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Efficacy and Safety of Talquetamab in Chinese Patients With Relapsed/Refractory Multiple Myeloma From the Phase 1/2 MonumenTAL-1 Study

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Key Takeaway

In Chinese patients with RRMM, talquetamab led to rapid and deep responses, with low rates of discontinuation due to AEs, none of which were due to on-target, off-tumor AEs. These results were generally consistent with the global MonumenTAL-1 population

Conclusions

Talquetamab showed ORRs of ≥67% and VGPR or better rates of ≥58% across the 0.4 mg/kg QW and 0.8 mg/kg Q2W China cohorts

PK data were consistent with results from the global MonumenTAL-1 population, supporting selection of the 2 RP2Ds

Talquetamab represents an important new treatment option in China

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Disclosures
JJ has no conflicts of interest to disclose.

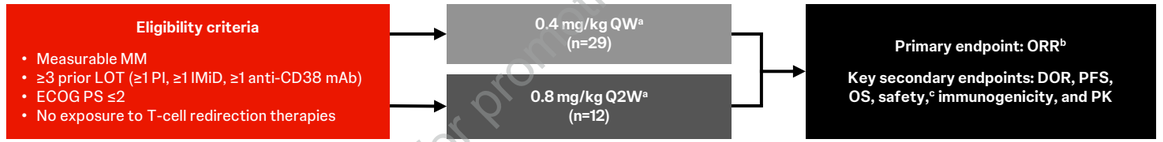
Introduction

- Talquetamab is the first approved bispecific antibody targeting the novel antigen G protein–coupled receptor class C group 5 member D (GPRC5D) in the US and EU for the treatment of patients with relapsed/refractory multiple myeloma (RRMM)[1-3]
- Approval was based on data from the MonumenTAL-1 study demonstrating high overall response rates (ORRs) at the recommended phase 2 doses (RP2Ds) of talquetamab in patients with RRMM[1-4]
  - ORRs were >71% in patients naïve to prior T-cell redirection therapy (in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts)[4]
  - ORR was 65% in patients with prior T-cell redirection therapy (receiving either dosing schedule)[4]
- Patients from China were not included in the previously reported MonumenTAL-1 study results
- Here, we report the first analysis of the efficacy and safety of talquetamab in the China cohorts from phase 2 of the MonumenTAL-1 study

Methods

- MonumenTAL-1 is a first-in-human, phase 1/2, open-label, multicenter study of talquetamab monotherapy in patients with RRMM
  - Phase 1 identified 2 RP2Ds, subcutaneous 0.4 mg/kg weekly (QW) and 0.8 mg/kg every other week (Q2W), which were further assessed in phase 2
- Chinese patients were enrolled in phase 2 (Feb 2022–Feb 2023) China cohorts and received the 2 RP2Ds (**Figure 1**)

Figure 1: MonumenTAL-1 China cohort study design



[a]With 2–3 step-up doses. [b]Assessed by independent review committee using International Myeloma Working Group criteria.[5,6] [c]CRS and ICANS were graded by ASTCT criteria[7]; all other AEs were graded by CTCAE v4.03.
AE, adverse event; ASTCT; American Society for Transplantation and Cellular Therapy; 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; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics.

Results

Baseline characteristics

- Baseline characteristics of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts are shown in **Table 1**

Table 1: Baseline characteristics

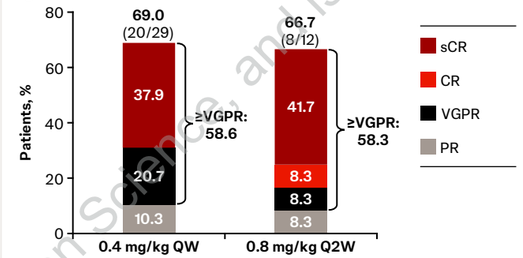
Characteristic	0.4 mg/kg QW (n=29)	0.8 mg/kg Q2W (n=12)
Age, median (range), years	63.0 (44–78)	60.0 (45–74)
Male, n (%)	21 (72.4)	3 (25.0)
Bone marrow plasma cells ≥60%,[a] n (%)	2 (6.9)	3 (25.0)
Extramedullary plasmacytomas ≥1, n (%)	6 (20.7)	1 (8.3)
High-risk cytogenetics,[b] n (%)	10 (37.0)	3 (30.0)
ISS stage,[c] n (%)		
I	15 (51.7)	7 (58.3)
II	12 (41.4)	4 (33.3)
III	2 (6.9)	1 (8.3)
Prior LOT, median (range)	4 (3–9)	4 (3–5)
Exposure status, n (%)		
Triple-class[d]	29 (100.0)	12 (100.0)
Penta-drug[e]	11 (37.9)	5 (41.7)
Refractory status, n (%)		
Triple-class[d]	15 (51.7)	6 (50.0)
Penta-drug[e]	3 (10.3)	2 (16.7)
To last LOT	27 (93.1)	12 (100.0)

[a]Maximum value from bone marrow biopsy or bone marrow aspirate is selected if both the results are available. [b]Defined as del(17p), t(4;14), and/or t(14;16); % calculated from n=27 for the QW cohort and n=10 for the Q2W cohort. [c]ISS staging is derived based on serum β_2-microglobulin and albumin. [d]≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb. [e]≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb. ISS, International Staging System.

