4th Cuneo City ImmunoTherapy Conference (CCITC)

Immunotherapy in Hematological Malignancies 2024

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News and views in aggressive lymphomas

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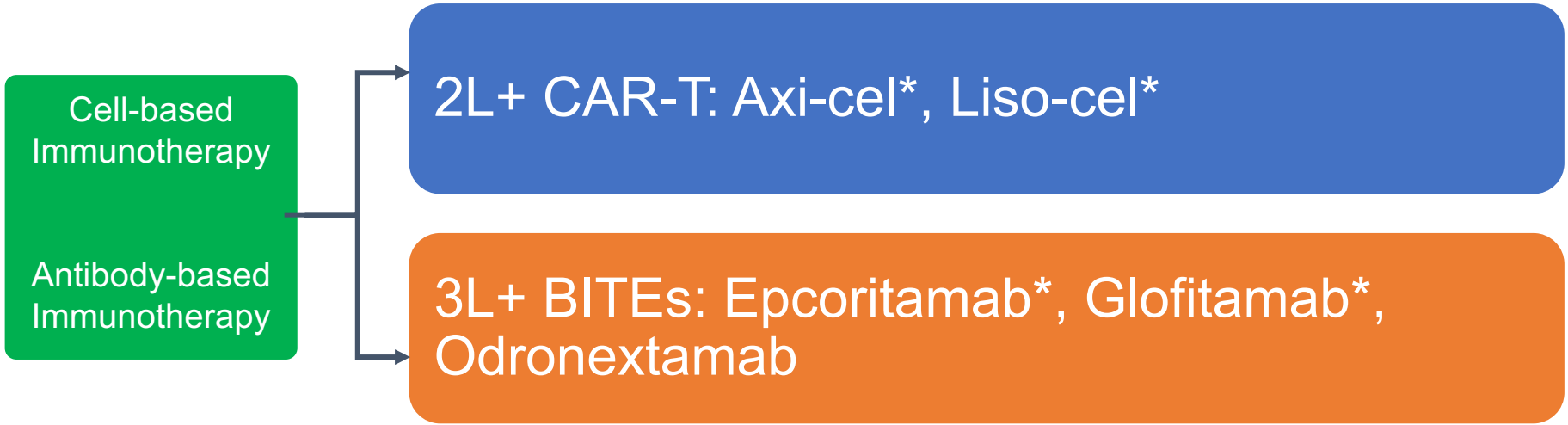
Organized by Prof. Massimo Massaia, SC Ematologia AO S.Croce e Carle, Cuneo - Italy and
Centro Interdipartimentale di Biotecnologie Molecolari "Guido Tarone" (MBC), Torino - Italy

Disclosures of C. Carlo-Stella

Company name	Research support	Consultant	Stockholder	Advisory board	Other
ADC Therapeutics	X	X		X	Honorarium
Karyopharm Tx				X	
Celgene/BMS				X	Honorarium
Incyte					Honorarium
Hoffmann-La Roche Ltd	X			X	Honorarium
Janssen Oncology					Honorarium
Takeda					Honorarium
Merck Sharp & Dohme				X	Honorarium
AstraZeneca					Honorarium
Gilead					Honorarium
SOBI				X	Honorarium
AbbVie				X	
Genmab				X	

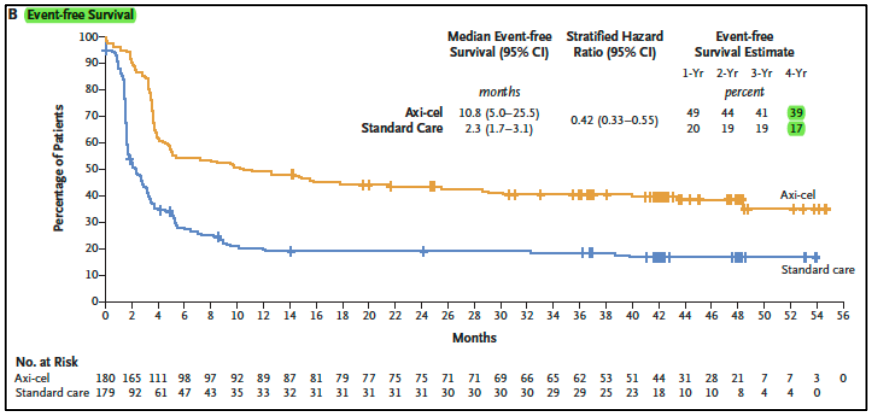
News & Views - Changes of Therapeutic Algorythm for R/R DLBCL

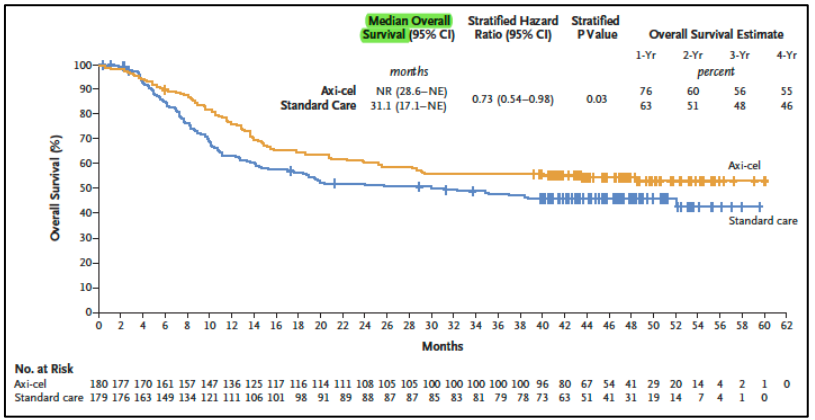


*FDA and/or EMA approved

Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma

J.R. Westin, O.O. Oluwole, M.J. Kersten, D.B. Miklos, M.-A. Perales, A. Ghobadi, A.P. Rapoport, A. Sureda, C.A. Jacobson, U. Farooq, T. van Meerten, M. Ulrickson, M. Elsawy, L.A. Leslie, S. Chaganti, M. Dickinson, K. Dorritie, P.M. Reagan, J. McGuirk, K.W. Song, P.A. Riedell, M.C. Minnema, Y. Yang, S. Vardhanabhuti, S. Filosto, P. Cheng, S.A. Shahani, M. Schupp, C. To, and F.L. Locke, for the ZUMA-7 Investigators and Kite Members*

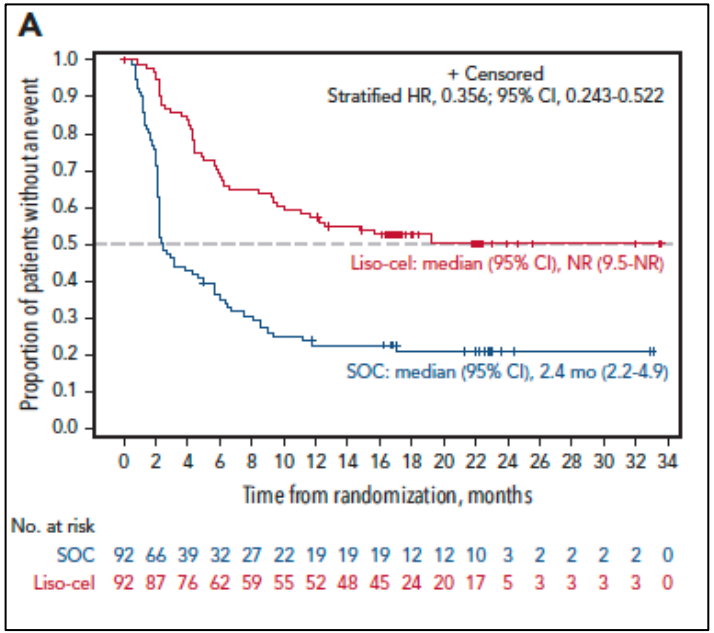


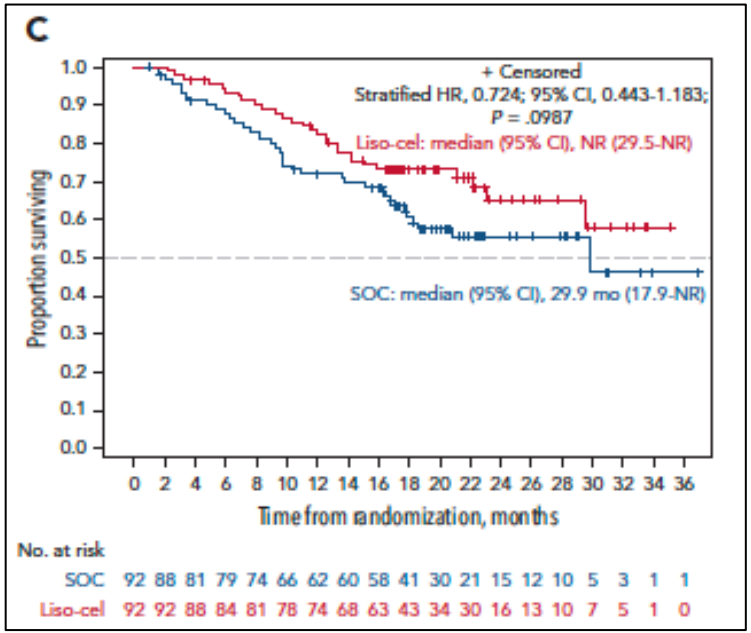


ZUMA-7 – Westin J et al, NEJM, 2023

Lisocabtagene maraleucel as second-line therapy for large B-cell lymphoma: primary analysis of the phase 3 TRANSFORM study

