

Clinical Features and Management of GPRC5D-Related AEs in Chinese Relapsed/Refractory Multiple Myeloma Patients Treated With Talquetamab: MonumenTAL-1 China Cohort Experience

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Key Takeaway



Management of GPRC5D-related AEs may enable prolonged time on talquetamab, allowing pts to experience the full benefit of treatment

Conclusions



Talquetamab produced deep responses in Chinese pts with heavily pretreated RRMM



GPRC5D-related AEs were predominantly mild in severity and manageable, and did not lead to dose modification



Clinical features of GPRC5D-related AEs were similar to those observed in the global cohort



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Introduction

- Talquetamab is a first-in-class bispecific antibody targeting the novel antigen G protein-coupled receptor class C group 5 member D (GPRC5D),^{1,2} and is the only approved agent of its kind³
- Talquetamab is approved globally, including in the US, EU, and China, to treat patients (pts) with relapsed/refractory multiple myeloma (RRMM), based on the global phase 1 (NCT03399799)/ 2 (NCT04634552) MonumenTAL-1 study^{2,4-6}
 - Overall response rates (ORRs) of 67% to 74% were reported²
 - GPRC5D-related "on-target, off-tumor" adverse events (AEs) were observed, including oral (dysgeusia, dry mouth), skin (rash, non-rash), and nail toxicities⁷
 - Early onset of GPRC5D-related AEs, including dysgeusia, is associated with a higher likelihood of response to talquetamab; prior data support flexible dosing in responders to mitigate AEs while maintaining efficacy^{2,8}
- In the China cohort, efficacy and safety data were generally consistent with the global cohort; however, rates of taste-related events were lower, at 25.0% to 41.1% versus 71.0% to 72.0%^{8,9}
- Here, we report a post-hoc analysis of the clinical management of GPRC5D-related AEs in the China cohort of MonumenTAL-1

Results

Baseline characteristics

- The baseline characteristics of pts in the QW and Q2W China cohorts are presented in Table 1

Table 1: Baseline characteristics

Characteristic	0.4 mg/kg QW (n=29)	0.8 mg/kg Q2W (n=12)
Age, mean±SD, years	62.1±9.2	61.2±9.7
Male, n (%)	21 (72.4)	3 (25.0)
ECOG PS, n (%)		
0	17 (58.6)	7 (58.3)
1	10 (34.5)	3 (25.0)
2	2 (6.9)	2 (16.7)
Time from diagnosis to 1st dose, years, median (range)	3.7 (0.9-11.2)	3.5 (1.5-11.9)
ISS stage, ^a n (%)		
I	15 (51.7)	7 (58.3)
II	12 (41.4)	4 (33.3)
III	2 (6.9)	1 (8.3)
Prior LOTs, median (range)	4 (3-9)	4 (3-5)
Refractory status, n (%)		
Triple-class ^b	15 (51.7)	6 (50.0)
Penta-drug ^c	3 (10.3)	2 (16.7)

^aISS staging was derived based on serum β_2 -microglobulin and albumin. ^b≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb. ^c≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb. IMiD, immunomodulatory drug; ISS, International Staging System; LOT, line of therapy; mAb, monoclonal antibody; PI, protease inhibitor; QW, once per week; Q2W, every other week; SD, standard deviation.

Updated efficacy summary

- Treatment efficacy was similar between the 2 cohorts (Figure 2, Table 2)

GPRC5D-related AEs

- GPRC5D-related oral AEs included dysgeusia and dry mouth; all were grade 1 or 2 (Table 3) and none required talquetamab dose modification
- Median time to onset (TTO) of dysgeusia was 15 to 17 days, with a median duration of 160 to 231 days across the 2 cohorts
 - 2 pts (both in the QW cohort) reported concurrent decreased appetite, and 4 reported a ≥10% weight decrease
 - Dysgeusia resolved by data cutoff in 58.3% (QW) and 50.0% (Q2W) of events; the case of dry mouth also resolved
 - 4 pts with dysgeusia required concomitant medications (Table 4)
- GPRC5D-related skin AEs included rash and non-rash skin toxicity; none required talquetamab dose modification
- Rash: grade ≥3 events were reported for 1 pt (QW cohort) (Table 3)
 - Median TTO (all grades) was 9 to 25 days, with a median duration of 17 to 23 days across the 2 cohorts
- Non-rash skin toxicity included skin exfoliation, dry skin, and pruritus; grade ≥3 events occurred in 1 pt (QW cohort)
 - Median TTO (all grades): 19 to 62 days; median duration: 28 to 40 days (Table 3)
 - Supportive care was required for 11 (QW) and 2 (Q2W) pts (Table 4)
- Nail disorders occurred in 4 pts in each cohort (13.8% [QW] and 33.3% [Q2W]) and all at grade 1 to 2; none led to dose modification, and 1 (3.4%) pt (QW cohort) received treatment (paraffin and vitamin E) (Table 3, Table 4)

