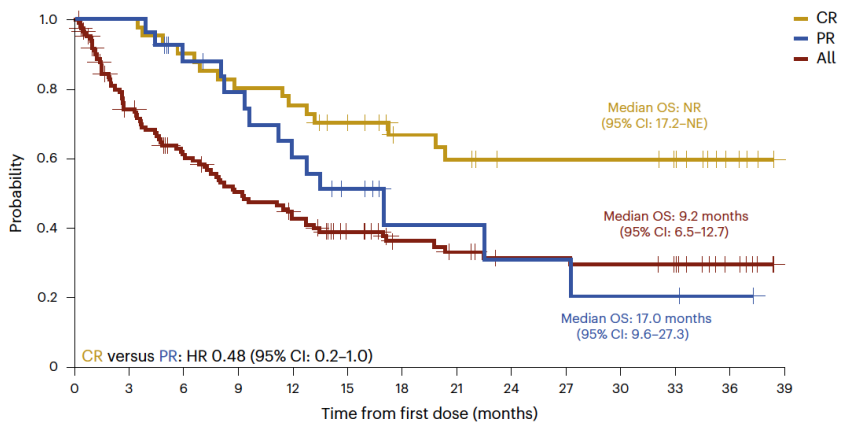
a



No. at risk:

CR	40	40	35	30	26	18	15	12	11	10	8	4	1	0
PR	26	25	9	6	5	4	3	3	3	3	2	1	0	0
All	127	72	44	36	31	22	18	15	14	13	10	5	1	0

b



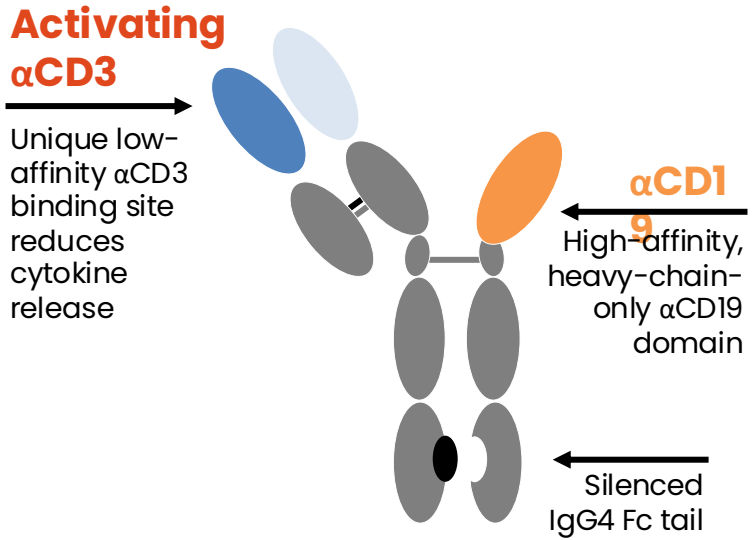
No. at risk:

CR	40	40	36	32	30	25	19	17	14	14	14	12	5	0
PR	26	26	20	17	13	9	4	4	3	3	2	2	1	0
All	127	87	68	55	46	35	24	21	17	17	16	14	6	0

Kim et al, Nat Cancer. 2025 Mar;6(3):528-539.

Surovatamig (AZD0486): Novel CD19 x CD3 Bispecific Antibody

Surovatamig (AZD0486)



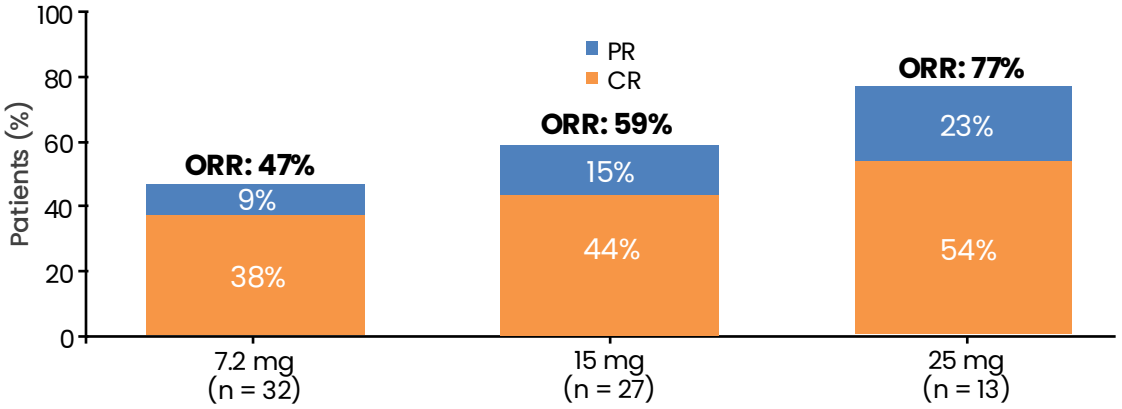
- Fully human CD3 x CD19 IgG4 bispecific T-cell engager
- Key design features:
  - Low-affinity αCD3 reduces cytokine release
  - Silenced Fc tail prolongs half-life and prevents nonspecific binding/ ADCC

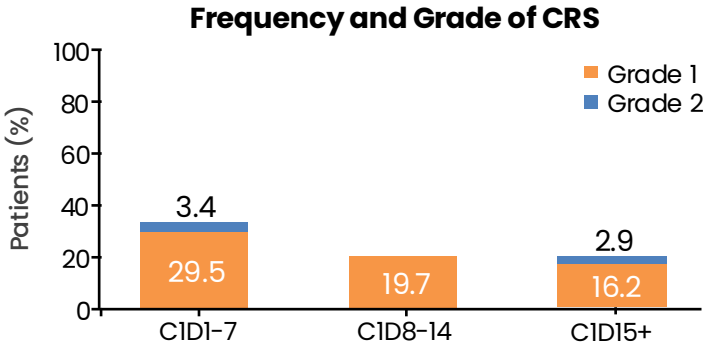
Gaballa. ASH 2024. Abstr 868.