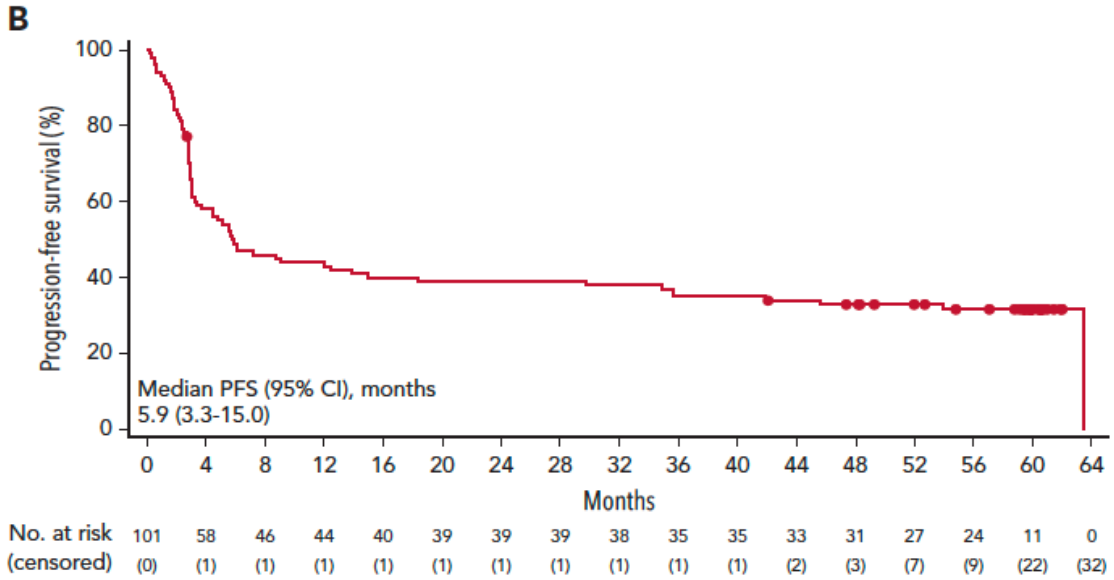
Jeremy S. Abramson,[1] Scott R. Solomon,[2] Jon Arnason,[3] Patrick B. Johnston,[4] Bertram Glass,[5] Veronika Bachanova,[6] Sami Ibrahimi,[7] Stephan Mielke,[8] Pim Mutsaers,[9] Francisco Hernandez-Ilizaliturri,[10] Koji Izutsu,[11] Franck Morschhauser,[12] Matthew Lunning,[13] Alessandro Crotta,[14] Sandrine Montheard,[14] Alessandro Previtali,[14] Ken Ogasawara,[15] and Manali Kamdar,[16] for the TRANSFORM Investigators





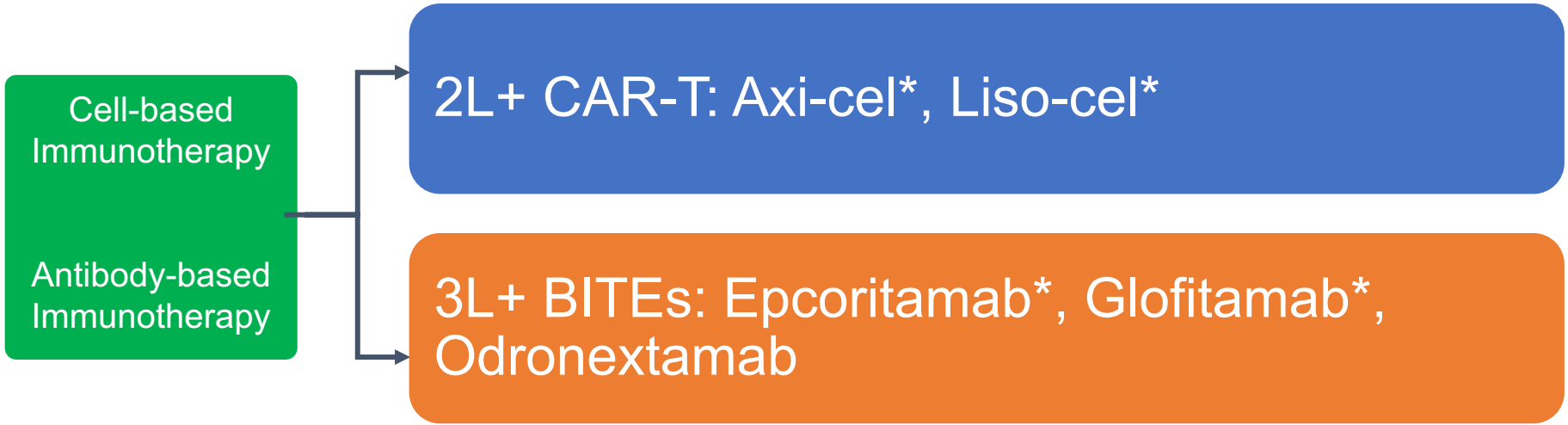
Abramson JS et al, Blood 2023

ZUMA 1 – Progression-Free Survival



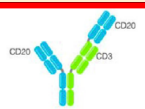
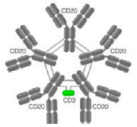
ZUMA-1. Neelapu S et al, Blood 2023

2024 News & Views - Changes of Therapeutic Algorythm for R/R DLBCL



*FDA and/or EMA approved

Comparative characteristics of CD20XCD3 BsAb currently in development

Product name	Schematic depiction	Format	Technology	CD20:CD3 ratio	CD3 clone	CD20 clone	Fc silencing mutations*
Mosunetuzumab[18]		IgG1	Knobs-into-holes (different Fabs)	1:1	UCHT1v9 (CD3δε)	2H7 (type 1 epitope, identical to rituximab)	N297G (no FcγR binding)
Glofitamab[15]		IgG1	Head-to-tail fusion	2:1	SP34-der.(CD3ε)	By-L1 (type 2 epitope, identical to obinutuzumab)	IgG1-P329G-LALA (no FcγR binding)
Epcoritamab[16]		IgG1	Controlled Fab-arm exchange	1:1	huCACAO (SP34-der.)(CD3ε)	7D8 (type 1 epitope, shared by ofatumomab)	L234F,L235E,D265A (no FcγR,C1q binding)
Odronexamab[17]		IgG4	Heavy chains with different affinity	1:1	REG1250 (CD3δε)	3B9-10 (type 1 epitope, shared by ofatumomab)	Modified IgG4 (no FcγRIII binding)
Plamotamab[90]		IgG1	Fab-Fc x scFv-Fc	1:1	α-CD3_H1.30 (SP34-der.)(CD3ε)	C2B8_H1_L1 (type 1 epitope, shared by rituximab)	G236R, L328R (no FcγR binding)
IgM 2323[19]		IgM	IgM + modified J chain	10:1	Not reported	Not reported	No

*These Fc-silencing mutations do not abolish the binding of BsAb to neonatal FcR.

Delivery and Scheduling

Treatment	Route	Cycles	Duration	CRS Mitigation
Glofitamab	IV	2 weekly steps to target then Q3W to C12 RP2D 30 mg	Fixed	Obinutuzumab Step up dosing Steroids
Epcoritamab	SC	QW C1-3 Q2W C4-9 Q4W 10+ RP2D 48mg	Until PD	Step up dosing Steroids
Odronextamab	IV	6 doses C1 3 weekly doses C2-4 then Q2W RP2D 160 mg	Until PD	Step up dosing Steroids

BsAb, bispecific antibody; C, cycle; CRS, cytokine release syndrome; D, day; FL, follicular lymphoma; IV, intravenous; Q2W, every 2 weeks; Q4W, every 4 weeks; QW, every week; SC, subcutaneous.
Adapted from: 1. Dreyling M, et al. *J Clin Oncol*. 2017;35(35):3898-3905. 2. Budde LE, et al. *Lancet Oncol*. 2022;23(8):1055-1065. 3. Kim T-M, et al. Presented at: ASH 2022.

