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ORAL ABSTRACTS

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

A Multicenter Phase2 Trial of Linperlisib in Relapsed or Refractory Peripheral T/NK Cell Lymphomas

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Introduction
Peripheral T/NK cell lymphomas (PTCLs) are a group of aggressive heterogeneous non-Hodgkin's lymphomas where in relapsed or refractory (r/r) disease, the approved standard therapies are limited with a median progression free survival (mPFS) of only 3-4 months. PI3Kdelta inhibitors have demonstrated clinical activities in T-cell and B-cell lymphomas, owing to the multiple cellular activities in the T, B, and myeloid cell tumor microenvironment. However, application of these agents has

been hampered by poor tolerabilities, particularly with toxicities such as diarrhea/colitis, hepatotoxicity, pneumonitis, hyperglycemia, and rash. As a new PI3Kdelta-selective oral agent, linperlisib was shown to be efficacious and indicated a favorable safety profile in phase 1 and 2 clinical trials in r/r Follicular Lymphoma (FL) and PTCL. Linperlisib received marketing approval in China in 2022 for r/r FL patients (pts) with 2 prior systemic therapies. Here we report the efficacy and safety findings for linperlisib in a pivotal phase 2 trial in r/r PTCL.

Methods

Ninety-eight pts were enrolled in the open-label phase 2 registration trial (CTR20210333) from May 2021 to October 2022 at 25 sites in China. The trial had a representation of different PTCL subtypes: AITL (48 pts), PTCL-NOS (24 pts), NKT (8 pts), ALCL (2 pts), MEITL (2 pts), Other (4 pts), and 10pt did not qualify as PTCL confirmed by independent pathology review, yielding a Full Analysis Set (FAS) of 88 pts for efficacy evaluation. Linperlisib was orally dosed at 80 mg QD (RP2D) continuously until disease progression, intolerable toxicity, or study withdrawal. Tumor assessments performed every 2 treatment cycles (28-day cycle) were evaluated with Lugano 2014 criteria by an Independent Review Committee. Safety was evaluated according to CTCAE v5.0.

Results

In this phase 2 study, the median age was 57 years, ECOG 0-1 (100%). Most patients were diagnosed with Lugano 2014 Stage III (29 pts, 33%), or IV (49pts, 56%) diseases, and were refractory or relapsed to a median of 2 prior systemic therapies. Sixty-four pts (73%) had refractory diseases, 59 pts (67%) had relapsed diseases, and 35 pts (40%) were with both r/r.

Treatment related adverse events (TRAE) were observed in 94 pts (95.9%) , with the most common TRAEs (≥10%) being neutropenia (59%), leukopenia (47%), thrombocytopenia (32%), anaemia (24%), elevated alanine aminotransferase (23%), elevated aspartate aminotransferase (20%), pneumonia (20%), lymphocytopenia (17%), hypertriglyceridemia (15%), fever (15%), diarrhea (14%), elevated lipase (13%), hyperuricemia (13%), rash (13%), hypercholesterolemia (12%), hyponatremia (11%), elevated lactate dehydrogenase (10%), elevated creatinine (10%). AEs of ≥Grade 3 (≥5%) were neutropenia (32%), pneumonia (14%), leukopenia (10%), anaemia (6%), thrombocytopenia (5%), upper respiratory tract infection (5%) and lymphocytopenia (5%). The most frequent Serious Adverse Event (drug-related) was pneumonia (11%). Twenty-two pts (22.4%) had dose reductions, and 9 pts (9.2%) discontinued from the study due to AEs. The safety profile was consistent with all previously reported in linperlisib clinical studies.

Among the 88 FAS pts, the objective response rate (ORR) was 48%, including 30% (26 pts) complete response, 18% (16 pts) partial response, and 20% (18 pts) stable disease. The disease control rate was 68%. Responses were demonstrated in all subtypes, including AITL, PTCL-NOS, NKT, and others. As of April 24, 2023, the median duration of response had not been reached (95%CI: 7.8, NR), and mPFS was 5.5 months (95%CI: 3.5, 15.6). All pts had ≥6 months of follow-up as of the safety and efficacy analysis data cut off (April 24, 2023); median follow-up was 13.9 months. The 6-month OS rate was 75% (95% CI: 64.51%, 82.74%), the median OS was 14.2 months (95%CI: 7.9, NR), 16 pts continued to receive linperlisib treatment.

Conclusions

Linperlisib, as a new PI3Kdelta-selective oral agent, showed a well-tolerated safety profile with low levels of severe gastrointestinal and liver toxicities seen with other PI3K agents. In r/r PTCL, linperlisib had promising durable efficacies, with 48% ORR (30% CR) and a median duration of response that was not reached. As in previous lymphoma studies with linperlisib, a high proportion of responses were CRs, and responses were observed across almost all PTCL subtypes. A phase 2 r/r PTCL and CTCL trial in the US/EU is ongoing.

Disclosures No relevant conflicts of interest to declare.

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