Combination of mitoxantrone hydrochloride liposome with pegaspargase in patients with extranodal NK/T-cell lymphoma: A phase I/II clinical trial


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Background
Extranodal NK/T-cell lymphoma (ENKTCL) remains a high unmet clinical need for improving outcome. This trial aimed to explore the safety, pharmacokinetics (PK) and efficacy of mitoxantrone hydrochloride liposome (PLM60) plus pegaspargase in patients (pts) with ENKTCL.

Methods
Adult pts with histologically confirmed treatment-naïve or relapsed/refractory ENKTCL were recruited. Phase I was 3+3 dose-escalation design with four dose levels of PLM60 (12, 16, 20 and 24 mg/m²) plus pegaspargase 2000 IU/m² administered on day 1 of every cycle (21 days) for 4-6 cycles. Phase II was dose expansion at the recommended phase 2 dose (RP2D) in pts with treatment-naïve ENKTCL. The primary endpoints were safety and PK. The secondary endpoint was efficacy including complete response (CR) rate, objective response rate (ORR) as per Lugano 2014.

Results
At the cut-off data of February 15, 2022, 31 eligible pts were enrolled (phase I, n = 21 and phase II, n = 10). Phase I included 9 relapsed/refractory pts and 12 treatment-naïve pts. Two dose-limiting toxicities (grade-4 neutropenia in 20 mg/m²; grade-3 abdominal pain in 24 mg/m²) occurred. RP2D was PLM60 24 mg/m² plus pegaspargase 2000 IU/m². Treatment-related adverse events (TRAEs) of any grade occurred in all 31 pts, in which 27 (87.1%) were ≥ grade 3. The most common ≥ grade 3 TRAEs was neutropenia (77.4%), leucopenia (74.2%), anemia (54.8%), thrombocytopenia (45.2%), hypertriglycerideremia (22.6%), infectious pneumonia (16.1%), lymphocytopenia (16.1%), decreased fibrinogen level (16.1%), hypoglycemia (12.9%) and elevated bilirubin (12.9%). 31 pts were evaluable for response. CR rate and ORR were 61.3% (19/31, 95% CI 42.2%-78.2%) and 87.1% (27/31, 95% CI 70.2%-96.4%), respectively. Median PFS was not reached. Among 22 treatment-naïve pts (13 males) with a median age of 40.5 (range, 23-70), 9 pts (40.9%) had the presence of B symptoms and 6 pts (27.3%) were at the stage III or IV (Lugano classification). The CR rate and ORR of this cohort was 68.2% (15/22, 95% CI 45.1%-86.1%) and 90.9% (20/22, 95% CI 70.8%-98.9%).

Conclusions
PLM60 plus pegaspargase had an encouraging efficacy especially in treatment-naïve ENKTCL pts with manageable safety profiles.

Clinical trial identification
NCT04509466.

Legal entity responsible for the study
CSPC Zhongqi Pharmaceutical Technology Co., Ltd.
Funding
This trial is funded by National key R&D Program of China (2017YFA0205604), and supported by CSPC Zhongqi Pharmaceutical Technology Co., Ltd.

Disclosure

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