Abstract: PB3076

Title: GOLSEEK-1: A PHASE 3, DOUBLE-BLIND, RANDOMIZED STUDY COMPARING THE EFFICACY AND SAFETY OF GOLCADOMIDE PLUS R-CHOP VS R-CHOP IN PATIENTS WITH PREVIOUSLY UNTREATED, HIGH-RISK, LARGE B-CELL LYMPHOMA

Abstract Type: Publication Only

Topic: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

Diffuse large B-cell lymphoma (DLBCL) and other LBCLs account for 35–40% of non-Hodgkin lymphoma cases in North America and Europe. Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), typically administered for 6 cycles, is the standard therapy for DLBCL, and is curative in ~60–70% of patients (pts). However, 30–40% of pts have refractory/relapsed (R/R) DLBCL following R-CHOP, with poor clinical outcomes. First-line therapy represents the greatest opportunity for curing LBCL via the use of improved treatment options. Golcadomide is a potential first-in-class oral CELMoDTM agent purposefully designed for the treatment of lymphoma. Golcadomide co-opts cereblon to induce targeted degradation of the transcription factors Ikaros/Aiolos, inducing deep, rapid, and extensive tumor killing independent of cell of origin as well as enhanced immunostimulatory activity. In the phase 1b study CC-220-DLBCL-001, golcadomide combined with R-CHOP was well tolerated, and showed promising activity and combinability in pts with previously untreated aggressive BCL, including those with high-risk disease (Hoffmann et al. ASH 2023, #4459). Additionally, golcadomide has shown promising efficacy and safety profiles as monotherapy (Michot et al. ICML 2023, #90) and combined with rituximab (Chavez et al. ASH 2023, #4496) in pts with R/R DLBCL. The efficacy and safety data observed in early-phase studies suggest promising activity and a manageable safety profile, supporting further investigation of the golcadomide + R-CHOP combination in the phase 3 setting.

Aims:

To evaluate the efficacy and safety of golcadomide + R-CHOP vs placebo + R-CHOP in pts with previously untreated high-risk LBCL.

Methods:

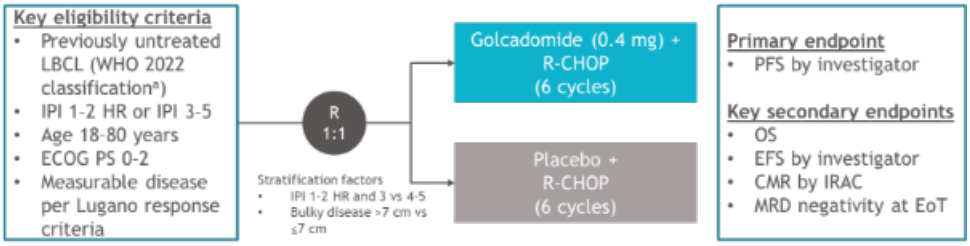
Approximately 850 pts with previously untreated LBCL will be randomized 1:1 to either golcadomide + R-CHOP or placebo + R-CHOP. Pts must have histologically confirmed diagnosis of LBCL according to WHO 2022 classification (Figure). Other key inclusion criteria include International Prognostic Index (IPI) score 1 or 2 considered high-risk (LDH ≥1.3 × upper limit of normal and/or bulky disease, defined as a single lesion of ≥7 cm, Maurer et al. ASH 2023, #4512), or IPI score ≥3; measurable disease as defined by the Lugano classification; and Ann Arbor stage II–IV disease. Key exclusion criteria include other lymphoma subtypes such as primary mediastinal LBCL, primary cutaneous DLBCL-leg type, grade 3b follicular lymphoma (FL), transformed FL, ALK-positive LBCL, primary effusion lymphoma, and Burkitt lymphoma, as well as documented or suspected central nervous system involvement. Randomization will be stratified by IPI score (1-2 with risk factors and 3 vs. 4-5) and bulky disease (>7 cm vs. ≤7 cm). After a screening period of ≤4 wks, pts will receive golcadomide (0.4 mg) or placebo orally once daily for 7 consecutive days in each of 6 cycles in combination with R-CHOP in 21-day cycles.

Results:

The primary endpoint is progression-free survival, assessed by investigator based on the Lugano Response Criteria. Key secondary endpoints include overall survival, event-free survival, independently assessed complete metabolic response rate, and minimal residual disease negativity (defined as having undetectable circulating tumor DNA levels at end of treatment).

Summary/Conclusion:

The addition of golcadomide to the current induction therapy is a rational approach with the potential to improve outcomes for pts with high-risk LBCL. Importantly, this trial includes high-risk pts categorized as low or intermediate IPI score, but with bulky disease and/or very high LDH.



[a]DLBCL, NOS (including GCB and ABC types); high-grade BCL, with MYC and BCL2 rearrangements; high-grade BCL, NOS; T-cell/histiocyte/rich LBCL; or EBV+ DLBCL. ABC, activated B-cell; BCL, B-cell lymphoma; CMR, complete metabolic response; DLBCL, diffuse large B-cell lymphoma; EBV+, Epstein-Barr virus positive; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; EoT, end of treatment; GCB, germinal center B-cell; HR, high-risk; IPI, International Prognostic Index; IRAC; Independent Response Adjudication Committee, LBCL, large B-cell lymphoma; MRD, minimal residual disease; NOS, not otherwise specified; OS, overall survival; PFS, progression-free survival; R, randomized; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; WHO, World Health Organization.

Keywords: CHOP, High risk, Rituximab, Diffuse large B cell lymphoma