(PB3864) A MULTICENTER, OPEN-LABEL, PHASE 3, RANDOMIZED TRIAL OF DUVELISIB VS INVESTIGATOR'S CHOICE (GEMCITABINE OR BENDAMUSTINE) IN RELAPSED/REFRACTORY NODAL T-CELL LYMPHOMA WITH T-FOLLICULAR HELPER PHENOTYPE

Topic: 20. Other aggressive lymphomas

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Background

Peripheral T cell lymphomas (PTCL) are a rare, heterogeneous group of aggressive lymphomas. The current World Health Organization classification of lymphoid neoplasms groups PTCL subtypes angioimmunoblastic T-cell lymphoma (AITL), PTCL-NOS with T-follicular helper (TFH) phenotype, and follicular T-cell lymphoma under the category of nodal TFH lymphoma (nTFHL). nTFHL entities have similarities in clinical, immunophenotypic, and genetic characteristics.
Most patients diagnosed with PTCL will develop relapsed/refractory (R/R) disease. Currently, the only agent approved in the EU/UK for treatment of R/R PTCL is brentuximab vedotin for anaplastic large-cell lymphoma. Novel agents such as romidepsin, belinostat, and pralatrexate have received accelerated approvals outside the EU/UK, but to date, none have received full approval. As such, there are no novel agents approved and available for these patients in EU/UK.
Duvelisib (DUV) is an oral inhibitor of phosphatidylinositol 3-kinase-δ/γ. US indications: adults with R/R chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after ≥2 prior lines of systemic therapy. EU/UK indications: adults with R/R CLL after ≥2 prior therapies and for follicular lymphoma refractory to ≥2 prior systemic therapies. The use of DUV in PTCL is investigational.
The phase 2 PRIMO study evaluated DUV in R/R PTCL (NCT03372057). Outcomes included objective response rate (ORR) 48.0%, median progression-free survival (mPFS) 3.4 mo, and median overall survival (mOS) 12.4 mo. In patients with AITL (a subtype of nTFHL), outcomes were ORR 62.2%, mPFS 8.3 mo, and mOS 18.1 mo.
Outcomes in the AITL subgroup of the PRIMO study provided rationale to initiate the TERZO™ study (NCT06522737; EU CT: 2024-516605-23-00), which is evaluating DUV versus investigator's choice of gemcitabine (GEM) or bendamustine (BEN), two standard of care regimens commonly used in patients with R/R nTFHL.

Methods

TERZO is a multicenter, open-label, phase 3, randomized study expected to enroll 124 patients with R/R nTFHL who have progressed on ≥1 line of systemic anticancer therapy. Study duration will be 48 months; patients are randomized 1:1 and stratified by number of prior therapies and AITL score.
Arm 1: DUV 75 mg orally twice daily (BID) for cycles 1 and 2, followed by DUV 25 mg BID for cycles ≥3, in 28-day cycles. Arm 2: either GEM 1200 mg/m^2 IV on Day 1, 8, and 15 of each 28-day cycle (≤6 cycles) or BEN 90-120 mg/m^2 IV on Day 1 and 2 of each 21-day cycle (≤6 cycles).
Primary endpoint is Independent Review Committee-assessed PFS, a key secondary endpoint is OS, and additional secondary endpoints include investigator (INV)-assessed PFS, ORR, complete response rate, duration of response, safety, quality-of-life, percent of patients proceeding to stem cell transplant (SCT), INV-assessed PFS in patients proceeding to SCT, and PK parameters derived from blood concentrations of DUV and its metabolites. Eligibility criteria include adults with R/R nTFHL, ≥1 prior line of systemic therapy, measurable disease, ECOG performance status ≤2, and no prior history of allogeneic SCT or PI3K inhibitor use.

Summary/Conclusion

DUV monotherapy has demonstrated activity in R/R PTCL, with more pronounced effects in AITL. TERZO will test the hypothesis that DUV monotherapy is associated with improved outcomes versus GEM or BEN in patients with R/R nTFHL. TERZO is the only phase 3 study dedicated to nTFHL in the EU/UK, designed to address this serious unmet need.