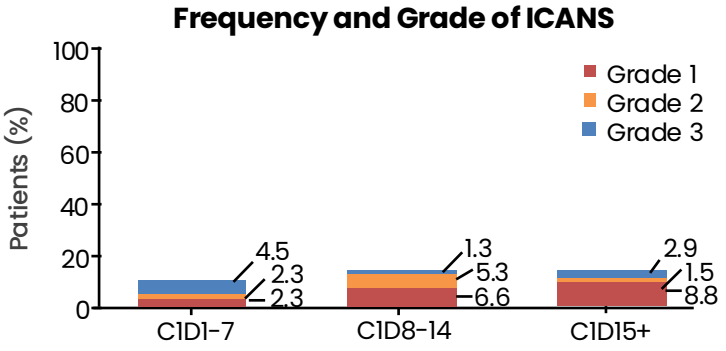
Surovatamig for R/R DLBCL

- Phase I study of surovatamig for R/R CD19+ B-NHL that was R/R to ≥2 prior lines of therapy (N = 106)

Baseline Characteristics	N = 106
Median age, yr (range)	68 (22-94)
Median prior tx (range)	3 (2-13)
Prior CAR T-cell tx, %	42
Refractory to last line of therapy, %	75

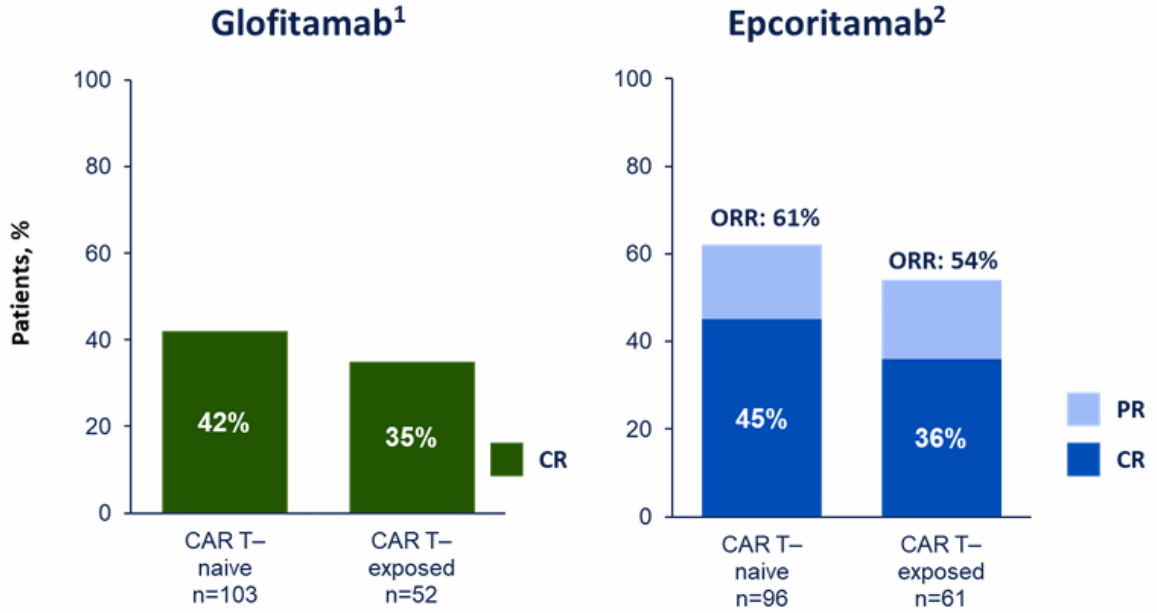






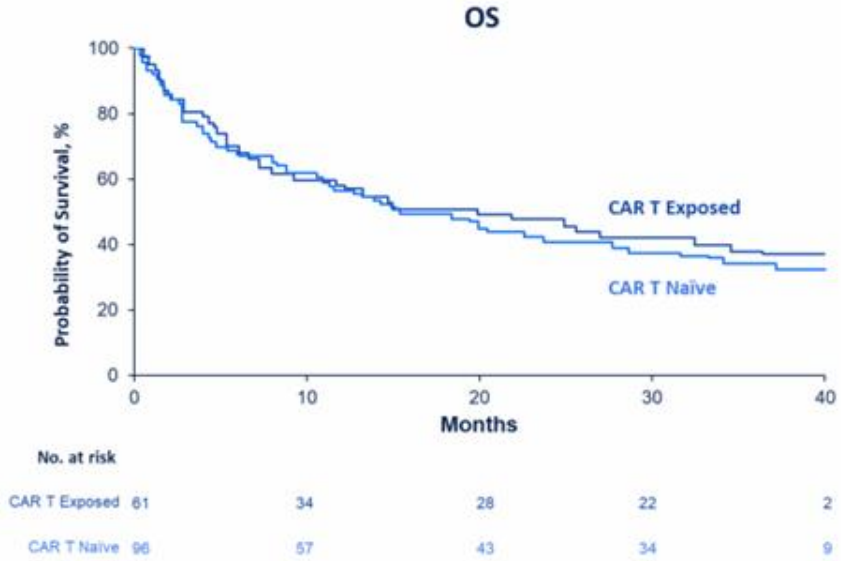
Kim. ASH 2025. Abstr 5514.

Phase II studies of glofitamab and epcoritamab in patients with R/R LBCL – CART exposed vs. CART naïve patients



1. Dickinson MJ, et al. N Engl J Med. 2022;387(24):2220-2231. 2. Karimi Y, et al. Oral 1737. ASH. Dec 7-10, 2024.

Phase II dose expansion study of epcoritamab in patients with R/R LBCL – CART exposed vs. CART naïve patients



Best response, n (%)	CAR T Exposed N=61	CAR T Naïve n=96
ORR	33 (54)	59 (61)
CR	22 (36)	43 (45)
PR	11 (18)	16 (17)

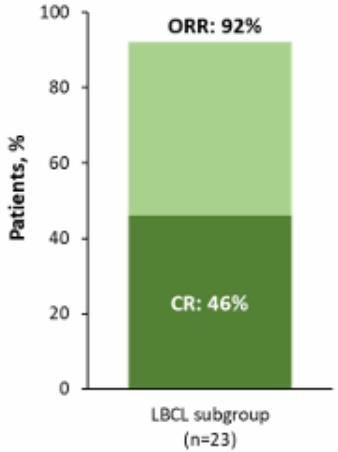
Safety	Overall N=157
Most common TEAEs, ≥20%	
CRS	60%
Diarrhea	24%
Pyrexia	23%
Neutropenia	22%
Fatigue	22%
Injection-site reaction	21%

Karimi Y, et al. Oral 1737. ASH. Dec 7-10, 2024.

