Safety Results From REALiTAL: A Multi-Country Observational Retrospective Study of Talquetamab in Patients With Relapsed/Refractory Multiple Myeloma Outside of Clinical Trials

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Key Takeaway

Treatment with talquetamab outside of clinical trials was generally safe and manageable with similar outcomes to those observed previously in the MonumenTAL-1 study

Conclusions

The majority of AEs in REALiTAL were clinically manageable, with no new safety signals identified

Infections were generally low grade and resolved with appropriate management. Taste-related changes and skin/nail reactions were reversible, with most events showing improvement. CRS was mostly low-grade and resolved, with limited use of tocilizumab or prophylactics in the study. ICANS events were rare and low grade, with no grade ≥3 cases reported

Only 5.4% of patients discontinued treatment due to GPRC5D-related AEs

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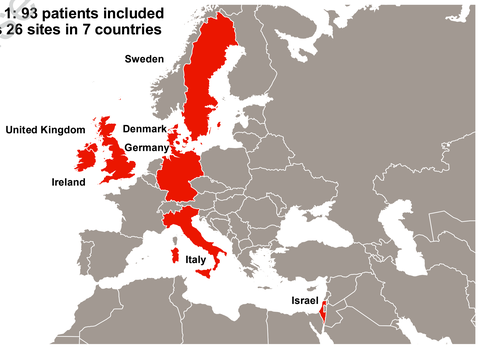
Introduction

- Talquetamab is the first G protein–coupled receptor family C group 5 member D (GPRC5D)-targeting bispecific antibody (BsAb) approved for the treatment of patients with relapsed/refractory multiple myeloma (RRMM)[1-3]
- With a median follow-up of over 30 months, the pivotal phase 1/2 MonumenTAL-1 (N=375) trial showed an overall response rate (ORR) of ≥66.7% across all cohorts[1]
  - Median duration of response (DOR) was 9.5 months for the weekly (QW) cohort and 17.5 months in the every-other-week (Q2W) cohort
  - Median progression-free survival (PFS) and overall survival (OS) were 7.5 and 34 months (QW) and 11.2 months and not reached (Q2W), respectively
  - Common adverse events (AEs) in MonumenTAL-1 included cytokine release syndrome (CRS), taste-related AEs, and non-rash skin-related AEs
- Previous REALiTAL data demonstrated deep and durable responses in hard-to-treat, heavily pretreated patients with RRMM outside of clinical trials.[4] Here, we report the safety and management profile in patients observed in the REALiTAL study

Methods

- REALiTAL is a retrospective, international, noninterventional study that aims to describe the management and outcomes of patients with RRMM treated with talquetamab outside of clinical trials
- REALiTAL included 26 sites across 7 countries (**Figure 1**)
- Data were collected from patient medical records, including demographics, disease characteristics, prior therapies, effectiveness, and safety
- Informed consent was obtained for all patients
- Safety data included incidence and severity of CRS, immune effector cell–associated neurotoxicity syndrome (ICANS), infections, and GPRC5D-related AEs
  - AEs were graded by Common Terminology Criteria for Adverse Events (CTCAE), v4.03
  - CRS and ICANS were graded by American Society for Transplantation and Cellular Therapy (ASTCT) criteria

Figure 1: 93 patients included across 26 sites in 7 countries



Results

Patients

- REALiTAL included 93 eligible patients receiving talquetamab on or before December 31, 2023; most patients had received talquetamab prior to commercial access programs
- Patient baseline characteristics are shown in **Table 1**

Table 1: Baseline demographics and disease characteristics

Characteristic	N=93[a]
Age, years, median (range)	65 (24–86)
ECOG PS ≥1, n (%)	21/35 (60.0)
Extramedullary plasmacytoma, n (%)	11/51 (21.6)
LDH >245 U/L, n (%)	43/80 (53.8)
Creatinine clearance mL/min/1.73 m^2	86
<30 mL/min/1.73 m^2	7 (8.1)
≥30 to <40 mL/min/1.73 m^2	7 (8.1)
≥40 mL/min/1.73 m^2	72 (83.7)
History of severe infections, n (%)	10 (10.8)
Cardiac conditions, n (%)[b]	9 (9.7)
Years since diagnosis, median (range)	6.03 (1.5–23.1)
Previous lines of therapy, median (range)	5 (2–16)
Refractory to the last line of therapy, n (%)	71 (76.3)
Autologous SCT, n (%)	70 (75.3)
Patients receiving prior BCMA, n (%)	57 (61.3)
CAR-T	11 (11.8)
ADC	24 (25.8)
BsAbs	22 (23.7)

[a]Data available added as denominators if some were missing and not available in the clinical chart for the whole cohort. [b]Cardiac conditions include myocardial infarction or coronary artery bypass graft. ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; SCT, stem cell transplant.

