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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

A Phase 1 First-in-Human Monotherapy Study of F182112, a B-Cell Maturation Antigen (BCMA)-CD3 Bispecific Antibody, in Patients with Relapsed or Refractory Multiple Myeloma

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Introduction:
Outcomes of relapsed or refractory Multiple Myeloma(RRMM) are generally poor after receiving current arsenal of therapies. Several novel kinds of drugs targeting BCMA are being developed to overcome resistance in this heavily treated patient population. F182112 is a BCMA x CD3 bispecific antibody that redirects $CD3^+$ T cells to mediate T-cell activation and subsequently caused lysis of BCMA-expressing myeloma cells. A phase 1 clinical trial, NTP-F182112-001, has been launched to evaluate the safety and efficacy of F182112 in patients with RRMM. Shan Dong New Time Pharmaceutical Co. Ltd provides the funding support for the research. Clinical trial information: NCT04984434.

Methods:
This is a first-in-human, open-label, multicenter, phase 1 study. It has enrolled patients with RRMM who aged ≥ 18 years and previously received at least 2 prior lines of therapy including at least a proteasome inhibitor and an immunomodulatory agent. F182112 was administered intravenously once a week. First four dose cohorts of F182112 (0.01, 0.1, 0.3 and 1μg/kg) were planned for accelerated titration phase and the following four dose cohorts (3, 10, 20, and 30 μg/kg) were planned for i3+3 dose escalation phase . Primary objectives were to access safety and tolerability by monitoring adverse events (AEs) per CTCAE v5.0, with exception of CRS grading per ASTCT 2018. The target rate of dose-limiting toxicity (DLT) was 25% (equivalence interval± 5%). In addition, soluble BCMA, cytokines and immunophenotyping were analysed in peripheral blood. The pharmacokinetics and immunogenicity of F182112 were also explored.

Results :
As of July 24, 2023, 22 patients have been treated with F182112 (0.01-30 μg/kg) at eight escalating dose levels. Median age was 64.5 years (range 52-74). All of patients were followed up at least five weeks and the median follow-up was 3 months (range 1-18). Fifteen (68.1%) patients received ≥4 prior lines of therapy and 15 (68.1%) patients were refractory to last lines of therapy.
Treatment-related AEs (TRAEs) were reported in 18 (82%) pts, with grade ≥3 and serious AEs occurring in 14 (64%) and 4 (18.2%) pts, respectively. The most common TRAEs(≥20%) were CRS (72.7%), lymphopenia (68.2%), neutropenia (54.6%), leukopenia (50%) and anemia (31.8%). All CRS was grade 1 or 2 and the median duration time was 2 days (1-5). One dose-limiting toxicities (ALT elevation, grade 3) occurred at 10 μg/kg dose level. No patients required F182112 dose reduction due to AEs.
As of this date cut-off, 20 of the 22 patients were evaluated for response(Figure 1). The overall response rate (ORR) was 45% (9/20), 30% (6/20) patients had stable disease (SD) and 25% (5/20) patients experienced disease progression (PD). At dose cohorts of 10ug/kg and 20ug/kg (n=9),ORR was 77.8%(7/9)with very good partial remission or better (≥VGPR) rate of 44% (4/9) and stringent complete remission (sCR) rate of 33% (3/9). At the dose cohort of 30ug/kg (n=4), ORR was 25% (1/4), one

patient of this dose cohort with extramedullary mass larger than 5cm in diameter at baseline experienced disease progression due to the mass enlargement, though his serum M protein decreased by 60.27%.
F182112 exhibited a favorable PK profile in its target patient population of RR MM, with F182112 exposures increasing in a dose-related manner.

Conclusions:
F182112 in patients with RRMM is well tolerated with preliminary antitumor activity and a favorable PK profile in patients,supporting further evaluation.

Disclosures No relevant conflicts of interest to declare.

