Outpatient step-up dosing and safety with talquetamab: a real-world Mayo Clinic study

Scott Soefje[1], Tyler Sandahl[1], Rafael Fonseca[2], Sikander Ailawadhi[3], Ricardo Parrondo[3], Nivedita Rangarajan[4], Hoa H Le[5], Purushotham K[4], Hannah Barman[4], Tyler E Wagner[4], Saurabh Patel[5], Xinke Zhang[5], Rohan C Parikh[5], Ming-Hui Tai[5], Yi Lin[1], Shaji K Kumar[1]

[1]Mayo Clinic, Rochester, MN, USA; [2]Mayo Clinic, Phoenix, AZ, USA; [3]Mayo Clinic, Jacksonville, FL, USA; [4]nference Inc., Cambridge, MA, USA; [5]Johnson & Johnson, Horsham, PA, USA

Key Takeaways

OP protocols for talquetamab SUD are being adopted by centers such as the Mayo Clinic

Most patients started their treatment in the OP setting, with 40.6% receiving all SUD care exclusively in the OP setting and 53.1% utilizing a hybrid IP/OP model, which ultimately resulted in reduced IP stays and potentially associated cost savings

Overall, the CRS profile was consistent with clinical trial data, with all events being mild and no grade ≥3 events

Conclusions

In this real-world analysis, on average, patients who received talquetamab SUD in the OP setting had a reduced LOS while maintaining a similar CRS profile to that previously shown for talquetamab without prophylactic tocilizumab

While further real-world research will provide additional insights into long-term talquetamab dosing in various settings, data from this study support the feasibility of OP talquetamab SUD administration

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Disclosure

RA is an employee of Johnson & Johnson.

Introduction

- Talquetamab is a first-in-class GPRC5D-targeted bispecific antibody approved in the United States for the treatment of patients with relapsed/refractory multiple myeloma (RRMM) who have received ≥4 prior lines of therapy (LOTs) and are triple-class exposed to a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 monoclonal antibody[1]
- Based on findings from the phase 1/2 MonumenTAL-1 study (ClinicalTrials.gov Identifiers: NCT03399799/ NCT04634552), in which talquetamab induced deep and durable responses in heavily pretreated patients with RRMM, initiation of talquetamab therapy included step-up dosing (SUD) before establishing a 0.4 mg/kg weekly or 0.8 mg/kg biweekly (Q2W) treatment schedule[1–3]
- Per the US prescribing information, patients should be hospitalized for 48 hours following all SUD doses to monitor for cytokine release syndrome (CRS)[1]; however, to facilitate access to and improve the patient experience with talquetamab, some centers, such as the Mayo Clinic, have established outpatient (OP) programs
- Currently, real-world evidence on talquetamab SUD in an OP setting is limited, as patients are likely to receive SUD in an inpatient (IP) setting[4]
- The objective of this retrospective, observational study was to describe patient characteristics, health care resource utilization, and safety in real-world patients with RRMM who initiated talquetamab SUD at the Mayo Clinic

Methods

Study design

- This was a real-world, retrospective, observational study using de-identified electronic medical records available from the Mayo Clinic

Study population

- Adult patients ≥18 years of age with ≥1 multiple myeloma diagnosis code who had received their first talquetamab SUD dose at the Mayo Clinic between August 9, 2023 (talquetamab approval date), and November 15, 2024 (data cutoff date), were included
  - Patients who received talquetamab as part of a clinical trial were excluded
- The index date was defined as the date of the first talquetamab SUD dose

Study outcomes

- Patient demographics and clinical characteristics were collected during the baseline period, which was defined as the 6 months prior to the index date
- SUD practices are reported, including IP admission and length of stay (LOS)
- Risk and severity of CRS and immune effector cell–associated neurotoxicity syndrome (ICANS), as well as management strategies, are reported

