Abstract: P961

Title: A PHASE I MONOTHERAPY STUDY ASSESSING THE SAFETY AND EFFICACY OF GR1803, A BCMA×CD3 BISPECIFIC ANTIBODY, IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

Outcomes remain poor for patients with relapsed or refractory Multiple Myeloma（RRMM）. GR1803 is a BCMA x CD3 bispecific antibody that redirects cytotoxic T cells to BCMA expressing myeloma cells. We report here initial findings from an ongoing, single-agent phase I study of GR1803 in patients with RRMM.

Aims:

The objective for this phase 1 study is to assess the safety, tolerability, efficacy, pharmacokinetics (PK), and immunogenicity of GR1803 in RRMM patients.

Methods:

Adult patients with RRMM that relapsed after or were refractory to prior therapies, including a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody received GR1803 weekly by intravenous injection in 24-week cycles. Patients had measurable disease per the International Myeloma Working Group (IMWG) criteria (2016). The study is divided into 2 parts: Dose Escalation (Part 1) and Expansion (Part 2). 16 patients were enrolled into 1 of 8 dose-escalation cohorts (0.02-360 ug/kg). Dose escalation began at 0.02 ug/kg dose with single patient accelerated titration phase for the first 3 cohorts, followed by a standard titration phase with a “3 + 3” design. 180 and 240 ug/kg dose levels were further expanded with 22 and 12 patients respectively.

Results:

As of January 18, 2024, this project has enrolled 50 subjects. At data cutoff date of January 31, 2024, 49 (98%) subjects experienced at least one treatment emergent adverse event (TEAE) and 48(96%) subjects had a TEAE grade ≥ 3. Common (≥ 20%) TEAEs include infection 70% (38% Gr ≥ 3), cytokine release syndrome 80% (6% Gr ≥ 3), fever 40% (4% Gr ≥ 3), anemia 70% (32% Gr ≥ 3), neutropenia 76% (50% Gr≥ 3), thrombocytopenia 64% (48% Gr ≥ 3), leukocytopenia 66% (32% Gr ≥ 3), lymphocytopenia 62% (60% Gr≥ 3), hypokalemia 52% (16% Gr ≥ 3) and diarrhea 38% (8% Gr ≥ 3). 2 patients were evaluable for dose limiting toxicities (DLTs) in the 360ug/kg dose treatment cohorts.

40 patients have now undergone at least one efficacy assessment. The overall ORR for the 40 evaluable subjects was 85% (34/40), and the vast majority of patients in remission were still on treatment, with follow-up time up to 44 weeks. The 180ug/kg dose cohort enrolled a total of 25 subjects, the median follow-up time was 28 weeks (range, 3 weeks-32 weeks). Among the 25 patients, 23 subjects have received at least one efficacy assessment, with an ORR of 96% (22/23), an incidence of VGPR of 43%, and an incidence of CR of 13%. The follow up time for 13 patients with extramedullary multiple myeloma (EMM) who received 180ug/kg dose injection was 20 weeks (range, 10 weeks-25 weeks). The overall efficacy assessment ORR was 100% (13/13), with 7 VGPRs and 6 PRs.

The majority of patients achieved PR and above remission at the first efficacy assessment, with a median onset of 3 weeks. Subjects’ remission was sustained and improved further with continued treatment. For patients who had not yet achieved remission (SD, MR), or who had achieved PR but had not yet achieved VGPR and higher efficacy, all efficacy metrics were in progressive decline. At a median follow-up of 7 mo for 25 patients, median progression-free survival (mPFS) was not reached and the median duration of remission (mDOR) was not

reached. All subjects in remission have not experienced disease progression yet.

Summary/Conclusion: Treatment with GR1803 was well tolerated with excellent anti-myeloma activity, especially in patients with EMM. GR1803 is expected to improve the prognosis of patients with RRMM. With longer follow-up, additional efficacy/safety data will be presented.

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Keywords: B-cell maturation antigen, Multiple myeloma, Bispecific