MM-215

Efficacy and Safety From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma: Analyses at an Extended Median Follow-Up

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Key Takeaway

At an extended mFU (30–38 months), patients with RRMM treated with talquetamab continue to demonstrate deep and durable responses and tolerable safety with no new discontinuations due to GPRC5D-related AEs

Conclusions

High ORRs elicited by talquetamab were durable and led to promising 36-month OS rates (45–61%)

The safety profile continued to show lower risk of high-grade infections relative to approved anti-BCMA BsAbs,[8,9] potentially contributing to the OS benefit with talquetamab and highlighting the humoral immune preservation that enables versatile use of talquetamab including in combination

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Disclosures

DO is an employee and stockholder of Johnson & Johnson.

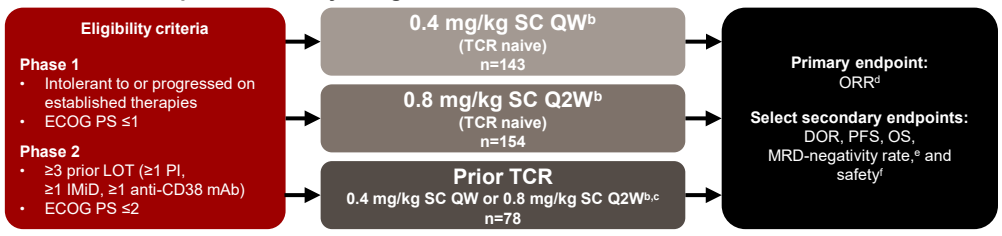
Introduction

- Talquetamab is the first and only approved bispecific antibody (BsAb) targeting G protein–coupled receptor class C group 5 member D (GPRC5D) for the treatment of relapsed/refractory multiple myeloma (RRMM)[1-3]
- In previous results from the phase 1/2 MonumenTAL-1 study (clinical cut-off: Jan 2024; median follow-up [mFU], 21–30 months), talquetamab elicited deep, durable responses with low discontinuation rates[4]

We report efficacy and ongoing safety from MonumenTAL-1 at an extended mFU of 30–38 months, the longest mFU for any anti-GPRC5D agent

Methods

MonumenTAL-1[a] phase 1/2 study design

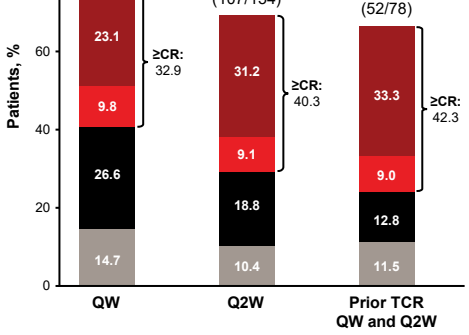


[a]NCT03399799/NCT04634552. [b]With 2–3 step-up doses. [c]Patients received QW (n=70) or Q2W (n=8) dosing. [d]Assessed by IRC using International Myeloma Working Group criteria.[5,6] [e]MRD was assessed using bone marrow aspirates and evaluated via next-generation sequencing. [f]CRS and ICANS were graded by ASTCT criteria[7]; all other AEs were graded by CTCAE v4.03.
AE, adverse event; ASTCT, American Society of Transplantation and Cellular Therapy; CR, complete response; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMiD, immunomodulatory drug; IRC, independent review committee; LOT, line of therapy; mAb, monoclonal antibody; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; Q2W, every other week; QW, weekly; SC, subcutaneous; TCR, T-cell redirection therapy.

