Analysis of Infections and Parameters of Humoral Immunity in Patients With Relapsed/Refractory Multiple Myeloma Treated With Talquetamab Monotherapy in MonumenTAL-1

Paula Rodríguez-Otero[1], Carolina Schinke[2], Ajai Chari[3], Brea Lipe[4], Noa Lavi[5], Leo Rasche[6], Deeksha Vishwamitra[7], Sheri Skerget[7], Raluca I Verona[7], Xuewen Ma[7], Sheetal Khedkar[7], Brandi W Hilder[7], Tara Masterson[7], Michela Campagna[8], Thomas Renaud[9], Jaszianne Tolbert[7], Christoph Heuck[7], M Damiette Smit[10], Niels WCJ van de Donk[11]

[1]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [2]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [3]Mount Sinai School of Medicine, New York, NY, USA; [4]University of Rochester Medical Center, Rochester, NY, USA; [5]Rambam Health Care Campus, Haifa, Israel; [6]University Hospital of Würzburg, Würzburg, Germany; [7]Janssen Research & Development, Spring House, PA, USA; [8]Janssen Research & Development, Madrid, Spain; [9]Janssen Research & Development, Raritan, NJ, USA; [10]Janssen Biologics Europe, Leiden, Netherlands; [11]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, Netherlands

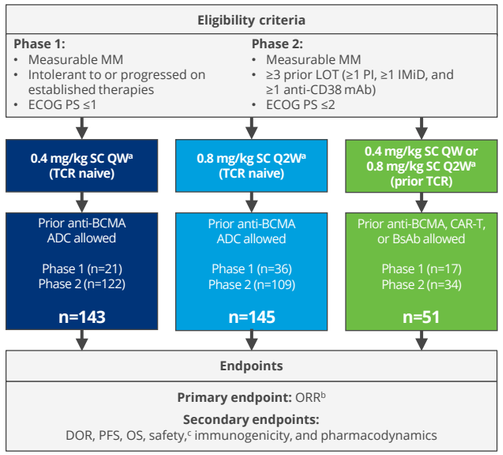
INTRODUCTION

- Infection is a common complication of multiple myeloma (MM), and immunotherapies that impact normal immune cells may increase risk of infections[1,2]
- G protein–coupled receptor family C group 5 member D (GPRC5D) is a novel target expressed on plasma cells, with significantly higher expression on malignant vs normal plasma cells[3]
  - GPRC5D has been shown to have limited expression on normal human hematopoietic cells, such as B cells and bone marrow progenitors[3,4]
- In the phase 1/2 MonumenTAL-1 study, talquetamab, a first-in-class bispecific antibody (BsAb) targeting GPRC5D, yielded responses in >70% of patients with relapsed/refractory MM (RRMM)[5]
- We report data on the infection profile and aspects of immune function from patients treated with talquetamab in the MonumenTAL-1 study

METHODS

- MonumenTAL-1 (NCT03399799/NCT04634552) enrolled patients who were naive or exposed to prior T-cell redirection therapy (TCR) (**Figure 1**)

FIGURE 1: MonumenTAL-1 phase 1/2 study design



[a]With 2–3 step-up doses. [b]Assessed by independent review committee using International Myeloma Working Group criteria. [c]Cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) were graded by American Society for Transplantation and Cellular Therapy criteria; all other adverse events (AEs) were graded by Common Terminology Criteria for Adverse Events (CTCAE) v4.03. ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; LOT, line of prior therapy; mAb, monoclonal antibody; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; Q2W, every other week; QW, weekly; SC, subcutaneous.

MULTIPLE MYELOMA

RESULTS

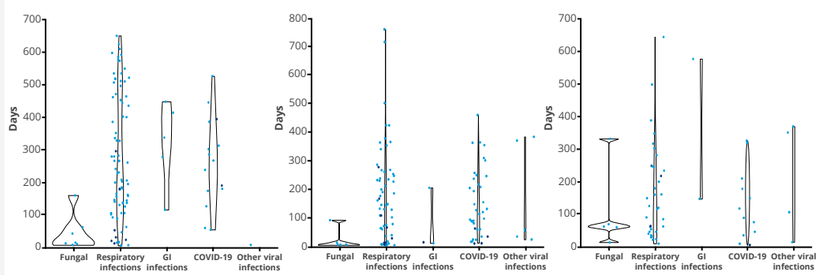
- Of 339 patients, any-grade infections occurred in 64.0% (18.6% grade 3/4) after median follow-up of 18.8, 12.7, and 14.8 months in the QW, Q2W, and prior TCR cohorts, respectively; there were few opportunistic infections, and 1.5% of infections led to death (**Table**)
- Overall, most infections were low grade; hypogammaglobulinemia or postbaseline immunoglobulin G (IgG) laboratory values <500 mg/dL occurred in 64.3%, 67.6%, and 72.5% of patients in QW, Q2W, and prior TCR cohorts, respectively
  - Few patients received intravenous immunoglobulin (IVIG; 14.7%, 13.1%, and 15.7% of patients, respectively)
- New-onset grade 3/4 infections were most prevalent during the first 100 days in all 3 cohorts; across clinically relevant infections, the most common were respiratory infections and COVID-19 (**Figure 2**)
- Neutrophil counts decreased during cycle 1 but showed a steady recovery beginning at cycle 2 (**Figure 3**)
- CD19+ B-cell levels showed no reduction over time (**Figure 4**), with an increasing trend noted at cycle 7; in addition, there was no decrease in polyclonal IgG (**Figure 5**)

