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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Combination of Mitoxantrone Hydrochloride Liposome with Tislelizumab in Patients with Relapsed or Refractory NK/T Cell Lymphoma: A Phase Ib/II Clinical Trial

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Background : Extranodal NK/T cell lymphoma (ENKTL) is a highly aggressive malignancy associated with Epstein-Barr virus (EBV) infection, and remains a high unmet clinical need for improving prognosis. Mitoxantrone hydrochloride liposome (PLM60) is a nano-drug that has been approved as the first treatment option for relapsed/refractory (r/r) PTCL, and has shown certain efficacy and safety in a pivotal phase II study. Tislelizumab is a humanized immunoglobulin G4 variant monoclonal antibody against PD-1. This trial aims to investigate the safety and efficacy of combining PLM60 with tislelizumab in patients (pts) with r/r ENKTL.

Methods: Pts with r/r ENKTL were recruited in this ongoing, prospective, multicenter, open-label phase Ib/II study (NCT05464433). Phase Ib was 3+3 design with two dose levels of PLM60 (d1, 16 mg/m ^{2} and 20 mg/m ^{2}) plus tislelizumab 200 mg (d1, Q4W) induction therapy for up to 6 cycles, then tislelizumab 200 mg (Q3W) to continue maintenance therapy until disease progression, discontinuation, withdrawal or one year of therapy (including induction therapy period). Phase II was a dose expansion at the recommended phase II dose (RP2D). The primary endpoints were to assess the tolerability (i.e. dose-limiting toxicity (DLT)) and explore RP2D of PLM60 in phase Ib, and the objective response rate (ORR) of phase II. Secondary endpoints were complete response (CR) rate, ORR, disease control rate (DCR) and safety of phase Ib, and DCR, progression-free survival (PFS), overall survival (OS) and safety of phase II.

Results: At data cut-off on 11 July 2023, 13 eligible pts were enrolled (phase Ib, n=6 and phase II, n=7). 6 pts of phase Ib were evaluable for response with a median age of 29.5 (range, 22-47) years, and 5 pts (83.3%) were ECOG 1. 3 pts (50.0%) had advanced stage III or IV (Ann Arbor). No DLT occurred at 16 mg/m ^{2} and 20 mg/m ^{2}in phase Ib study. RP2D was PLM60 20 mg/m ^{2} plus tislelizumab 200 mg. The CR rate, ORR and DCR were 33.3% (2/6, 95% CI 4.3%-77.7%), 100.0% (6/6, 95% CI 54.1%-100.0%) and 100.0% (6/6, 95% CI 54.1%-100.0%), respectively.

At data cutoff, the phase II study is being enrolled. Overall, the 11 pts evaluated in phase Ib and phase II had an ORR of 81.8% (9/11) (Figure 1). Furthermore, a decrease in EBV viral load was observed during treatment with PLM60 and tislelizumab except for one pt who experienced viral load rebounded and disease progression after 3 cycles of therapy (Figure 2). With a median follow-up of 2.1 (range, 1.0-5.6) months currently, the median PFS and OS will be reported after long-term follow-up. Treatment-related adverse events (TRAEs) of any grade occurred in all 13 enrolled pts, in which 7 (53.8%) pts were grade 3/4. The common grade 3/4 TRAEs were leucopenia (38.5%), neutropenia (30.8%), lymphocyte count decreased (30.8%), thrombocytopenia (7.7%), alanine aminotransferase increased (7.7%) and diarrhea (7.7%). Three patients had treatment delayed because of AEs. Moreover, no adverse cardiac events occurred during this study.

Conclusions: PLM60 plus tislelizumab proves an encouraging efficacy in r/r ENKTL pts with manageable safety profiles.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Mitoxantrone hydrochloride liposome (PLM60) is a nano-drug approved by NMPA. PLM60 has been shown good efficacy and safety in r/r PTCL from prior studies with objective response rate (ORR) 41.7% and complete response rate (CRR) 23.1%.

