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Glofitamab Plus Gemcitabine and Oxaliplatin (Glofit-GemOx) in Patients With Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL): 2 Year Follow-Up of the Phase 3 STARGLO Trial

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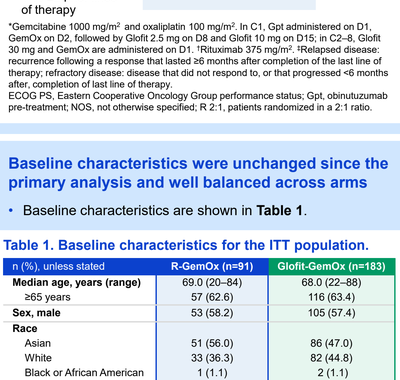
Background

- Glofitamab, a CD20xCD3 bispecific antibody, has shown durable responses as fixed-duration monotherapy in R/R DLBCL after ≥2 prior lines of therapy.[1]
  - High complete response (CR) rates were observed, with the majority of CRs lasting ≥2 years,[2] leading to the approval of glofitamab as a monotherapy for R/R DLBCL after ≥2 prior therapies.
- In the primary analysis of STARGLO (NCT04408638), glofitamab in combination with GemOx showed a statistically significant and clinically meaningful benefit in overall survival (OS), progression-free survival (PFS), and CR rate, over rituximab (R)-GemOx in autologous stem cell transplant (ASCT)-ineligible R/R DLBCL.[3]
- We present the updated efficacy and safety of Glofit-GemOx versus R-GemOx in patients with R/R DLBCL after ≥1 line of therapy from the Phase 3 STARGLO trial, including landmark analyses of patients with a CR at end of treatment (EOT).

Methods

- STARGLO is a randomized, global, Phase 3 trial (**Figure 1**), with a primary endpoint of OS and key secondary endpoints of independent review committee (IRC)-assessed PFS, CR rate, and duration of CR (DOCR).
- Safety endpoints include the incidence, nature, and severity of adverse events (AEs).
- Additional analyses include landmark analyses by response at EOT and circulating tumor DNA (ctDNA) status at Cycle (C) 3 Day (D) 1, and immune recovery.
- ctDNA analyses were performed using the AVENIO non-Hodgkin lymphoma assay, with a modified ctDNA CAPP-Seq workflow (research use only); undetectable ctDNA status was defined using a detection cutoff of p=0.005.[4]
- B-cell counts and immunoglobulin G (IgG) and M (IgM) values were measured locally.
- Clinical cut-off date (CCOD) was June 17, 2024.

Figure 1. Study design of STARGLO (NCT04408638).



*Gemcitabine 1000 mg/m^2 and oxaliplatin 100 mg/m^2. In C1, Gpt administered on D1, GemOx on D2, followed by Glofit 2.5 mg on D8 and Glofit 10 mg on D15; in C2–8, Glofit 30 mg and GemOx are administered on D1. †Rituximab 375 mg/m^2. ‡Relapsed disease: recurrence following a response that lasted ≥6 months after completion of the last line of therapy; refractory disease: disease that did not respond to, or that progressed <6 months after, completion of last line of therapy.
ECOG PS, Eastern Cooperative Oncology Group performance status; Gpt, obinutuzumab pre-treatment; NOS, not otherwise specified; R 2:1, patients randomized in a 2:1 ratio.

Baseline characteristics were unchanged since the primary analysis and well balanced across arms

- Baseline characteristics are shown in **Table 1**.

Table 1. Baseline characteristics for the ITT population.

