## CORRESPONDENCE

**Open Access**

# Glofitamab therapy for diffuse large B cell lymphoma: latest updates from the 2022 ASH Annual Meeting

Chaoyu Wang and Yao Liu[*]

## Abstract

Over one-third of B cell lymphomas are not effectively treated by R-CHOP chemotherapy. When lymphoma relapses or is refractory, the prognosis becomes very poor. Due to this fact, there is an urgent and clear requirement for a more effective, novel treatment option. Glofitamab is a CD20xCD3 T-cell-engaging, bispecific antibody capable of recruiting T cells to tumor cells. We have summarized several of the latest reports on glofitamab use in B cell lymphoma therapy from the 2022 ASH Annual Meeting (ASH2022).

### To the editor

The prognosis for patients with relapsed or refractory (R/R) B-cell lymphoma is generally poor. New therapeutic methods are urgently required within clinical settings. Glofitamab is a CD20xCD3 T-cell-engaging bispecific antibody with a 2:1 (CD20:CD3) configuration. It confers high-avidity bivalent binding to CD20 on B cells, and recruits T cells directly to tumor cells [1, 2]. We have summarized several of the latest reports on glofitamab in B cell lymphoma therapy from the 2022 ASH Annual Meeting (ASH2022).

### Glofitamab for newly diagnosed diffuse large B cell lymphoma (DLBCL)

A phase Ib study [3] assessed the role of the glofitamab inclusion in an R-CHOP regimen in patients with newly diagnosed, untreated DLBCL. In total, 56 patients were enrolled. The median age of the patients was 68 years (from 21 to 84 years of age), and 96.4% presented with advanced stage B cell lymphoma (III/IV). Among the 46 patients who were evaluable, the overall response rate (ORR) and complete response (CR) rate were 93.5% and 76.1%, respectively. With respect to the safety of this treatment, grade ≥ 3 adverse events (AEs) related to glofitamab were observed in 13 (23.2%) patients. No reports of grade 3–5 cytokine release syndrome (CRS) events were presented.

### Glofitamab for R/R B cell lymphoma

A phase I clinical trial study [4] reported on two bispecific monoclonal antibodies (RO7227166 and glofitamab) in R/R B-cell lymphoma. RO7227166 is a bispecific monoclonal antibody which targets CD19 and 4-1BB. In the presence of a T-cell receptor signal and strict dependence upon CD19 crosslinking, RO7227166 provides a strong stimulation to T-cells via 4-1BB agonism. 4-1BB upregulation was stimulated on immune cells by glofitamab. A total of 71 patients were enrolled in the trial. 44.3% of patients had advanced stage B-cell lymphoma, while 27.1% had received prior CAR-T therapy. The median number of prior therapeutic approaches was 3 (ranging from 1 to 7). In DLBCL, the ORR and CR were 67% and 39%, respectively. However, the ORR and CR were 91% and 73% in FL patients (Table 1). Grade ≥ 3 AEs were observed to occur in 57.2% patients (Table 2).

*Correspondence:
Yao Liu
liuyao77@cqu.edu.cn
Department of Hematology, Chongqing University Cancer Hospital,
Chongqing Key Laboratory of Translational Research for Cancer
Metastasis and Individualized Treatment, Chongqing 400030, China

**Table 1** Updates on glofitamab therapy for B cell lymphoma patients

| Author | Study type | Regimen | Patients | ORR | CR | Survival |
|---|---|---|---|---|---|---|
| Max S. Topp | Phase Ib | Glofitamab combined with R-CHOP | Newly diagnosed untreated DLBCL, N = 56 93.5% | | 76.1% | – |
| Martin Hutchings | Phase I | RO7227166 combined with glofitamab | R/R B-cell lymphoma, N = 71 DLBCL:67% (46 DLBCL, 24 FL, 1 MZL) FL:91% | | DLBCL:39% FL:73% | – |
| Anna Dodero | Retrospective | Glofitamab | R/R large B-cell lymphomas, N = 18 68% | | 38% | 1-year OS: 44% |
| Martin Hutchings | Retrospective | Glofitamab | R/R large B-cell lymphoma, N = 61 84% (41 DLBCL, 18 tFL, 1 HGBCL, 1 PMBCL) | | 56% | – |
| Burhan Ferhanoglu | Retrospective (compassionate use) | Glofitamab | R/R large B-cell lymphoma, N = 42 28.5% (2 tFL, 40 DLBCL), | | 19% | Median OS: 7 months |

*DLBCL* diffuse large B cell lymphoma, *tFL* transformed follicular lymphomas, *PMBCL* primary mediastinal B-Cell lymphoma, *HGBCL* high-grade B-cell lymphoma, *MZL* marginal zone lymphoma, *R/R* relapsed/refractory, *CR* complete response, *ORR* overall response rate, *PFS* progression free survival, *OS* overall survival

**Table 2** Reported adverse events from glofitamab therapy

| Author | Study | Regimen | Grade ≥ 3 AEs | Grade 1–2 CRS | Grade 3–5 CRS |
|---|---|---|---|---|---|
| Max S. Topp | Phase Ib | Glofitamab combined with R-CHOP | 71.4% | 10.7% | 0 |
| Martin Hutchings | Phase I | RO7227166 combined with glofitamab | 57.2% | 54.3% | 0 |
| Anna Dodero | Retrospective | Glofitamab | – | – | – |
| Martin Hutchings | Retrospective | Glofitamab | – | – | – |
| Burhan Ferhanoglu | Retrospective (compassionate use) | Glofitamab | 23% | 28.6% | 8.6% |

