PS1766

Real-world analysis of talquetamab in heavily pretreated and high-risk patients with relapsed/refractory multiple myeloma

Tala Shekarkhand[1], David Nemirovsky[2], Andriy Derkach[2], Kylee Maclachlan[1], Malin Hultcrantz[1], Hani Hassoun[1], Sham Mailankody[1], Urvi Shah[1], Sridevi Rajeeve[1], Hamza Hashmi[1], Gunjan Shah[3], Michael Scordo[3], Heather J Landau[3], Sergio A Giralt[3], Alexander Lesokhin[1], Neha Korde[1], Saad Z Usmani[1], Yi-Hsuan Liu[4], Elissa E Min[4,5], Xinke Zhang[4], Saurabh Patel[4], Carlyn Rose Tan[1]

[1]Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Department of Biostatistics and Epidemiology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Adult Bone Marrow Transplant Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]Johnson & Johnson, Horsham, PA, USA; [5]Purdue University College of Pharmacy, West Lafayette, IN, USA

Key Takeaway

Our study demonstrated that patients treated with talquetamab achieved an ORR of 57% and a median PFS of 6.8 months, despite high proportions of patients with aggressive disease biology and prior exposure to BCMA-DT

Conclusions

- In this retrospective study of patients with RRMM, patients were more heavily pretreated than those of the MonumenTAL-1 study, with 66% of patients having received prior BCMA-DT and 88% having aggressive disease biology (≥1 HRCA, extramedullary disease, and/or circulating plasma cells)
- Despite the heavily pretreated nature of the patient population, talquetamab achieved an ORR of 57% and a median PFS of 6.8 months
- No significant difference in PFS was observed based on prior BCMA-DT exposure, although receiving a BCMA-targeting BsAb as the most recent BCMA-DT prior to talquetamab may impact PFS

Please scan QR code

Poster

https://www.congresshub.com/EHA2025/Oncology/Talquetamab/Tan

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Acknowledgments

This study was sponsored by Johnson & Johnson. Medical writing and editorial support were provided by Jessica A Weaver, PhD, of Lumanity Communications Inc., and funded by Johnson & Johnson.

Disclosures

CRT served in an advisory role for Johnson & Johnson and Sanofi; and served on a steering committee for Johnson & Johnson.

Introduction

- Talquetamab is the first GPRC5D×CD3-directed T-cell bispecific antibody (BsAb) approved in the United States for patients with relapsed/refractory multiple myeloma (RRMM) who have received ≥4 prior lines of therapy (LOTs) and are triple-class exposed, which is defined as exposure to a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 monoclonal antibody[1]
- The phase 1/2 MonumenTAL-1 study (ClinicalTrials.gov Identifiers: NCT03399799/NCT04634552) demonstrated the safety and efficacy of talquetamab in heavily pretreated patients with RRMM[1-3]
  - High overall response rates (ORRs) of 74%, 70%, and 67% were demonstrated for patients in the 0.4 mg/kg weekly (QW) dosing, 0.8 mg/kg biweekly (Q2W) dosing, and prior T-cell–redirecting therapy cohorts, respectively, with both 0.4 mg/kg QW and 0.8 mg/kg Q2W dosing used for the prior T-cell–redirecting therapy cohort[3]
    - Additionally, within the prior T-cell–redirecting therapy cohort, the ORR was 71% for patients who had previously undergone chimeric antigen receptor T-cell (CAR-T) therapy and 58% for patients who had undergone prior BsAb therapy[3]
  - The median progression-free survival (PFS) was 7.5, 11.2, and 7.7 months for the QW, Q2W, and prior T-cell–redirecting therapy cohorts, respectively[3]
    - Within the prior T-cell–redirecting therapy cohort, patients with prior CAR-T therapy had a median PFS of 12.3 months, whereas those with prior BsAb treatment had a median PFS of 4.1 months[3]
- While these results highlight the efficacy of talquetamab in achieving encouraging response rates and PFS in heavily pretreated patients with RRMM, including those with prior exposure to T-cell–redirecting therapies, real-world data on characteristics and outcomes of this patient population are limited[4,5]
- The objective of this retrospective, observational study was to examine real-world characteristics and outcomes of patients with RRMM who were treated with talquetamab

