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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Glofitamab Plus R-CHOP Induces High Response Rates with a Manageable Safety Profile in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma (DLBCL): A 12-Month Analysis from a Phase Ib Study

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Background: Over a third of patients (pts) with DLBCL do not respond or relapse after first-line (1L) treatment with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP; Sarkozy and Sehn. Ann Lymphoma 2019); these pts have limited curative options. Glofitamab (Glofit) is a T-cell engaging bispecific antibody with a novel 2:1 (CD20:CD3) format that allows bivalent binding to CD20 on B cells; this enables combination with anti-CD20 antibodies, including rituximab. Glofit monotherapy has shown durable responses in pts with relapsed/refractory DLBCL (Dickinson et al. NEJM 2022). In the safety run-in and expansion phases of the ongoing NP40126 trial (NCT03467373), Glofit + R-CHOP demonstrated promising efficacy and manageable safety in pts with 1L DLBCL (Topp et al. ASH 2022). Here, we report durability of response beyond 12 months in Glofit + R-CHOP-treated pts with 1L DLBCL from the NP40126 trial.
Methods: Pts received R-CHOP for 6-8 three-weekly cycles. Intravenous Glofit was given with step-up dosing during Cycle (C)2 (Day [D]8, 2.5mg; D15, 10mg) and at the target dose (30mg) from C3D8 onwards. Glofit maintenance was allowed for up to one year. Efficacy was analyzed in all pts who had been on the study long enough to have a protocol scheduled end-of-treatment response assessment. Safety was analyzed in all pts who received at least one dose of any study drug.
Response was assessed by PET-CT using Lugano criteria (Cheson et al. JCO 2014). Cytokine release syndrome (CRS) events were graded using the American Society for Transplantation and Cellular Therapy criteria (Lee et al. Biol Blood Marrow Transplant 2019) and other adverse events (AEs) by the Common Terminology Criteria for Adverse Events (v4.0). Hospitalization was not mandated for Glofit.
Results: As of April 4, 2023, 56 pts were enrolled in this cohort. Median age was 68 years (range: 21-84), 54 pts (96.4%) had Ann Arbor stage III/IV disease, and median International Prognostic Index (IPI) score was 3 (IPI 1: 3.6% [2/56], IPI 2: 33.9% [19/56], IPI 3: 35.7% [20/56], IPI 4: 23.2% [13/56], IPI 5: 3.6% [2/56]). The cell of origin was germinal center B-cell (GCB) in 25 (44.6%) pts and non-GCB in 11 (19.6%) pts.

After 17.1 (range: 0-26) months of median follow-up, the best overall response rate was 92.9% (52/56) and the complete metabolic response (CMR) rate was 83.9% (47/56). Median time to CMR was 1.8 months (95% confidence interval [CI]: 1.6-4.7). Most CMRs (44/47; 93.6%) were ongoing at data cut-off (**Figure**). Among complete responders, the Kaplan-Meier estimated probability of ongoing responses at 12 months was 91.5% (95% CI: 82.2-100). Median duration of response and duration of complete response were not reached at data cut-off.

The incidence of AEs and serious AEs (SAEs) were similar compared with earlier analyses. Grade (Gr) ≥3 AEs occurred in 42 (75.0%) pts and Gr ≥3 AEs related to Glofit in 14 (25.0%) pts. SAEs were reported in 20 (35.7%) pts and SAEs related to Glofit in six (10.7%) pts. Gr 5 AEs were reported in four (7.1%) pts (COVID-19 pneumonia, n=3; infusion related reaction associated with rituximab, n=1). AEs leading to dose interruption of Glofit occurred in 12 (21.4%) pts. Median dose intensity was 100% for all R-CHOP components. AEs leading to discontinuation of Glofit occurred in one (1.8%) patient.

CRS events were reported in six (10.7%) pts: Gr 1, n=4; Gr 2, n=2; no Gr 3/4 CRS events were reported. All CRS events occurred during C2-3. Tocilizumab was used in two (33.3%) pts with CRS. Neurologic AEs (NAEs) occurred in 23 (41.1%) pts (most common NAEs (>5%) were peripheral neuropathy, n=7 [12.5%]; paraesthesia, n=5 [8.9%]; insomnia, n=4 [7.1%]; headache, n=3 [5.4%]); Gr 3 NAEs included cerebrovascular accident (n=1) and herpes zoster (n=1). No Glofit-related NAEs consistent with immune effector cell-associated neurotoxicity syndrome were reported. Neutropenia was reported in 26 (46.4%) pts (Gr ≥3 neutropenia: Gr 3, n=5; Gr 4, n=19). Infections and infestations were reported in 27 (48.2%) pts (of which the majority were Gr ≤2 [17/27]); Gr 3, n=7; Gr 5, n=3.

Conclusions: Glofit + R-CHOP had a manageable safety profile with a low incidence of CRS, and continued to demonstrate durable responses with an improved CMR rate since the last data cut-off. These findings support the potential for favorable long-term outcomes with Glofit + R-CHOP as 1L treatment of DLBCL. Further analyses, including circulating tumor DNA data, will be presented.