Data analysis

- Data were analyzed and summarized for patients who had completed the SUD schedule
  - Data for the subset of these patients who had initiated SUD in an OP setting are also presented
- Patient numbers and percentages were determined for categorical variables, and patient numbers, percentages, and descriptive statistics (mean, standard deviation [SD], median, interquartile range [IQR]) were determined for continuous variables

Results

Patient characteristics

- Overall, 32 patients who had completed talquetamab SUD and met the inclusion criteria were included in this analysis
  - Baseline demographics and clinical characteristics are summarized in **Table 1**
    - The mean (SD) age was 67 (8) years, 12 (37.5%) patients were female, and 29 (90.6%) patients were White
    - The mean (SD) number of prior LOTs before the index date was 6.3 (3.8)
  - The median (IQR) duration of follow-up was 7 (4.6–11.6) months
- Similar clinical characteristics were observed among the 25 patients who had initiated SUD in an OP setting
  - Key clinical characteristics for these patients are summarized in **Table 2**

Table 1: Demographics and clinical characteristics

Characteristic	Patients with complete SUD (n=32)
Age at index, years	
Mean (SD)	67 (8)
Median (IQR)	68 (62–74)
Sex, n (%)	
Male	20 (62.5)
Female	12 (37.5)
Race, n (%)	
White	29 (90.6)
Black or African American	2 (6.3)
Asian	0
Other/unknown	1 (3.1)
Site of administration, n (%)	
Rochester, MN	25 (78.1)
Phoenix/Scottsdale, AZ	4 (12.5)
Jacksonville, FL	3 (9.4)
Payer, n (%)	
Medicare	19 (59.4)
Commercial	10 (31.3)
Other	2 (6.3)
Weight at index, kg	
Mean (SD)	79.8 (21.3)
Median (IQR)	75.4 (67.0–89.2)
Duration of MM diagnosis, years	
Mean (SD)	6.8 (3.8)
Median (IQR)	6.4 (4.0–9.4)
ECOG PS score, n (%)	
0	6 (18.8)
1	15 (46.9)
2	5 (15.6)
≥3	3 (9.4)
Unknown	3 (9.4)
ISS disease stage, n (%)	
I	3 (9.4)
II	5 (15.6)
III	6 (18.8)
Unknown	18 (56.3)
Cytogenetic risk at diagnosis, n (%)	
High	16 (50.0)
Standard	15 (46.9)
Unknown	1 (3.1)
QCCI score	
Mean (SD)	3.7 (1.6)
Median (IQR)	3.0 (2.0–4.3)
Number of prior LOTs	
Mean (SD)	6.3 (3.8)
Median (IQR)	6 (4–8)

SUD, step-up dosing; SD, standard deviation; IQR, interquartile range; MM, multiple myeloma; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; QCCI, Quan Charlson Comorbidity Index; LOT, line of therapy.

Table 2: Clinical characteristics among patients initiating SUD in an OP setting

Characteristic	Patients initiating SUD in an OP setting (n=25)
ECOG PS score, n (%)	
0	5 (20.0)
1	13 (52.0)
2	4 (16.0)
≥3	2 (8.0)
Unknown	1 (4.0)
ISS disease stage, n (%)	
I	3 (12.0)
II	4 (16.0)
III	5 (20.0)
Unknown	13 (52.0)
Cytogenetic risk at diagnosis, n (%)	
High	11 (44.0)
Standard	13 (52.0)
Unknown	1 (4.0)
Number of prior LOTs	
Mean (SD)	6.2 (3.3)
Median (IQR)	6 (4–8)

SUD, step-up dosing; OP, outpatient; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; LOT, line of therapy; SD, standard deviation; IQR, interquartile range.

