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LETTER

Glofitamab *vs.* real-world regimens in Chinese patients with third- or later-line relapsed/refractory diffuse large B-cell lymphoma: an external control study

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Diffuse large B-cell lymphoma (DLBCL), the most common subtype of non-Hodgkin's lymphoma (NHL) worldwide, accounts for 39% and 44% of nodal and extranodal NHL cases in China, respectively[1]. Standard first-line treatment for DLBCL is chemo-immunotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, which cures 50%–60% of patients[2]. Therefore, approximately 40% of DLBCL patients are refractory to or relapse after treatment. Glofitamab is a T cell-engaging bispecific monoclonal antibody targeting CD20 expressed on B cells and CD3 on the surface of T cells, inducing tumor cell lysis and T cell activation, proliferation, and cytokine release[3]. Glofitamab has promising efficacy and safety in global and Chinese phase 1/2 studies involving patients with relapsed/refractory DLBCL[4,5] with overall response rates (ORRs) of 52% and 67% and complete response rates (CRRs) of 40% and 52%, respectively[4-6]. Among these studies the most common adverse event (AE) was cytokine release syndrome (63%)[4,6]. Indeed, the incidence of grade ≥ 3 cytokine release syndrome was 4%[4]. Based on these promising results, glofitamab was approved for the treatment of relapsed/refractory DLBCL in China in November 2023. However, clinical studies comparing glofitamab with regimens frequently used in real-world Chinese practice are lacking. Therefore, this study aimed to compare the efficacy and safety of glofitamab versus real-world regimens in Chinese patients with third- or later-line relapsed/refractory DLBCL.

This study compared data from a multicenter glofitamab cohort with an external control [real-world data (RWD) cohort]. The study schema for the glofitamab cohort and observation period is provided in **Figure S1**. The glofitamab cohort was constructed using data from a prospective, open-label, single-arm phase 1 study conducted in five sites in China[6]. The RWD cohort was derived from a non-interventional, retrospective, observational cohort involving secondary data use with information originating from routine clinical practice. The primary efficacy endpoint was CRR. The secondary endpoints were ORR and time-to-next treatment (TTNT). The exploratory endpoints included the incidence and severity of hematologic AEs with severity determined according to National Cancer Institute Common Terminology Criteria for Adverse Events (version 5.0) and routine blood laboratory tests (neutrophil count, white blood cell count, platelet count,

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hemoglobin concentration, and bilirubin, creatinine, lactate dehydrogenase, aspartate aminotransferase, and alanine aminotransferase levels). Additional details regarding the study design, study population, endpoint definitions, and statistical analysis are provided in the **Supplementary methods**.

The patient disposition is shown in **Figure S2**. In total, 30 (100%) and 27 (90.0%) patients were included in the glofitamab safety set and full analysis set (FAS), respectively. The final FAS and safety set for the RWD cohort included 162 (73.6%) patients. Baseline covariates for inverse probability weighting-average treatment effect on the treated weights using the propensity score method are summarized in **Table S1**. The median (min, max) treatment duration was 24.9 (0, 39) weeks in the glofitamab cohort and 4.0 (0, 65) weeks in the RWD cohort. The median [95% confidence interval (CI)] follow-up time was 14.52 (13.50, 19.68) months in the glofitamab cohort and 17.74 (10.78, 28.48) months in the weighted RWD cohort.

CRR

The unweighted CRR was 51.9% (95% CI: 31.95%, 71.33%) in the glofitamab cohort. The unweighted and weighted CRRs were 9.9% (95% CI: 5.75%, 15.54%) and 10.1% (95% CI: 0.00%, 21.38%) in the RWD cohort, respectively (**Table 1**). The CRR for the glofitamab cohort was significantly higher than the RWD cohort in the weighted [rate difference (95% CI): 41.8% (19.80%, 63.76%), odds ratio (95% CI): 9.617 (2.235, 41.383); $P = 0.0024$] and unweighted groups [rate difference: 42.0% (22.58%, 61.37%), odds ratio: 9.827 (3.938, 24.523); $P < 0.0001$].

