TPS7099

Poster Session

Phase 3 trial evaluating the efficacy and safety of odronextamab plus chemotherapy versus rituximab plus chemotherapy in previously untreated follicular lymphoma (OLYMPIA-2).

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Background: Odronextamab, an off-the-shelf, CD20×CD3 bispecific antibody, has shown compelling efficacy and generally manageable safety as monotherapy in patients with heavily pretreated relapsed/refractory (R/R) follicular lymphoma (FL), including those with rituximab-refractory disease (Villasboas et al. ASH 2023). In the Phase 2 ELM-2 study, odronextamab demonstrated objective and complete response (CR) rates of 80% and 73%, respectively, and median duration of response of 22.6 months; median overall survival was not reached. Treatment-related adverse events led to treatment discontinuation in 7.8% of patients. These encouraging results support an investigation into whether odronextamab plus chemotherapy is superior to the current FL first-line standard of care of rituximab plus chemotherapy. This study will also evaluate whether odronextamab maintenance is required to achieve progression-free survival (PFS), given the risks associated with sustained B-cell depletion. **Methods:** OLYMPIA-2 (NCT06097364) is a Phase 3, randomized, open-label, multicenter study of odronextamab plus chemotherapy (Odro-CHOP/Odro-CVP) versus R-CHOP/R-CVP in patients with previously untreated FL. The study consists of Part 1A (dose escalation), Part 1B (dose optimization), and Part 2 (randomization). In Part 1, patients will receive six 21-day cycles (induction) of Odro-CHOP, in which intravenous odronextamab will be administered in a step-up regimen starting on Cycle (C) 1 Day (D) 8 to mitigate the risk of cytokine release syndrome, followed by full dose starting from C2D8. Patients with CR or partial response at the end of induction will receive 12 doses of odronextamab maintenance given Q8W. In Part 2, patients will be randomized 1:1:1 to receive induction of 6 cycles of Odro-CHOP/Odro-CVP with no maintenance (Arm A), Odro-CHOP/Odro-CVP followed by odronextamab maintenance (Arm B), or R-CHOP/R-CVP followed by rituximab maintenance (Arm C). Key inclusion criteria: aged ≥18 years; CD20+ FL Grade 1–3a, stage II bulky or stage III/IV; measurable disease; and ECOG performance status 0–2. Part 1: patients with FL that is R/R (Part 1A only) or previously untreated with Follicular Lymphoma International Prognostic Index-1 (FLIPI-1) score 3–5. Part 2: previously untreated patients with FLIPI-1 score 0–5. Patients with central nervous system lymphoma or histological Grade 3b are excluded. The Part 2 primary endpoint is CR rate at 30 months (CR30) by independent central review. Key secondary endpoints include PFS, event-free survival, investigator-assessed CR30, and patient-reported outcomes. Biomarkers (including minimal residual disease by ctDNA) will be evaluated as exploratory endpoints. This trial is currently recruiting and is expected to enroll up to 64 patients in Part 1 and ~669 patients in Part 2 at ~200 global sites. Clinical trial information: NCT06097364. Research Sponsor: Regeneron Pharmaceuticals, Inc.