What about the efficacy of CART in patients previously exposed to bispecifics? Data from the DESCARTES registry:

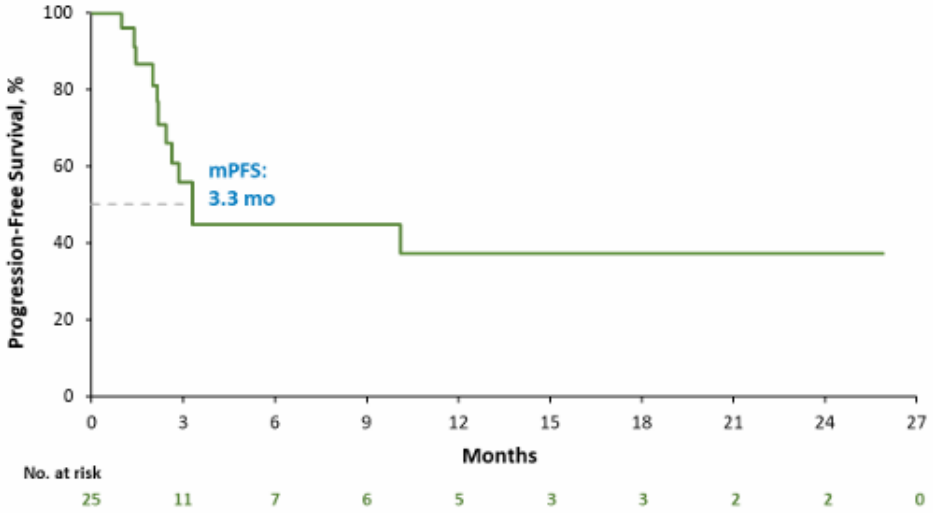
ORR: CAR T after BsAb in LBCL

Median follow-up = 12.3 months



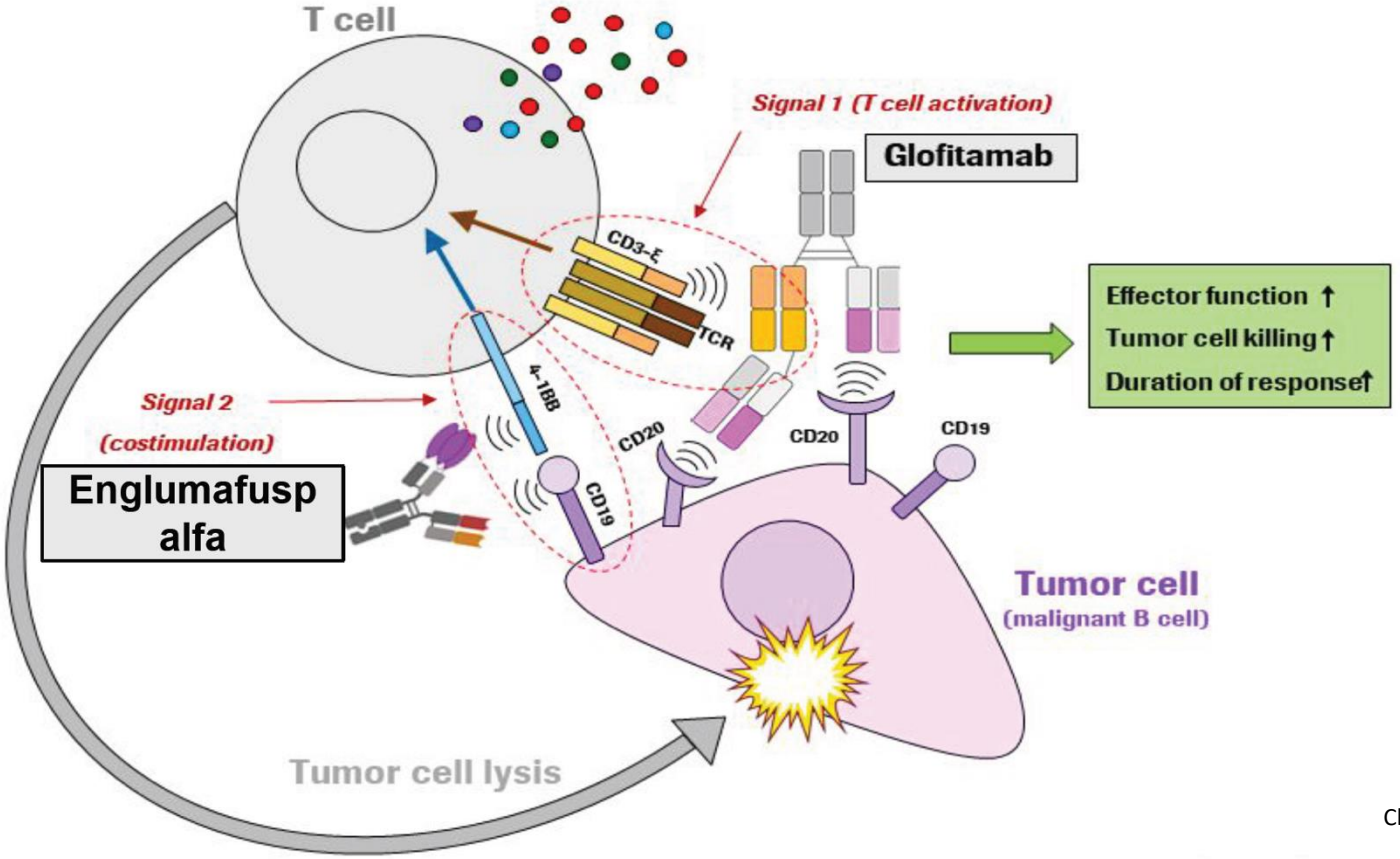
PFS: CAR T after BsAb in LBCL

Median follow-up = 12.3 months



Crochet G, et al. Blood 2024; 144(3): 334-338.

Englumafusp alfa mechanism of action



Claus et al, Sci Transl Med 2019.