ORR and TTNT

The unweighted ORR was 66.7% (95% CI: 46.04%, 83.48%) in the glofitamab cohort. The unweighted and weighted ORRs were 30.2% (95% CI: 23.29%, 37.95%) and 31.1% (95% CI: 13.72%, 48.52%) in the RWD cohort, respectively (**Table 1**). The ORR for the glofitamab cohort was significantly higher than the RWD cohort in the weighted [rate difference (95% CI): 35.5% (10.67%, 60.42%), odds ratio (95% CI): 4.426 (1.416, 13.837); $P = 0.0105$] and unweighted groups [rate difference: 36.4% (17.28, 55.56), odds ratio 4.612 (1.937, 10.982); $P = 0.0002$].

The median (95% CI) TTNT was not reached (6.64 months, not estimated) in the glofitamab cohort. The median (95% CI) TTNT was 3.84 (3.02, 5.52) and 3.94 (2.83, 7.52) months in the unweighted and weighted RWD cohorts, respectively. The 12-month TTNT rate (95% CI) was 60.9% (41.92%, 79.88%) in the glofitamab cohort, 29.8% (21.59%, 37.96%) in the unweighted RWD cohort (**Figure 1A**), and 30.6% (19.96%, 41.23%) in the weighted RWD cohort (**Figure 1B**). Hazard ratios (95% CI) in the glofitamab cohort for TTNT versus the RWD cohort were 0.432 (0.231, 0.808; $P = 0.0086$) before weighting and 0.450 (0.208, 0.974; $P = 0.0426$) after weighting.

Table 1 Complete and overall response rates based on ATT weights

	Glofitamab cohort $n = 27$	Unweighted RWD cohort $n = 162$	Weighted RWD cohort $n = 27.2$
Complete response	14 (51.9)	16 (9.9)	2.7 (10.1)
95% CI	31.95, 71.33	5.75, 15.54	0.00, 21.38
Rate difference (95% CI), glofitamab *vs.* RWD cohort	–	42.0 (22.58, 61.37)	41.8 (19.80, 63.76)
Odds ratio (95% CI) *vs.* glofitamab cohort	–	9.827 (3.938, 24.523)	9.617 (2.235, 41.383)
P value *vs.* glofitamab cohort	–	< 0.0001	0.0024
Overall response	18 (66.7)	49 (30.2)	8.5 (31.1)
95% CI	46.04, 83.48	23.29, 37.95	13.72, 48.52
Rate difference (95% CI), glofitamab *vs.* RWD cohort	–	36.4 (17.28, 55.56)	35.5 (10.67, 60.42)
Odds ratio (95% CI), glofitamab *vs.* RWD cohort	–	4.612 (1.937, 10.982)	4.426 (1.416, 13.837)
P value *vs.* glofitamab cohort	–	0.0002	0.0105

Data are shown as *n* (%) unless otherwise stated. ATT, average treatment effect on the treated; CI, confidence interval; RWD, real-world data