Clinical Characteristics – Pivotal data in 3L+ DLBCL

Characteristics	Glofitamab (n=155)*	Epcoritamab (n=157)**	Odronextamab*** (n=141)
Age (median, range)	66 (21-90)	64 (20-83)	66 (24-88)
Prior lines of therapy (median, range)	3 (2-7)	3 (2-11)	2 (2-8)
Primary refractory	58%	61%	57%
Refractory to last therapy	86%	83%	86%
HGBCL	7%	6%	18%
Transformed lymphoma	17%	25%	17%
PMBCL	4%	3%	0%
Prior CAR-T	33%	39%	0%
Prior ASCT	18%	20%	17%

*Dickinson M, NEJM 387:2220-2231, 2022; **Thieblemont C, JCO, 41:2238-2247, 2023; ***Ayyappan S, Blood 142: 436-38, 2023

Response rates at RP2D – Pivotal data in 3L+ DLBCL

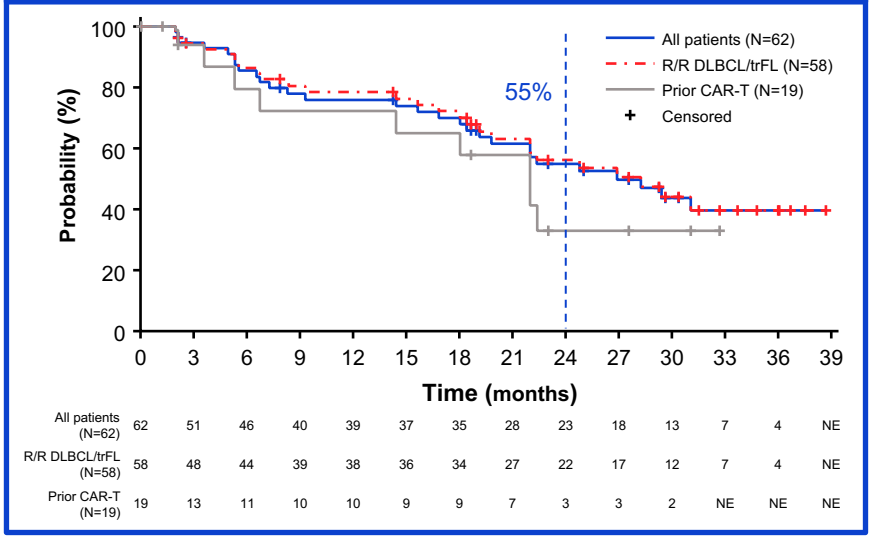
Characteristics	Glofitamab (n=155)*	Epcoritamab (n=157)**	Odronextamab*** (n=141)
CRR	61 (39.5%) [95% CI: 31.6%, 47.5%]	61 (39%) [95% CI: 31–47]	39 (31%)
ORR	80 (51.6) [95% CI: 43.5%, 59.7%]	99 (63) [95% CI: 55–71]	66 (52%)

*Dickinson M, NEJM 387:2220-2231, 2022; **Thieblemont C, JCO, 41:2238-2247, 2023; ***Ayyappan S, Blood 142: 436-38, 2023

Glofitamab CR Remained Durable

	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)	26.9 (19.8–NR)	28.3 (19.8–NR)	22.0 (6.7–NR)
24-month DoCR, % (95% CI)	55.0 (41.1–68.8)	56.2 (41.9–70.4)	33.1 (7.2–59.0)
Median CR follow-up, months (range)	29.6 (0–39)	29.6 (0–39)	23.0 (0–33)
Ongoing CRs, n/N (%)	34/62 (55)	32/58 (55)	10/19 (53)

DoCR by IRC



- Median time on study: 32.1 months (range: 0–43)

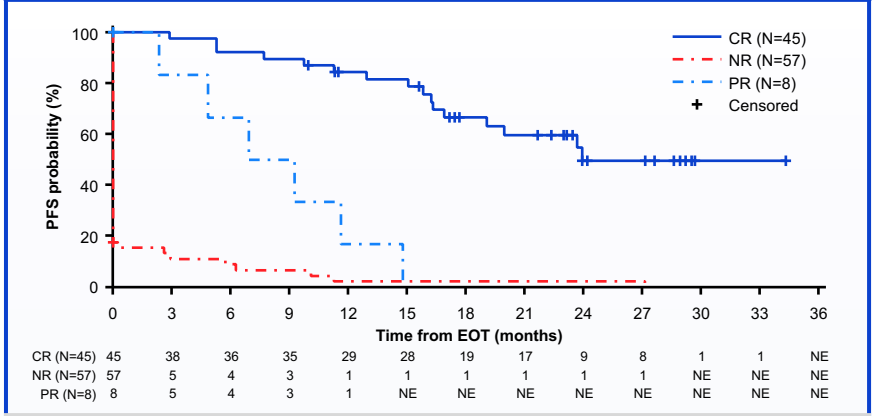
With 32 months median follow-up, glofitamab showed high response rates and durable remissions across subgroups

*Intent-to-treat population (DLBCL, trFL, HGBCL, and PMBCL); †Patients in this subgroup had similar baseline characteristics to the overall population; ‡Primary efficacy population reported in the glofitamab USPI, all patients received at least one dose of glofitamab. CI, confidence interval; NE, not estimable; NR, not reached; USPI, United States prescribing information.

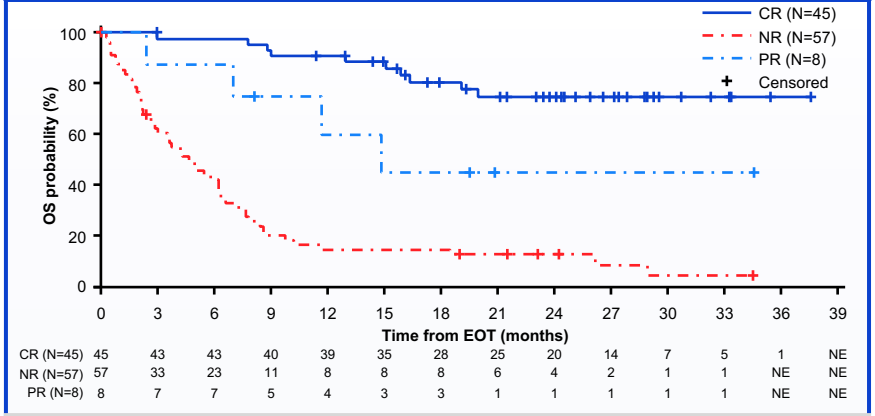
1. COLUMVI USPI. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761309s000lbl.pdf.

Landmark analysis by response at EOT

PFS



OS



Landmark PFS from EOT in patients with CR at EOT*	N=45
Median PFS, months (95% CI)	24.0 (19.1–NE)
18-month PFS rate, % (95% CI)	66.6 (51.0–82.2)

Landmark OS from EOT in patients with CR at EOT*	N=45
Median OS, months (95% CI)	NE (NE)
18-month OS rate, % (95% CI)	80.7 (68.6–92.8)

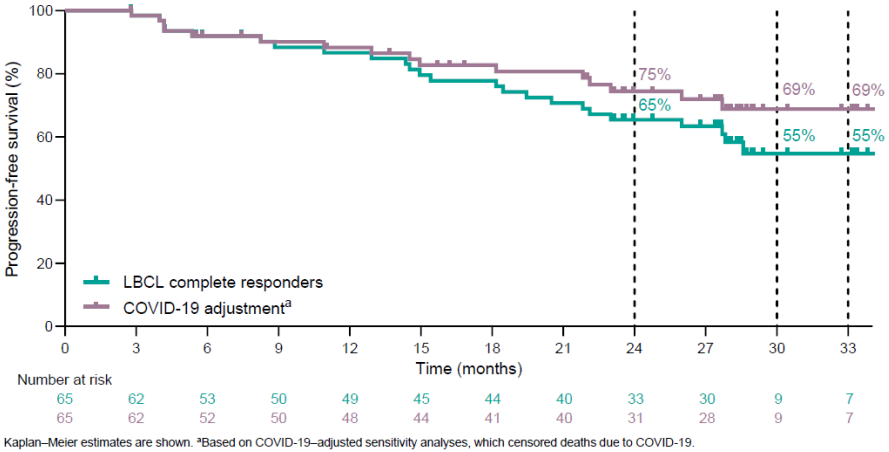
Majority of patients with a CR at EOT remained progression-free and alive at 18 months after EOT

*KM estimates.
EOT, end-of-treatment.

Hutchings M, et al. ASH 2023; oral presentation (abstract #433).

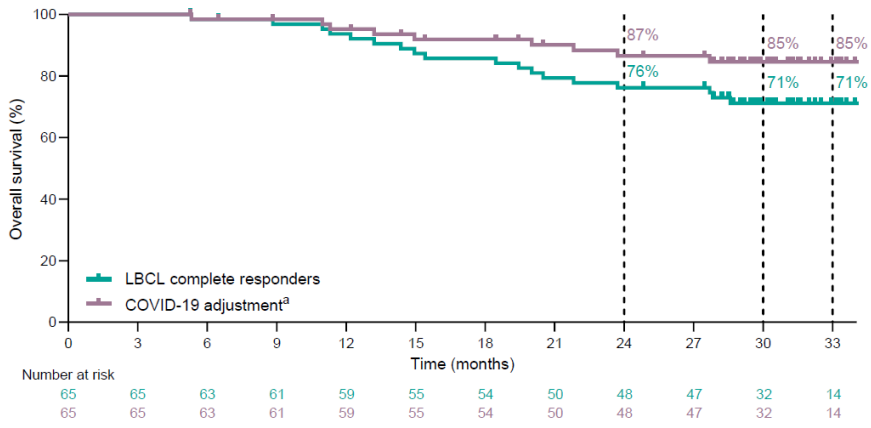
Epocoritamab CR Remained Durable

PFS



Kaplan–Meier estimates are shown. [a]Based on COVID-19–adjusted sensitivity analyses, which censored deaths due to COVID-19.

