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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Supplementary material

https://www.congresshub.com/Oncology/AM2025/Talquetamab/Donk-Talq

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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

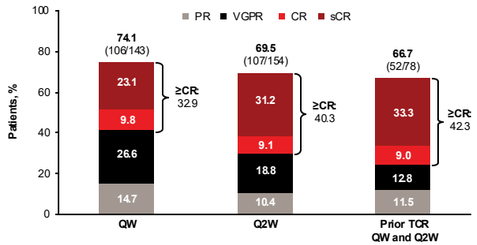
MonumenTAL-1[a] phase 1/2 study design

[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; VGPR, very good partial response.

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 (≥VGPR, most ≥CR), and 2 subsequently progressed during this time

Results

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



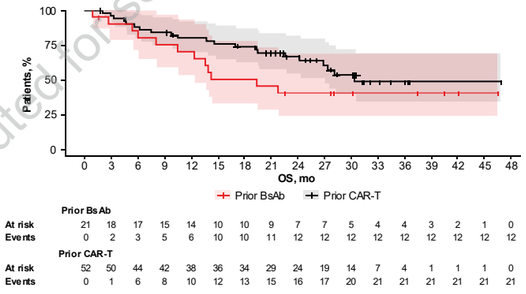
[a]Due to rounding, individual response rates may not sum to the ORR. Since previous disclosure, 1 patient in the prior TCR QW and Q2W cohort deepened in response (CR to sCR). PR, partial response; sCR, stringent complete response.

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. See **Supplemental Table 1** for efficacy outcomes in the USPI population (≥4 prior LOT). mDOR, median duration of response; mPFS, median progression-free survival; MRD neg, minimal residual disease negativity; USPI, US prescribing information.

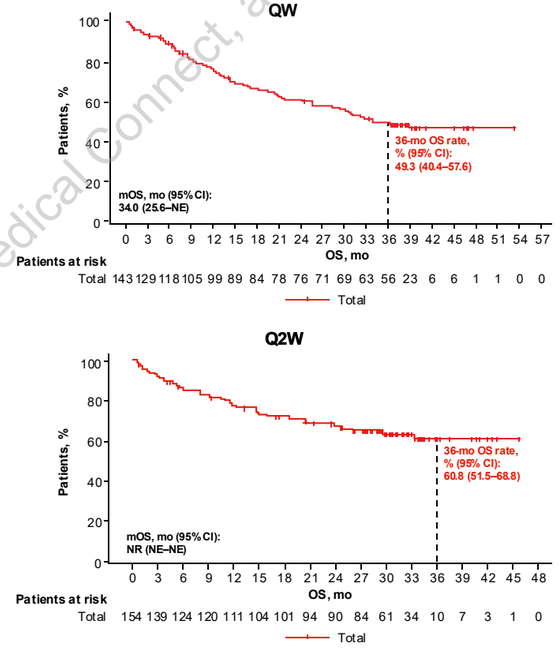
Figure 2. Patients receiving prior CAR-T therapy had higher observed OS rates vs patients receiving prior BsAb therapy, although numbers were small



Prior BsAb																	
At risk	21	18	17	15	14	10	10	9	7	7	5	4	4	3	2	1	0
Events	0	2	3	5	6	10	10	11	12	12	12	12	12	12	12	12	12
Prior CAR-T																	
At risk	52	50	44	42	38	36	34	29	24	19	14	7	4	1	1	1	0
Events	0	1	6	8	10	12	13	15	16	17	20	21	21	21	21	21	21

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.

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]

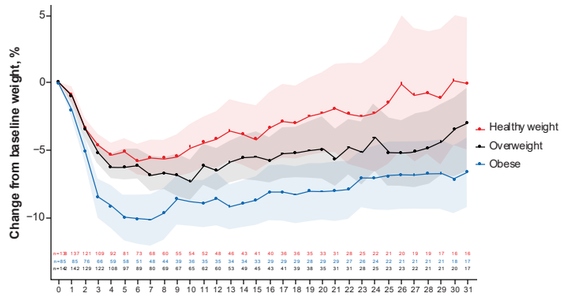


[a]Data not mature in the Q2W cohort. mOS, median overall survival; NE, not estimable; NR, not reached.

The safety profile was consistent with previous results (Supplemental Table 2)[4]; discontinuation rates due to AEs remained low, and no new discontinuations occurred due to GPRC5D-related AEs

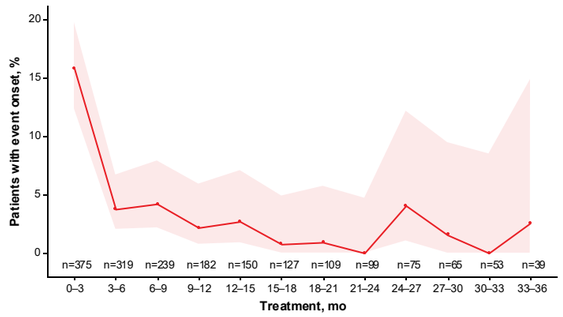
A new safety signal, ataxia/balance disorders, was recently identified in association with talquetamab and had low prevalence in MonumenTAL-1

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.