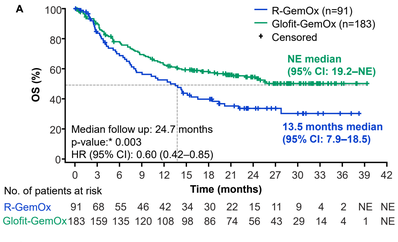
n (%), unless stated	R-GemOx (n=91)	Glofit-GemOx (n=183)
Median age, years (range)	69.0 (20–84)	68.0 (22–88)
≥65 years	57 (62.6)	116 (63.4)
Sex, male	53 (58.2)	105 (57.4)
Race		
Asian	51 (56.0)	86 (47.0)
White	33 (36.3)	82 (44.8)
Black or African American	1 (1.1)	2 (1.1)
Unknown	6 (6.6)	13 (7.1)
ECOG PS	(n=88)	(n=180)
0/1	80 (90.9)	160 (88.9)
2	8 (9.1)	20 (11.1)
Ann Arbor stage	(n=90)	(n=183)
III/IV	70 (77.8)	122 (66.7)
No. of prior lines of therapy		
1	57 (62.6)	115 (62.8)
≥2	34 (37.4)	68 (37.2)
Primary refractory disease*	47 (51.6)	106 (57.9)
R/R status to last therapy		
Relapsed	37 (40.7)	71 (38.8)
Refractory	54 (59.3)	112 (61.2)
Bulky disease	(n=90)	(n=183)
≥10 cm	14 (15.6)	23 (12.6)
Prior CAR T-cell therapy	8 (8.8)	14 (7.7)

*Primary refractory disease: disease that did not respond to, or that progressed <6 months after completion of first-line therapy.
CAR, chimeric antigen receptor; ITT, intention-to-treat.

A sustained OS and PFS benefit was observed with Glofit-GemOx versus R-GemOx after 2 years of follow-up

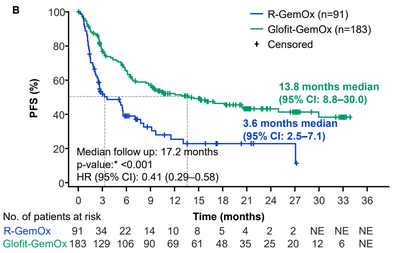
- With a median follow-up of 24.7 months, Glofit-GemOx continued to confer a clinically meaningful OS benefit versus R-GemOx (**Figure 2A**), with 24-month OS rates of 54.4% (95% confidence interval [CI]: 46.8–62.0) versus 33.6% (95% CI: 22.9–44.2), respectively.
  - Overall, 26.9% of Glofit-GemOx-treated patients received ≥1 new anti-lymphoma treatment compared with 57.1% of R-GemOx-treated patients.
- Glofit-GemOx was associated with a PFS benefit versus R-GemOx (**Figure 2B**); 72% of patients with a CR had an ongoing CR at CCOD (**Table 2**).

Figure 2. OS (A) and IRC-assessed PFS (B) with ~2 years of follow-up.



No. of patients at risk

R-GemOx	91	68	55	46	42	34	30	22	15	11	9	4	2	NE	NE
Glofit-GemOx	183	159	135	120	108	98	86	74	56	43	29	14	4	1	NE



No. of patients at risk

R-GemOx	91	34	22	14	10	8	5	4	2	2	NE	NE
Glofit-GemOx	183	129	106	90	69	61	48	35	25	20	12	6	NE

*p-value is descriptive. HR, hazard ratio; NE, not evaluable.

Table 2. Outcomes by IRC assessment.

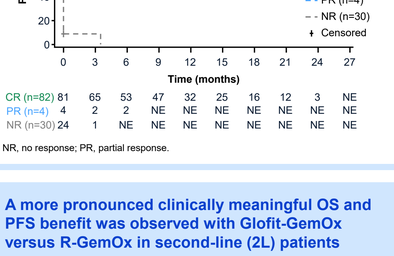
Outcome	R-GemOx (n=91)	Glofit-GemOx (n=183)
Median PFS, months (95% CI)	3.6 (2.5–7.1)	13.8 (8.8–30.0)
18-month PFS, % (95% CI)	23.0 (11.5–34.4)	46.5 (38.5–54.5)
ORR, % (95% CI)	40.7 (30.5–51.5)	68.3 (61.0–75.0)
CR rate, % (95% CI)	25.3 (16.8–35.5)	58.5 (51.0–65.7)
Median DOCR, months (95% CI)	24.2 (6.9–NE)	NE (27.2–NE)
Ongoing CR, % (n/n)	69.6 (16/23)	72.0 (77/107)

ORR, overall response rate.

