Abstract: P915

Title: LONG-TERM EFFICACY AND SAFETY RESULTS FROM THE PHASE 1/2 MONUMENTAL-1 STUDY OF TALQUETAMAB, A GPRC5D×CD3 BISPECIFIC ANTIBODY, IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

Talquetamab (tal) is the first approved GPRC5D-targeting bispecific antibody (BsAb) for treatment of patients (pts) with relapsed/refractory multiple myeloma (RRMM). In the phase 1/2 MonumenTAL-1 study, tal demonstrated high ORRs in pts naive (>71%) and exposed (65%) to prior T-cell redirection therapy (TCR, including CAR-T and BsAbs, mostly BCMA-targeting). Early onset of GPRC5D-related AEs was associated with a higher likelihood of response. Tal was associated with low discontinuation rates and a notable favorable infections profile compared with published studies of BCMA-targeting BsAbs.

Aims:

We report efficacy and safety results across 3 RRMM cohorts in MonumenTAL-1 with a longer median follow-up (mFU) of 20–30 months and additional pts in the analysis.

Methods:

Eligible pts were intolerant to or progressed on established therapies (phase 1, NCT03399799) or had ≥3 prior lines of therapy, including ≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 antibody (phase 2, NCT04634552). Pts received recommended phase 2 doses (RP2Ds) of subcutaneous tal 0.4 mg/kg QW or 0.8 mg/kg Q2W, with step-up doses. Response was assessed by an independent review committee based on IMWG criteria. AEs were graded by CTCAE v4.03. CRS and ICANS were graded by ASTCT criteria.

Results:

As of Jan 2024, 375 pts were enrolled: 143 pts in the QW cohort with mFU of 29.8 mo, 154 pts in the Q2W cohort with mFU of 23.4 mo, and 78 pts in the prior TCR cohort who received either RP2D (89.7% dosed QW) with mFU of 20.5 mo. Baseline characteristics were similar to previous reports, with the exception of a greater number of African American pts in the current analysis (n=32). ORRs ranged from 67–74% (≥VGPR, 55–59%) across cohorts (**Table**). In the prior TCR cohort, ORR was 71.4% (40/56) and 57.7% (15/26) in pts with prior CAR-T and prior BsAb, respectively. ORRs were consistent across clinically relevant subgroups, except pts with EMD who had lower ORRs (48.5% [QW], 41.5% [Q2W], 44.0% [prior TCR]). DOR and PFS results suggest better durability in the Q2W vs QW cohort (**Table**). The safety profile was also consistent with previous results. Common AEs in the QW, Q2W, and prior TCR cohorts, respectively, included CRS (79.0%, 74.7%, 73.1%), taste-related AEs (72.0%, 71.4%, 75.6%), non-rash skin-related AEs (56.6%, 73.4%, 64.1%), nail-related AEs (55.2%, 53.2%, 59.0%), and rash-related AEs (39.9%, 29.9%, 32.1%); most were grade 1/2. Weight loss, assessed by vital signs (weight decrease ≥10% from baseline), occurred in 38.5% (QW), 34.4% (Q2W), and 38.5% (prior TCR) of pts. The most common grade 3/4 AEs were hematologic AEs, including anemia (31.5%, 25.3%, 26.9%) and neutropenia (30.8%, 21.4%, 47.4%). Infection rates were comparable to previous reports (any grade, 60.8%, 70.1%, 76.9%; grade 3/4, 22.4%, 20.1%, 25.6%). Dose reductions (15.4%, 9.7%, 11.5%) and discontinuations (4.9%, 9.7%, 5.1%) due to AEs remained low. There were no treatment-related deaths.

Summary/Conclusion:

With additional pts in the analysis, high ORRs were maintained across cohorts (>69% and 67% in pts naive and exposed to prior TCR, respectively). With longer follow-up, pts continued to demonstrate durable responses, with longer DOR in Q2W vs QW dosing in pts naive to prior TCR. The safety profile was consistent with previous

reports and continues to show GPRC5D as a B-cell–sparing target with a lower risk of severe infections relative to approved BCMA-targeting BsAbs. These data support tal as a versatile treatment for pts with RRMM, delivering robust and durable responses across broad pt populations.

TABLE: Efficacy outcomes in patients with and without prior TCR in MonumenTAL-1

Outcomes	Tal 0.4 mg/kg QW (n=143)[a]	Tal 0.8 mg/kg Q2W (n=154)[a]	Prior TCR (n=78)
Median follow-up, months	29.8	23.4	20.5
ORR, n (%)	106 (74.1)	107 (69.5)	52 (66.7)
≥VGPR, n (%)	85 (59.4)	91 (59.1)	43 (55.1)
≥CR, n (%)	47 (32.9)	62 (40.3)	33 (42.3)
Median DOR, months	9.5	17.5	N/A[b]
(95% CI)	(6.7–13.4)	(12.5–NR)	
12-month DOR rate, %	43.8	60.6	55.8
(95% CI)	(34.1–53.1)	(50.4–69.4)	(40.8–68.4)
Median PFS, months	7.5	11.2	7.7
(95% CI)	(5.7–9.4)	(8.4–14.6)	(4.1–14.5)
12-month PFS rate, %	34.9	46.8	44.7
(95% CI)	(27.0–42.9)	(38.5–54.8)	(33.1–55.7)

[a]0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts did not have prior exposure to TCR.
[b]Not reported due to heavy censoring from 12 to 20 months; the estimate may not be reliable at this time point.
CR, complete response; DOR, duration of response; N/A, not applicable; NR, not reached; ORR, overall response rate; PFS, progression-free survival; Q2W, every other week; QW, weekly; tal, talquetamab; TCR, T-cell redirection therapy; VGPR, very good partial response.

Keywords: Myeloma, Bispecific, G-protein-coupled receptors, Multiple myeloma