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Multiple Myeloma

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Supplemental Table 1: Efficacy Outcomes in the USPI Population

Outcome	QW (n=100)	Q2W (n=90)	Prior TCR QW and Q2W[a] (n=58)
ORR, %	73.0	71.1	72.4
≥CR	35.0	43.3	50.0
VGPR	22.0	17.8	8.6
PR	16.0	10.0	13.8
Median time to best response of ≥CR,[b] mo (range)	2.27 (1.1–12.7)	6.24 (1.2–16.8)	2.66 (1.2–17.5)
Median time to best response of VGPR,[c] mo (range)	1.97 (1.1–6.2)	3.06 (0.3–18.9)	2.04 (1.2–2.1)
Median time to best response of PR,[d] mo (range)	1.28 (1.1–2.9)	2.07 (1.2–2.8)	1.13 (1.1–3.0)
Median DOR, mo (95% CI)[e]	10.2 (6.6–15.7)	17.9 (12.5–26.0)	19.2 (6.7–NE)
≥CR[b]	28.8 (18.9–NE)	26.1 (18.0–NE)	24.7 (19.2–NE)
VGPR[c]	6.4 (4.4–9.5)	9.3 (7.4–15.2)	4.8 (2.1–NE)
PR[d]	3.0 (1.9–5.6)	5.5 (0.9–6.5)	2.4 (1.9–4.6)
Median PFS (95% CI), mo	6.8 (5.5–10.4)	12.4 (9.6–18.2)	11.3 (4.8–21.4)
36-mo PFS, %	17.6 (10.7–26.0)	NE (NE–NE)	28.2 (16.0–41.7)
Median OS (95% CI), mo	NR (21.7–NE)	NR (33.2–NE)	30.6 (20.2–NE)
36-mo OS, %	50.5 (40.0–60.0)	NE (NE–NE)	46.4 (29.2–61.9)

Data are reported from phase 2 only.
[a]Phase 2 data include the 0.4 mg/kg QW cohort only. [b]n=35 (QW), n=39 (Q2W), n=29 (prior TCR QW and Q2W). [c]n=22 (QW), n=16 (Q2W), n=5 (prior TCR QW and Q2W). [d]n=16 (QW), n=9 (Q2W), n=8 (prior TCR). [e]n=73 (QW), n=64 (Q2W), n=42 (prior TCR QW and Q2W).
CR, complete response; DOR, duration of response; NE, not estimable; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; Q2W, every other week; QW, weekly; TCR, T-cell redirection therapy; USPI, US prescribing information; VGPR, very good partial response.

Supplemental Table 2: Hematologic and Nonhematologic AEs

AE (≥30% in any cohort), n (%)	QW (n=143)		Q2W (n=154)		Prior TCR QW and Q2W (n=78)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic AE						
Anemia	65 (45.5)	46 (32.2)	67 (43.5)	39 (25.3)	38 (48.7)	22 (28.2)
Neutropenia	50 (35.0)	44 (30.8)	44 (28.6)	33 (21.4)	40 (51.3)	37 (47.4)
Thrombocytopenia	39 (27.3)	29 (20.3)	46 (29.9)	28 (18.2)	30 (38.5)	22 (28.2)
Nonhematologic AE						
CRS	113 (79.0)	3 (2.1)	116 (75.3)	1 (0.6)	57 (73.1)	1 (1.3)
Dysgeusia[a]	103 (72.0)	NA	111 (72.1)	NA	59 (75.6)	NA
Infections[b]	87 (60.8)	33 (23.1)	109 (70.8)	33 (21.4)	61 (78.2)	20 (25.6)
Skin related[c]	85 (59.4)	0	113 (73.4)	1 (0.6)	53 (67.9)	0
Nail related[d]	80 (55.9)	0	84 (54.5)	0	47 (60.3)	0
Weight decreased	59 (41.3)	3 (2.1)	64 (41.6)	9 (5.8)	29 (37.2)	1 (1.3)
Rash related[e]	57 (39.9)	2 (1.4)	48 (31.2)	8 (5.2)	25 (32.1)	2 (2.6)
Pyrexia	57 (39.9)	4 (2.8)	44 (28.6)	2 (1.3)	27 (34.6)	0
Dry mouth	38 (26.6)	0	60 (39.0)	0	34 (43.6)	0
Fatigue	36 (25.2)	5 (3.5)	44 (28.6)	1 (0.6)	25 (32.1)	1 (1.3)

[a]Including ageusia, dysgeusia, hypogeusia, and taste disorder. Per CTCAE, the maximum possible grade of dysgeusia is 2. [b]Infections are reported as a System Organ Class. [c]Including skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [d]Including nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [e]Including rash, maculopapular rash, erythematous rash, and erythema.
AE, adverse event; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; NA, not applicable; Q2W, every other week; QW, weekly, TCR, T-cell redirection therapy.