Englumafusp alfa

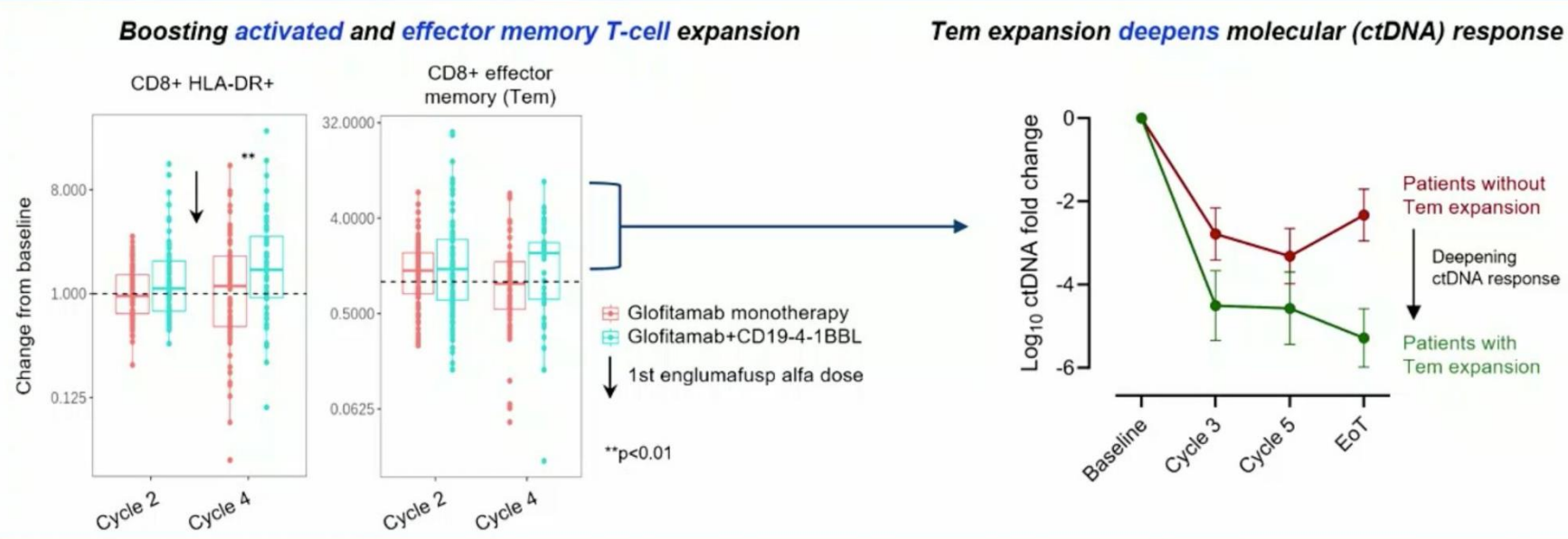
Response rates across all dosing levels in evaluable patients with 2L+ R/R aNHL

n (%)	n	BOR	CR
R/R aNHL			
2L+	83	56 (67.0)	47 (57.0)
3L+	70	46 (65.7)	37 (52.8)
R/R aNHL with prior CAR-T	42	26 (61.9)	20 (47.6)
R/R aNHL without prior CAR-T			
2L+	41	30 (73.2)	27 (66.0)
3L+	28	20 (71.4)	17 (60.7)
2L	13	10 (77.0)	10 (77.0)
R/R aNHL with *TP53* mutation	22	17 (77.0)	15 (68.0)

Morschhauser F et al, EHA 2024 (S237).

Englumafusp alfa boosts memory formation that leads to deeper molecular response

Englumafusp alfa boosts effector memory expansion and deepening of ctDNA response



Significantly greater expansion of activated and effector memory T cells in combination setting vs monotherapy
Effector memory boost is more pronounced in CMR patients and associated with deep ctDNA response at EoT

Morschhauser F et al, EHA 2024 (S237).

STARGLO: Study design (GO41944; NCT04408638)

Phase 3, open-label, randomised trial

Patients with R/R DLBCL (N=274)

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

Stratification factors

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

R 2:1

Glofitamab (C1 SUD;* 30mg C2–12)
Gem (1000mg/m²) + Ox (100mg/m²)
Gpt (1000mg)

D:1 2 8 15 1 1 1 1 1 1 1 1 1 1 1

C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8 | C9 | C10 | C11 | C12

Glofit-GemOx (n=183)

21-day cycles

Rituximab (375mg/m²)
Gem (1000mg/m²) + Ox (100mg/m²)

D: 1 2 1 1 1 1 1 1 1

C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8

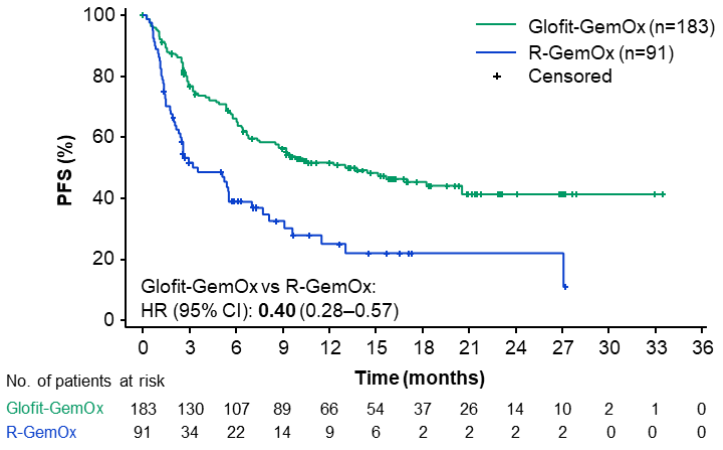
R-GemOx (n=91)

*Glofit 2.5mg on D8 and 10mg on D15. †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. C, cycle; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; DLBCL, diffuse large B-cell lymphoma; Gem-Ox, gemcitabine and oxaliplatin; Glofit, glofitamab; Gpt, obinutuzumab pretreatment; NOS, not otherwise specified; R 2:1, patients randomised in a 2:1 ratio; R, rituximab.

Abramson JS, et al. EHA 2024; Oral presentation (abstract#LB3438);
Abramson JS, et al. Lancet 2024;404(10466, Suppl).