OS

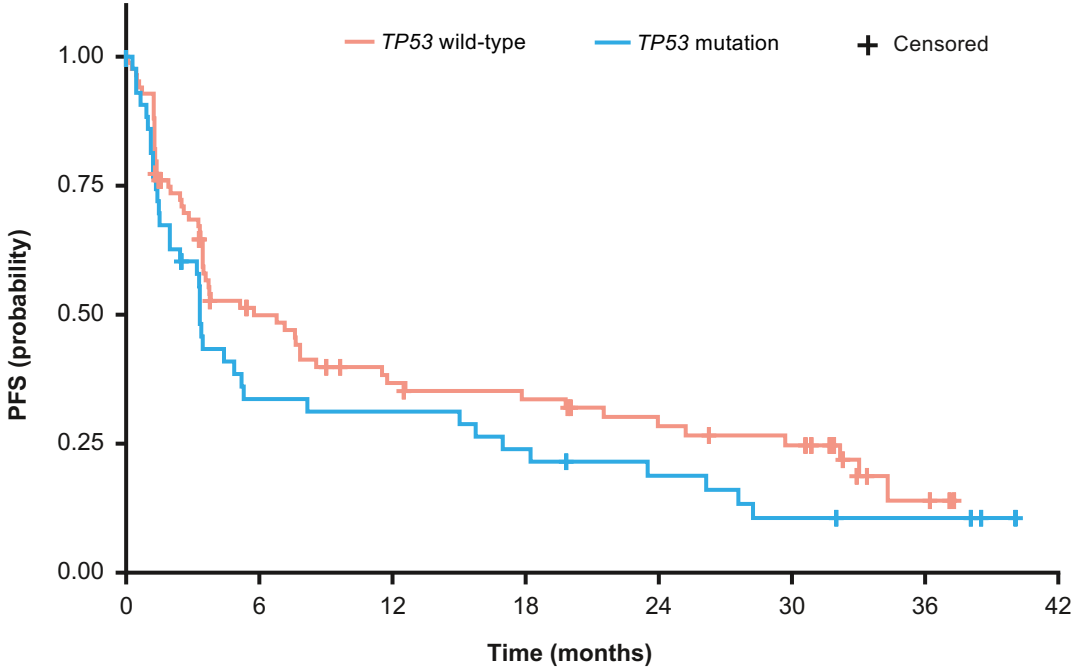


Kaplan–Meier estimates are shown. [a]Based on COVID-19–adjusted sensitivity analyses, which censored deaths due to COVID-19.

Thieblemont C. et al. P1151, EHA 2024

Progression-Free Survival by TP53 Status

- At Baseline, TP53 mutations were detected in 33% (44/132) of patients
- CR rate for TP53 mutation was 25% (11/44) vs 43% (38/88) for TP53 wild-type patients
- Patients with TP53 mutation had a PFS comparable to TP53 wild-type patients (HR 1.34, 95% CI: 0.89–2.02)



Number at risk

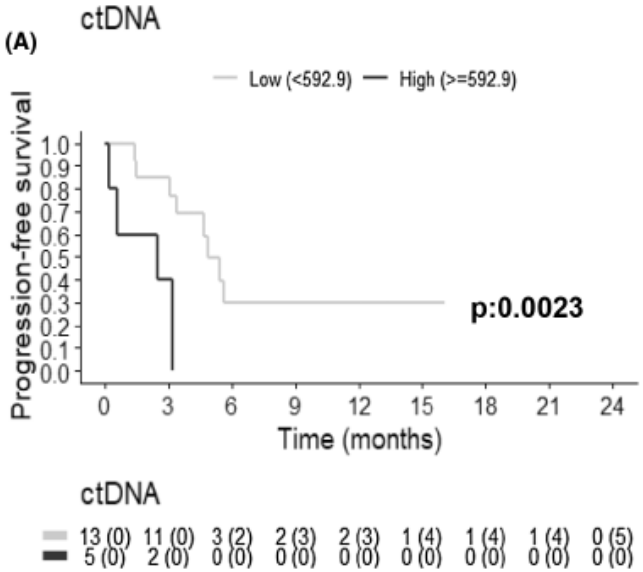
88	35	24	21	16	13	3	0
44	14	13	10	7	4	3	0

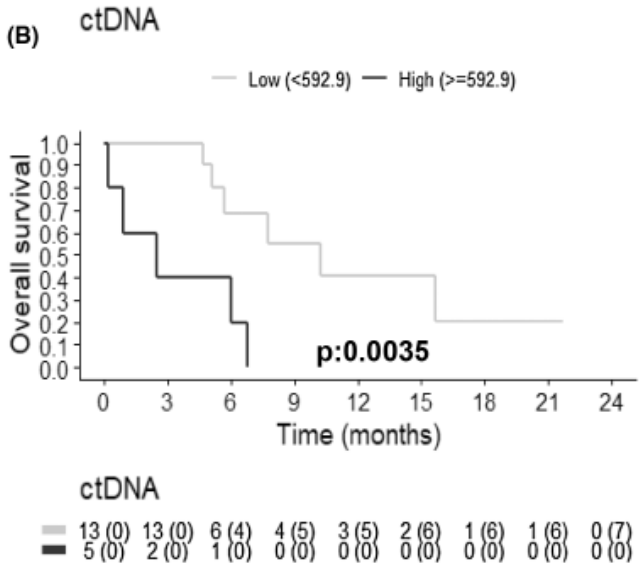
C. Carlo-Stella et al, poster, EHA 2024

Outcome after chimeric antigen receptor (CAR) T-cell therapy failure in large B-cell lymphomas

Anna Dodero[1] | Stefania Bramanti[2] | Martina Di Trani[2] | Martina Pennisi[1] | Silva Ljevar[3] | Annalisa Chiappella[1] | Magagnoli Massimo[2] | Anna Guidetti[1,4] | Francesco Corrado[5] | Paulina Maria Nierychlewska[6] | Alice Di Rocco[7] | Daniele Lorenzini[8] | Rahal Daoud[9] | Chiara De Philippis[2] | Armando Santoro[2,5] | Carmelo Carlo-Stella[2,5] | Paolo Corradini[1,4]

Br. J. Haematol, 2023

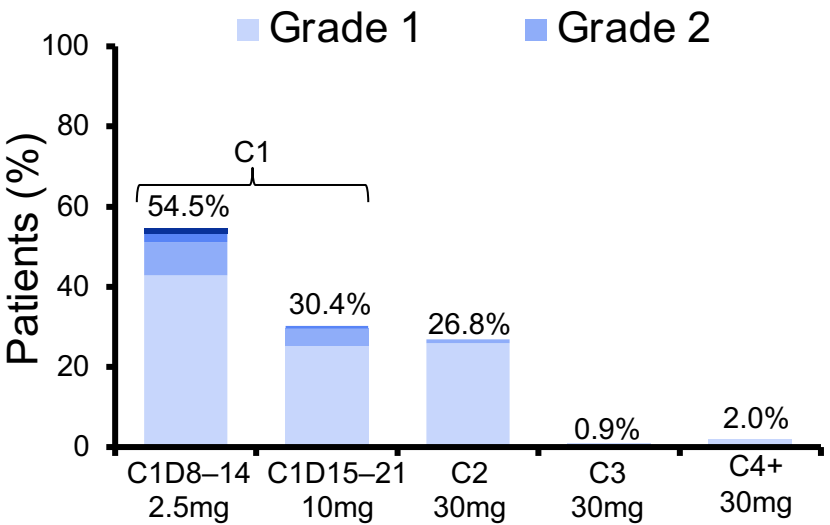




6-month PFS: 0% vs. 30%

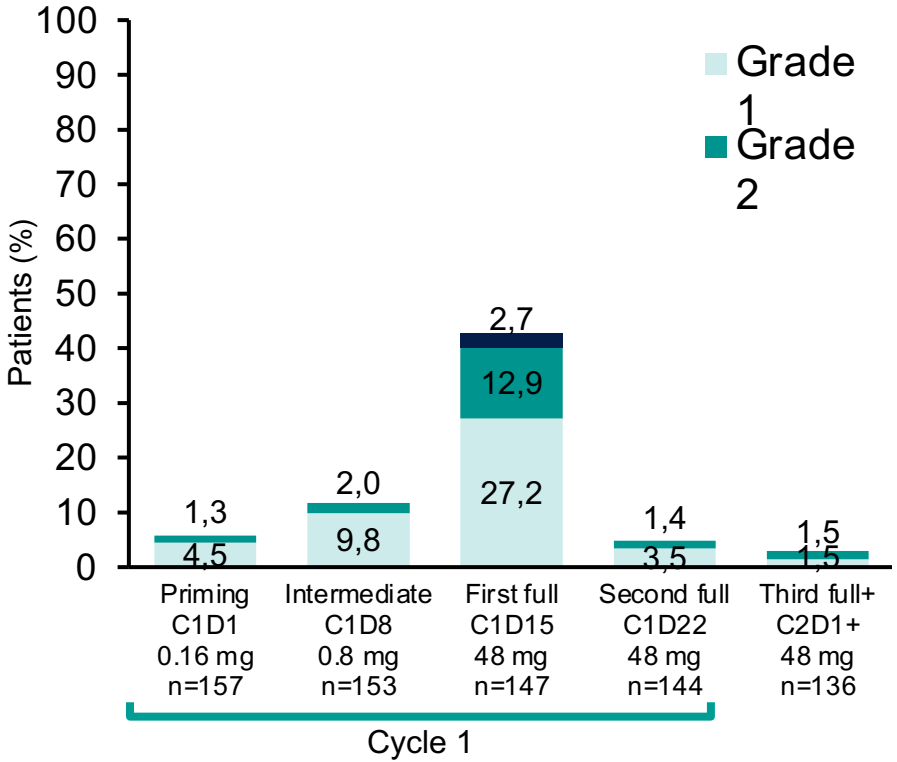
6-month OS: 20% vs. 68%

CRS Rates and Grades – Glofit *vs* Epco



CRS was mostly low grade, time of onset was predictable, and most events occurred during C1