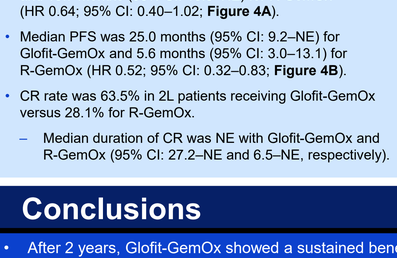
Over 80% of Glofit-GemOx-treated patients with a CR at EOT remained alive and progression-free 12 months after EOT

- In landmark analyses by response at EOT in Glofit-GemOx-treated patients, median OS (**Figure 3A**) and PFS (**Figure 3B**) were NE in patients with a CR at EOT.
  - 12-month OS rate: 89.3% (95% CI: 82.3–96.4).
  - 12-month PFS rate: 82.4% (95% CI: 72.2–92.5).

Figure 3. Landmark analyses of OS (A) and IRC-assessed PFS (B) by response at EOT in Glofit-GemOx-treated patients.



CR (n=82)	82	78	73	64	54	47	31	21	13	3	1	NE
PR (n=4)	4	3	2	2	NE	NE	NE	NE	NE	NE	NE	NE
NR (n=30)	30	15	10	8	5	4	3	2	1	NE	NE	NE



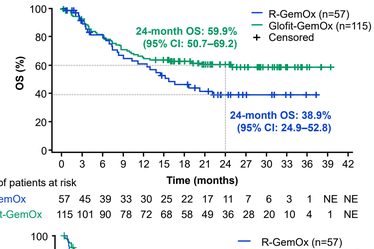
CR (n=82)	81	65	53	47	32	25	16	12	3	NE
PR (n=4)	4	2	2	NE	NE	NE	NE	NE	NE	NE
NR (n=30)	24	1	NE	NE	NE	NE	NE	NE	NE	NE

NR, no response; PR, partial response.

A more pronounced clinically meaningful OS and PFS benefit was observed with Glofit-GemOx versus R-GemOx in second-line (2L) patients

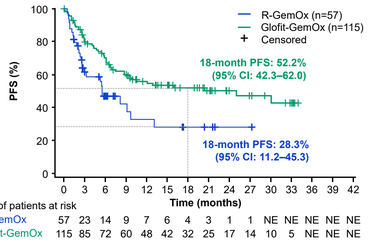
- Median OS was NE (95% CI: 25.0–NE) for Glofit-GemOx and 15.7 months (95% CI: 10.3–NE) for R-GemOx (HR 0.64; 95% CI: 0.40–1.02; **Figure 4A**).
- Median PFS was 25.0 months (95% CI: 9.2–NE) for Glofit-GemOx and 5.6 months (95% CI: 3.0–13.1) for R-GemOx (HR 0.52; 95% CI: 0.32–0.83; **Figure 4B**).
- CR rate was 63.5% in 2L patients receiving Glofit-GemOx versus 28.1% for R-GemOx.
  - Median duration of CR was NE with Glofit-GemOx and R-GemOx (95% CI: 27.2–NE and 6.5–NE, respectively).

Figure 4. OS (A) and IRC-assessed PFS (B) in 2L patients treated with Glofit-GemOx or R-GemOx.



No. of patients at risk

R-GemOx	57	45	39	33	30	25	22	17	11	7	6	3	1	NE	NE
Glofit-GemOx	115	101	90	78	72	68	58	49	36	28	20	10	4	1	NE



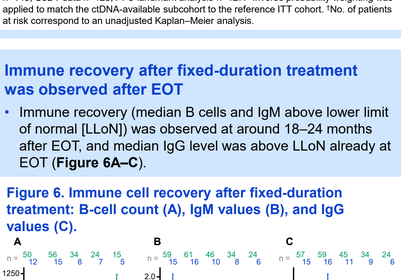
No. of patients at risk

R-GemOx	57	23	14	9	7	6	4	3	1	1	NE	NE	NE	NE	NE
Glofit-GemOx	115	85	72	60	48	42	32	25	17	14	10	5	NE	NE	NE

Deep and early molecular responses were observed with Glofit-GemOx

- In a landmark analysis, ctDNA undetected status at C3D1 was prognostic of superior PFS (**Figure 5A**).
- Glofit-GemOx drove a deep and early molecular response, with a higher proportion of patients with undetected ctDNA at C3D1 compared with R-GemOx (**Figure 5B**).

