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623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Safety and Efficacy of a-319 (a CD3xCD19 T cell engager) in Patients with Relapsed or Refractory B-Cell Non-Hodgkin Lymphoma

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Background: A-319 is a CD19 x CD3 bispecific T cell engager to treat B-cell non-Hodgkin Lymphoma (B-NHL). A-319 contains a scFV domain derived from SP34 CD3 antibody and a CD19 binding domain in a Fab format without Fc. A-319 has the same mechanism of action as that of blinatumomab, and may benefit B-NHL patients. We report the phase I study results of A-319 in patients with relapsed/refractory B-NHL.
Methods: The current study is a multi-center, open-label, dose-escalation phase I clinical study. The primary endpoint was to determine the dose-limiting toxicity (DLT) and maximum tolerated dose (MTD) of A-319. The secondary endpoints were to evaluate the pharmacokinetics (PK) and efficacy.
During dose escalation stage, one treatment cycle contains one week of A-319 priming doses and three weeks of treatment doses. During priming doses, A-319 was administered three times per week (day 1, day 3 and day 5) at dose level of 0.05 ug/kg/day by 24 hr IV infusion. Dose escalation started at week two at dose level of 0.05, 0.15, 0.3, 0.6, 1.2, 1.8 and 2.4 ug/kg/day, respectively, by 6 hr IV infusion three times per week. The study was registered at ClinicalTrials.gov (NCT04056975).
Results: A total of 21 B-NHL patients (CD19+) were treated with A-319 for at least 1 cycle. Eighteen (85.7%) patients experienced adverse events and 12 (57.1%) patients experienced treatment-related adverse events (TRAEs). The most common TRAE was cytokine release syndrome (CRS, 23.8%, n=5), followed by fever (66.7%, n=14) and decreased immunoglobulin (23.8%, n=5). Most of the reported adverse events were CTCAE Grade I-II. Five patients experienced CRS (Grade I-II, n=5;≥Grade III, n=0). Six patients experienced immune effector cell-associated neurotoxicity syndrome (Grade I-II, n=6;Grade III, n=2). The serious adverse events were reported in 3 patients, which included lung infection (Grade III, n=1), interstitial pneumonia (Grade I, n=1), and pulmonary embolism (Grade III, n=1). There was no reported DLT. No fatal cases were reported during treatment. The preliminary pharmacokinetic (PK) results showed that A-319 has linear PK properties with an estimated $T_{1/2}$ of 6-10 hrs. Preliminary responses were reported that one patient achieved complete remission (CR), 3 achieved partial remission (PR), and 7 achieved stable disease (SD) after one cycle of treatment. In the 5 th cohort (at the dose level of 1.2 ug/kg/day), one patient with diffuse large B cell lymphoma (DLBCL) achieved CR, one with follicular lymphoma (FL) achieved PR and on with DLBCL achieved SD.
Conclusions: A-319 was well tolerated in relapsed/refractory B-NHL. A-319 at the dose level of 1.2 ug/kg/day showed encouraging disease control and warranted further clinical investigation.

Disclosures Zhao: *ITabMed Ltd:* Current Employment. **Zhong:** *ITabMed Ltd:* Current Employment. **Tan:** *ITabMed Ltd:* Current Employment. **Yu:** *ITabMed Ltd:* Current Employment. **Xue:** *ITabMed Ltd:* Current Employment. **Shen:** *ITabMed Ltd:* Current Employment. **Tu:** *ITabMed Ltd:* Current Employment. **Yang:** *ITabMed Ltd:* Current Employment. **Chen:** *ITabMed Ltd:* Current Employment. **Liu:** *ITabMed Ltd:* Current Employment. **Yan:** *ITabMed Ltd:* Current Employment.

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