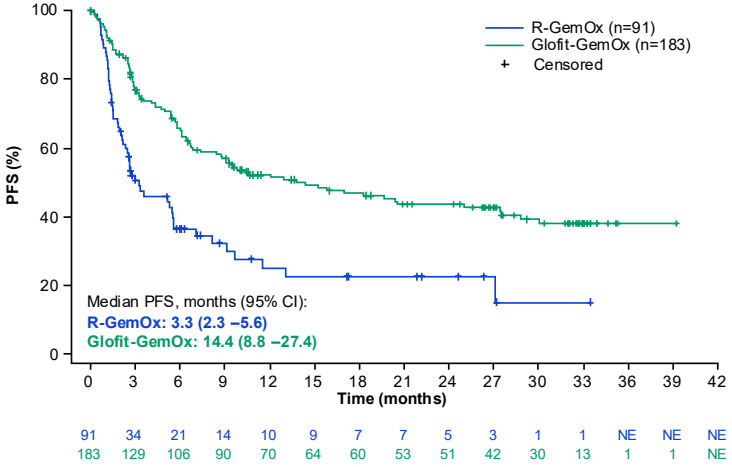
Progression-free survival by IRC assessment

Updated analysis



	R-GemOx (n=91)	Glofit-GemOx (n=183)
Updated analysis (median follow-up: 16.1 months)		
PFS, median (95% CI); months	3.6 (2.5–7.1)	13.8 (8.7–20.5)
HR (95% CI)	**0.40** (0.28–0.57)	
p-value*†	<0.0001	
12-month PFS, % (95% CI)	25.2 (13.6–36.9)	51.7 (44.0–59.4)

Extended follow-up analysis

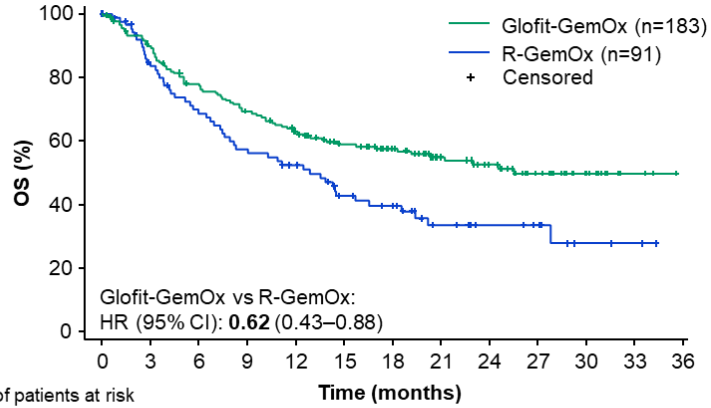


Outcome	R-GemOx (n=91)	Glofit-GemOx (n=183)
PFS, median (95% CI); months	**3.3** (2.3–5.6)	**14.4** (8.8–27.4)
30-month PFS, % (95% CI)	**15.2** (0.9–29.5)	**38.1** (29.8–46.3

Abramson JS, et al. EHA 2024; Oral presentation (abstract#LB3438), Abramson JS, et al. Lancet 2024;404(10466):1940–54 Abramson JS, et al. ASH 2025; Poster presentation (P-5519).

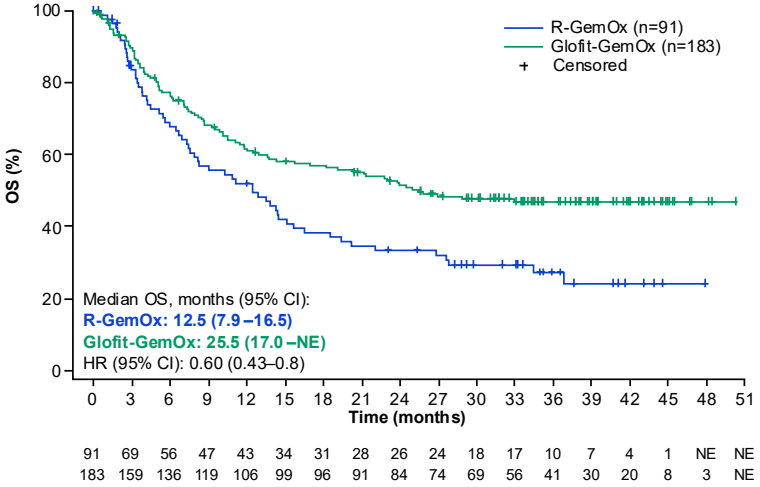
STARGLO: Primary endpoint: Overall survival

Updated analysis



	R-GemOx (n=91)	Glofit-GemOx (n=183)
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)

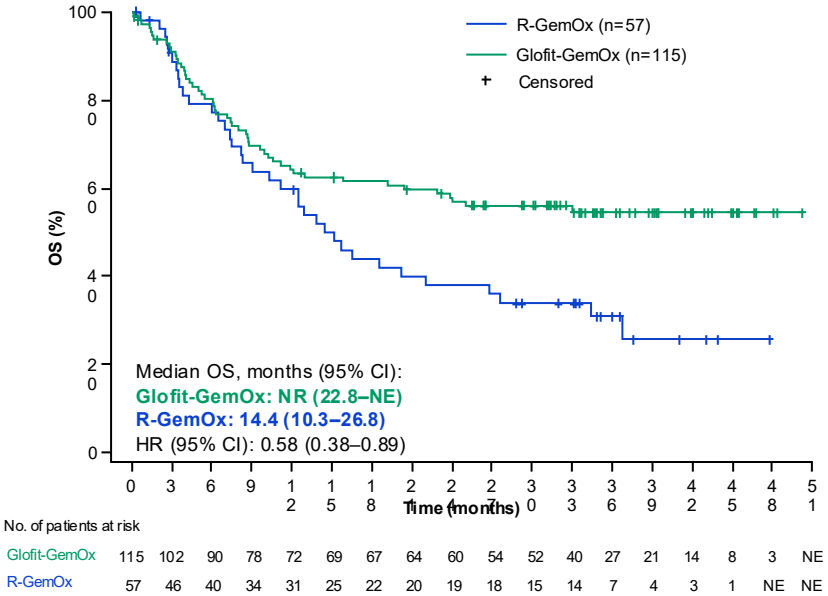
Extended follow-up analysis



Outcome	R-GemOx (n=91)	Glofit-GemOx (n=183)
3-year follow-up analysis (median follow-up: 35.1 months [95% CI: 33.6–37.6])		
OS, median (95% CI); months	**12.5** (7.9–16.5)	**25.5** (17.0–NE)
36-month OS, % (95% CI)	**27.4** (17.3–37.5)	**47.1** (39.5–54.6)