Methods

Study design

- In this real-world, retrospective, observational study, patients in the United States with RRMM who were treated with talquetamab therapy at Memorial Sloan Kettering Cancer Center between August 1, 2023, and March 1, 2025, were identified from patient charts
  - The index date was defined as the date of the first talquetamab dose
  - Data were aggregated and de-identified at the patient level
- The cutoff date of the analysis was April 1, 2025

Study population

- Adult patients ≥18 years of age with a confirmed diagnosis of RRMM who had completed commercial talquetamab step-up dosing with ≥1 month of follow-up were included

Study outcomes

- Patient baseline clinical characteristics and prior LOTs were directly extracted from patient charts; in instances where the number of prior LOTs was not available, this information was determined using published guidelines[6]
- Clinical outcomes were assessed from the index date to the data cutoff date
  - Patient responses were evaluated using the International Myeloma Working Group uniform response criteria
  - Time-to-event outcomes included PFS and overall survival (OS)

Statistical analysis

- All study variables were summarized descriptively, with means, standard deviations, medians, and interquartile ranges (IQRs) reported for continuous variables and numbers and percentages reported for categorical variables
- Time-to-event outcomes were analyzed using the Kaplan–Meier method

Results

Patient characteristics

- Overall, 59 patients completed talquetamab step-up dosing with a follow-up period of ≥1 month
- Patient characteristics at baseline are summarized in **Table 1**
  - The median (IQR) age was 66 (61–72) years
  - 30 of 59 (51%) patients were male; 11 of 57 (19%) patients were Black or African American; 24 of 51 (47%) patients had extramedullary disease within 3 months prior to initiating talquetamab therapy; 31 of 36 (86%) patients had high-risk cytogenetic abnormalities (HRCAs) prior to initiating talquetamab therapy, including 18 of 36 (50%) patients with ≥2 HRCAs; and 6 of 59 (10%) patients had circulating plasma cells
  - The median (IQR) number of prior LOTs before the index date was 7 (5–9)
- 39 (66%) patients had received prior B-cell maturation antigen–directed therapy (BCMA-DT; **Table 1**); this included 19 (49%) patients who had received CAR-T, 17 (44%) patients who had received BsAb, 1 (3%) patient who had received an antibody-drug conjugate, 15 (38%) patients who had received ≥2 BCMA-DT agents, and 2 (5%) patients who had received an unknown BCMA-DT agent
  - 22 (37%) patients had received BCMA-DT as the last LOT immediately prior to talquetamab, and 14 of these patients were primary refractory to T-cell–redirecting therapies
  - The median (IQR) time from last BCMA-DT to initiation of talquetamab was 4 (1–10) months; specifically, the median (IQR) time from last BCMA-targeting BsAb was 1 (0–6) month
- 7 (12%) patients received other prior T-cell–redirecting therapies (1 patient received GPRC5D-targeted therapy and 6 patients received Fc receptor-homolog 5 [FcRH5]–targeted therapy)

Table 1: Patient characteristics

Characteristic	Patients with RRMM (N=59)
Age at index, years	
Median (IQR)	66 (61–72)
Sex, n (%)	
Male	30 (51)
Female	29 (49)
Race, n/N (%)[a]	
White	39/57 (68)
Black or African American	11/57 (19)
Asian	5/57 (9)
Other	2/57 (4)
ECOG PS score, n/N (%)[a]	
0	7/38 (18)
1	26/38 (68)
2	5/38 (13)
Cytogenetic risk prior to initiating talquetamab therapy, n/N (%)[a]	
High[b]	31/36 (86)
Standard	5/36 (14)
ISS disease stage, n/N (%)[a]	
1	19/43 (44)
2	12/43 (28)
3	12/43 (28)
EMD,[c] n/N (%)[a]	
Yes	24/51 (47)
Circulating plasma cells, n (%)	
Present	6 (10)
Number of prior LOTs	
Median (IQR)	7 (5–9)
2–4, n (%)	13 (22)
5–7, n (%)	25 (42)
≥8, n (%)	21 (36)
Triple-class refractory,[d] n (%)	51 (86)
Penta-drug refractory,[e] n (%)	21 (36)
Prior BCMA-DT, n (%)	39 (66)
BCMA-DT as the last LOT immediately prior to talquetamab	22 (37)
Primary refractory to T-cell–redirecting therapies	14 (24)
Median (IQR) time from last BCMA-DT to talquetamab initiation, months	4 (1–10)
CAR-T (n=19)	9 (2–15)
BsAb (n=17)	1 (0–6)

