Abstract: S191

Title: PIVOTAL PHASE 2 MONUMENTAL-1 RESULTS OF TALQUETAMAB (TAL), A GPRC5DXCD3 BISPECIFIC ANTIBODY (BSAB), FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM)

Abstract Type: Oral Presentation

Session Title: MM Clinical: New combinations and novel targets

Background:

Tal is a first-in-class BsAb targeting the novel antigen G protein–coupled receptor family C group 5 member D. In MonumenTAL-1 (NCT03399799/NCT04634552), tal showed promising efficacy and clinically manageable safety in patients (pts) with RRMM.

Aims:

We report pivotal phase 2 results from MonumenTAL-1 in pts with and without prior T-cell redirection therapy.

Methods:

All pts provided informed consent. Eligible pts were intolerant to or progressed on established therapies (phase 1) or had ≥3 prior lines of therapy (LOT), including ≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 antibody (phase 2). Pts received RP2Ds of SC tal 0.4 mg/kg QW or 0.8 mg/kg Q2W with step-up doses. CRS and ICANS were graded by ASTCT criteria; all other AEs were graded by CTCAE v4.03. Response was assessed by IMWG criteria. Data cut-off was Sep 12, 2022 for efficacy and Oct 19, 2022 for safety. Data will be updated for the meeting.

Results:

From the pivotal cohorts, 288 pts received tal 0.4 mg/kg QW (n=143) or 0.8 mg/kg Q2W (n=145), and 51 pts with prior T-cell redirection therapy received either dose. In the QW, Q2W, and prior T-cell redirection cohorts, respectively, median prior LOT was 5–6; 74%, 69%, and 84% were triple-class refractory and 29%, 23%, and 41% were penta-drug refractory; 15%, 11%, and 12% received prior belantamab. In the prior T-cell redirection cohort, 71% received CAR-T therapy, 35% received a BsAb, and 6% received both. In the pivotal cohorts, ORR was 74% (QW, 14.9 mo median follow-up [mF/U]) and 73% (Q2W, 8.6 mo mF/U), with very good partial response or better (≥VGPR) in 59% (QW) and 57% (Q2W). ORR was consistent across subgroups, including baseline ISS stage III disease, cytogenetic risk, number of prior LOT, and belantamab exposure. In pts with baseline plasmacytomas, ORR was 49% in both pivotal cohorts. In the prior T-cell redirection cohort, ORR was 63% (53% ≥VGPR) at 11.8 mo mF/U. Median PFS was 7.5, 11.9 (61% censored), and 5.1 mo in the QW, Q2W, and prior T-cell redirection cohorts, respectively. Common AEs included CRS (79%, 75%, 77%), skin-related AEs (56%, 71%, 69%), nail-related AEs (54%, 53%, 61%), and dysgeusia (50%, 48%, 61%); most were grade 1/2 and clinically manageable. ICANS occurred in 11%, 11%, and 3% of pts. Infections occurred in 58%, 65%, and 71% (grade 3/4: 22%, 16%, 26%) of pts, with low rates of opportunistic infections. AEs resulted in dose reductions in 15%, 8%, and 10% of pts and discontinuation in 5%, 8%, and 6%. There were no tal-related deaths. Responders to tal had higher T cell counts and lower frequencies of exhausted T cells and CD38+ Tregs vs non-responders.

Summary/Conclusion: Pivotal phase 2 tal data showed >70% ORR in heavily pretreated pts with RRMM. High response rates were also seen in pts with prior T-cell redirection therapy. The safety profile was clinically manageable with low rates of high-grade infections and tal discontinuations.

Keywords: Phase I/II, G-protein-coupled receptors, Bispecific, Multiple myeloma