Dickinson M, et al. ASCO 2022

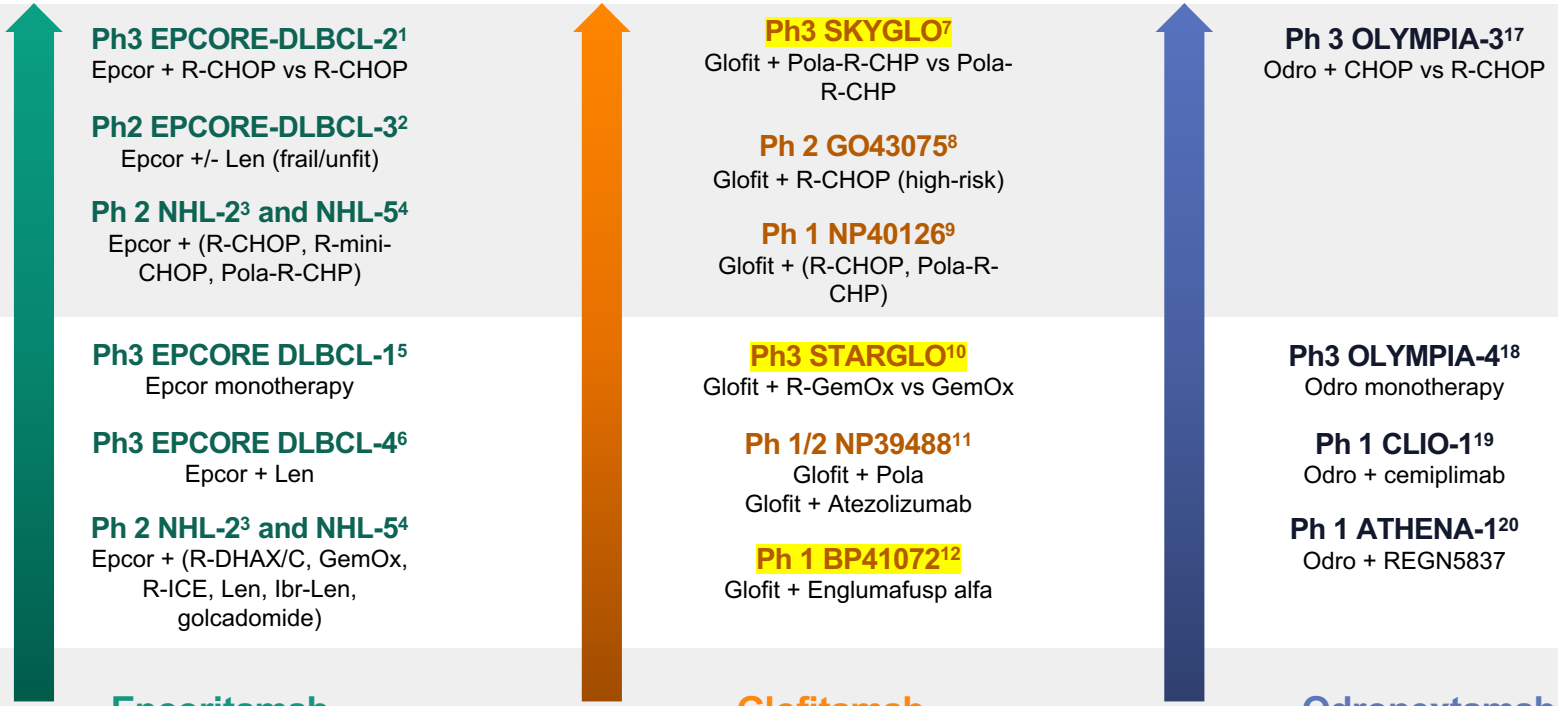


Thieblemont C, et al. EHA 2022

Characteristics of Bispecific Abs

- Off-the-shelf treatment – eventually administered at fixed duration, reducing overall treatment burden
- Premedication but no lymphodepletion or bridging therapy
- Monotherapy induces high CR rates, even in high-risk pts (CAR-T exposed, P53mut)
- Durable CR in DLBCL with a high proportion of pts in CR beyond two years
- Predictable and manageable safety profile supports long-term disease control
- Limited CNS toxicity compared to other therapies
- MoA makes the bispecifics ideal for combination strategies
- Potential to enhance effectiveness and use in earlier lines of therapy

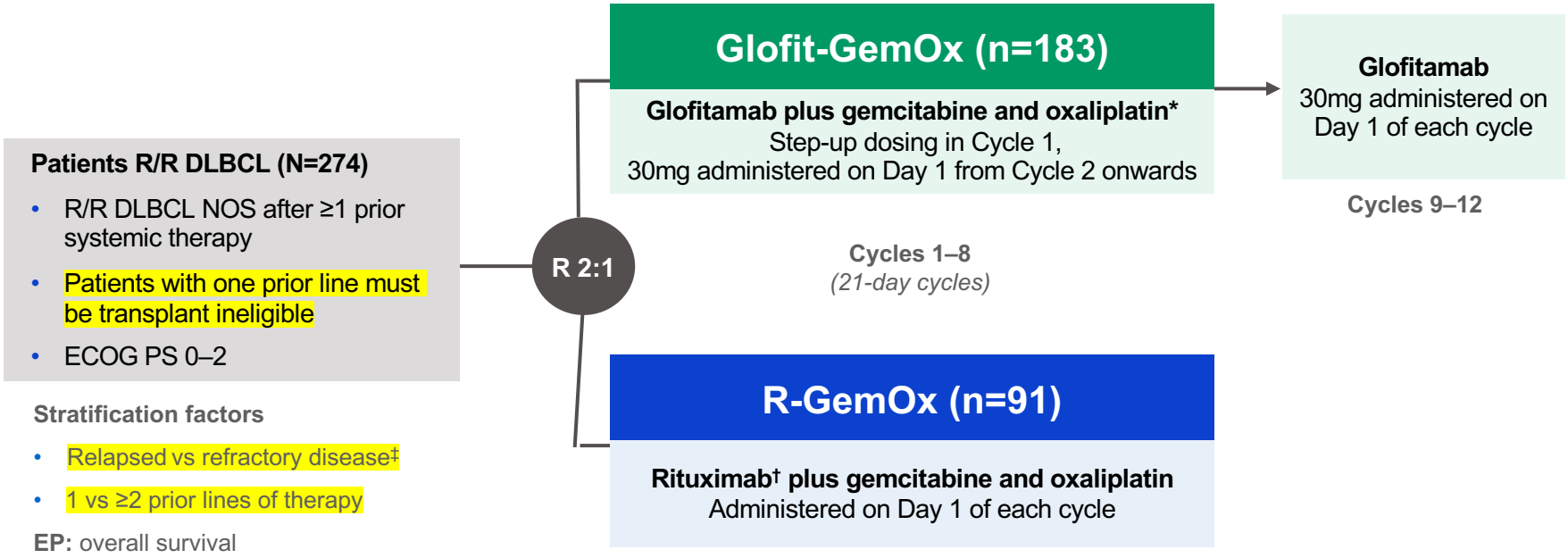
Bispecific Development in DLBCL



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.

STARGLO: study design



*Gemcitabine 1000mg/m2 and oxaliplatin 100mg/m2. In C1, Gpt administered on D1, GemOx on D2, followed by glofit 2.5mg on D8 and glofit 10mg on D15; in C2–8, glofit 30mg and GemOx are administered on D1. †Rituximab 375mg/m2. ‡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. ASCT, autologous stem cell transplant; C, cycle; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; DLBCL, diffuse large B-cell lymphoma; Glofit-GemOx, glofitamab plus gemcitabine and oxaliplatin; Gpt, obinutuzumab pre-treatment; NOS, not otherwise specified; R 2:1, patients randomized in a 2:1 ratio; R-GemOx, rituximab plus gemcitabine and oxaliplatin.