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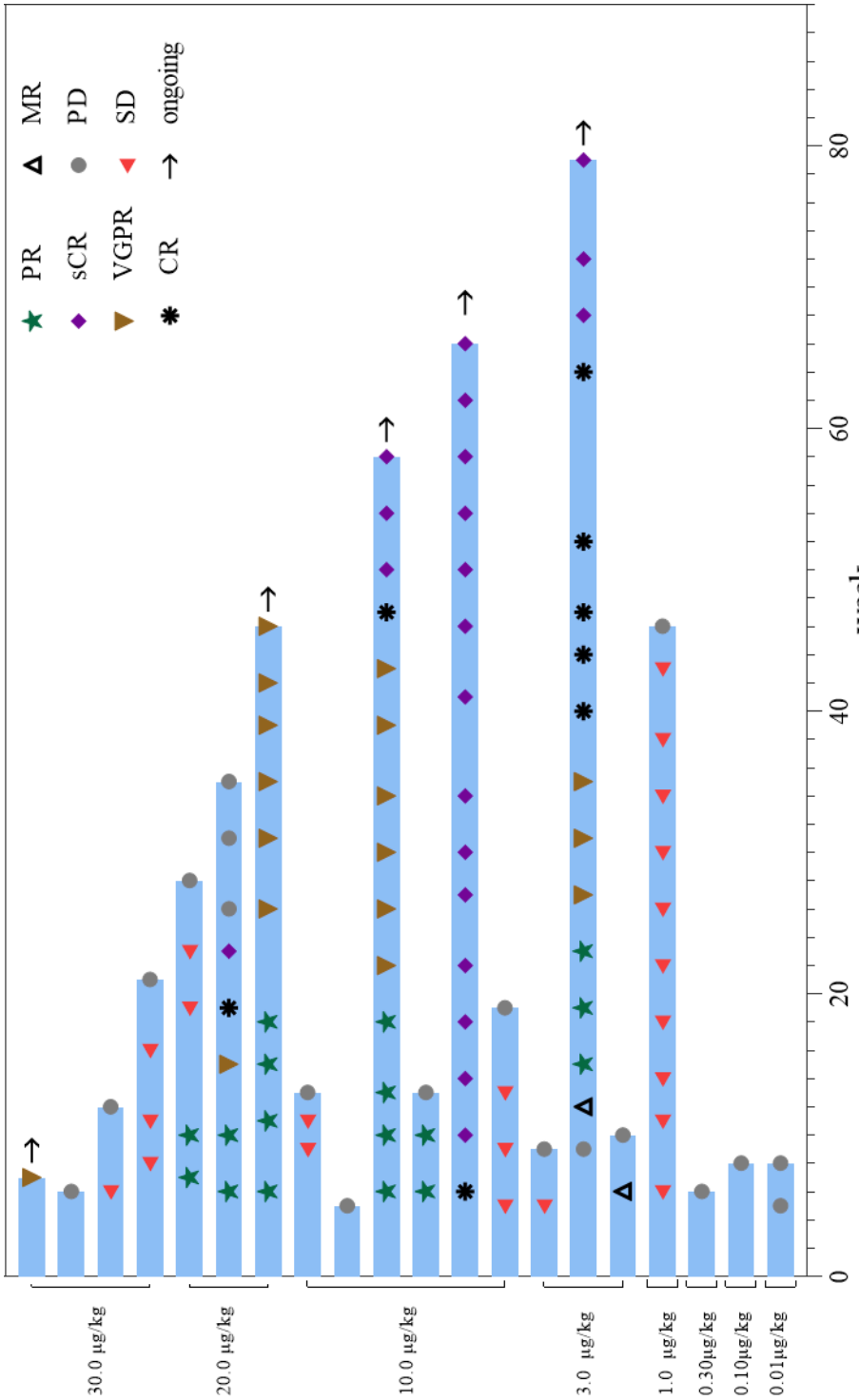

Figure1. F182112 exposure and tumor response

Figure 1