Abstract: LB3438

Title: GLOFITAMAB PLUS GEMCITABINE AND OXALIPLATIN (GLOFIT-GEMOX) FOR RELAPSED/REFRACTORY (R/R) DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): RESULTS OF A GLOBAL RANDOMIZED PHASE III TRIAL (STARGLO)

Abstract Type: Oral Presentation

Session Title: Plenary Abstracts Session

Background:

Glofitamab is a CD20:CD3 bispecific antibody that is well tolerated with durable responses when given as fixed-duration monotherapy in R/R DLBCL after ≥2 prior lines of therapy (Dickinson, et al. NEJM 2022).

Aims:

We present efficacy and safety results of Glofit-GemOx versus rituximab (R)-GemOx in patients (pts) with R/R DLBCL after ≥1 prior line of therapy from the global, randomized, Phase III STARGLO trial (NCT04408638).

Methods:

Pts were randomized 2:1 to receive either Glofit-GemOx (8 cycles, plus 4 cycles glofitamab monotherapy) or R-GemOx (8 cycles) and stratified by number of prior therapies (1 vs ≥2) and refractoriness to last treatment. Following obinutuzumab pretreatment, glofitamab was administered during Cycle 1 as weekly step-up doses (2.5/10mg), then the 30mg target dose every 21 days from Cycle 2 Day 1. Pts enrolling after 1 prior therapy were considered ineligible for autologous stem cell transplant (ASCT) based on age ≥70 years, organ dysfunction, ECOG performance status ≥2, patient refusal for ASCT, or other investigator-assessed comorbidities.

Primary endpoint was overall survival (OS). Secondary endpoints included independent review committee (IRC)-assessed progression-free survival (PFS), and complete remission (CR) rate. All pts provided informed consent. All study therapy constituted investigational or off-label use.

Results:

In total, 274 pts with DLBCL were enrolled (Glofit-GemOx, n=183; R-GemOx, n=91), including 172 (62.8%) after 1 prior therapy and 102 (37.2%) after ≥2 prior therapies. Overall, 153 (55.8%) had primary refractory disease and 166 (60.6%) were refractory to last therapy.

At primary analysis (cut-off date Mar 29, 2023), there was a significant OS benefit with Glofit-GemOx versus R-GemOx (hazard ratio [HR] 0.59, 95% confidence interval [CI]: 0.40–0.89; p=0.011). With a median follow-up of 11.3 months, median OS was not reached (95% CI: 13.8–not evaluable) for Glofit-GemOx versus 9 months for R-GemOx (95% CI: 7.3–14.4). Significant benefit of Glofit-GemOx was also observed in IRC-assessed PFS (HR 0.37, 95% CI: 0.25–0.55; p<0.0001) and CR rate (50.3 vs 22.0%; 95% CI: 16.3–40.3, p<0.0001).*

A follow-up analysis was conducted once all pts had completed therapy (cut-off date Feb 16, 2024; median follow-up of 20.7 months). Glofit-GemOx continued to demonstrate superior median OS (25.5 vs 12.9 months; HR 0.62, 95% CI: 0.43–0.88; **Figure**), median PFS (13.8 vs 3.6 months; HR 0.40, 95% CI: 0.28–0.57), and CR rate (58.5 vs 25.3%) versus R-GemOx, respectively.

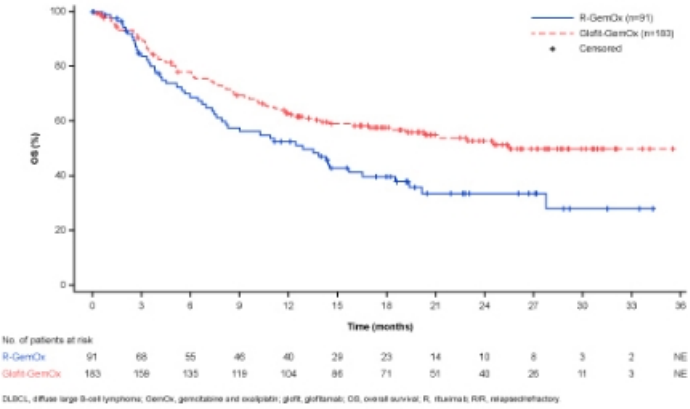
Median number of cycles received was higher with Glofit-GemOx versus R-GemOx (11 vs 4). Adverse event (AE) rates were higher with Glofit-GemOx versus R-GemOx, including Grade (Gr) 3–4 AEs (69.4 vs 36.4%), Gr 5 AEs (8.3 vs 4.5%; primarily driven by an imbalance of COVID-19 AEs), and serious AEs (54.4 vs 17.0%; primarily CRS). Adjusting for exposure differences, AE rates were similar between arms. In pts exposed to glofitamab, CRS was the most frequently reported AE (Gr 1: 31.4%, Gr 2: 10.5%, and Gr 3: 2.3%), and events consistent with immune effector cell-associated neurotoxicity syndrome were reported in four pts (2.3%), all of which were

concurrent with CRS.

Summary/Conclusion:

Glofit-GemOx demonstrated statistically significant and clinically meaningful benefit in OS, PFS, and CR rate over R-GemOx in ASCT-ineligible pts with R/R DLBCL. Glofitamab is the first CD20:CD3 bispecific antibody to demonstrate survival benefit in DLBCL in a randomized Phase III trial. Glofit-GemOx, a fixed-duration, off-the-shelf regimen, was well tolerated with a safety profile consistent with known risks of each individual agent.

Figure. OS with R-GemOx versus Glofit-GemOx in patients with R/R DLBCL from the follow-up analysis (cut-off date Feb 16, 2024)



DLBCL, diffuse large B-cell lymphoma; GemOx, gemcitabine and oxaliplatin; glofit, glofitamab; OS, overall survival; R, rituximab; R/R, relapsed/refractory

Keywords: CD20, Bispecific, Diffuse large B cell lymphoma