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

STARGLO: Patient demographics and baseline characteristics (ITT population)

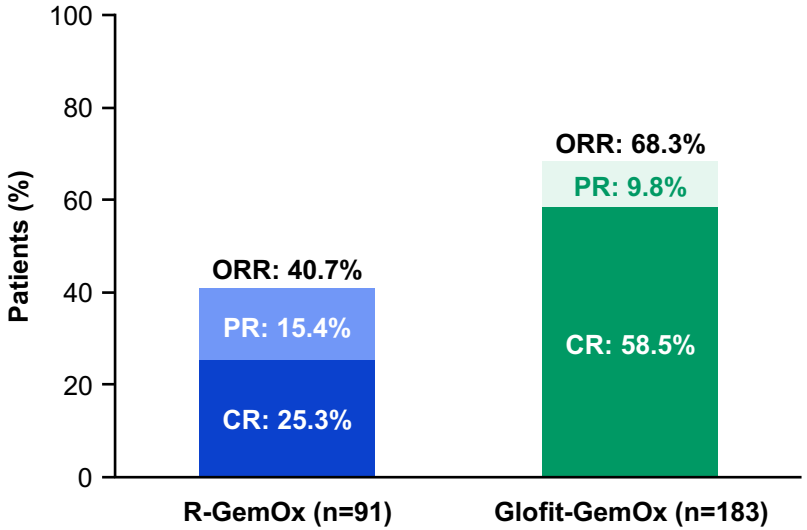
n (%), unless otherwise stated		R-GemOx (n=91)	Glofit-GemOx (n=183)
Age, years	Median (range) ≥65 years	68.0 (20–84) 56 (61.5)	68.0 (22–88) 116 (63.4)
Sex	Male	53 (58.2)	105 (57.4)
Race	Asian Black or African American White Unknown	51 (56.0) 1 (1.1) 33 (36.3) 6 (6.6)	86 (47.0) 2 (1.1) 82 (44.8) 13 (7.1)
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)

ABC, activated B-cell-like; CAR, chimeric antigen receptor; ECOG PS, Eastern Cooperative Oncology Group performance status; GCB, germinal center B-cell-like; Glofit-GemOx, glofitamab plus gemcitabine and oxaliplatin; ITT, intention to treat; R-GemOx, rituximab plus gemcitabine and oxaliplatin; R/R, relapsed/refractory.

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

STARGLO: Response rates by IRC assessment

Response rates at the updated analysis



- **33.2%** difference in CR rate between treatment arms (95% CI: 19.7–44.5)
- CR rate significantly better with Glofit-GemOx vs R-GemOx (descriptive p-value **<0.0001***)

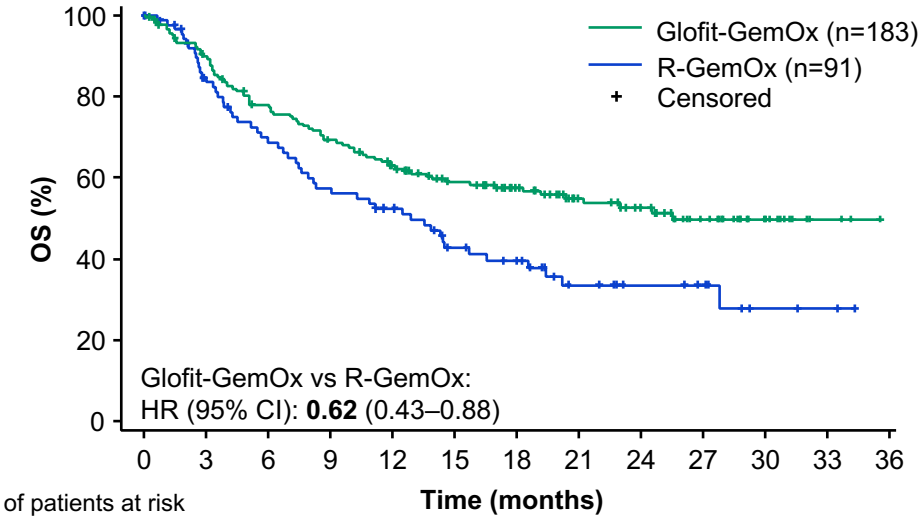
- CR rate was statistically significant at primary analysis, with increased difference between treatment arms at the updated analysis

Difference in duration of CR between treatment arms had not reached statistical significance at the time of analysis.
*p-value based on Cochran-Mantel-Haenszel method.
CI, confidence interval; CR, complete response;Glofit-GemOx, glofitamab plus gemcitabine and oxaliplatin; IRC, Independent Review Committee; ORR, overall response rate; PR, partial response; R-GemOx, rituximab plus gemcitabine and oxaliplatin.

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

STARGLO: Primary endpoint - overall survival

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)

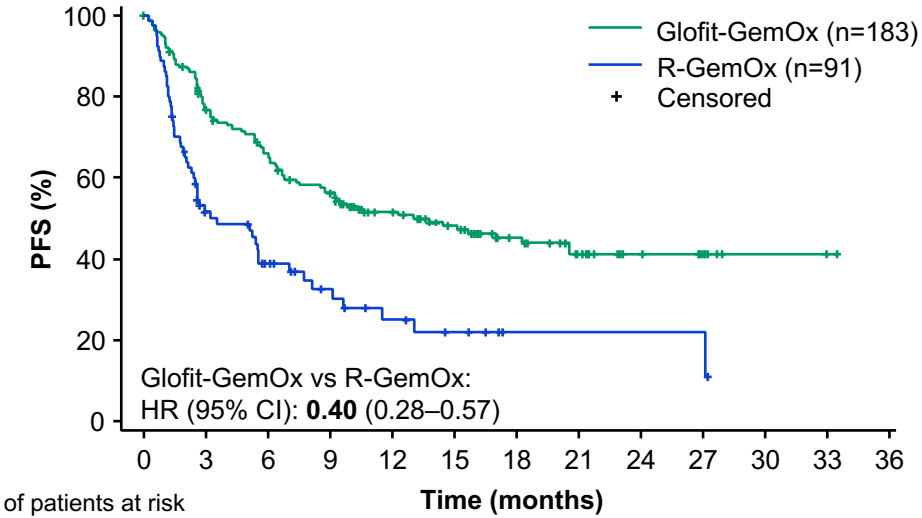
- Statistically significant and clinically meaningful **OS benefit for Glofit-GemOx** versus R-GemOx

24-month OS not reported at the primary analysis as data were not sufficiently mature.
*p-value is alpha controlled at the primary analysis and descriptive at updated analysis.
CI, confidence interval; Glofit-GemOx, glofitamab plus gemcitabine and oxaliplatin; HR, hazard ratio; NE, not evaluable; OS, overall survival; R-GemOx, rituximab plus gemcitabine and oxaliplatin.

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

STARGLO: Progression-free survival by IRC assessment

Updated analysis



	R-GemOx (n=91)	Glofit-GemOx (n=183)
Primary analysis (median follow-up: 9.6 months)		
PFS, median (95% CI); months	3.3 (2.5–5.6)	12.1 (6.8–18.3)
HR (95% CI)	**0.37** (0.25–0.55)	
p-value*	<0.000001	
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*	<0.000001*	
12-month PFS (95% CI)	25.2% (13.6–36.9)	51.7% (44.0–59.4)

- Statistically significant and clinically meaningful **PFS benefit for Glofit-GemOx** versus R-GemOx

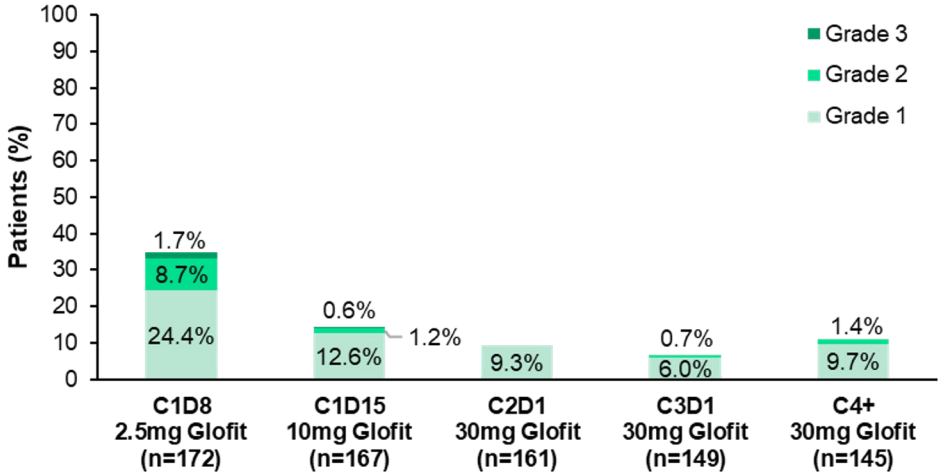
12-month PFS not reported at the primary analysis as data were not sufficiently mature. Three patients proceeded to ASCT after study treatment, all three patients are alive as of today. *p-value is alpha controlled at the primary analysis and descriptive at updated analysis.
ASCT, autologous stem cell transplant; CI, confidence interval; Glofit-GemOx, glofitamab plus gemcitabine and oxaliplatin; HR, hazard ratio; IRC, Independent Review Committee; PFS, progression-free survival; R-GemOx, rituximab plus gemcitabine and oxaliplatin.

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

STARGLO: Cytokine release syndrome

n (%) of patients with ≥1 CRS AE*	Glofit-GemOx (Glofit exposed) n=172
Any grade†	76 (44.2)
Grade 1	54 (31.4)
Grade 2	18 (10.5)
Grade 3	4 (2.3)‡
Median time to CRS onset, hours (range)	
2.5mg glofitamab (C1D8)	13.5 (4.4–134.9)
10mg glofitamab (C1D15)	32.4 (7.4–564.3)
Median CRS duration, hours (range)	
2.5mg glofitamab (C1D8)	22.7 (0.0–168.0)
10mg glofitamab (C1D15)	24.0 (0.0–248.5)
Tocilizumab for CRS management, n / n (%)	28 / 76 (36.8)
Corticosteroids for CRS management, n / n (%)	39 / 76 (51.3)

CRS by cycle and grade in the updated analysis



- CRS mainly occurred in C1 and was predominantly low grade

Dexamethasone premedication was mandated to prevent/mitigate CRS prior to step-up doses and prior to at least two 30mg doses of glofitamab, until no additional CRS was observed.
*Unless otherwise specified. †No Grade 4 or 5 CRS events were reported. ‡One patient had a Grade 3 CRS event confounded by a concurrent Grade 5 Septic Shock that required multiple pressors. AE, adverse event; C, cycle; CRS, cytokine release syndrome; D, day; Glofit-GemOx, glofitamab plus gemcitabine and oxaliplatin; R-GemOx, rituximab plus gemcitabine and oxaliplatin.

