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POSTER ABSTRACTS

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

A Phase I Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Preliminary Antitumor Activity of Dual CK1ε/PI3Kδ Inhibitor HZ-H08905 in Adult Patients with Relapsed and/or Refractory Hematologic Malignancies

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Background: HZ-H08905 is a first-class and potent CK1ε/PI3Kδ dual inhibitor, which was previously reported (Abstract 5502, ASH 2022). Phase I study is ongoing in China, and here we present preliminary results of HZ-H08905 monotherapy in hematologic malignancies.
Methods: HZ-H08905-101 is an ongoing Phase 1, first-in-human, open-label, multicenter, multiple-dose escalation and expansion study in China (CTR20213233). Primary objectives: safety/tolerability, maximum tolerated dose (MTD), and recommended phase 2 dose (RP2D) of HZ-H08905 monotherapy; secondary objectives: pharmacokinetic properties and preliminary anti-tumor activity of HZ-H08905 in patients with relapsed/refractory (R/R) non-Hodgkin lymphoma (NHL), including B-cell lymphoma (BCM) and T-cell lymphoma (TCL). HZ-H08905 was administered orally once daily in 28-day cycles until disease progression or unacceptable toxicity. The dose escalation part was initiated with a dose titration in the initial cohort (50mg once daily), followed by a 3 + 3 design (100mg, 300 or 450 mg once daily). Dose-limiting toxicity (DLT) for each cohort was evaluated in the first 28-day cycle. Dose expansion was conducted in selected doses and cohorts. Safety was assessed per CTCAE 5.0 and efficacy was measured according to IWWM-7 for WM, or IWCLL 2018 for CLL/SLL, or Lugano 2014 criteria for other NHL.
Results: At the data cutoff date of 25 May 2023, 38 pts were analyzed, including 26 R/R TCL [12 AITL, 10 PTCL-NOS, 2 ALK negative ALCL, 1 NKTCL 1 EATCL] and 12 R/R BCM [5 DLBCL, 3 FL, 2 WM, 1 CLL, 1 MCL]. 1 pt received 50mg/d, 9 pts received 100mg/d, 14 pts received 200mg/d, 13 pts received 300mg/d and 1pts received 450mg/d. No DLT occurred and MTD was not reached. Pts were with a median age of 61 years (range: 38-78), median ECOG 1 (range: 0-2) and a median of 2 prior systemic therapies (range: 1-5). 35 of 38 pts (92%) experienced a treatment related adverse event (TRAE). TRAEs of ≥Grade 3 (≥5%) were neutropenia (26.3%), pneumonia (7.9%), leukopenia (5.3%), elevated aspartate aminotransferase (5.3%), elevated alanine aminotransferase (5.3%) and herpes zoster (5.3%). 10 pts (26.3%) had dose interruption, 3pts (7.9%) had dose reduction, and 1 pt (2.6%) discontinued from the study due to TRAEs. Of 35 pts available for tumor assessment (26 TCL; 12 BCM), the overall response rate (ORR) was 60% (95%CI: 42.11, 76.13), including 17% (6 pts) complete response (CR), 40% (14 pts) partial response (PR), 3% (1 pt) minor response (MR) and 20% (7 pts) stable disease (SD), contributing to an 80% (95%CI: 63.06, 91.56) disease control rate (DCR). The median time to response (mTTR) was 1.9 months (95%CI: 1.87, 2.10). The median duration of response (mDOR) and median progression free survival (mPFS) had not been reached, with 21 pts (55%) are still on HZ-H08905 treatment. HZ-H08905 exhibited excellent antitumor efficacy in several NHL subtypes, including CLL, DLBCL, FL, MCL, PTCL and WM, with ORR ranged from 50%~100% and DCR ranged from 76%~100%.

Conclusions: These results demonstrated that HZ-H08905 monotherapy was well tolerated and showed promising efficacy in patients with R/R NHL. A Phase 2 R/R PTCL registration study in China is currently planned.

Disclosures No relevant conflicts of interest to declare.

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