Glofitamab Monotherapy in Relapsed or Refractory Large B-Cell Lymphoma: Extended Follow-Up from a Pivotal Phase II Study and Subgroup Analyses in Patients with Prior Chimeric Antigen Receptor T-Cell Therapy and by Baseline Total Metabolic Tumor Volume

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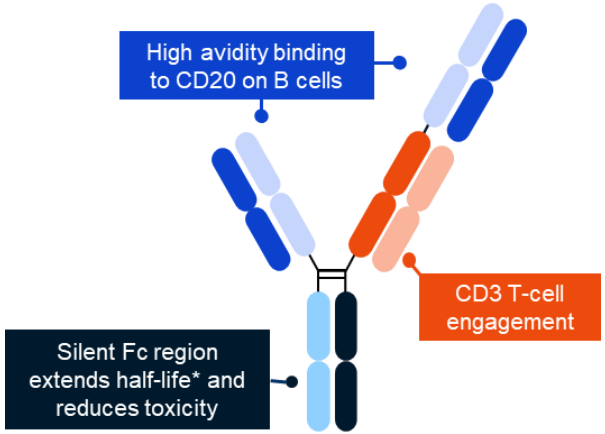
Background

- **Patients with R/R DLBCL after ≥2 prior therapies have a poor prognosis[1,2]**
  - CAR T-cell therapy has shown benefits in the third-line setting, however, ~50% of patients with a CR subsequently relapse[3]
  - Treatment options are limited for patients who experience disease progression on CAR T-cell therapy[4]
- **Glofitamab is an off-the-shelf, fixed-duration treatment[5]**
  - Engages and redirects T cells to eliminate B cells
  - Approved in more than 30 countries for the treatment of patients with R/R LBCL after ≥2 prior therapies
- **Glofitamab induced high CR rates with a manageable toxicity profile in patients with R/R DLBCL in a Phase II study (NCT03075696)[6,7]**

Glofitamab: *CD20xCD3 bispecific antibody with 2:1 format for increased potency vs 1:1 format[5]*



Here we present data with an extended follow-up, along with subgroup analyses in patients with prior CAR T-cell therapy and by baseline TMTV

*Compared with non-Fc bearing T-cell engaging bispecific antibodies.
CAR, chimeric antigen receptor; CR, complete response; DLBCL, diffuse large B-cell lymphoma; LBCL, large B-cell lymphoma; R/R, relapsed/refractory; TMTV, total metabolic tumor volume.

1. Chien HC, et al. Future Oncol 2020;17:411–22; 2. Crump M, et al. Blood 2017;130(16):1800–8; 3. Neelapu SS, et al. Blood 2023;141:2307–15; 4. Byrne M, et al. Biol Blood Marrow Transplant 2019;25:e344–51; 5. Bacac M, et al. Clin Cancer Res 2018;24:4785–97; 6. Dickinson M, et al. N Engl J Med 2022;387:2220–31; 7. Dickinson M, et al. ICML 2023; Oral 095.

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

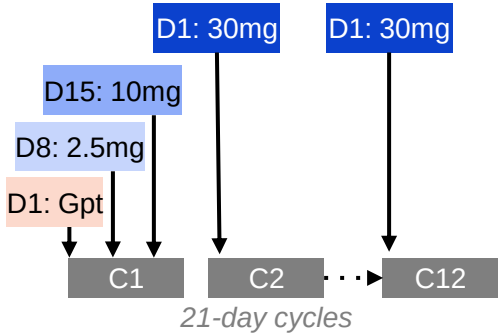
Glofitamab IV administration

Fixed-duration treatment:

- Up to 12 cycles (8.3 months)

CRS mitigation:

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



Endpoints

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

*By PET-CT (Lugano criteria)[1]; †By IRC and investigator. C, cycle; CRS, cytokine release syndrome; D, day; DoR, duration of response; DoCR, duration of complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; Gpt, obinutuzumab pre-treatment; HGBCL, high-grade B-cell lymphoma; 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.