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

Conclusions

- Fixed duration glofitamab added to GemOx demonstrated a statistically significant and clinically meaningful OS benefit in patients with R/R DLBCL, who were ineligible for ASCT
  - Median OS of 25.5 months with Glofit-GemOx compared with 12.9 months with R-GemOx (HR 0.62)
  - Glofit-GemOx improved median PFS (13.8 vs 3.6 months) and CR rate (58.5 vs 25.3%) versus R-GemOx
- Glofit-GemOx was tolerable; AEs were consistent with the known risks of the study drugs
  - CRS primarily occurred in C1 and was mostly low grade
- Glofitamab is the first CD20xCD3 bispecific antibody to demonstrate a survival benefit in DLBCL in a randomized Phase III trial; these results support the use of Glofit-GemOx for the treatment of R/R DLBCL

AE, adverse event; ASCT, autologous stem cell transplant; C, cycle; CR, complete response; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; Glofit-GemOx, glofitamab plus gemcitabine and oxaliplatin; HR, hazard ratio; PFS, progression-free survival; OS, overall survival; R/R, relapsed/refractory; R-GemOx, rituximab plus gemcitabine and oxaliplatin.

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

Glofitamab Monotherapy in Patients with Heavily Pretreated Relapsed/Refractory (R/R) Mantle Cell Lymphoma (MCL): Updated Analysis from a Phase I/II Study

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NP30179 Phase I/II study design

Study design[1]

- Multicenter, open-label, dose-escalation and dose-expansion study of glofitamab with Gpt

Glofitamab IV administration

- Fixed-duration treatment: maximum 12 cycles

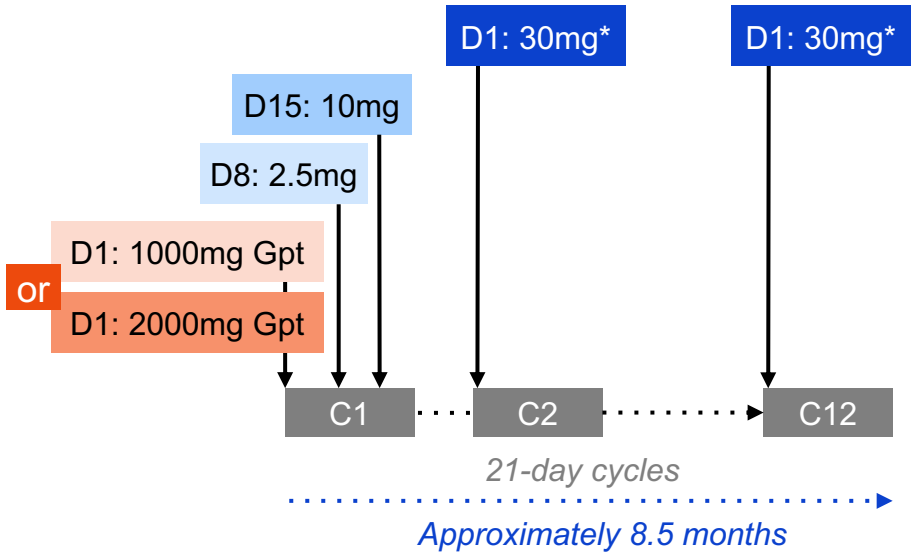
Population characteristics

- Age ≥18 years
- ≥1 prior systemic therapy
- ECOG PS 0 or 1

CRS mitigation

- Obinutuzumab pretreatment (1000mg or 2000mg)
- C1 step-up dosing
- Monitoring after first dose (2.5mg)

Dosing schedule



Clinical cut-off date: September 04, 2023.
*In the 1000mg Gpt cohort, two patients had 16mg glofitamab as their target dose in the dose escalation phase.
C, cycle; CRS, cytokine release syndrome; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; Gpt, obinutuzumab pretreatment; IV, intravenous.

1. NCT03075696. Available at: https:www.clinicaltrials.gov.

Baseline characteristics

n (%) of patients unless stated		Prior BTKi (n=31)*	BTKi naïve (n=29)*	All patients (N=60)*
Median age, years (range)		70.0 (41–84)	72.0 (52–86)	72.0 (41–86)
Male		23 (74.2)	21 (72.4)	44 (73.3)
Ann Arbor stage III/IV		28 (90.3)	24 (82.8)	52 (86.7)
MIPI score ≥6		7 (22.6)	8 (27.5)	15 (25.0)
Median no. of prior lines (range)		3.0 (1–5)	2.0 (1–4)	2.0 (1–5)
Median time since last prior therapy to first study treatment, months (range)		1.3 (0.1–53.2)	7.4 (1.1–132.5)	2.4 (0.1–132.5)
Median time since last anti-CD20 therapy to first study treatment, months (range)		15.1 (0.7–159.0)	25.1 (1.4–132.5)	16.3 (0.7–159.0)
Refractory status	Refractory to any prior therapy	30 (96.8)	20 (69.0)	50 (83.3)
	Refractory to 1L therapy	17 (54.8)	14 (48.3)	31 (51.7)
	Refractory to last prior therapy	27 (87.1)	17 (58.6)	44 (73.3)

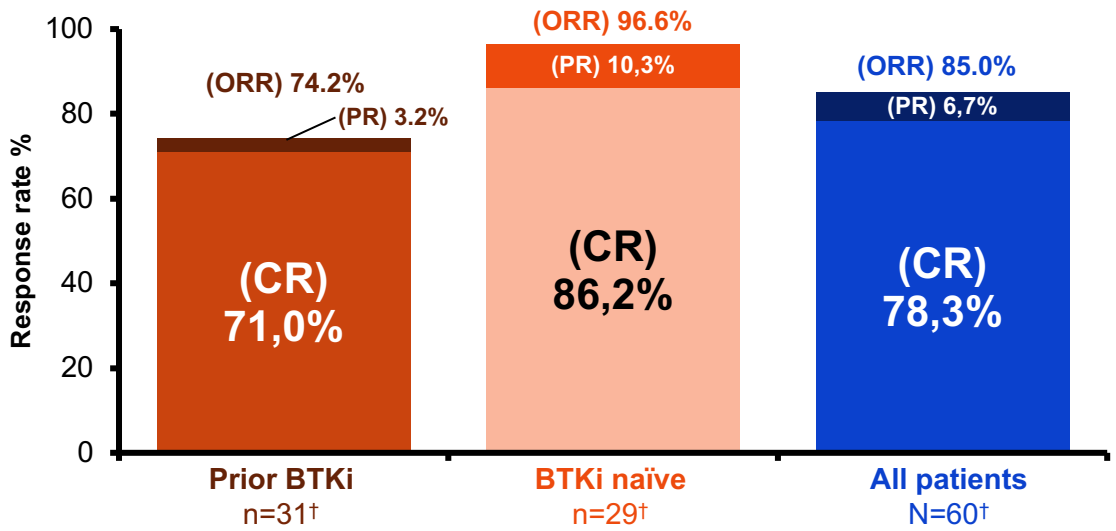
Patients with R/R MCL were heavily pretreated and highly refractory to their last prior therapy

A higher proportion of patients with prior BTKi therapy were refractory to their last prior therapy compared with BTKi-naïve patients

Clinical cut-off date: September 04, 2023.
*Efficacy evaluable population.
MIPI, mantle cell lymphoma international prognostic index.

Response rates

Response rates* in patients with R/R MCL



- Median time to first response among responders (n=51): **42 days** (95% CI: 42.0–45.0)

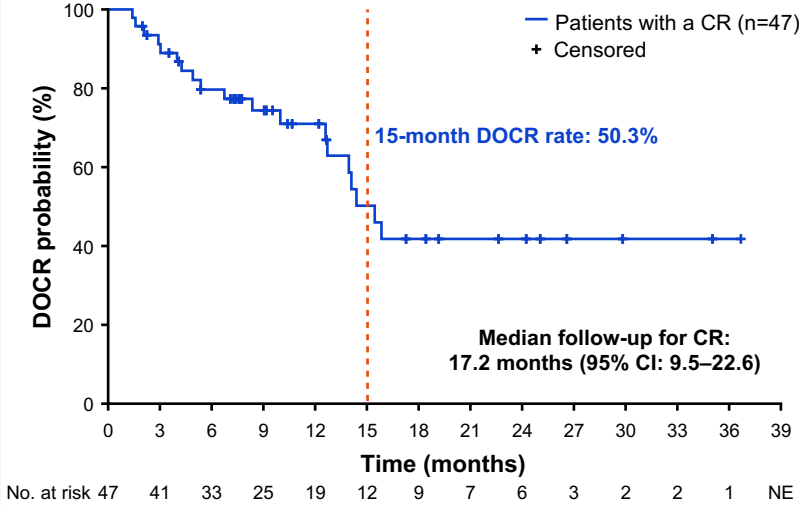
High CR and OR rates were observed in the overall population and in both BTKi-naïve patients and those with prior BKTi therapy

Clinical cut-off date: September 04, 2023.
*Investigator-assessed. †Efficacy evaluable population.
CI, confidence interval; ORR, overall response rate; PR partial response.

