Abstract: P1115

Title: ODRONEXTAMAB IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: RESULTS FROM A PRESPECIFIED ANALYSIS OF THE PIVOTAL PHASE 2 STUDY ELM-2

Abstract Type: Poster Presentation

Session Title: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

Odronextamab is a CD20×CD3 bispecific antibody (Ab). In the Phase 1 ELM-1 study (NCT02290951), odronextamab demonstrated encouraging activity and a generally manageable safety profile in patients (pts) with heavily pretreated diffuse large B-cell lymphoma (DLBCL) (Bannerji, et al. Lancet Haematol, 2022).

Aims:

To conduct a prespecified analysis of the efficacy and safety of odronextamab monotherapy in the DLBCL cohort from the Phase 2 ELM-2 study (NCT03888105).

Methods:

ELM-2 is a global, multicenter study that enrolled adult pts with DLBCL who were relapsed/refractory (R/R) after ≥2 prior lines of therapy (LOT) including an anti-CD20 Ab and an alkylator; previous CAR T therapy was not permitted. Informed consent was obtained for all pts. Intravenous odronextamab was administered in 21-day cycles with steroid prophylaxis and step-up dosing during Cycle (C) 1. The initial step-up regimen was 1 mg split over C1 Day (D) 1 and C1D2, and 20 mg split over C1D8 and C1D9, followed by the 160 mg full dose on C1D15 (1/20 regimen). This regimen was revised during the study to further mitigate risk of cytokine release syndrome (CRS), with the modified regimen consisting of 0.7 mg split over C1D1 (0.2 mg) and C1D2 (0.5 mg), 4 mg split over C1D8 (2 mg) and C1D9 (2 mg), and 20 mg split over C1D15 (10 mg) and C1D16 (10 mg), then the full 160 mg dose on C2D1 (0.7/4/20 regimen). 160 mg QW continued until the end of C4, followed by 320 mg odronextamab Q2W until disease progression or unacceptable toxicity. Primary endpoint was ORR assessed by independent central review (ICR).

Results:

As of Sept 15, 2022, 140 pts had been treated: median age 66 years (range 24–88); male, 59%; Ann Arbor stage III–IV, 80%; IPI score ≥3, 56%; median prior LOT, 2 (range 2–8); primary refractory, 57%; double refractory to anti-CD20 Ab and an alkylator in any LOT, 66%. Median duration of study follow-up was 21.3 months. ORR and CR rate by ICR were 49% (64/130) and 31% (40/130), respectively, and were consistent across high-risk subgroups. CRs were durable; median duration was 17.9 months (95% CI 10.2 months–not estimable) and the probability of an ongoing CR at 18 months was 48%.

TEAEs occurred in 139 (99%) pts, considered treatment-related in 123 (88%). Treatment-related Grade (Gr) 5 AEs occurred in 5 (4%) pts, and treatment-related AEs led to discontinuation in 11 (8%) pts. The most common TEAEs (>30% all grades) were CRS (55%), anemia (42%), and pyrexia (39%). With the 0.7/4/20 regimen (n=73), 1 (1%) pt had Gr 3 CRS and there were no cases of Gr 4 or 5 CRS; no pts required mechanical ventilation or ICU admission for CRS management. ICANS was reported in only 1 pt (Gr 1/2) with the 0.7/4/20 regimen.

Summary/Conclusion:

In the ELM-2 trial, odronextamab showed clinically meaningful efficacy, durable CRs, and a manageable safety profile. These data confirm odronextamab efficacy in hard-to-treat, highly aggressive R/R DLBCL. The 0.7/4/20 odronextamab step-up regimen mitigates the risk of high-grade CRS, which is consistently observed with other bispecifics and CAR T therapies, and may present an important future option for the management of R/R DLBCL.

Keywords: Diffuse large B cell lymphoma, Bispecific, Non-Hodgkin's lymphoma, Relapsed lymphoma