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Title: REAL-WORLD ANALYSIS OF GLOFITAMAB FOR RELAPSED/REFRACTORY LARGE B-CELL LYMPHOMA IN GERMANY, AUSTRIA AND SWITZERLAND

Abstract Type: Poster Presentation

Topic: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

Recently, glofitamab, a CD20xCD3 T-cell engaging bispecific antibody, has received approval for the treatment of adult patients with r/r DLBCL not otherwise specified or large B-cell lymphoma arising from follicular lymphoma, following at least 2 lines of systemic therapy. In the pivotal trial, the efficacy was highly encouraging, with an overall response rate (ORR) of 52% and a complete response rate (CR) of 39% (Dickinson, NEJM 2022). However, there is a scarcity of data on the efficacy and safety of glofitamab in the real-world setting.

Aims:

To assess the efficacy/feasibility of glofitamab in the real-world setting, we conducted this retrospective, multicenter study.

Methods:

This is a retrospective, multicenter analysis, enrolling 70 patients with r/r DLBCL treated with glofitamab within the National Compassionate Use Program (CUP) in 20 centers from Germany, Austria, and Switzerland. Patients were considered eligible for if they had experienced treatment failure after ≥ 3 lines of therapy, or were ineligible for next-in-line therapy including autologous/allogeneic stem cell transplantation or CAR-T therapy. The study focused on assessing the efficacy (ORR, CR, PR, mPFS, mOS) and safety profile (non-hematologic toxicity) of glofitamab in the real-world setting.

Results:

We enrolled 70 patients, of which 71% underwent prior CAR-T cell therapy. The majority of patients had an IPI >3, with a median age of 62. Seventy-one percent were refractory to last treatment and patients had a median of 4 prior lines of therapy (4 in non-CAR-T; 4.5 in CAR-T, p = 0.042). Overall, 44% of patients responded to glofitamab, with 26% achieving CR and 18% partial response (PR). The median progression-free survival (PFS) was 3.6 months (mo), while the median overall survival (OS) was 5.7 mo. Surprisingly, estimated mPFS (p = 0.006) and mOS (p = 0.004) were better in the CAR-T than in the non - CART group: 4.5 mo and 8.2 mo vs. 1.2 and 3.0. Moreover, durable responses were observed only for patients, who had a CR at day 90 following glofitamab treatment. Lower PFS was documented for patients with bendamustin administration within 6 months before glofitamab [HR=1.96, p=0.018], no previous CAR-T cell therapy [HR=2.24, p=0.018], refractoriness to last therapy [HR=2.63, p=0.007], bulky disease (>7.5 cm) [HR=2.95, p<0.01] and LDH > 400 U/L [HR=2.11, p=0.01]. Specifically, of the 24 patients receiving bendamustin within 6 mo before glofitamab 59% were refractory to glofitamab vs 48% in the non-bendamustin-population. The frequency of cytokine release syndrome (CRS) was 40%, with grades 3-4 documented only in 2%. Seven patients (10%) presented with ICANS grade 1-2 and one patient (1%) with grade 3. Infections occured in 31% of patients with grades ^{3} 3 in 12% and two patients with grade 5.

Summary/Conclusion:

As expected, the response rates in the real world analysis are slightly lower than in the pivotal trial. However, glofitamab demonstrates efficacy and a manageable safety profile in highly pretreated r/r DLBCL patients in the real-world scenario, reinforcing its potential as a valuable addition to the therapeutic armamentarium for DLBCL patients. The worse outcomes in non-CAR-T patients in our study may be attributed to a selection bias

for highly aggressive, refractory DLBCL patients ineligible for CAR-T. Notably, our data suggests that patients pretreated with bendamustin-containing regimens responded less well to glofitamab, highlighting that the optimal sequence of treatments before glofitamab should not include T-cell depleting agents.

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