STARGLO: OS by line of therapy – 2L sub-group analysis

Overall survival in 2L patients[1]



Outcome	R-GemOx 2L (n=57)	Glofit-GemOx 2L (n=115)	R-GemOx 3L+ (n=34)	Glofit-GemOx 3L+ (n=68)
Median follow-up: 35.1 months (95% CI: 33.6–37.6)				
OS, median (95% CI); months	**14.4** (10.3–26.8)	**NR** (22.8–NE)	**6.7** (4.2–14.3)	**17.0** (10.7–25.8)
36-month OS, % (95% CI)	**30.8** (17.7-44.0)	**54.6** (45.2–64.0)	**21.8** (6.7–36.9	**33.2** (21.2–45.3)

A clinically meaningful OS benefit was observed for Glofit-GemOx versus R-GemOx in 2L and 3L+ patients[1–3]

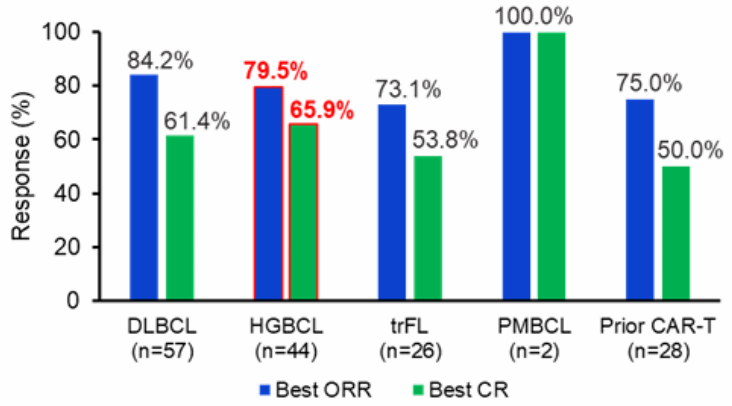
CCOD: May 1, 2025. 2L, second-line; 3L, third line; CI, confidence interval; GemOx, gemcitabine plus oxaliplatin; Glofit, glofitamab; HR, hazard ratio; NE, not evaluable; NR, not reached; OS, overall survival; R, rituximab.

1. Abramson JS, et al. ASH 2025; Poster presentation (P-5519;
2. Abdulhaq H, et al. ASH 2025; Poster presentation (P-3743);
3. Herbaux C, et al. ESH 2025; Poster presentation (P-6986893).

Glofitamab and Polatuzumab vedotin in r/r DLBCL

n (%) [95% CI]	By INV N=129	By IRC N=129
ORR	104 (**80.6**) [72.7–87.1]	101 (**78.3**) [70.2–85.1]
CR	80 (**62.0**) [53.1–70.4]	77 (**59.7**) [50.7–68.2]
PR	24 (18.6) [12.3–26.4]	24 (18.6) [12.3–26.4]
PD	16 (12.4) [7.3–19.4]	16 (12.4) [7.3–19.4]
DOR, median (months) [95% CI]	24.3 [15.0–37.8]	26.4 [10.9–44.3]

Best ORR and CR by histology and prior CAR T-cell therapy (INV-assessed)

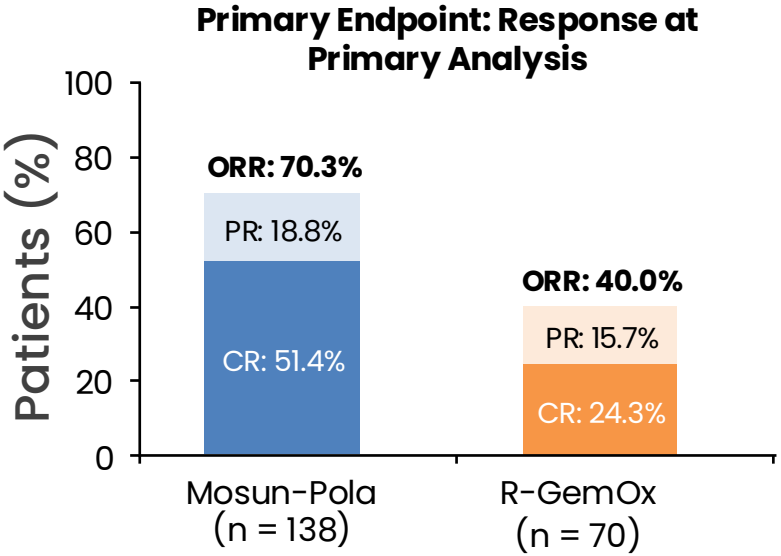


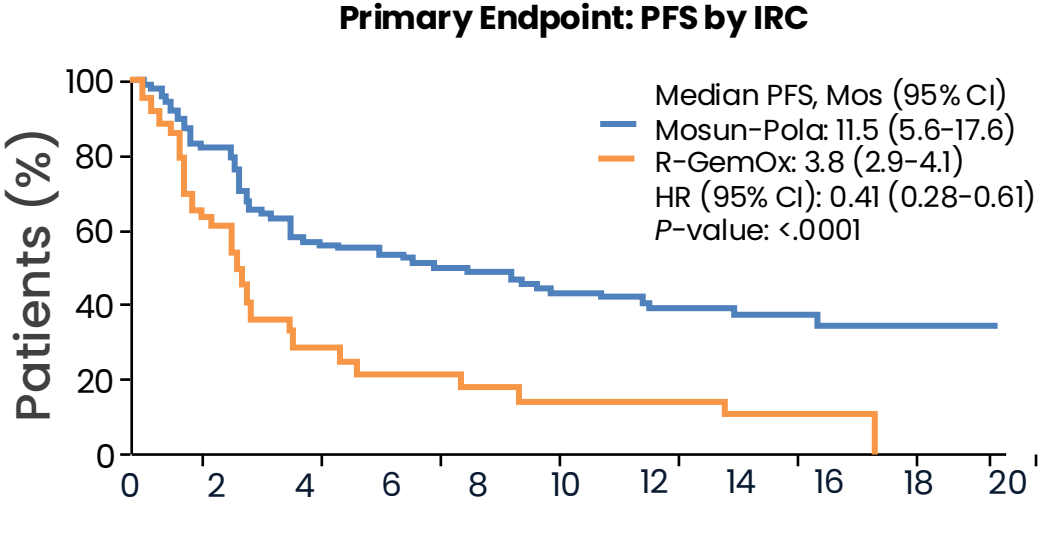
Impressive responses observed (**66% CR**) amongst patients with HGBCL

Hutchings M, et al. J Clin Oncol. 2025 43(36):3788-3798.