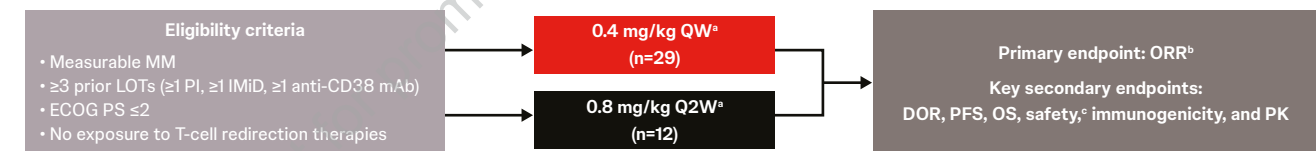
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Methods

- MonumenTAL-1 is a first-in-human, phase 1/2, open-label, multicenter study of talquetamab monotherapy in pts with RRMM
 - 2 recommended phase 2 doses were identified in phase 1: 2 subcutaneous 0.4 mg/kg weekly (QW cohort) and 0.8 mg/kg every other week (Q2W cohort)
- Chinese pts enrolled in phase 2 (February 2022 to September 2023) received either the QW or Q2W dosing regimen (Figure 1)
- The aim of this post-hoc analysis was to assess GPRC5D-related AEs, including oral, skin, and nail toxicities (data cutoffs: February 29, 2024, and August 26, 2024, for the QW and Q2W cohorts, respectively)

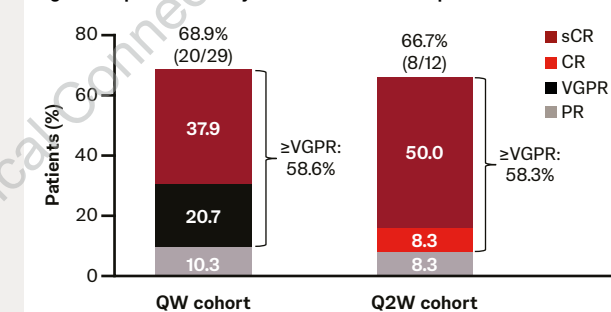
Figure 1: MonumenTAL-1 China cohort study design



^aWith 2-3 step-up doses. ^bAssessed by independent review committee using International Myeloma Working Group criteria.^{4,4} CRs and ICANS were graded by ASTCT criteria;⁵ all other AEs were graded by CTCAE v4.03. AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; CR, complete response; 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; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; QW, once per week; Q2W, every other week.

Efficacy summary

Figure 2: Updated efficacy outcomes – tumor response^a



^aDue to rounding, individual response rates may not sum to the ORR. CR, complete response; ORR, objective response rate; PR, partial response; QW, once per week; Q2W, every other week; sCR, stringent complete response; VGPR, very good partial response.

