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Prophylactic Tocilizumab to Mitigate Cytokine Release Syndrome and Outpatient Dosing of Talquetamab in Relapsed/Refractory Multiple Myeloma: Updated Phase 1/2 MonumenTAL-1 Results

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Key Takeaway

A single dose of tocilizumab before the first talquetamab SUD with daily dexamethasone for 48 hours after talquetamab step-up and first full treatment doses reduced CRS incidence and severity vs the overall MonumenTAL-1 population

Conclusions

No increased neutropenia, ICANS, GPRC5D-associated AEs, or infection rates were observed in patients treated with prophylactic tocilizumab vs the overall MonumenTAL-1 population

ORR was similar to the overall MonumenTAL-1 population in patients who received prophylactic tocilizumab before talquetamab

These results support further exploration of prophylactic tocilizumab to facilitate outpatient administration of talquetamab SUDs and the first full treatment doses

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Disclosures

OP is an employee and stockholder of Johnson & Johnson.

Introduction

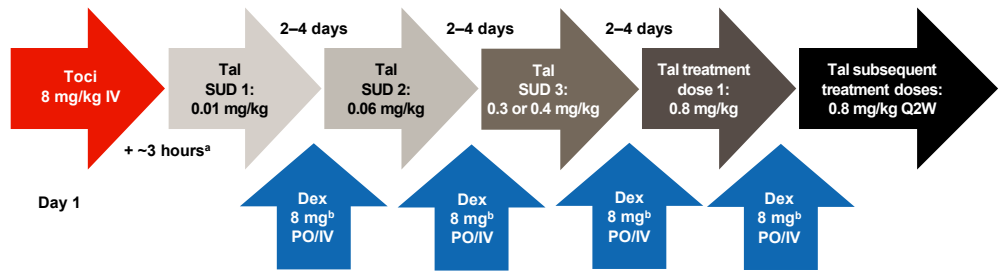
- Talquetamab is the first and only approved bispecific antibody targeting G protein–coupled receptor class C group 5 member D (GPRC5D) for the treatment of relapsed/refractory multiple myeloma (RRMM)[1-3]
- In MonumenTAL-1, cytokine release syndrome (CRS) occurred in 73–79% of patients across cohorts without prophylactic tocilizumab, and 35–47% received tocilizumab for the treatment of CRS (± other interventions)[3]
- Tocilizumab treatment for CRS reduced the incidence of repeat events,[3] promoting investigation of prophylactic tocilizumab before talquetamab to reduce the incidence and severity of CRS

We evaluated the impact of prophylactic tocilizumab on CRS with talquetamab to enable safe and effective outpatient dosing of step-up doses (SUDs) and the first full dose

Methods

- Eligible patients were from phase 2 of MonumenTAL-1 (NCT04634552)
- 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 [mAb])
- Patients could be treated on an inpatient or outpatient basis
- 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 tocilizumab



[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; Toci, tocilizumab.

Results

Table 1: Baseline characteristics were representative of the overall MonumenTAL-1 population, with 10 patients treated as inpatients and 17 patients treated as outpatients

Parameter	Prophylactic tocilizumab (N=27)
Follow-up, months, median (range)	4.4 (0.5–18.4)
Age, years, median (range)	69.0 (51.0–79.0)
Male, n (%)	16 (59.3)
ECOG PS 0, n (%)	8 (29.6)
ECOG PS 1, n (%)	18 (66.7)
ECOG PS 2, n (%)	1 (3.7)
Extramedullary plasmacytomas, n (%)	
0	22 (81.5)
≥1	5 (18.5)
High-risk cytogenetics,[a] n (%)	7 (31.8)
ISS stage I,[b] n (%)	15 (60.0)
ISS stage II,[b] n (%)	7 (28.0)
ISS stage III,[b] n (%)	3 (12.0)
Prior LOT, median (range)	4.0 (3.0–11.0)
Refractory status, n (%)	
Triple-class[c]	19 (70.4)
Penta-drug[d]	6 (22.2)
To last LOT	24 (88.9)

[a]Defined as del(17p), t(4;14), and/or t(14;16); calculated from n=22. [b]ISS staging is derived based on serum β_2-microglobulin and albumin; calculated from n=25 (n=2 had missing assessments). [c]≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb. [d]≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb. ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System.

Table 2: Reduced incidence and severity of CRS vs overall MonumenTAL-1 population

Parameter	Prophylactic tocilizumab (N=27)	MonumenTAL-1 overall (N=402)
CRS, n (%)		
Grade 1	5 (18.5)	223 (55.5)
Grade 2	0 (0)	63 (15.7)
Grade 3	0 (0)	5 (1.2)
Onset of CRS,[a] days, median (range)	2.5 (2.0–12.0)	2.0 (1.0–22.0)
Duration of CRS, days, median (range)	1.0 (1.0–6.0)	2.0 (1.0–29.0)
Supportive measures for CRS,[b] n (%)	4 (14.8)	274 (68.2)
Tocilizumab	3 (11.1)	147 (36.6)
Oxygen	0 (0)	25 (6.2)
Corticosteroids	0 (0)	22 (5.5)
Paracetamol	3 (11.1)	206 (51.2)
Other	1 (3.7)	130 (32.3)
CRS recovered or resolved,[c] n (%)	6 (100.0)	496 (99.8)

[a]Relative to the most recent dose. [b]Patients could receive ≥1 supportive therapy. [c]Patients could have ≥1 event.

