Abstracts

A PHASE I STUDY OF A NOVEL BCMA×CD3 BISPECIFIC ANTIBODY EMB06 IN RELAPSED OR REFRACTORY MULTIPLE MYELOMA

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Background Despite recent advances in T-cell engager based multiple myeloma therapies, high rate of cytokine release syndrome (CRS) and severe neurotoxicity remains a challenge in clinic. EMB-06 is a novel 2+2 BCMA×CD3 T-Cell engaging bispecific antibody developed based on the Epimab’s proprietary Fabs-In-Tandem-Immunoglobulin (FIT-Ig®) platform. Differentiated from existing T-cell engagers, EMB-06 comprises tetravalent binding domains in cis-configuration and proprietary anti-CD3 arms with optimized affinity. It induced modest levels of cytokine release yet retained robust anti-tumor activity in preclinical studies. Here we report the initial results from an ongoing multicenter, first-in-human, Phase I study of EMB-06 in relapsed or refractory multiple myeloma (RRMM).

Methods The Phase I study evaluates escalating doses of once weekly IV administrations of EMB-06 in patients (pts) with RRMM who have failed or are intolerant to standard therapies. Dose escalation was guided by the Bayesian optimal interval (BOIN) design. Primary objectives were to assess safety, tolerability, and determine the MTD and/or RP2Ds. Secondary objectives were to assess pharmacokinetics (PK), pharmacodynamics (PD), immunogenicity, and preliminary anti-tumor activities.

Results As of Aug 28, 2023, 33 pts had been treated with EMB-06 at 0.2mg to 200mg. Median age was 66 y (46–82). Median prior lines of therapies were 3 (2–6) and 26 (79%) pts were refractory to the most recent line of therapy. Treatment-related AEs (TRAEs) were reported in 20 (61%) pts, with Gr ≥3 occurring in 7 (21%) pts. The most common TRAEs include ALT increase (18%), leukopenia (18%), ALP increase (15%), neutropenia (15%), anemia (12%), AST increase (12%), GGT increase (12%), lymphopenia (12%) and CRS (12%). All CRS were Grade 1. Only 1 patient experienced treatment related neurotoxicity (Gr.1 paresthesia). One DLT (pneumonia, cardiac failure, creatinine increased and hepatic insufficiency) was observed at 60mg cohort. EMB-06 shows dose proportional increase in PK exposure across 0.2–120 mg, and the median half-life after single dosing is 4.4 days. PD activity (T cell redistribution and activation along with transient release of low-level cytokines) was observed at doses ≥0.6mg. The ORR was 29% (9/31) among 31 response evaluable pts. Of the 5 evaluable pts treated with doses ≥120mg, the ORR was 100% (1 CR, 2 VGPR, 2 PR).

Conclusions EMB-06 demonstrated a differentiated safety profile in RRMM pts with exceptionally low CRS and neurotoxicity rates so far. An initial ORR of 100% has been observed at doses ≥120mg. Updated data will be shared at the meeting.

Trial Registration The clinical trial was registered with www.clinicaltrials.gov (NCT04735575).

Ethics Approval The trial was done according to Good Clinical Practice and the Declaration of Helsinki. The protocol and amendments were approved by the institutional review board or ethics committee at each site. And all participants gave informed consent before taking part in the trial. The name of the ethics committee(s) or institutional review board(s), the number/ID of the approval(s) are as follow:

- Epworth health – No. 2020-12-1350
- Sunshine Coast Haematology and Oncology Clinic- No. 2020-12-1350-AA
- One Clinical Research - No. 2020-12-1350-AB
- Ethics Committee of Ruijin Hospital Affiliated to Shanghai Jiaotong University School Of Medicine-No. 2021-73
- Henan Cancer Hospital Medical Science Research Ethics Committee-No. 2021-381-002
- Clinical Trial Ethics Committee of Huazhong University of Science and Technology-No. 2021-218
- Ethics Committee of the First Affiliated Hospital, School Of Medicine, Zhejiang University-No. 2021-627
- Ethics Committee of Beijing Jishuitan Hospital-No. 20210902-01
- Peking University Third Hospital Medical Science Research Ethics Committee-No.2022-220-02
- Ethics Committee of Guangdong Provincial People’s Hospital-No. YW2023-011-02

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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