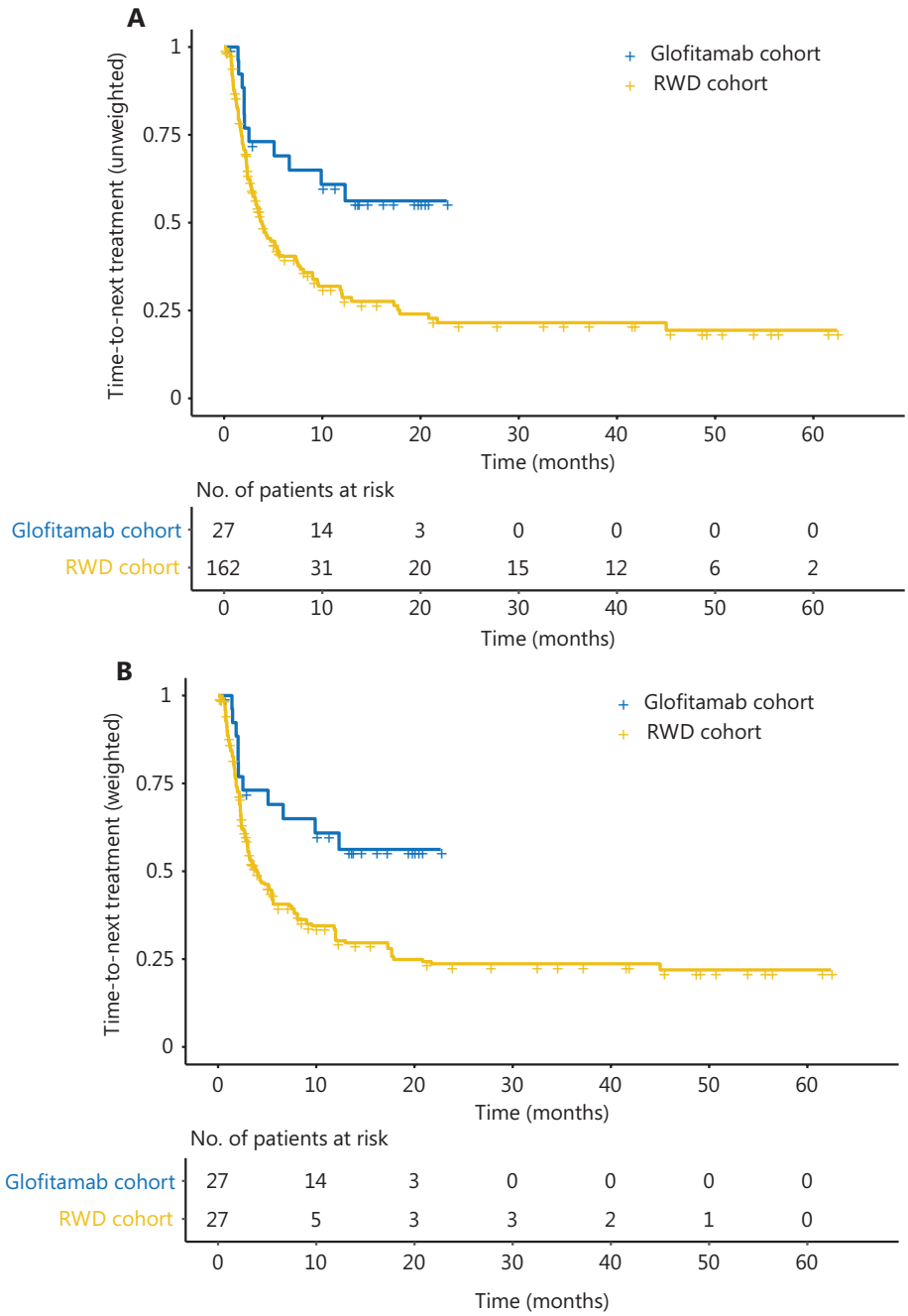


Figure 1 Time-to-next treatment in the glofitamab cohort and the real-world data cohort. Time-to-next treatment for each cohort was analyzed in (A) unweighted and (B) weighted populations. The numbers of patients at risk in the weighted population are rounded to the nearest integer. RWD, real-world data.

Safety

The incidence rate (95% CI) of hematologic AEs was 56.7% (37.4%, 74.5%) in the glofitamab cohort, 60.5% (52.5%, 68.1%) in the unweighted RWD cohort, and 60.9% (43.5%, 78.3%) in the weighted RWD cohort. There were no significant differences in the incidence rate of hematologic AEs in the glofitamab cohort versus the unweighted RWD cohort [odds ratio (95% CI): 0.854 (0.388, 1.878); P = 0.6944] or the weighted RWD cohort [0.839 (0.300, 3.331); P = 2.343].

Table S2 lists the hematologic AEs reported during this study. **Table S3** summarizes the key changes in routine blood tests from baseline-to-worst post-baseline measure by clinical significance in the RWD cohort.

Sensitivity analysis

Sensitivity analysis showed that glofitamab was associated with significantly greater CRRs and ORRs, as well as longer TTNTs compared to the unweighted and weighted RWD cohorts, even after considering patients without prior chimeric antigen receptor T therapy and using an alternate definition of TTNT.

CRRs and ORRs improved with glofitamab compared to frequently used real-world regimens. The higher CRRs in the glofitamab cohort compared to the RWD cohort could indicate that patients with DLBCL have deeper tumor responses. The findings are supported by previous studies in which other bispecific antibodies were used[7,8]. The 12-month TTNT rate was significantly higher in the glofitamab cohort than the RWD cohort, indicating a longer remission time for patients with DLBCL treated with glofitamab compared to patients receiving other therapies in a real-world setting. These findings are consistent with previous clinical trial data that demonstrated prolonged TTNTs with bispecific antibody therapies versus standard treatments or historical controls[8,9]. In addition, the findings of the current study supported the existing literature regarding the safety of glofitamab[10]. The present study had some limitations, including the variability of data sources, retrospective RWD cohort data, lack of control over the study variables and potential unmeasured factors, and reliance on existing data sources that may result in incomplete or inconsistent data. Residual confounding may have existed even though the key prognostic factors were adjusted, which bias efficacy comparisons due to the limited sample size and an inability to adjust for all prognostic factors.