SUNMO: Mosunetuzumab + Polatuzumab Vedotin vs R-GemOx for R/R Transplant-Ineligible DLBCL

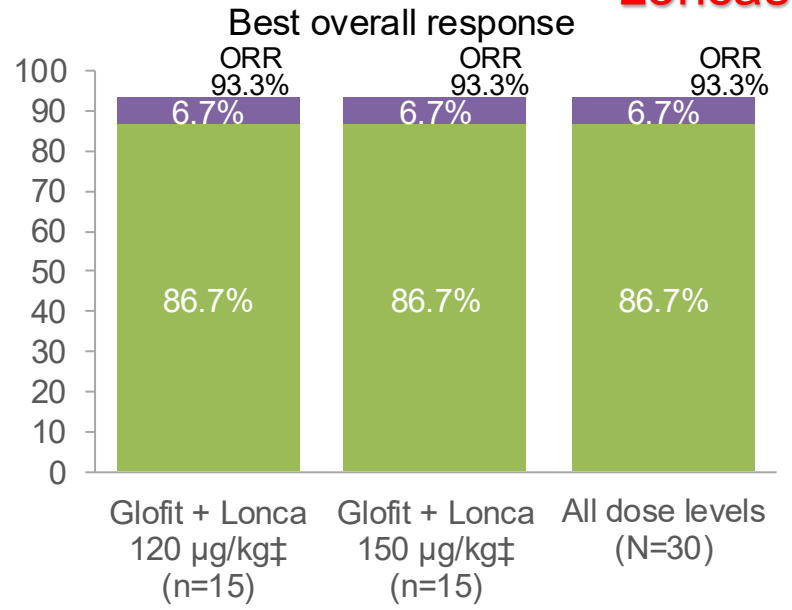
- Randomized phase III study of SC mosunetuzumab + polatuzumab vedotin vs rituximab + gemcitabine + oxaliplatin for CD20+ aggressive NHL (DLBCL or NOS, HGBCL DH/TH or NOS, tFL, FL grade 3b); ≥1 prior systemic therapy; ineligible for ASCT



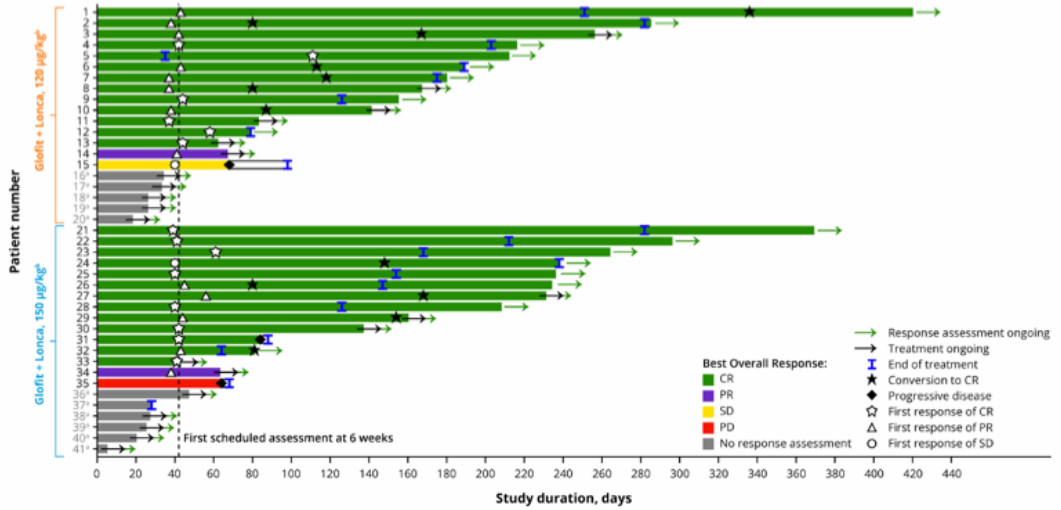


Budde E et al, J Clin Oncol 2025 Dec 20;43(36):3799-3811.

Loncastuximab + glofitamab



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

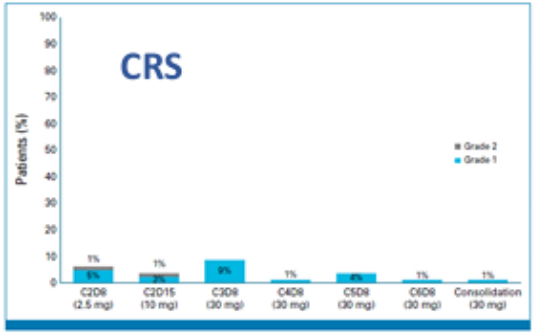


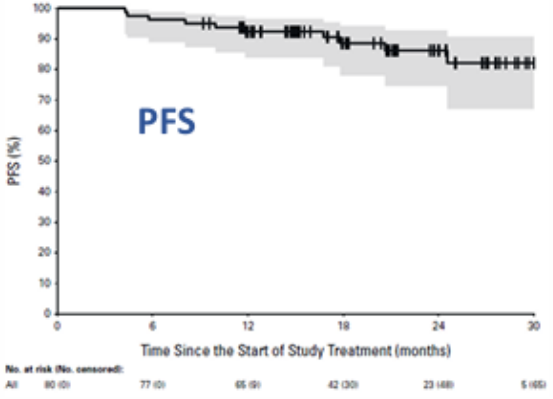
Alderuccio et al. ICML 2025; Oral presentation #078.