Duration of response

DOCR*	Prior BTKi n=22	All patients n=47
Median DOCR, months (95% CI)	12.6 (5.4–NE)	15.4 (12.7–NE)
15-month DOCR rate, % (95% CI)	33.5 (10.6–56.4)	50.3 (32.0–68.6)
Ongoing CR, n (%)	10 (45.5)	28 (59.6)
DOR*	**n=23**	**n=51**
Median DOR, months (95% CI)	12.6 (7.4–NE)	16.2 (12.6–NE)
15-month DOR rate, % (95% CI)	NA	59.7 (44.1–75.3)
Ongoing response, n (%)	10 (43.5)	28 (54.9)

DOCR*

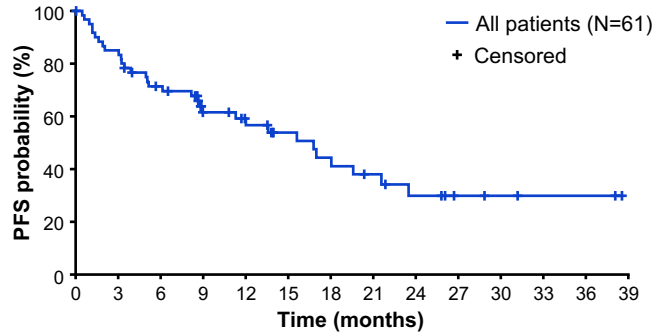


With 17 months' median follow-up, fixed-duration glofitamab monotherapy achieved **durable CRs** with the **majority of CRs (59.6%) still ongoing at data cut-off**

Clinical cut-off date: September 04, 2023.
*Investigator-assessed.
DOR, duration of response; DOCR, duration of complete response; NA, not available; NE, not estimable.

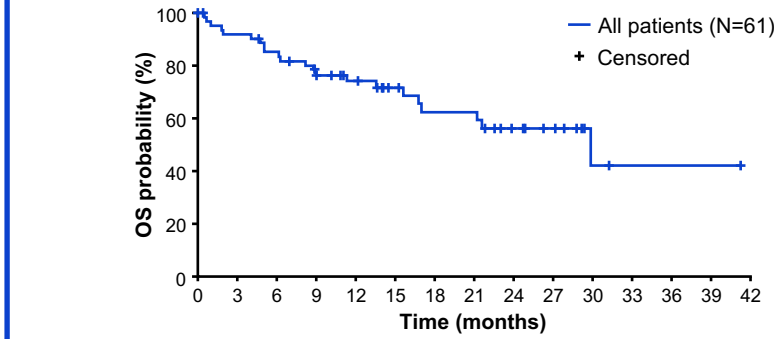
Time-to-event endpoints

PFS



	Prior BTKi n=32*	All patients N=61*
Median PFS follow-up, months (95% CI)	26.1 (13.5–31.2)	19.6 (11.9–26.1)
Median PFS, months (95% CI)	8.6 (3.4–15.6)	16.8 (8.9–21.6)
15-month PFS rate, % (95% CI)	33.0 (14.8–51.1)	54.0 (40.1–67.8)

OS†



	Prior BTKi n=32*	All patients N=61*
Median OS follow-up, months (95% CI)	24.7 (13.6–28.8)	21.8 (14.0–24.9)
Median OS, months (95% CI)	21.2 (9.0–NE)	29.9 (17.0–NE)
15-month OS rate, % (95% CI)	55.0 (36.5–73.6)	71.4 (59.3–83.5)

Clinically significant PFS and OS at 15 months were achieved with fixed-duration glofitamab

Clinical cut-off date: September 04, 2023.

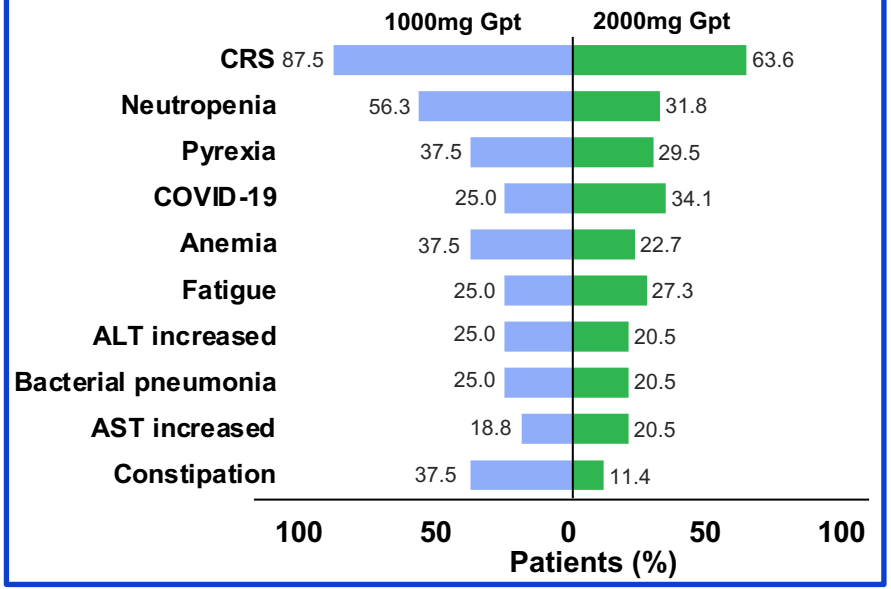
*ITT population. †At the time of analysis, 22 patients had died, the majority due to PD (n=7) or COVID-19 (n=7); other causes of death were pneumonia (n=1), septic shock (n=1), cardiac arrest (n=1), and unknown/other (n=5). All patients who died due to COVID-19 had achieved a CR.

OS, overall survival; PD, progressive disease; PFS, progression-free survival.

Safety summary

AEs, n (%)	1000mg Gpt cohort (n=16)	2000mg Gpt cohort (n=44)	All patients (N=60)
Any grade AE	16 (100)	44 (100)	60 (100)
Glofitamab related	16 (100)	39 (88.6)	55 (91.7)
Serious AE	15 (93.8)	32 (72.7)	47 (78.3)
Glofitamab related	12 (75.0)	24 (54.5)	36 (60.0)
Grade 3/4 AE	13 (81.3)	26 (59.1)	39 (65.0)
Glofitamab related	13 (81.3)	22 (50.0)	35 (58.3)
Grade 5 AE	2 (12.5)	7 (15.9)	9 (15.0)
Glofitamab related	0	0	0

AEs with an incidence of ≥15% in all patients (N=60)



The incidence and severity of AEs were consistent with the known safety profile of glofitamab[1]

Clinical cut-off date: September 04, 2023.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate transaminase.

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

CRS summary

n (%)	1000mg Gpt cohort (n=16)	2000mg Gpt cohort (n=44)	All patients (N=60)
Any grade CRS*	14 (87.5)	28 (63.6)	42 (70.0)
Grade 1	4 (25.0)	18 (40.9)	22 (36.7)
Grade 2	6 (37.5)	7 (15.9)	13 (21.7)
Grade 3	2 (12.5)	3 (6.8)	5 (8.3)
Grade 4	2 (12.5)	0	2 (3.3)
Serious AE of CRS†	11 (68.8)	12 (27.3)	23 (38.3)

n (%)	1000mg Gpt cohort (n=16)	2000mg Gpt cohort (n=44)	All patients (N=60)
CRS management			
Tocilizumab	11 (68.8)	11 (25.0)	22 (36.7)
Corticosteroid	8 (50.0)	10 (22.7)	18 (30.0)
Tocilizumab and corticosteroids	6 (37.5)	7 (15.9)	13 (21.7)
ICU admission	5 (31.3)	4 (9.1)	9 (15.0)

The majority of CRS events were Grade 1/2, and a lower incidence of CRS was observed in the 2000mg versus 1000mg cohort

Clinical cut-off date: September 04, 2023.

*CRS by ASTCT consensus grading criteria.[1] †Serious AE of CRS is defined as per International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

ASTCT, American Society for Transplantation and Cellular Therapy; ICU, intensive care unit.

1. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625–38.

Conclusions

- Fixed duration glofitamab monotherapy induced high response rates and durable responses in heavily pretreated patients with R/R MCL, including in patients with prior BTKi therapy
  - Durable responses were maintained beyond EOT
- The majority of patients with a CR at EOT remained progression-free and were alive 15 months post-EOT
- The observed safety profile was manageable and consistent with the known safety profile of glofitamab
  - CRS events were predominantly Grade 1/2 and most occurred during Cycle 1
  - A lower incidence of CRS was observed following glofitamab treatment in the higher Gpt dose cohort (2000mg vs 1000mg), this regimen is being used in the ongoing Phase III GLOBRYTE study[1]
  - Strategies to minimize COVID-19 related events will be implemented going forward
- Glofitamab monotherapy is a promising treatment option for patients with R/R MCL

1. NCT06084936. Available at: https:www.clinicaltrials.gov.