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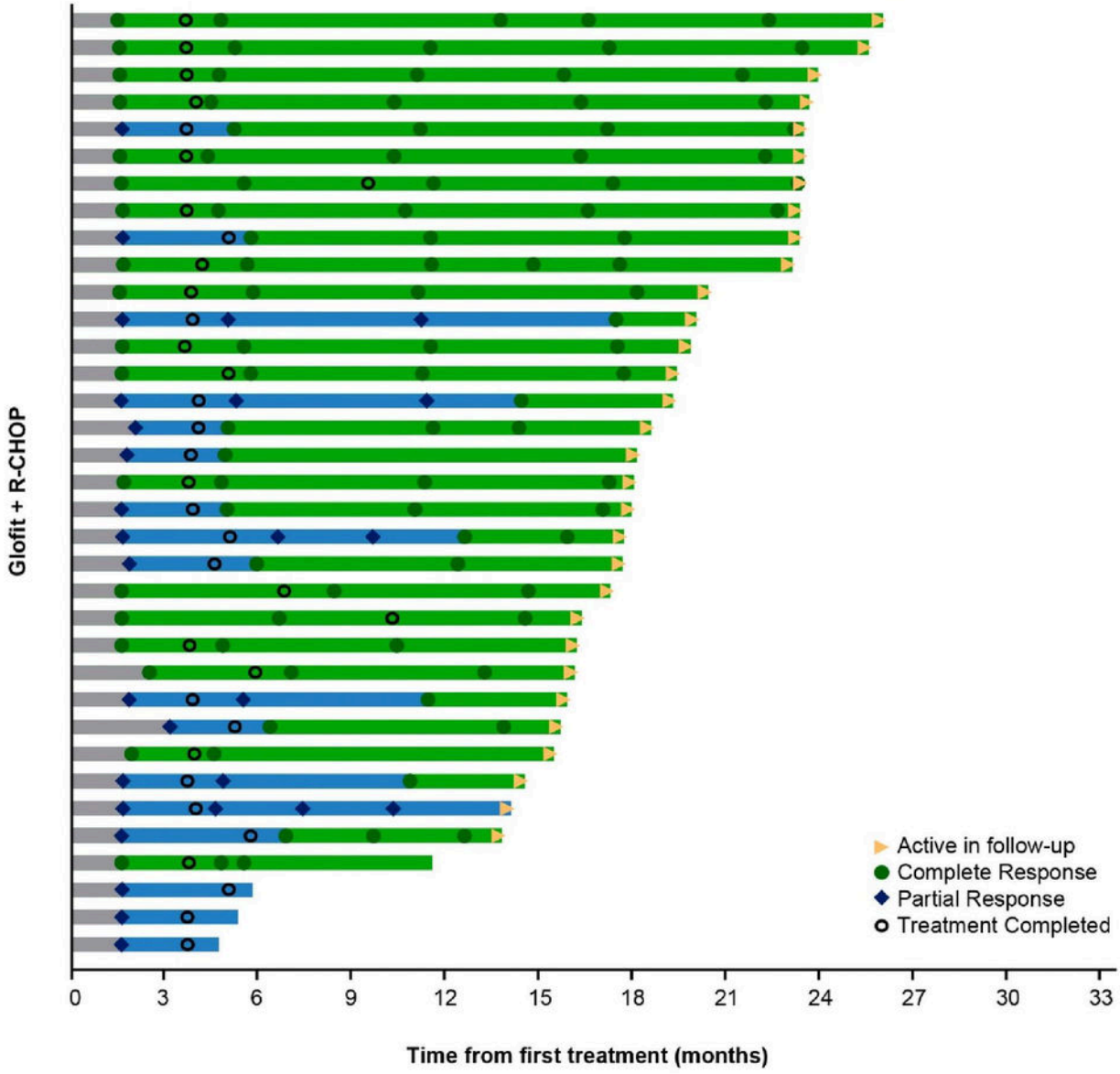
OffLabel Disclosure: Glofitamab (Columvi) is a bispecific CD20-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory DLBCL, NOS or large B-cell lymphoma arising from FL, after two or more lines of systemic therapy. Rituximab (Rituxan) is a CD20-directed cytolytic antibody indicated for the treatment of adult pts with: relapsed or refractory, low grade or follicular, CD20-positive, B-cell NHL as a single agent; previously untreated follicular, CD20-positive, B-cell NHL in combination with first-line chemotherapy (chemo) and, in pts achieving a CR or PR to a rituximab product in combination with chemo, as single-agent maintenance therapy; non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line CVP chemo; previously untreated diffuse large B-cell, CD20-positive, NHL in combination with CHOP or other anthracycline-based chemo regimens; previously untreated and previously treated CD20-positive CLL in combination with fludarabine and cyclophosphamide. Rituxan Hycela is a combination of rituximab, a CD20-directed cytolytic antibody, and hyaluronidase human, an endoglycosidase, indicated for the treatment of adult pts with: relapsed or refractory FL as a single agent; previously untreated FL in combination with first-line chemotherapy (chemo); a CR or PR to rituximab in combination with chemo, as single agent maintenance therapy; non-progressing (including stable disease) FL, as a single agent after first-line CVP chemo; previously untreated DLBCL in combination with CHOP or other anthracycline-based chemo regimens; previously untreated and previously treated CLL in combination with fludarabine and cyclophosphamide.

Figure. Durability of response in patients with previously untreated DLBCL who received Glofit + R-CHOP



Clinical cut-off date: April 4, 2023; DLBCL, diffuse large B-cell lymphoma; Glofit, glofitamab; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Figure 1

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