RRMM, relapsed/refractory multiple myeloma; IQR, interquartile range; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; EMD, extramedullary disease; LOT, line of therapy; BCMA-DT, B-cell maturation antigen–directed therapy; CAR-T, chimeric antigen receptor T cell; BsAb, bispecific antibody; PI, proteasome inhibitor; IMiD, immunomodulatory drug; mAb, monoclonal antibody.
[a]Patients with available data were included in the denominator.
[b]High risk includes 1q+, t(4;14), t(14;16), t(14;20), and/or del(17p) or monosomy 17.
[c]EMD within 3 months of talquetamab start.
[d]Refractory to ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb therapy.
[e]Refractory to ≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb therapy.

- The majority of patients (n=52 [88%]) would not have met the eligibility criteria for the MonumenTAL-1 trial, with cytopenias being the most common reason for study ineligibility
- 38 (64%) patients initiated treatment with talquetamab at a dose of 0.8 mg/kg Q2W

Efficacy

- At a median follow-up of 13 months (95% confidence interval [CI], 9.4–16.0), the ORR was 57% among 56 response-evaluable patients (**Table 2**)
  - Notably, 23 of 56 (41%) patients achieved a very good partial response or better
- Among the 32 patients who responded to talquetamab, the 6-month rate for duration of response was 72% (95% CI, 56%–92%)

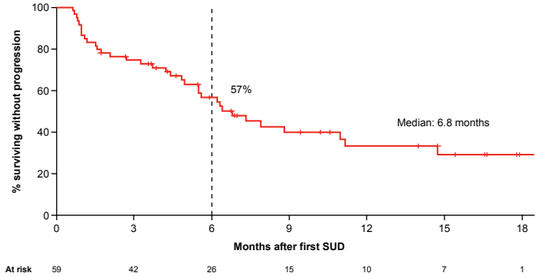
Table 2: Response rates

Response category	Patients with RRMM (N=59)
Best response, n (%)	
CR	5 (9)
VGPR	18 (31)
PR	9 (15)
MR	2 (3)
SD	11 (19)
POD	11 (19)
Not evaluable	3 (5)
ORR, n/N (%)	32/56 (57)
Unknown, n	3

RRMM, relapsed/refractory multiple myeloma; CR, complete response; VGPR, very good partial response; PR, partial response; MR, minimal response; SD, stable disease; POD, progression of disease; ORR, overall response rate.

- The median PFS was 6.8 months (95% CI, 5.5–15.0), with a 6-month PFS rate of 57% (95% CI, 45%–72%; **Figure 1**)

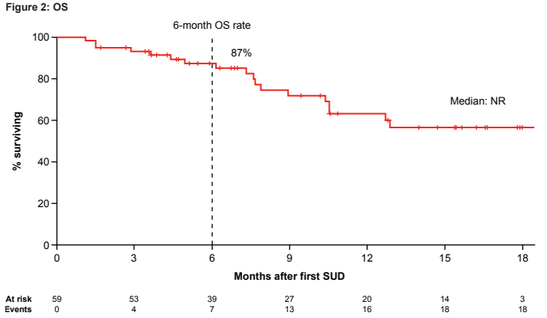
Figure 1: PFS



PFS, progression-free survival; SUD, step-up dosing.