As of Sept 2024, 17, 27, and 18 patients remained on talquetamab in the QW, Q2W, and prior TCR QW and Q2W cohorts, respectively. All were responders (very good partial response [VGPR] or better, most ≥CR), and 2 subsequently progressed during this time

Results

Figure 1. ORR[a] remained high, consistent with previous results[4]



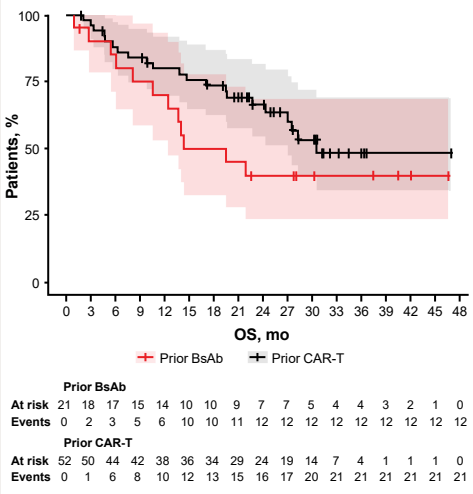
[a]Due to rounding, individual response rates may not sum to the ORR. Since previous disclosure, 1 patient in the prior TCR QW and Q2W cohort deepened in response (CR to sCR). PR, partial response; sCR, stringent complete response.

Table. mDOR and mPFS continued to demonstrate superior outcomes in the Q2W vs QW cohort

Outcome	QW (n=143)	Q2W (n=154)	Prior TCR QW and Q2W (n=78)
mFU, mo	38.2	31.2	30.3
mDOR, mo (95% CI)[a]	9.5 (6.7–13.4)	17.5 (12.5–25.1)	19.2 (8.1–24.7)
mPFS, mo (95% CI)	7.5 (5.7–9.4)	11.2 (7.7–14.6)	7.7 (4.1–14.5)
MRD neg (10^{-5}), % (95% CI)[b]	64.3 (51.9–75.4)	65.2 (52.8–76.3)	57.1 (37.2–75.5)

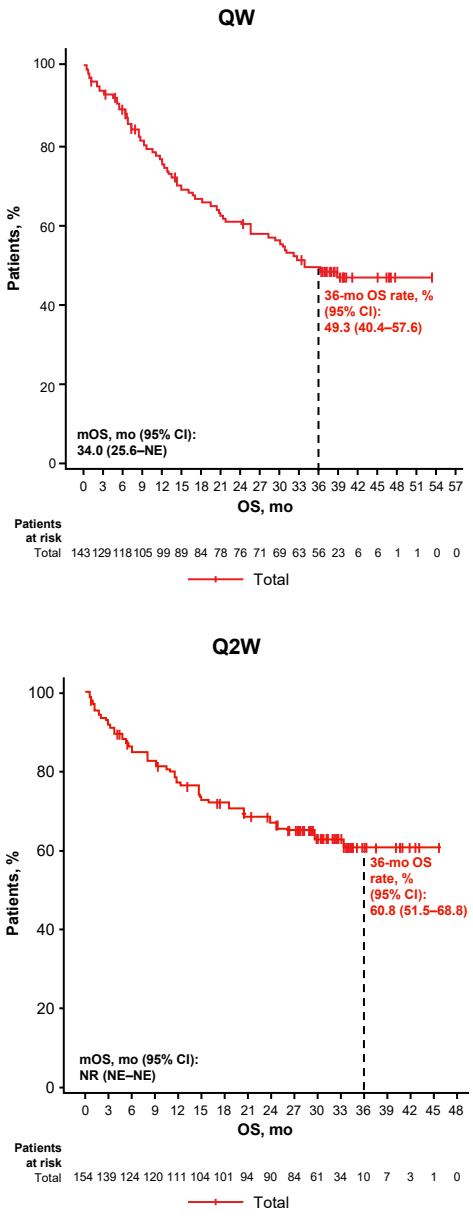
[a]n=106 (QW), n=107 (Q2W), n=52 (prior TCR QW and Q2W). [b]Assessed in patients with evaluable samples: n=70 (QW), n=69 (Q2W), n=28 (prior TCR QW and Q2W). Only MRD assessments (10^{-5}) within 3 months of achieving CR or sCR until death, disease progression, or subsequent therapy are considered.
mDOR, median duration of response; mPFS, median progression-free survival; MRD neg, minimal residual disease negativity; USPI, United States Prescribing Information.

Figure 2. Patients receiving prior CAR-T therapy had higher observed OS rates vs patients receiving prior BsAb therapy, although numbers were small



Data are shown for patients in the prior TCR QW and Q2W cohort only (n=78, majority [96%] BCMA targeted); 5 patients who received both prior BsAb and prior CAR-T were excluded from the analysis. CAR, chimeric antigen receptor; mo, month.