Efficacy

- As of February 29, 2024, ORRs were 69.0% and 66.7% in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively (**Figure 2**)
- Median time to first response was 1.3 months in both cohorts
- ORRs were consistent among clinically relevant subgroups – including cytogenetic risk profile, ISS stage, and number of prior LOT – but were lower in patients with vs without extramedullary disease, as seen in the global MonumenTAL-1 population[4]
- Responses were durable, with comparable 6-month DOR in each cohort; PFS at 6 months was also comparable between cohorts (**Table 2**)

Figure 2: ORR[a]



[a]Due to rounding, individual response rates may not sum to the ORR.
CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Table 2: Efficacy outcomes

Outcome	0.4 mg/kg QW (n=29)	0.8 mg/kg Q2W (n=12)
mFU, mo	16.7	9.4
mDOR (95% CI),[a] mo	15.7 (5.7–NE)	NR (2.8–NE)[b]
6-mo DOR rate, %	70.0 (45.1–85.3)	85.7 (33.4–97.9)
9-mo DOR rate, %	60.0 (35.7–77.6)	Not mature[b]
mPFS (95% CI), mo	8.3 (6.3–NE)	NR (2.3–NE)[b]
6-mo PFS rate, %	73.3 (52.0–86.3)	61.4 (26.6–83.5)
9-mo PFS rate, %	48.9 (28.6–66.4)	Not mature[b]

[a]n=20 for the QW cohort and n=8 for the Q2W cohort. [b]Data are still maturing. mDOR, median duration of response; mFU, median follow-up; mPFS, median progression-free survival; NE, not estimable; NR, not reached.

Safety overview

- CRS was the most common AE, and hematologic AEs were the most common grade 3/4 AEs (**Table 3**)
- ICANS occurred in 1 patient (0.4 mg/kg QW cohort; grade 5)
- AEs led to treatment discontinuation in 3.4% and 16.7% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively
- AEs resulted in 2 deaths in the 0.4 mg/kg QW cohort and no deaths in the 0.8 mg/kg Q2W cohort

CRS

- CRS was generally grade 1 (62.1% and 75.0%) or 2 (20.7% and 8.3%) in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively, and occurred during step-up and first treatment doses
- Median time to CRS onset and duration were each 2 days in both the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts
- Recurrent CRS events occurred in 62.1% (17/18 grade 1/2) and 58.3% (all grade 1/2) of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively; recurrent CRS events primarily occurred with step-up and cycle 1 doses
- No patients discontinued treatment due to CRS, and all but 1 CRS event resolved

Infections

- COVID-19 and pneumonia were the most common infections in both cohorts, reflecting the impact of the pandemic

On-target, off-tumor GPRC5D AEs

- AEs related to taste, skin (non-rash and rash), and nails were mainly grade 1/2 (**Table 3**), and none resulted in discontinuation
- Taste-related events were lower in the China cohorts (25.0–41.1%) compared with the global MonumenTAL-1 cohorts (71.0–72.0%)[4]

PK

- Mean talquetamab concentrations throughout treatment were maintained at or above the target maximal concentration associated with 90% maximal drug effect identified from an ex vivo cytotoxicity assay

Table 3: Hematologic and nonhematologic AEs

AEs (≥30% in any cohort), n (%)	0.4 mg/kg QW (n=29)		0.8 mg/kg Q2W (n=12)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic AEs				
Anemia	22 (75.9)	8 (27.6)	8 (66.7)	3 (25.0)
Neutropenia	21 (72.4)	9 (31.0)	8 (66.7)	2 (16.7)
Thrombocytopenia	9 (31.0)	5 (17.2)	4 (33.3)	1 (8.3)
Nonhematologic AEs				
CRS	26 (89.7)	2 (6.9)	10 (83.3)	0
Infections[a]	23 (79.3)	15 (51.7)	5 (41.7)	2 (16.7)
Pyrexia	19 (65.5)	0	4 (33.3)	0
Weight decreased	15 (51.7)	0	6 (50.0)	0
Skin related[b]	15 (51.7)	1 (3.4)	5 (41.7)	0
Hypokalemia	11 (37.9)	4 (13.8)	6 (50.0)	1 (8.3)
Taste related[c]	12 (41.4)	NA	3 (25.0)	NA
Cough	11 (37.9)	0	3 (25.0)	0
Hypocalcemia	11 (37.9)	1 (3.4)	3 (25.0)	0
Rash related[d]	11 (37.9)	1 (3.4)	3 (25.0)	0
Decreased appetite	8 (27.6)	0	4 (33.3)	0
Insomnia	9 (31.0)	0	2 (16.7)	0
Constipation	9 (31.0)	0	0	0
Diarrhea	9 (31.0)	0	0	0
Nail related[e]	4 (13.8)	0	5 (41.7)	0
Increased C-reactive protein	0	0	4 (33.3)	0

AEs are listed in descending order per incidence in the total study population. [a]Infections are reported at the system organ class level. [b]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Includes ageusia, dysgeusia, hypogeusia, and taste disorder; per CTCAE, the maximum possible grade of dysgeusia is 2. [d]Includes rash, maculopapular rash, erythematous rash, and erythema. [e]Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. NA, not applicable.

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Multiple Myeloma