- All patients had extensive prior treatment exposure (**Table 3**)

Table 3: Prior treatment exposure

Prior treatment type, n (%)	Patients with complete SUD (n=32)
PI	32 (100)
Bortezomib	32 (100)
Carfilzomib	29 (90.6)
Ixazomib	17 (53.1)
IMiD	31 (96.9)
Lenalidomide	31 (96.9)
Pomalidomide	29 (90.6)
Thalidomide	9 (28.1)
Anti-CD38 mAb	30 (93.8)
Daratumumab	29 (90.6)
Isatuximab	9 (28.1)
Penta-exposed[a]	27 (84.4)
Selinexor	13 (40.6)
BCMA-targeted therapy	19 (59.4)
CAR-T (cilta-cel, ide-cel)	12 (37.5)
ADC (belantamab)	4 (12.5)
Teclistamab	10 (31.3)

SUD, step-up dosing; PI, proteasome inhibitor; IMiD, immunomodulatory drug; mAb, monoclonal antibody; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; ide-cel, idecabtagene vicleucel; ADC, antibody-drug conjugate
[a]Exposed to 2 PIs, 2 IMiDs, and 1 anti-CD38 mAb

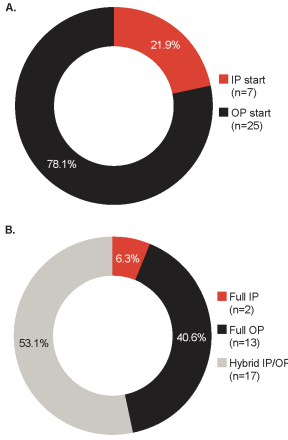
SUD setting and schedule

- Of the 32 patients who completed all 4 doses of the SUD schedule (all of whom were on a talquetamab Q2W dosing schedule), most patients (25 [78.1%]) had started treatment with talquetamab in an OP setting and 7 (21.9%) patients had started treatment with talquetamab in an IP setting (**Figure 1A**)
  - Only 2 (6.3%) patients completed SUD in a full IP setting, while 13 (40.6%) and 17 (53.1%) patients completed SUD in an all-OP and hybrid IP/OP setting, respectively (**Figure 1B**)

Admissions and LOS

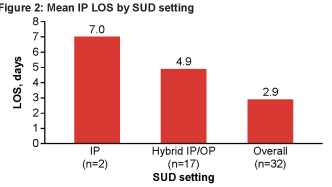
- Among the 32 patients who completed SUD, the mean (SD) number of admissions was 0.9 (1.1)
  - The mean (SD) total LOS was 7.0 (0) days, 4.9 (3.8) days, and 2.9 (3.7) days for patients who completed SUD in an all-IP setting, a hybrid IP/OP setting, and overall, respectively (**Figure 2**)
  - Among all 32 patients who completed SUD, the median (IQR) total LOS was 2 (0–4.0) days
- Of the 19 patients with IP admissions, the mean (SD) number of admissions was 1.7 (0.9)
  - The mean (SD) total LOS of these 19 patients was 5.1 (3.7) days, and the median (IQR) was 4 (2.0–6.5) days
- Compared with patients who completed SUD in an all-IP setting or a hybrid IP/OP setting, the mean (SD) total LOS (1.6 [2]) was shorter for patients initiating SUD in an OP setting (**Figure 2** and **Table 4**)

Figure 1: Setting of care for administration of (A) the first talquetamab SUD and (B) all 4 doses of the talquetamab SUD schedule



SUD, step-up dosing; IP, inpatient; OP, outpatient

Figure 2: Mean IP LOS by SUD setting



IP, inpatient; LOS, length of stay; SUD, step-up dosing; OP, outpatient

CRS and supportive care

- Among all patients who completed SUD, dexamethasone and acetaminophen were each received by 28 (87.5%) patients as their primary prophylaxis for CRS (**Table 5**)
- A total of 19 (59.4%) patients who completed SUD developed CRS during SUD, with 10 (31.3%) patients experiencing only 1 CRS event, 6 (18.8%) patients experiencing 2 events, and 3 (9.4%) patients experiencing ≥3 events
  - Most CRS events were of low severity and associated with the first 2 SUD doses
  - Supportive care treatment for CRS events that developed during SUD included tocilizumab (n=12; 37.5%), dexamethasone (n=19; 59.4%), and acetaminophen (n=19; 59.4%)
- One (3.1%) patient developed grade 1 ICANS during SUD
- Similar trends were observed among patients initiating SUD in an OP setting