Table 3: Similar CRS incidence and severity in patients treated in an inpatient vs outpatient setting

Outcome	Inpatient (n=10)	Outpatient (n=17)
CRS, n (%)	3 (30.0)	2 (11.8)[a]
Grade 1	3 (30.0)	2 (11.8)[a]
Grade 2	0 (0)	0 (0)
Grade 3	0 (0)	0 (0)
Onset of CRS,[b] days, median (range)	2.0 (2.0–12.0)	5.5 (3.0–8.0)
Duration of CRS, days, median (range)	1.0 (1.0–6.0)	2.0 (1.0–3.0)
During SUD dose period,[c] n (%)	3 (30.0)	0 (0)
During 1st full cycle,[c] n (%)	0 (0)	2 (11.8)
During 2nd full cycle or after,[c] n (%)	1 (10.0)	0 (0)
CRS recovered or resolved,[c] n (%)	4 (100.0)	2 (100.0)

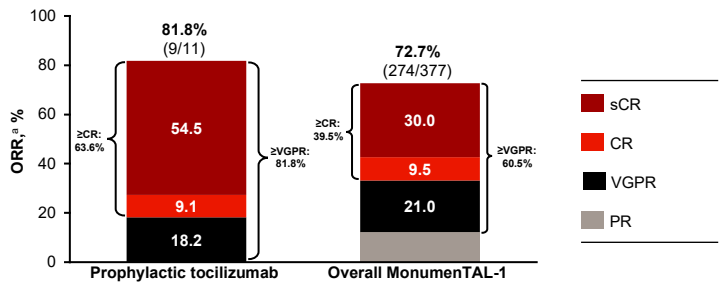
[a]1 patient treated on an outpatient basis had CRS while hospitalized for bone pain. [b]Relative to the most recent dose. [c]Patients could have ≥1 event.

Table 4: No increased neutropenia, infections, ICANS, or GPRC5D-associated AEs compared with the overall MonumenTAL-1 population

Most common AEs (≥20% of total population) and AEs of interest, n (%)	Prophylactic tocilizumab (N=27)	
	Any Grade	Grade 3/4
Hematologic AEs		
Neutropenia	9 (33.3)	6 (22.2)
Anemia	7 (25.9)	3 (11.1)
Lymphopenia	6 (22.2)	5 (18.5)
Nonhematologic AEs		
Taste changes[a]	18 (66.7)	NA
Skin AEs[b]	13 (48.1)	0 (0)
Dry mouth	12 (44.4)	0 (0)
Weight decrease	8 (29.6)	0 (0)
Nail AEs[c]	7 (25.9)	0 (0)
Cough	6 (22.2)	0 (0)
Fatigue	6 (22.2)	0 (0)
Other AEs of interest		
Infections[d]	15 (55.6)	5 (18.5)
ICANS	2 (7.4)	0 (0)

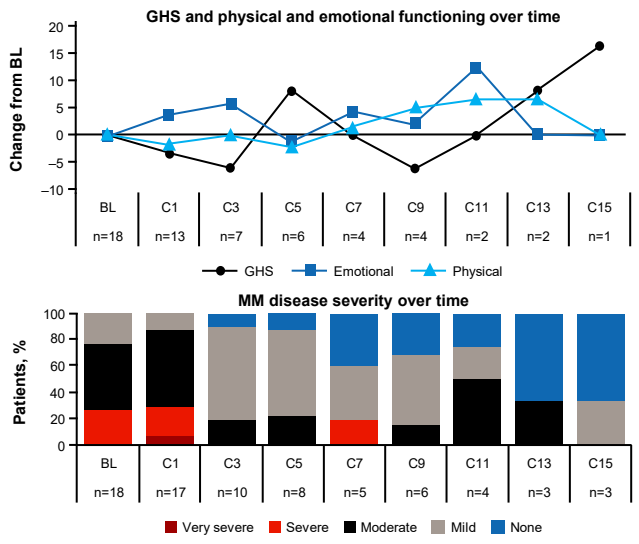
[a]Dysgeusia, ageusia, hypogeusia, and taste disorder; maximum grade for taste changes is 2 per CTCAE. [b]Skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [d]Infections described on a System Organ Class basis, and thus not grouped with Preferred Term data in terms of incidence.

Figure 2: Similar ORR to overall MonumenTAL-1 population in the prophylactic tocilizumab cohort



[a]Results presented based on the latest available data assessed by independent committee review per International Myeloma Working Group criteria. CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Figure 3: GHS and physical and emotional functioning did not worsen vs BL over time, and MM disease severity generally improved over time in the prophylactic tocilizumab cohort



GHS and physical and emotional functioning are measured with European Organisation for Research and Treatment of Cancer quality of life questionnaire core-30 scales, which range from 0–100, with higher values indicating improvements. BL, baseline; C, cycle; GHS, global health status; MM, multiple myeloma.

Prophylactic tocilizumab reduced CRS incidence and severity and did not exacerbate other AEs of interest, including GPRC5D-associated AEs, infections, or ICANS

Patients in the prophylactic tocilizumab cohort of MonumenTAL-1 experienced similar improvements in quality of life to patients from the overall MonumenTAL-1 population

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Multiple Myeloma

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