- Patients were heavily pretreated, with a median 5 previous lines of therapy; almost all (n=91; 97.8%) were triple-class exposed, and most (n=80; 86.0%) were penta-class exposed
- 82 (88.2%) patients started Q2W administration and 11 (11.8%) started QW
  - 6 (24%) out of 25 patients switching from QW to Q2W or from Q2W to monthly (QM) did so due to AEs
- Median duration of follow-up was 14.95 (range, 0.36–25.26) months
  - 68 (73.1%) patients discontinued treatment
  - The primary reasons for discontinuation were 57 (61.3%) due to disease progression, 5 (5.4%) due to treatment-emergent adverse events (TEAEs), and 3 (3.2%) due to physician decision

Efficacy

- Efficacy data for the overall population have been reported previously[4]
- ORR was 66.7% with 53 (57.0%) experiencing a very good partial response or better
- Median DOR was 12.3 (95% CI, 7.9–not estimable [NE]) months, median PFS was 8.2 (95% CI, 6.1–10.7) months, and median OS was 25.3 (95% CI, 17.3–NE) months over a median treatment duration of 7.9 (95% CI, 5.7–9.9) months

Safety

- The overall safety profile is shown in **Table 2**
- The most common TEAEs were skin/nail toxicity (67.7%), oral toxicity (66.7%), dysgeusia (57.0%), CRS (55.9%), and infections (47.3%)
- CRS occurred in 52 (55.9%) patients, mostly grade 1/2; 1 (1.1%) patient had a grade 3 event
  - Median duration of event for CRS was 2 (range, 1–368) days. 91.2% of CRS events occurred in the step-up phase and the rest (8.8%) of events started in any consequent dose
- There were 2 (2.2%; both grade 1) cases of ICANS
  - 1 patient reported a grade 3/4 nervous system disorder; no ataxia/balance disorders were reported
- 44 (47.3%) patients had an infection; 8 (8.6%) were grade 3/4, and only 1 (1.1%) patient discontinued due to infection (grade 5, septic shock)
- Skin and nail AEs occurred in 63 (67.7%) patients; all were grade 1/2 except 1 (1.1%) grade 3 AE
  - 4 (4.3%) patients interrupted talquetamab due to skin and nail AEs, but none discontinued
- Oral toxicity occurred in 62 (66.7%) patients, mostly grade 1/2, with 1 case of grade 4 stomatitis that did not lead to discontinuation
  - 2 (2.2%) patients interrupted study drug, 1 (1.1%) reduced dose, and 1 (1.1%) discontinued due to oral toxicity
- 75% of skin and nail toxicity events and 58% of oral toxicity events resolved or were resolving at the time of data collection
- Median duration of events for skin and nail AEs was 63.5 (range, 3–458) days and 125 (range, 6–473) days for oral toxicity
- There were 8 (8.6%) grade 5 AEs, none were considered related to talquetamab (4 general disorders and site conditions, 2 infections and infestations, 1 gastrointestinal disorder, and 1 metabolism and nutrition disorder)
- For those with prior BCMA, infections occurred in 53.1% of patients and 8.2% were grade 3/4

Table 2: TEAEs of clinical interest

TEAE, n (%)	N=93	
	Any Grade, n (%)	Grade 3/4, n (%)
Any TEAE, n (%)	92 (98.9)	28 (30.1)
Infections	44 (47.3)	8 (8.6)
COVID-19	7 (7.5)	1 (1.1)
Pneumonia	6 (6.5)	3 (3.2)
Upper respiratory tract infection	6 (6.5)	0 (0.0)
Urinary tract infection	5 (5.4)	1 (1.1)
Hematological TEAEs		
Anemia	13 (14.0)	8 (8.6)
Neutropenia	9 (9.7)	6 (6.5)
Thrombocytopenia	7 (7.5)	6 (6.5)
Nonhematological TEAEs		
Skin/nail toxicity	63 (67.7)	1 (1.1)
Oral toxicity	62 (66.7)	3 (3.3)
Dysgeusia[a]	53 (57.0)	NA
CRS	52 (55.9)	1 (1.1)
Neurological TEAEs of interest		
ICANS	2 (2.2)	0 (0.0)

[a]Includes dysgeusia, ageusia, and taste disturbance. Maximum grade is 2. NA, not applicable.

AE Management

- The AE management profile by concomitant medication is shown in **Tables 3–5**
- 77 (82.8%) patients received medications for infections, 50 (53.8%) for CRS, 35 (37.6%) for skin/nail toxicity, and 28 (30.1%) for oral toxicity
- 42 (45.2%) patients received immunoglobulin replacement, 35 (37.6%) as primary prophylaxis for infection and 4 (4.3%) as secondary prophylaxis

Table 3: Concomitant medications for CRS management

Concomitant medications, n (%)	Total
Patients receiving ≥1 medication, n (%)	50 (53.8)
AE treatment	41 (44.1)
Tocilizumab	22 (23.7)
Prophylaxis	19 (20.4)

Table 4: Concomitant medications for infection management

Concomitant medications, n (%)	Total
Patients receiving ≥1 medication, n (%)	77 (82.8)
AE treatment	39 (41.9)
Antibiotics	34 (36.6)
Antiviral	6 (6.5)
Antifungal	2 (2.2)
Prophylaxis, n (%)	65 (69.9)
Antibiotics	48 (51.6)
Antiviral	52 (55.9)
Antifungal	5 (5.4)
IgRT use	42 (45.2)
Primary prophylaxis	35 (37.6)
Secondary prophylaxis	4 (4.3)
Other	3 (3.2)

IgRT, immunoglobulin replacement therapy.

Table 5: Concomitant medications for skin/nail and oral toxicity management

Skin/nail, n (%)	Total
Patients receiving ≥1 medication, n (%)	35 (37.6)
AE treatment	32 (34.4)
Emollients and moisturizers	12 (12.9)
Corticosteroids	19 (20.4)
Antihistamines	5 (5.4)
Prophylaxis	3 (3.2)
Oral, n (%)	
Patients receiving one or more medication, n (%)	28 (30.1)
AE treatment	25 (26.9)
Corticosteroids	9 (9.7)
Anti-infectives	10 (10.8)
Prophylaxis	3 (3.2)

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Multiple Myeloma

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