Table 4: HCRU among patients initiating SUD in an OP setting

	Patients initiating SUD in an OP setting (n=25)
Completed SUD in an all-OP setting, n (%)	13 (52.0)
Completed SUD in a hybrid IP/OP setting, n (%)	12 (48.0)
LOS, days	
Mean (SD)	3.3 (1.5)
Median (IQR)	4 (2–4)
IP admission due to any AE, n (%)	4 (16.0)
Admission due to CRS	4 (16.0)
Admission due to GPRC5D-related events	0
Total LOS per patient for CRS admissions, days	
Mean (SD)	4 (2.6)
Median (IQR)	3 (3–5)
LOS per admission for CRS admissions, days	
Mean (SD)	2 (0.7)
Median (IQR)	2 (2–2)
Among all 25 patients initiating SUD in an OP setting	
Mean (SD) number of admissions	0.8 (0.9)
Mean (SD) total LOS, days	1.6 (2)
Median (IQR) LOS, days	0 (0–4)
Mean (SD) LOS per admission, days	1.9 (2.5)
Median (IQR) LOS per admission, days	2 (0–2)
Among the 12 patients with admissions	
Mean (SD) number of admissions	1.4 (0.6)
Mean (SD) total LOS, days	3.3 (1.5)
Median (IQR) LOS, days	4 (2–4)
Mean (SD) LOS per admission, days	2.3 (1)
Median (IQR) LOS per admission, days	2 (2–2)
SUD schedule pattern, n (%)	
Exact 3-day interval	2 (8.0)
Exact 2-day interval	17 (68.0)
Other	6 (24.0)

HCRU, health care resource utilization; SUD, step-up dosing; OP, outpatient; IP, inpatient; LOS, length of stay; SD, standard deviation; IQR, interquartile range; AE, adverse event; CRS, cytokine release syndrome.

Table 5: CRS and supportive care

Patients, n (%)	Patients with complete SUD (n=32)	Patients initiating SUD in an OP setting (n=25)
Patients who received primary prophylaxis		
Dexamethasone	28 (87.5)	21 (84.0)
Acetaminophen	28 (87.5)	21 (84.0)
Diphenhydramine	27 (84.4)	20 (80.0)
Patients who experienced CRS during SUD	19 (59.4)	14 (56.0)
Grade 1[a,b]	14 (43.8)	12 (48.0)
Grade 2[a]	5 (15.6)	2 (8.0)
Patients with only 1 CRS event	10 (31.3)	8 (32.0)
Patients with 2 CRS events	6 (18.8)	4 (16.0)
Patients with ≥3 CRS events	3 (9.4)	2 (8.0)
CRS associated with each SUD		
SUD dose 1	12 (37.5)	8 (32.0)
SUD dose 2	9 (28.1)	6 (24.0)
SUD dose 3	8 (25.0)	6 (24.0)
SUD dose 4	2 (6.3)	2 (8.0)
Patients who received supportive care treatment for CRS		
Tocilizumab	12 (37.5)	8 (32.0)
Dexamethasone	19 (59.4)	14 (56.0)
Acetaminophen	19 (59.4)	14 (56.0)
Patients who developed ICANS during SUD	1 (3.1)	1 (4.0)
Grade 1	1 (3.1)	1 (4.0)

CRS, cytokine release syndrome; SUD, step-up dosing; OP, outpatient; ICANS, immune effector cell–associated neurotoxicity syndrome.
[a]Per CRS grading.
[b]It remains uncertain whether 1 patient experienced grade 1 CRS or fever attributable to an underlying infection. Notably, the event did not necessitate the administration of corticosteroids or tocilizumab for management.

References

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Multiple Myeloma

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