*CRS* cytokine release syndrome, *AEs* adverse events

In another retrospective study, Anna Dodero [5] enrolled 51 patients who did not respond to axi-cel (n = 17) or tisa-cel (n = 34) therapies. Failure after CAR T-cell treatment occurred at a median of 49 days, with 9 patients (18%) experiencing early progression (≤ 30 days). In total, 22 (43%) patients were enrolled in a clinical trial, some of which were given glofitamab (n = 18), while others were adminstered loncastuximab + ibrutinib (n = 4). The ORR and CR were 68% and 38% in patients receiving glofitamab, respectively.

Martin Hutchings [6] presented data related to the CR in end-of-treatment patients with R/R large B-cell lymphoma. A total of 61 patients who received glofitamab were in CR by the end-of-treatment. The median number of prior therapeutic approaches was 3 (range, 2–9), with 61% of patients having received ≥ 3 prior therapies. The ORR and CR were 84% and 56% after 12 months post-end-of-treatment, respectively. This study is one of the first to describe sustained responses lasting after the end of the therapy.

In another real-world study, Burhan Ferhanoglu [7] retrospectively analyzed 42 patients who received glofitamab via compassionate use in Turkey. The median number of prior therapeutic approaches for the patients was 4 (range 3–6). The ORR and CR were 28.5% and 19%, respectively. The median overall survival was 7 months (95% CI 4.02–10.03). Observed reduced response rates may be related to an increased number of patients being refractory to the first lines of therapy.

In R/R lymphoma, a reported phase I, dose-escalation preclinical study suggested a strong rationale for combination of RG6333, which is a CD19-targeted affinity-optimized CD28 bispecific antibody, with glofitamab to deepen and prolong treatment responses [8]. Optimal scheduling, including alternation of costimulatory bispecific antibodies suggests a powerful off-the-shelf T cell redirection approach as a potential alternative to CAR-T cell therapies. Given the encouraging long-term data, it seems probable that glofitamab may be used prior to CAR-T due to the off-the-shelf availability of glofitamab treatment as well as the lack of requirement for specialized centers to administer it.

## Abbreviations

| | |
|---|---|
| ASH | American Society of Hematology |
| DLBCL | Diffuse large B cell lymphoma |
| CRS | Cytokine release syndrome |
| CR | Complete response |
| ORR | Overall response rate |
| PFS | Progression free survival |
| OS | Overall survival |

## Author contributions

YL designed the study. YL and CW drafted the manuscript. CW prepared the tables. All authors participated in the process of drafting and revising the manuscript. All authors read and approved the final manuscript.

## Availability of data and materials

The material supporting the conclusion of this study has been included within the article.

## Declarations

### Ethics approval and consent to participate

Not applicable for this summary.

### Consent for publication

Not applicable for this summary.

### Competing interests

The authors declare that they have no competing interests.

## References

1. Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for relapsed or refractory diffuse large B-cell lymphoma. N Engl J Med. 2022;387(24):2220–31.
2. Hou JZ, Ye JC, Pu JJ, et al. Novel agents and regimens for hematological malignancies: recent updates from 2020 ASH annual meeting. J Hematol Oncol. 2021;14(1):66.
3. Topp MS, Tani M, Dickinson M, et al. Glofitamab plus R-CHOP induces high response rates and a favorable safety profile in patients with previously untreated diffuse large B-cell lymphoma (DLBCL): results from a phase Ib study. Blood. 2022;140(Supplement 1):1775–7.
4. Hutchings M, Carlo-Stella C, Gritti G, et al. CD19 4–1BBL (RO7227166) a novel costimulatory bispecific antibody can be safely combined with the T-cell-engaging bispecific antibody glofitamab in relapsed or refractory B-cell non-Hodgkin lymphoma. Blood. 2022;140(Supplement 1):9461–3.
5. Dodero A, Bramanti S, Pennisi M, et al. Patients outcome after chimeric antigen receptor (CAR) T-cells failure in aggressive B-cell lymphomas: role of immunotherapy and prognostic factors. Blood. 2022;140(Supplement 1):9468–9.
6. Hutchings M, Carlo-Stella C, Morschhauser F, et al. Relapse is uncommon in patients with large B-cell lymphoma who are in complete remission at the end of fixed-course glofitamab treatment. Blood. 2022;140(Supplement 1):1062–4.
7. Ferhanoglu B, Gulbas Z, Uzay A, et al. Glofitamab in relapsed/refractory diffuse large B cell lymphoma: real world data. Blood. 2022;140(Supplement 1):6704–5.
8. Sam J, Hofer T, Kuettel C, et al. RG6333 (CD19-CD28), a CD19-targeted affinity-optimized CD28 bispecific antibody, enhances and prolongs the anti-tumor activity of glofitamab (CD20-TCB) in preclinical models. Blood. 2022;140(Supplement 1):3142–3.

## Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.