P-077

Prophylactic Tocilizumab to Mitigate Cytokine Release Syndrome in Patients Receiving Talquetamab for Relapsed/Refractory Multiple Myeloma: Results From the Phase 1/2 MonumenTAL-1 Study

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Key Takeaway

Prophylactic toci and increased dex use during SUD appears to be a safe and effective strategy to mitigate the risk of CRS with talquetamab

Conclusions

A single dose of toci before talquetamab and increased dex use post dose reduced the incidence and severity of CRS compared with the overall MonumenTAL-1 population

Similar rates and severity of neutropenia and infections were observed with prophylactic toci use compared with the overall MonumenTAL-1 population

These data support the exploration of outpatient administration of talquetamab SUDs to reduce the burden of hospitalization during initial talquetamab treatment

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Disclosures

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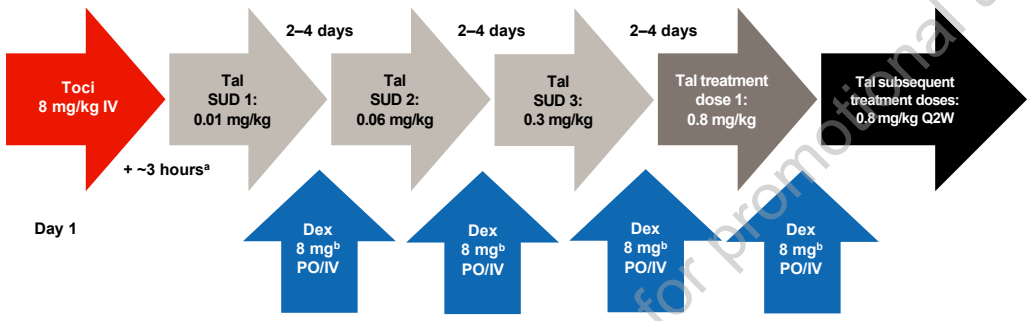
Introduction

- Talquetamab is the first and only approved G protein–coupled receptor family C group 5 member D (GPRC5D)-targeting bispecific antibody (BsAb) for the treatment of patients with triple-class exposed relapsed/refractory multiple myeloma (RRMM)[1-3]
- In the MonumenTAL-1 study, cytokine release syndrome (CRS) occurred in 73.1–79.0% of patients across cohorts, among whom, 35.0–47.4% were treated with tocilizumab (toci; ± other interventions)
- Data suggest that prophylactic toci before BsAb treatment may reduce the incidence and severity of CRS, which may facilitate outpatient administration of step-up doses (SUDs) and improve patient experience[4]
- The current analysis evaluated the effects of prophylactic toci on CRS parameters following talquetamab treatment

Methods

- Eligible patients were from phase 2 of MonumenTAL-1 (NCT04634552; **Figure 1**)
- Patients had RRMM and had received ≥3 prior lines of therapy (LOT; ≥1 proteasome inhibitor [PI], ≥1 immunomodulatory drug [IMiD], and ≥1 anti-CD38 monoclonal antibody)
- CRS and immune effector cell–associated neurotoxicity syndrome (ICANS) were graded by American Society for Transplantation and Cellular Therapy criteria; other adverse events (AEs) were graded by Common Terminology Criteria for Adverse Events (CTCAE) v4.03

Figure 1: Dosing schedule for patients receiving SC talquetamab and prophylactic toci



[a]With required pretreatments (glucocorticoid, antihistamine, and antipyretic). [b]Given daily for 2 days after each SUD and first full treatment dose. If posttreatment dex was scheduled on a day when premedication with dex was required, only the premedication dose was given. dex, dexamethasone; IV, intravenous; PO, oral; Q2W, every other week; SC, subcutaneous; tal, talquetamab.

Results

Patients

- 12 patients were included in the analysis, with median follow-up of 4.4 months (range, 0.3–8.8)
- Most patients were male (75.0%), and ~42% were Black or African American; patients had a median of 3 (range, 3–10) prior LOT (**Table 1**)
- 2 patients (16.7%) received prior B-cell maturation antigen–targeted T-cell redirection therapy (1 chimeric antigen receptor T-cell and 1 BsAb)

Table 1: Baseline characteristics

Characteristics	Prophylactic toci (N=12)
Age, years, median (range)	69 (51–77)
Male, n (%)	9 (75.0)
Race, n (%)	
White	7 (58.3)
Black or African American	5 (41.7)
ECOG PS, n (%)	
0	4 (33.3)
1	7 (58.3)
2	1 (8.3)
Extramedullary plasmacytomas, n (%)	
0	11 (91.7)
≥1	1 (8.3)
High-risk cytogenetics,[a] n (%)	2 (20.0)
ISS stage,[b] n (%)	
I	6 (50.0)
II	5 (41.7)
III	1 (8.3)
Prior LOT, median (range)	3 (3–10)
Refractory status, n (%)	
Triple-class[c]	6 (50.0)
Penta-drug[d]	1 (8.3)
To last LOT	11 (91.7)
% BMPCs (biopsy or aspirate),[e] n (%)	
<5	5 (41.7)
≥5 to ≤30	2 (16.7)
>30 to <60	2 (16.7)
≥60	3 (25.0)

[a]Defined as del(17p), t(4;14), and/or t(14;16); calculated from n=10. [b]ISS staging is derived based on serum β_2-microglobulin and albumin. [c]≥1 PI, ≥1 IMiD, and ≥1 anti–CD38 mAb. [d]≥2 PIs, ≥2 IMiDs, and ≥1 anti–CD38 mAb. [e]Maximum value from bone marrow biopsy or bone marrow aspirate is selected if both the results are available. BMPC, bone marrow plasma cell; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; mAb, monoclonal antibody.