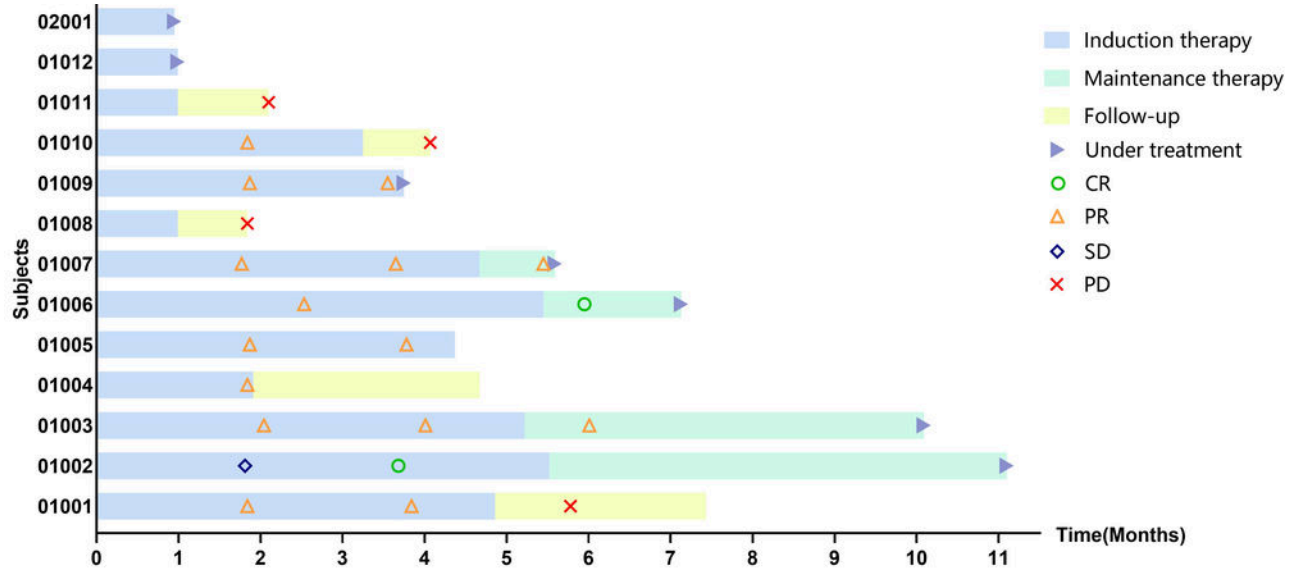

Figure 1 Efficacy and survival of r/r ENKTL patients after combination therapy with PLM60 and Tislelizumab. (Patient 01004 ended therapy due to withdrawal of informed consent)

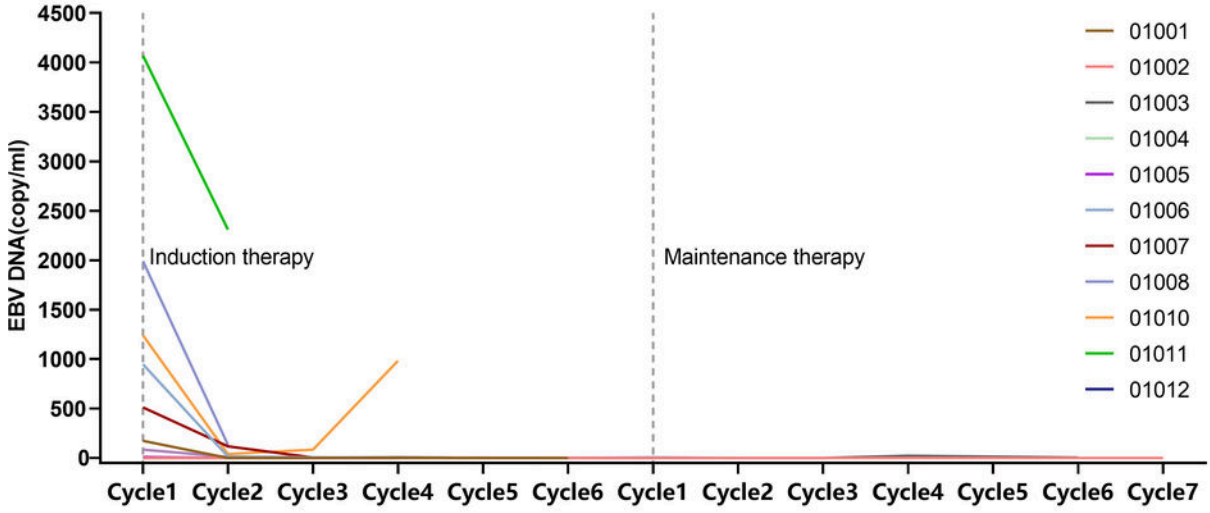

Figure 2 EBV viral load changes in the individual during and after therapy with PLM60 and Tislelizumab.

Figure 1

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