- The median OS was not reached (95% CI, 11 months–not reached), with a 6-month OS rate of 87% (95% CI, 79%–97%; **Figure 2**)

Figure 2: OS

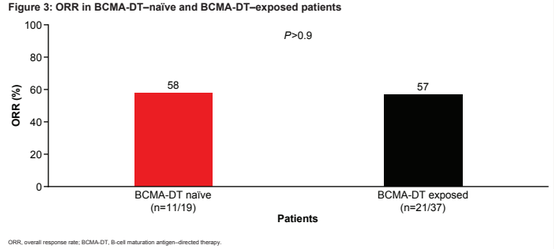


OS, overall survival; NR, not reached; SUD, step-up dosing.

Response rates and PFS in BCMA-DT–naïve and BCMA-DT–exposed patients

- In a subgroup analysis, the ORR was 58% for response-evaluable BCMA-DT–naïve patients and 57% for BCMA-DT–exposed patients (*P*>0.9; **Figure 3**)

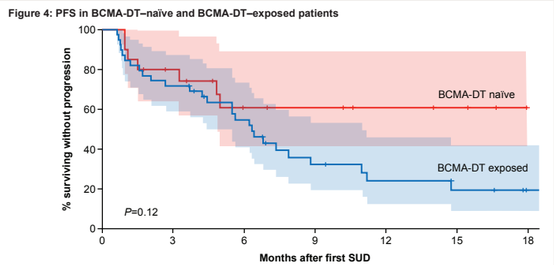
Figure 3: ORR in BCMA-DT–naïve and BCMA-DT–exposed patients



ORR, overall response rate; BCMA-DT, B-cell maturation antigen–directed therapy.

- There was no statistically significant difference in the 6-month PFS rate between patients with prior BCMA-DT (55% [95% CI, 41%–73%]) and BCMA-DT–naive patients (61% [95% CI, 41%–89%]; *P*=0.12; **Figure 4**)

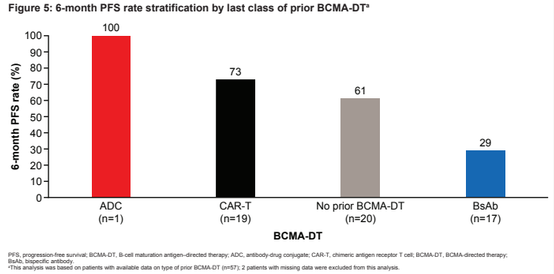
Figure 4: PFS in BCMA-DT–naïve and BCMA-DT–exposed patients



PFS, progression-free survival; BCMA-DT, B-cell maturation antigen–directed therapy; SUD, step-up dosing.

- When stratified by the last class of prior BCMA-DT, the 6-month PFS rate was 100% (95% CI, 100%–100%) for antibody-drug conjugates (n=1), 73% (95% CI, 55%–96%) for CAR-T therapy (n=19), 29% (95% CI, 14%–61%) for BsAb therapy (n=17), and 61% (95% CI, 41%–89%) for patients with no prior BCMA-DT (n=20; *P*=0.003; **Figure 5**)

Figure 5: 6-month PFS rate stratification by last class of prior BCMA-DT[a]



PFS, progression-free survival; BCMA-DT, B-cell maturation antigen–directed therapy; ADC, antibody-drug conjugate; CAR-T, chimeric antigen receptor T cell; BCMA-DT, BCMA-directed therapy; BsAb, bispecific antibody.
[a]This analysis was based on patients with available data on type of prior BCMA-DT (n=57); 2 patients with missing data were excluded from this analysis.

References

1. TALVEY™ (talquetamab-tgvs) [package insert]. Janssen Biotech, Inc.; 2023. 2. Chari A, et al. *N Engl J Med*. 2022;387(24):2232–2244. 3. Rasche L, et al. Presented at: European Hematology Association (EHA) Congress; June 13–16, 2024; Madrid, Spain. 4. Schinke C, et al. *Curr Med Res Opin*. 2024;40(10):1705–1711. 5. Chari A, et al. *Clin Lymphoma Myeloma Leuk*. 2024;24(10):665–693.e14. 6. Sweeney NW, et al. *JCO Clin Cancer Inform*. 2022;6:e2100141.

Multiple Myeloma

Presented by CR Tan at the 30th European Hematology Association (EHA) Congress; June 12–15, 2025; Milan, Italy