Figure 3. mOS was 34 months with QW dosing, not reached at 3 years with Q2W dosing, and 28 months in the prior TCR QW and Q2W cohort[a]

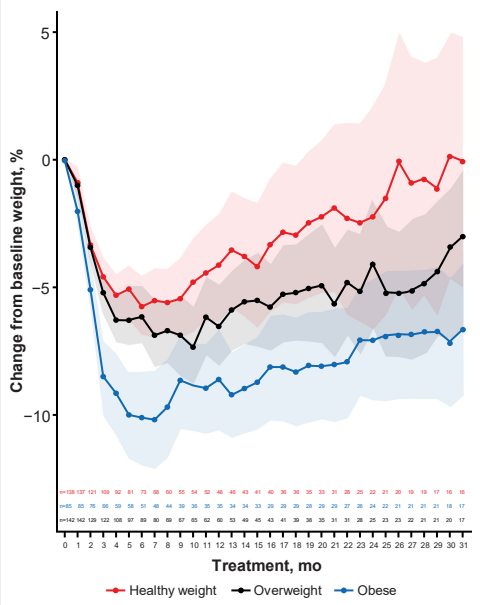


[a]Data not mature in the Q2W cohort. mOS, median overall survival; NE, not estimable; NR, not reached.

The safety profile was consistent with previous results[4]; discontinuation rates due to AEs remained low, and no new discontinuations occurred due to GPRC5D-related AEs

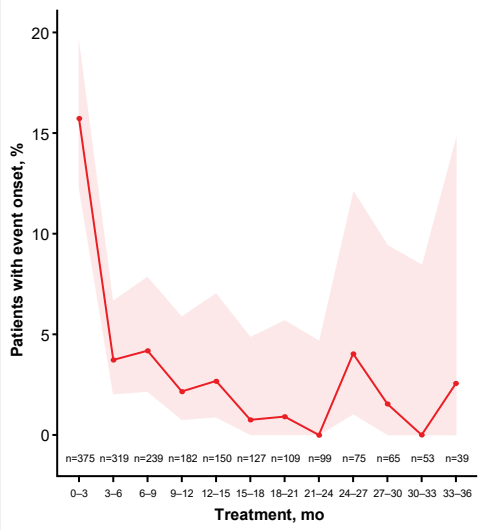
A new safety signal, ataxia/balance disorders, was recently identified in association with talquetamab and had low prevalence in MonumenTAL-1

Figure 4. Initial mean weight loss was observed in patients before stabilizing and improving; patients with a baseline "healthy weight" BMI who remained on treatment returned to their baseline weight over time



Data were plotted as mean percent change from baseline weight. BMI categories were defined as follows: healthy weight (18.5 to <25), overweight (25 to <30), obese (≥30). BMI was calculated as patient body weight (in kg) divided by patient height squared (in meters). Month 0 represents baseline and month 1 represents the first 30.4375 days of treatment. Shaded areas represent the 95% CIs. Data plotted if ≥15 patients remained within 30 days of last talquetamab treatment and had a measurement within the window. Data were averaged if multiple readings were taken on the same day, and the most recent reading was used if multiple readings were available within the same interval. BMI, body mass index.

Figure 5. Across combined cohorts, new-onset grade ≥3 infections were mostly limited to early treatment cycles



Shaded areas represent the 95% CIs. Data were plotted if ≥25 patients remained on treatment.

References

1. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 2. Chari A, et al. *Lancet Haematol* 2025;12:E269-E821. 3. TALVEY™ (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2023. 4. Rasche L, et al. Presented at EHA; June 13–16, 2024; Madrid, Spain. 5. Rajkumar SV, et al. *Blood* 2011;117:4691-5. 6. Kumar S, et al. *Lancet Oncol* 2016;17:328-46. 7. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25:625-38. 8. van de Donk NWCJ, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8011. 9. Tomasson M, et al. *Blood* 2023;142(supplement 1):3385.

Multiple Myeloma

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