Figure 5. PFS by ctDNA status (A) and proportion of patients with undetected ctDNA (B) at C3D1.



No. at risk†

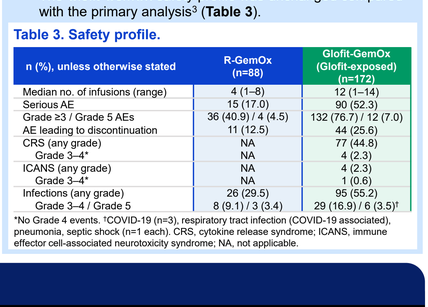
Yes	56	46	33	21	13	8
No	71	24	14	8	2	1

ctDNA analysis population, n=194 (no samples collected in China). Baseline ctDNA data n=149, C3D1 data n=128, PFS landmark analysis n=127. *Inverse probability weighting was applied to match the ctDNA-available subcohort to the reference ITT cohort. †No. of patients at risk correspond to an unadjusted Kaplan–Meier analysis.

Immune recovery after fixed-duration treatment was observed after EOT

- Immune recovery (median B cells and IgM above lower limit of normal [LLoN]) was observed at around 18–24 months after EOT, and median IgG level was above LLoN already at EOT (**Figure 6A–C**).

Figure 6. Immune cell recovery after fixed-duration treatment: B-cell count (A), IgM values (B), and IgG values (C).



Includes patients completing treatment with no events of disease progression ±45 days from the analyzed time point. Patients with available data at each time point are shown. Outliers falling outside the box plot whiskers are excluded. Solid line within each box shows the median. LLoN: B cells, 70 cells/µL; IgM, 0.3 g/L; IgG, 5 g/L. BL, baseline; mo, months.

The safety profile was consistent with the known risks of the individual study drugs

- The Glofit-GemOx safety profile was unchanged compared with the primary analysis[3] (**Table 3**).

Table 3. Safety profile.

n (%), unless otherwise stated	R-GemOx (n=88)	Glofit-GemOx (Glofit-exposed) (n=172)
Median no. of infusions (range)	4 (1–8)	12 (1–14)
Serious AE	15 (17.0)	90 (52.3)
Grade ≥3 / Grade 5 AEs	36 (40.9) / 4 (4.5)	132 (76.7) / 12 (7.0)
AE leading to discontinuation	11 (12.5)	44 (25.6)
CRS (any grade)	NA	77 (44.8)
Grade 3–4*	NA	4 (2.3)
ICANS (any grade)	NA	4 (2.3)
Grade 3–4*	NA	1 (0.6)
Infections (any grade)	26 (29.5)	95 (55.2)
Grade 3–4 / Grade 5	8 (9.1) / 3 (3.4)	29 (16.9) / 6 (3.5)†

*No Grade 4 events. †COVID-19 (n=3), respiratory tract infection (COVID-19 associated), pneumonia, septic shock (n=1 each). CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; NA, not applicable.

Conclusions

- After 2 years, Glofit-GemOx showed a sustained benefit in survival and response outcomes versus R-GemOx, with 82.4% of patients with a CR at EOT in remission 12 months after EOT.
- Deep and early molecular responses were seen with Glofit-GemOx; ctDNA status at C3D1 was prognostic of PFS.
- Immune recovery was observed at 18–24 months after EOT.
- The safety profile remained manageable and consistent with the known risks of each study drug.
- These data support Glofit-GemOx as a fixed duration, off-the-shelf therapy for ASCT-ineligible R/R DLBCL.

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