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

Baseline characteristics

n (%)*		All patients (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/II	35 (22.7)
	III/IV	116 (75.3)
NHL subtype	DLBCL	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 no. 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 prior therapy	131 (85.1)
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

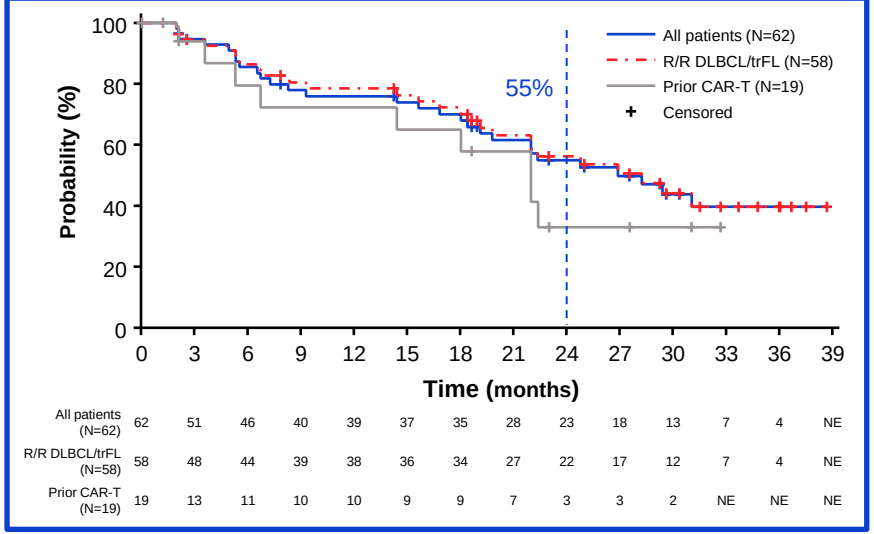
Clinical cut-off date: September 4, 2023. *Unless otherwise specified; †Safety-evaluable population (all treated patients; one patient enrolled in the intent-to-treat population did not receive any study drug and was excluded from the safety-evaluable population); ‡ECOG PS 2, n=1 (0.6%); one patient 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; NHL, non-Hodgkin lymphoma; trFL, transformed follicular lymphoma.

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

Response rates and DoCR

	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)

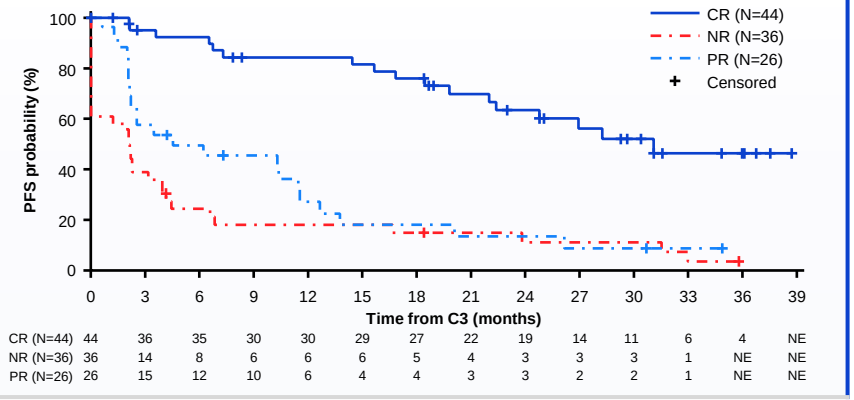
With 32 months median follow-up, glofitamab showed high response rates and durable remissions across subgroups

*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.

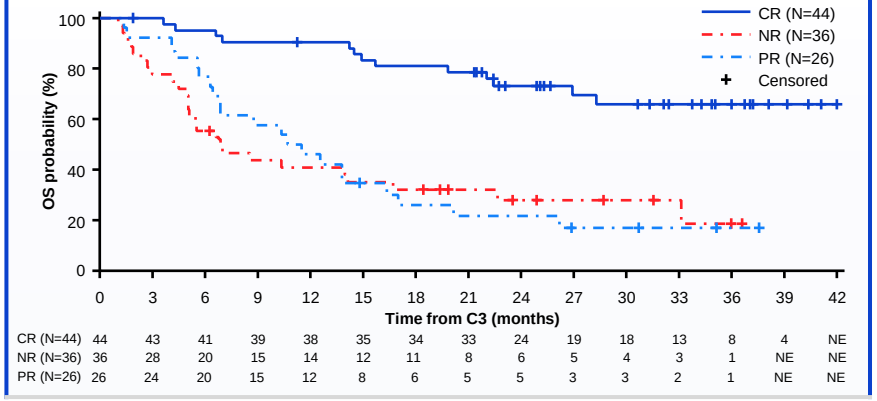
1. COLUMVI USPI. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761309s000lbl.pdf.

