Abstract: PB2998

Title: SELINEXOR COMBINED WITH TISLELIZUMAB IN PATIENTS WITH RELAPSED OR REFRACTORY EXTRANODAL NK/T-CELL LYMPHOMA (R/R ENKTL): RESULTS OF DOSE ESCALATION OF COHORT C FROM PHASE I/II STUDY TOUCH

Abstract Type: Publication Only

Topic: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

ENKTL is a rare and highly aggressive subtype of mature T and NK/T cell lymphoma. The prognosis remains extremely poor for R/R ENKTL patients (pts) with treatment failure of L-Aspariginase (L-Asp) based regimens, highlighting the need for novel approaches. Monotherapy of tislelizumab (Tis) showed preliminary clinical activity in R/R ENKTL. Selinexor (Sel), a novel XPO1 inhibitor, has demonstrated preclinical synergistic effects when combined with PD-1 antibody. The TOUCH study (NCT04425070) includes three cohorts investigating the combination of Sel with chemotherapy (ICE or GEMOX) or Tis in R/R ENKTL.

Aims:

Cohort C was designed to evaluate the safety, tolerability, preliminary efficacy of Sel plus Tis in R/R ENKTL.

Methods:

Pts who received at least one prior treatment containing L-Asp were enrolled. In the escalation stage, a 3+3 design was implemented to determine the RP2D of Sel. The starting dose of Sel was 40 mg QW, followed by 60 mg QW (dose level 2), administered orally on Days 1, 8, and 15 of each 21-day cycle. Tis was administered at a fixed dose of 200 mg every 3 weeks on Day 1. DLTs were assessed during the first cycle. Efficacy was evaluated per Lyric 2016 by investigators.

Results:

As of 25 Dec 2023, 12 R/R ENKTL pts were enrolled in the escalation stage including 3 pts in Sel 40mg cohort and 9 pts in Sel 60mg cohort. At study entry, the median age was 52 years (range 32-65); Five males and 7 females; 6 (50.0%) pts had stage III/IV disease; Seven (58.3%) pts had PINK score ≥2 and 6 (50.0%) pts were circular EBV-DNA positive. The median number of prior treatment lines was 2.5 (range 1-5); Ten (83.3%) pts were refractory to their last-line therapy. Eleven pts had prior exposure to PD-1/PD-L1 antibodies, including 7 pts who had received prior Tis.

No DLT was observed and MTD was not reached. The most common TEAEs were asthenia (83.3%), neutropenia (83.3%), nausea/vomiting (58.3%), decreased appetite, weight loss, anemia, thrombocytopenia (50.0%, respectively), lymphocytopenia (41.7%), pneumonia, AST increased and proteinuria (33.3%, respectively). Only 1 pt experienced an irAE with thyroiditis. Seven pts (58.3%) had Grade≥3 TEAEs. TESAEs occurred in 3 pts (25%) with only 1 (sepsis) considered treatment related. No pt discontinued or died due to TEAEs. Among 11 efficacy evaluable patients in escalation phase, ORR was 72.7% (8/11), and CR rate was 36.4% (4/11). In Sel 60mg cohort, 3 CRs and 4 PRs were observed. Of 7 Tis exposed pts, 2 achieved CR and 3 achieved PR. At a median follow-up of 6.8 months (range 5.5-12.6), the median PFS, DOR and OS of all pts were 6.1 months, 4.7 months, and not reached (6-month OS rate 90.9%), respectively. In Sel 60mg cohort, the median PFS, DOR and OS were 6.7 months, 4.7 months, and not reached (6-month OS rate 100%), respectively. The RP2D of Sel in Cohort C was determined to be 60mg QW.

Summary/Conclusion: Selinexor in combination of tislelizumab showed tolerable safety profile across 2 dose levels and promising efficacy results in R/R ENKTL. Expansion stage of Cohort C is ongoing.

Keywords: relapsed/refractory, Extranodal lymphoma, Phase I/II, Dose escalation