COALITION study: R-CHOP or Pola-R-CHOP + glofitamab in 1st line treatment of DLBCL

- Newly diagnosed LBCL and age ≤65 years
- Min. 1 high-risk feature: IPI ≥3, NCCN-IPI ≥4, or double-hit
- All received 1 x R-CHOP, then randomized to
  - 5 x Glofit-R-CHOP (n = 40), or
  - 5 x Glofit-Pola-R-CHP (n = 40)
- Followed by two cycles of glofitamab consolidation

- ORR 100% in both arms
- CRR 98% in both arms
- Estimated 2-y PFS (20.7-month median FU):
  - 86% in the Glofit-R-CHOP arm
  - 92% in the Glofit-Pola-R-CHP arm



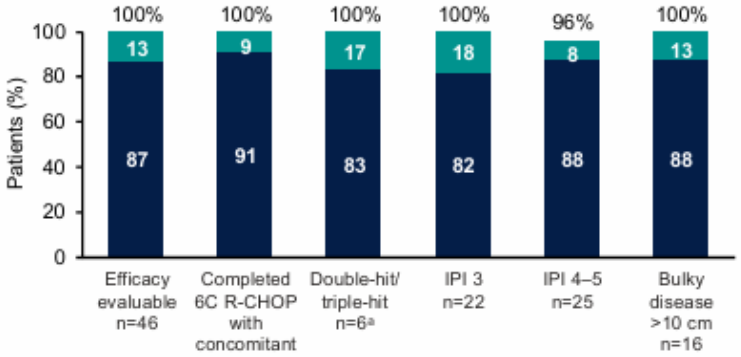


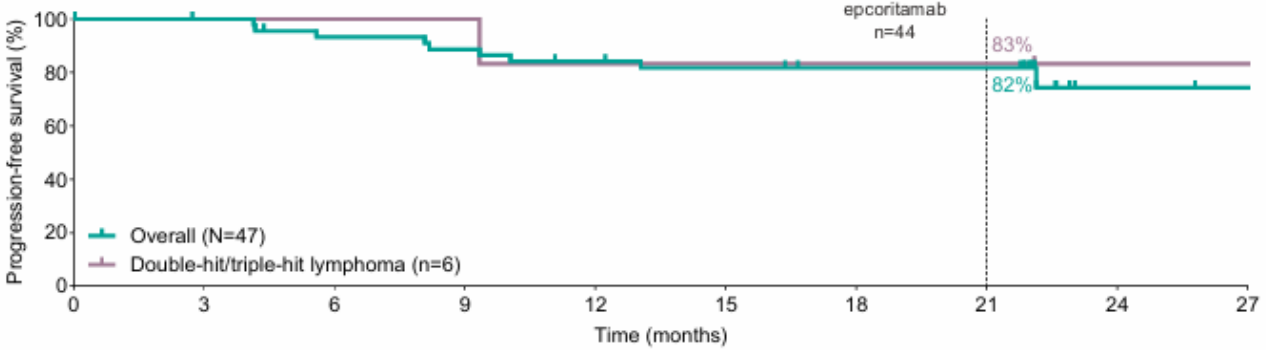
Minson A, et al. J Clin Oncol 2025, 43: 2595-2605.

Epcoritamab + R-CHOP in high-risk DLBCL: EPCORE NHL-2 Arm 1

Key inclusion criteria

- Newly diagnosed CD20⁺ LBCL[a]
- IPI score ≥3
- ECOG PS 0–2
- Adequate organ function

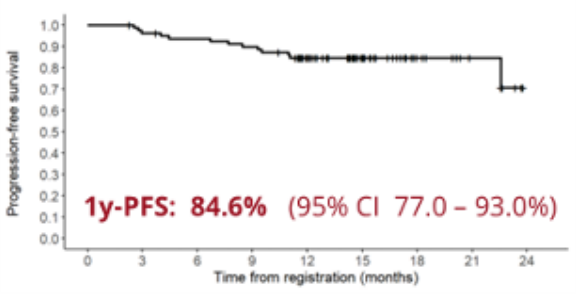




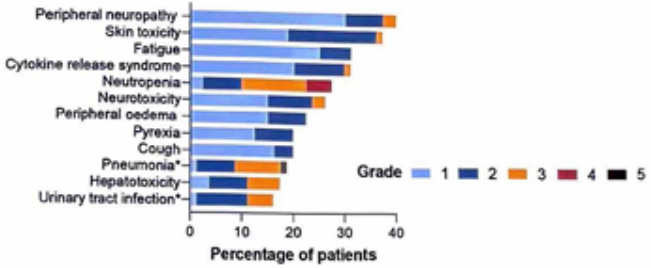
Falchi et al. ASH 2024

Phase II frontline chemolight R-pola-glo trial for elderly and medically unfit/frail patients with aggressive B-cell lymphoma

1-year Progression-free Survival (PFS)



Most common AE terms



RESULTS

Efficacy (n=20 evaluable):

- Median FU 15 month-1-year PFS 85% ; 1-year OS 90%
- After C2, C6 and EOT: ORR 96%, 94% and 90% (95% CI 89–99); CMR 58%, 75% and 81%
- Late conversions: 52% of early PR → CMR by C6; additional 40% converted during Glo consolidation, underscoring benefit of extended Glo exposure
- Alive at cut-off: 89% (71/80)
- Efficacy consistent across sGA risk groups; treatment mitigated adverse impact of IPI factors (e.g., LDH)

Safety:

- No grade 3–5 AEs in 34% (27/80)
- Infections grade 3–5: 26% (3 deaths: COVID 1, COVID+RSV 1, unknown 1)
- CRS: 31% (mostly early, low-grade; grade 3= 1; no grade 4/5; all resolved)
- ICANS: 4% (grade 2= 2; grade 3= 1)

CONCLUSIONS

- R-Pola-Glo delivers high and durable CMR with manageable safety in elderly/frail, medically unfit DLBCL
- 1-year survival metrics are favourable versus historical regimens for this population

Chapuy B, et al. ASH 2025

HO TERMINATO VOSTRO ONORE

e

GRAZIE MILLE PER L'ATTENZIONE

Guido Gini **Alice Di Rocco**
Ma MAGARI…