Landmark analysis by response at Cycle 3

PFS



OS



Landmark PFS from C3 in patients with CR at C3*	N=44
Median PFS, months (95% CI)	31.1 (22.4–NE)
24-month PFS rate, % (95% CI)	63.5 (47.5–79.6)

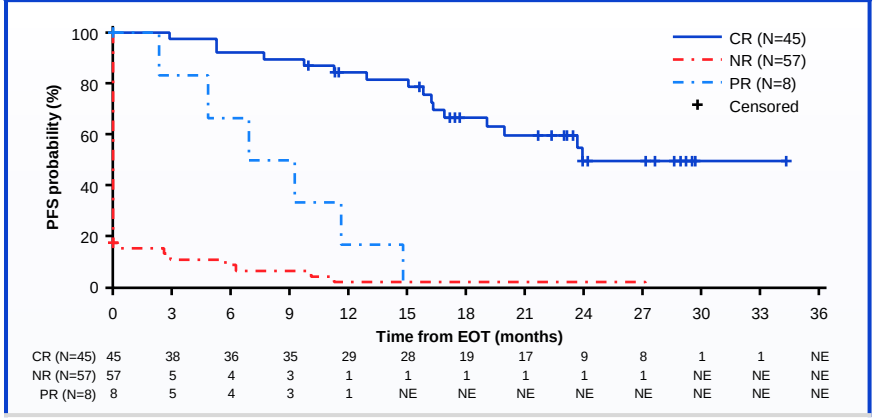
Landmark OS from C3 in patients with CR at C3*	N=44
Median OS, months (95% CI)	NE (NE)
24-month OS rate, % (95% CI)	73.4 (59.9–87.0)

A high proportion of patients with a CR at C3 remained progression-free and alive after 24 months

*KM estimates. NR, no response.

Landmark analysis by response at EOT

PFS



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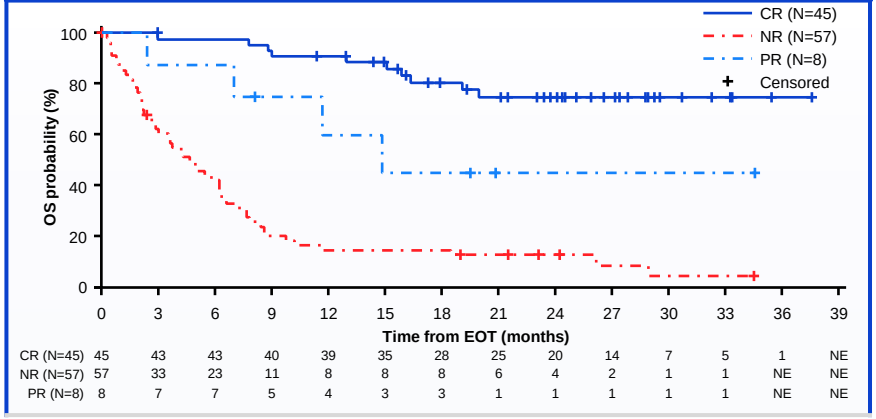


Landmark PFS from EOT in patients with CR at EOT*	N=45
Median PFS, months (95% CI)	24.0 (19.1–NE)
18-month PFS rate, % (95% CI)	66.6 (51.0–82.2)

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

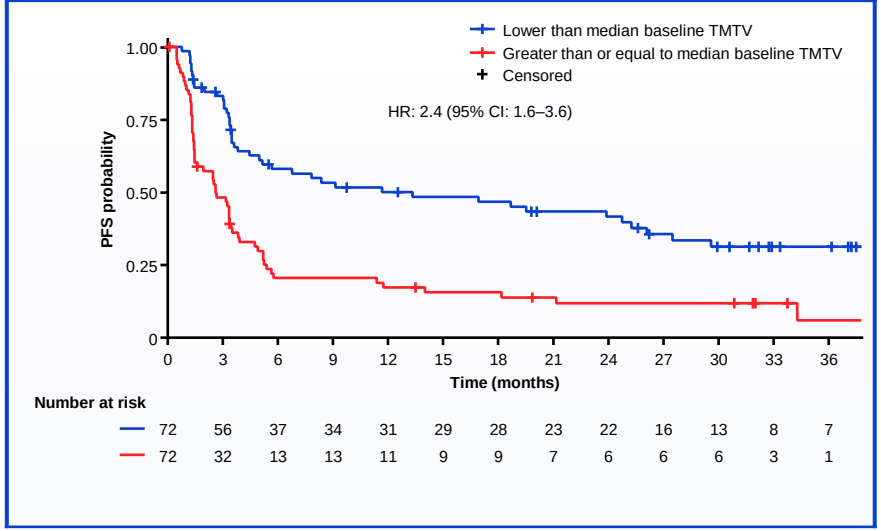
*KM estimates.
EOT, end-of-treatment; NR, no response.

Association between baseline TMTV and PFS

- Baseline TMTV was derived from baseline PET images 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*)

	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



Baseline TMTV may be prognostic for PFS

*Patients who received at least one dose of glofitamab. HR, hazard ratio; SUV, standardized uptake value; TMTV, total metabolic tumor volume.