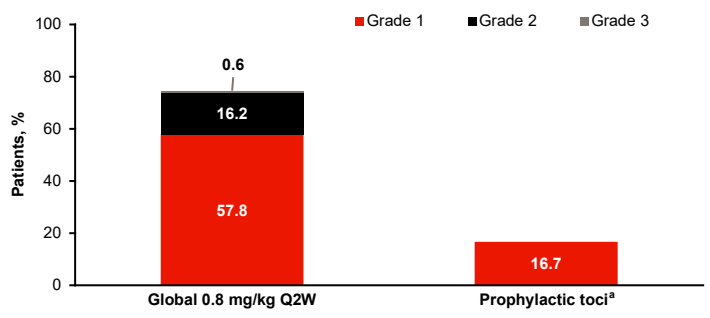
CRS incidence, severity, timing, and treatment

- Grade 1 CRS events occurred during SUD through cycle 1 in 2 patients (16.7%) (**Figure 2**); 1 patient (8.3%) experienced a grade 1 CRS event at cycle 2 day 1
  - 1 patient (8.3%) had a recurrent grade 1 CRS event during SUD
- Median time to CRS onset was 2.0 days (range, 2–12) and median duration was 2 days (range, 1–6)
  - Late median onset was due to the 1 patient with CRS at cycle 2 day 1
- All 3 patients received treatment for CRS, including toci (n=2) and paracetamol (n=3)

Disease characteristics in patients with and without CRS

- Prophylactic toci and postdose dex use appeared to lower CRS incidence and severity across varying levels of disease burden (**Table 2**)

Figure 2: Incidence and severity of CRS



[a]CRS events shown for those occurring during SUD through cycle 1 in the prophylactic toci cohort (n=2).

Table 2: Baseline characteristics of patients with and without CRS

	No CRS (n=9)	CRS during SUD through cycle 1 (n=2[a])
% BMPCs, n		
<5	4	1
≥5 to ≤30	2	–
>30 to <60	2	–
≥60	1	1
ISS stage, n		
I	4	1
II	4	1
III	1	–
EMD status, n		
Yes	1	–
No	8	2

[a]Patient with CRS at cycle 2 day 1 had the following baseline characteristics: ≥60% BMPCs; ISS stage I; no EMD. EMD, extramedullary disease.

Efficacy

- Overall response rate in response-evaluable patients was 70.0% (7/10) in the prophylactic toci cohort, similar to the global 0.8 mg/kg Q2W population (71.3%), although patient numbers were small in the prophylactic toci cohort

Other safety endpoints

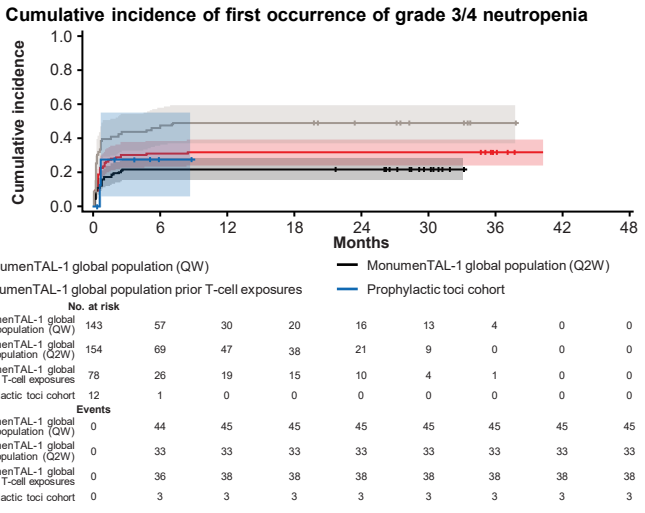
- No increase in rates of neutropenia, infections, or on-target, off-tumor AEs (GPRC5D-related AEs) was observed in the prophylactic toci cohort compared with the MonumenTAL-1 global population (**Table 3**)
  - Grade 3/4 neutropenia occurred early in the prophylactic toci cohorts, consistent with early timing in the global cohorts (plateauing around 5–6 months), although numbers were small (**Figure 3**)
  - 2 (16.7%) patients had grade 3/4 infections; both had significant medical history that may have impacted their risk for infection; 1 (8.3%) patient died due to lung infection
- 1 patient (8.3%) with 80% BMPCs developed ICANS (grade 2; concomitant with CRS)
- 1 patient (8.3%) discontinued treatment due to AEs (skin desquamation)

Table 3: Adverse events

AEs, n (%)	Prophylactic toci (N=12)	
	Any Grade	Grade 3/4
Hematologic AEs		
Leukopenia	4 (33.3)	4 (33.3)
Neutropenia	3 (25.0)	3 (25.0)
Lymphopenia	3 (25.0)	2 (16.7)
Anemia	2 (16.7)	1 (8.3)
Thrombocytopenia	2 (16.7)	1 (8.3)
Nonhematologic AEs		
Taste related[a]	8 (66.7)	NA
Skin related[b]	8 (66.7)	0
Infections	5 (41.7)	2 (16.7)
Weight loss	4 (33.3)	0
Nail related[c]	3 (25.0)	0
AST increase	3 (25.0)	0
Rash related[d]	2 (16.7)	1 (8.3)
ICANS	1 (8.3)	0
ALT increase	1 (8.3)	0

[a]Including ageusia, dysgeusia, hypogeusia, and taste disorder; maximum possible grade of dysgeusia per CTCAE is 2. [b]Including skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Including nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [d]Including rash, maculopapular rash, erythematous rash, and erythema. ALT, alanine transaminase; AST, aspartate aminotransferase; NA, not applicable.

Figure 3: Cumulative incidence of first occurrence of grade 3/4 neutropenia



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Multiple Myeloma

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