In conclusion, the glofitamab cohort had a favorable efficacy profile compared to RWD cohorts across various endpoints, with better tumor responses, longer response times, and generally better hematologic safety profiles than frequently used therapies in real-world settings among Chinese patients with relapsed/refractory DLBCL. These results supplement existing evidence from previous studies comparing bispecific antibodies with real-world regimens for relapsed/refractory DLBCL, filling gaps in comparative data, and therefore may provide guidance for clinicians making therapeutic choices in real-world clinical practice.

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Conflict of interest statement

Yukun Lan and Xiaohui Zhou declare current employment at Shanghai Roche Pharmaceuticals Ltd.; Jiahui Xu is a previous employee of Shanghai Roche Pharmaceuticals Ltd. All other authors declare no conflicts of interest.

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Data availability statement

For up-to-date details on the Roche' Global Policy on the Sharing of Clinical Information and how to request access to related clinical study documents, see: https://go.roche.com/data_sharing. Anonymized records for individual patients across more than one data source external to Roche cannot

and should not be linked due to a potential increase in the risk of patient re-identification.

References

1. Meng J, Chang C, Pan H, Zhu F, Xiao Y, Liu T, et al. Epidemiologic characteristics of malignant lymphoma in Hubei, China: a single-center 5-year retrospective study. Medicine (Baltimore). 2018; 97: e12120.
2. Liu Y, Barta SK. Diffuse large B-cell lymphoma: 2019 update on diagnosis, risk stratification, and treatment. Am J Hematol. 2019; 94: 604-16.
3. Shirley M. Glofitamab: first approval. Drugs. 2023; 83: 935-41.
4. Dickinson MJ, Carlo-Stella C, Morschhauser F, Bachy E, Corradini P, Iacoboni G, et al. Glofitamab for relapsed or refractory diffuse large B-cell lymphoma. N Engl J Med. 2022; 387: 2220-31.
5. Hutchings M, Carlo-Stella C, Morschhauser F, Falchi L, Bachy E, Cartron G, et al. ABCL-340 Glofitamab monotherapy in relapsed or refractory large B-cell lymphoma: extended follow-up from a pivotal phase 2 study and subgroup analyses in patients with prior chimeric antigen receptor T-cell therapy and by baseline total metabolic tumor volume. Clin Lymphoma Myeloma. 2024; 24: S473.
6. Song YQ, Zhang HL, Huang HQ, Zhang QY, Jing HM, Wang C, et al. Glofitamab monotherapy induces high complete response rates and manageable safety in Chinese patients with heavily pretreated relapsed or refractory diffuse large B-cell lymphoma. Haematologica. 2024; 109: 1269-73.
7. Ip A, Rosenthal A, Mutebi A, Wang T, Jun M, Wang A, et al. P1169: Comparison of real-world clinical outcomes in patients with relapsed/refractory large B-cell lymphoma treated with epcoritamab vs chemoimmunotherapy. Hemasphere. 2023; 7: e324937a.
8. McGough SF, Shamas N, Wang J, Jaber M, Swarup B, Blanchet Zumofen MH, et al. Comparative effectiveness between mosunetuzumab monotherapy clinical trial and real-world data in relapsed/refractory follicular lymphoma in third or subsequent lines of systemic therapy. Leuk Lymphoma. 2023; 64: 2269-78.
9. Sehn LH, Bartlett NL, Matasar MJ, Schuster SJ, Assouline SE, Giri P, et al. Long-term 3-year follow-up of mosunetuzumab in relapsed or refractory follicular lymphoma after ≥ 2 prior therapies. Blood. 2025; 145: 708-19.
10. Saleh K, Khoury R, Khalife N, Chahine C, Ibrahim R, Tikriti Z, et al. The evolving role of bispecific antibodies in diffuse large B-cell lymphoma. J Pers Med. 2024; 14: 666.

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