Safety summary

- **CRS* remained the most common AE**
  - CRS occurred in 64% of patients
  - CRS events were mostly Grade 1 (48%) or Grade 2 (12%); Grade 3 (3%) and Grade 4 (1%) events were uncommon
- **The incidence of AEs and SAEs was stable compared with earlier analyses[1,2]**
  - No new AEs were reported, including ICANS, CRS, infections, or Grade 5 AEs

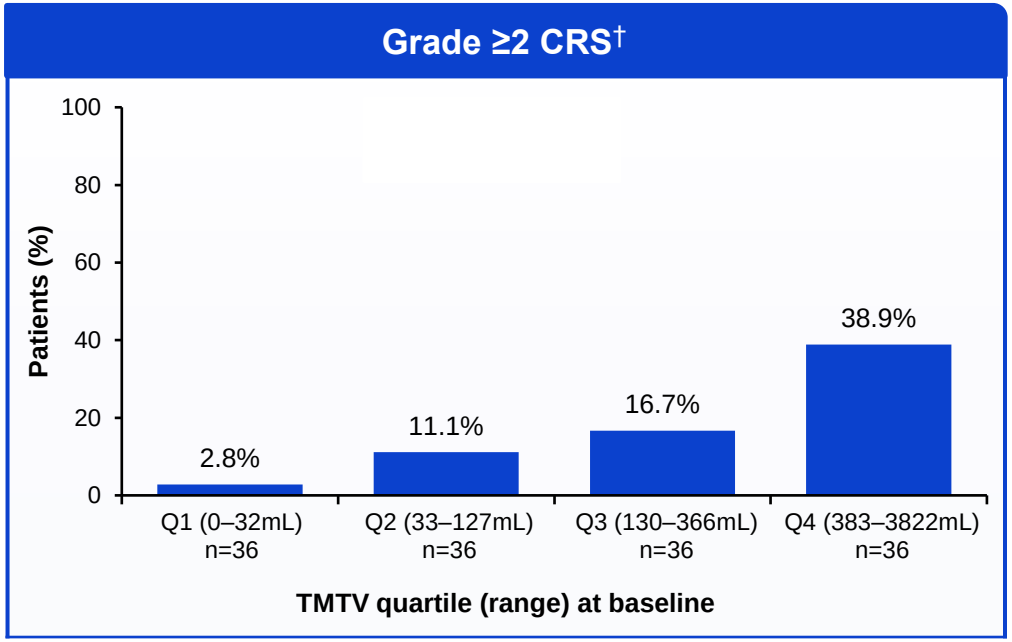
N (%)	N=154
AE Glofitamab-related	152 (99) 140 (91)
Grade ≥3 AE Glofitamab-related	100 (65) 69 (45)
SAE Glofitamab-related	75 (49) 46 (30)
Grade 5 (fatal) AE Glofitamab-related	11 (7) 0
AE leading to treatment discontinuation Glofitamab-related	14 (9) 5 (3)
AE leading to dose modification/interruption of glofitamab Glofitamab-related	29 (19) 16 (10)

The safety profile was consistent with previous analyses, with no new AEs reported[1,2]

*By ASTCT grade. AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy criteria; ICANS, immune effector cell-associated neurotoxicity syndrome; SAE, serious adverse event.

1. Dickinson M, et al. N Engl J Med 2022;387:2220–31;
2. Dickinson M, et al. ICML 2023; Oral 095.

Association between baseline TMTV* and CRS



- Most Grade ≥2 CRS events occurred with the first dose of glofitamab (C1D8, 2.5mg) and resolved before the next dose (C1D15, 10mg)

Higher baseline TMTV was associated with an increased risk of experiencing a Grade ≥2 CRS event

*Baseline TMTV (n=144) was derived from baseline PET images using a semi-automated method with a threshold for TMTV of 2x the SUV_{mean} of the liver; †Chi-square=16.273; degrees of freedom=1; p<0.0001.
Q, quartile.

Conclusions

- The majority of patients with a CR are in remission at 24 months' follow-up
  - CR rates and DoCR in patients with prior CAR T-cell therapy were consistent with the overall population
- Majority of patients with a CR at EOT were alive and event-free 18 months after EOT
- Higher baseline TMTV may be prognostic for lower PFS and was associated with an increased risk of experiencing Grade ≥2 CRS
- No new AEs were observed since the previous analysis, reflecting the advantage of the fixed duration of glofitamab treatment
- **Fixed-duration glofitamab provides long-lasting remissions for patients with R/R LBCL**

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