Table 3: Summary of GPRC5D-related TEAEs and their outcomes

TEAEs	0.4 mg/kg QW (n=29)	0.8 mg/kg Q2W (n=12)
Dysgeusia, n (%)		
Any grade, n (%) ^a	12 (41.4)	3 (25.0)
TTO, median (range), days	15 (6-64)	17 (5-73)
Duration, median (range), days	231 (93-417)	160 (47-263)
Resolved, n/N events (%)	7/12 (58.3)	2/4 (50.0)
Dry mouth		
Any grade, n (%) ^a	0	1 (8.3)
TTO, days	–	CI D15
Duration, days	–	163
Resolved, n/N events (%)	–	1/1 (100)
Rash		
Any grade, n (%) ^a	11 (37.9)	3 (25.0)
TTO, median (range), days	25 (11-247)	9 (2-173)
Duration, median (range), days	17 (1-202)	23 (1-49)
Resolved, n/N events (%)	11/14 (78.6)	3/3 (100)
Non-rash skin toxicity		
Any grade, n (%) ^a	15 (51.7)	5 (41.7)
TTO, median (range), days	62 (14-496)	19 (14-313)
Duration, median (range), days	40 (1-129)	28 (18-144)
Resolved, n/N events (%)	17/25 (68.0)	5/5 (100)
Nail disorder		
Any grade, n (%) ^a	4 (13.8)	4 (33.3)
TTO, median (range), days	46 (17-154)	39 (35-78)
Duration, median (range), days	223 (65-381)	301 (117-310)
Resolved, n/N events (%)	2/4 (50.0)	3/4 (75.0)

^aAll events were grade 1 or 2. ¹1 pt (QW cohort) experienced grade 3 events. GPRC5D, G-protein-coupled receptor class C group 5 member D; n/N, number of events that resolved/total number of events; QW, once per week; Q2W, every other week; TEAE, treatment-emergent adverse event; TTO, time to onset.

Table 2: Updated efficacy outcomes – survival

Outcome	0.4 mg/kg QW (n=29)	0.8 mg/kg Q2W (n=12)
mFU, months	16.3	13.9
mDOR (95% CI), ^a months	15.7 (5.7-NE)	NR (2.8-NE)
9-month DOR rate, % (95% CI)	60.0 (35.7-77.6)	87.5 (38.7-98.1)
mPFS (95% CI), months	8.3 (6.3-NE)	10.7 (2.3-NE)
9-month PFS rate, % (95% CI)	48.9 (28.6-66.4)	63.6 (29.7-84.5)
mOS (95% CI), months	NR (14.5-NE)	NR (9.7-NE)
12-month OS rate, % (95% CI)	82.2 (62.4-92.2)	81.8 (44.7-95.1)

^an=20 for the QW cohort and n=8 for the Q2W cohort. (m)DOR, (median) duration of response; mFU, median follow-up; (m)PFS, (median) progression-free survival; (m)OS, (median) overall survival; NE, not estimable; NR, not reached; QW, once per week; Q2W, every other week.

Table 4: Most common supportive measures and concomitant treatments for GPRC5D-related TEAEs

TEAEs	0.4 mg/kg QW (n=29)	0.8 mg/kg Q2W (n=12)
Dysgeusia, n (%) ^a		
No. of pts with concomitant medications (≥1 pt in either cohort) ^b	3 (10.3)	1 (8.3)
Dexamethasone acetate	0	1 (8.3)
Olanzapine	0	1 (8.3)
Prednisone	1 (3.4)	0
Riboflavin	1 (3.4)	0
Unspecified herbal	1 (3.4)	0
Dry mouth, n (%)		
No. of pts with concomitant medications	0	0
Rash, n (%) ^a		
No. of pts with concomitant medications (≥1 pt in either cohort) ^b	10 (34.5)	3 (25.0)
Oral ^b	8 (27.6)	2 (16.7)
Topical	4 (13.8)	1 (8.3)
Transdermal	1 (3.4)	0
Intramuscular	0	1 (8.3)
Intravenous	0	1 (8.3)
Other	2 (6.9)	1 (8.3)
Non-rash skin toxicity, n (%) ^a		
No. of pts with concomitant medications (≥2 pts in either cohort) ^b	11 (37.9)	2 (16.7)
Oral ^b	9 (31.0)	1 (8.3)
Topical	5 (17.2)	0
Transdermal	3 (10.3)	1 (8.3)
Nail disorders, n (%) ^a		
No. of pts with concomitant medications (≥1 pt in either cohort) ^b	1 (3.4)	0
Paraffin	1 (3.4)	0
Vitamin E NOS	1 (3.4)	0

^aPercentages calculated with the number of pts in the all-treated analysis set as the denominator. ^bPatients could appear in more than 1 category. GPRC5D, G-protein-coupled receptor class C group 5 member D; NOS, not otherwise specified; pt, patient; QW, once per week; Q2W, every other week; TEAE, treatment-emergent adverse event.

Multiple Myeloma