TABLE: Summary of all infection events in MonumenTAL-1

Patients, n (%)	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=145)	Prior TCR (n=51)
Infections			
Any Grade	84 (58.7)	96 (66.2)	37 (72.5)
Grade 3/4	28 (19.6)	21 (14.5)	14 (27.5)
Led to death	3 (2.1)[a]	2 (1.4)[b]	0
Led to discontinuation	2 (1.4)	0	1 (2.0)
Led to dose interruption	45 (31.5)	49 (33.8)	19 (37.3)
Opportunistic infections	5 (3.5)	8 (5.5)	3 (5.9)
Grade 3/4	2 (1.4)	0	1 (2.0)
Grade 3/4 neutropenia	45 (31.5)	32 (22.1)	27 (52.9)
Any infection + concomitant Grade 3/4 neutropenia	11 (7.7)	3 (2.1)	9 (17.6)
Grade 3/4 infection + concomitant Grade 3/4 neutropenia	4 (2.8)	1 (0.7)	1 (2.0)

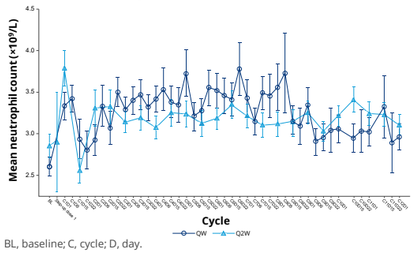
[a]Deaths were due to COVID-19 pneumonia, fungal sepsis, and septic shock. [b]Deaths were due to COVID-19 pneumonia and infection.

FIGURE 2: Timing and severity of clinically relevant infections in all cohorts[a]



[a]COVID-19 infections were irrespective of causal relation to talquetamab. GI, gastrointestinal.

FIGURE 3: Neutrophil counts over time



BL, baseline; C, cycle; D, day.

FIGURE 4: Absolute counts of B cells over time

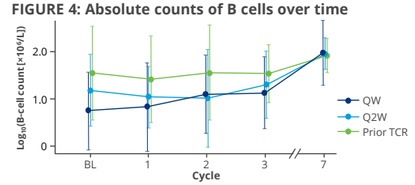
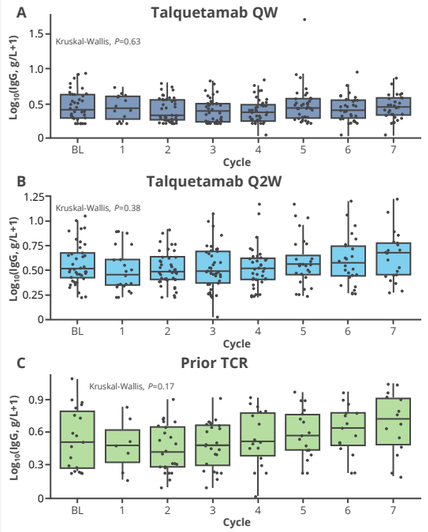


FIGURE 5: IgG levels over time in all cohorts[a]



[a]Data were censored for patients with IgG myeloma and after IVIG administration.

KEY TAKEAWAY

Patients treated with talquetamab showed effective myeloma control with concurrent preservation of humoral immune function and recovery of cytopenias, distinguishing talquetamab as an important emerging therapy for RRMM

CONCLUSIONS

- ~20% of patients experienced grade 3/4 infections, with low rates of opportunistic infections and discontinuations and deaths due to infections
- Infection rates, particularly rates of higher grade and fatal infections, occurred less frequently with talquetamab compared with those observed in BCMA-targeted T-cell–based therapies[2,6]
- No decreases in B cells or polyclonal IgG were observed, supporting talquetamab as a B-cell–sparing treatment and allowing maintenance of key elements of humoral immunity

ACKNOWLEDGMENTS

This study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Alana Dorfstatter, PharmD, of Eloquent Scientific Solutions, and funded by Janssen Scientific Affairs, LLC. This abstract was previously presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 2–6, 2023; Chicago, IL, USA & Virtual.

DISCLOSURES

PR-O has served in a consulting or advisory role with AbbVie, BMS, GSK, Janssen, Pfizer, and Sanofi; has received speakers' bureau fees from BMS, GSK, Janssen, and Sanofi; has received travel expenses from Pfizer; and has received honoraria from AbbVie, Celgene, GSK, H3 Biomedicine, Janssen, Pfizer, and Sanofi. **CS** has served in a consulting or advisory role with Janssen; and has received research funding and honoraria from Janssen. **AC** has served in a consulting or advisory role with AbbVie, Amgen, Antengene, BMS/Celgene, Genentech, Genzyme, GSK, Janssen Oncology, Karyopharm Therapeutics, OncoPeptides, Seagen, Secura Bio, Shattuck Labs, and Takeda; and has received research funding from Amgen, Celgene, Janssen, Pharmacyclics, Seagen, and Takeda. **BL** has served in a consulting or advisory role with BMS, GSK, Janssen Oncology, Karyopharm Therapeutics, Sanofi, and Takeda; and has received research funding from Amgen, Celgene, Cellectar, Janssen, Karyopharm Therapeutics, and Seagen. **NL** has no conflicts to disclose. **LR** has served in a consulting or advisory role with BMS, GSK, Janssen, Pfizer, and Sanofi; has received honoraria from Amgen, BMS, GSK, Janssen, Pfizer, and Sanofi; and has received research funding from BMS and Skyline Diagnostics. **DV**, **SS**, **RIV**, **XM**, **SK**, **BWH**, **TM**, **MC**, and **TR** are employees of Janssen; and may own stock in Johnson & Johnson/Janssen. **JT** is an employee of Janssen; may own stock in Johnson & Johnson/Janssen; has served in a consulting or advisory role with Janssen; and has received research funding from Janssen. **CH** is an employee of Janssen; may own stock in Johnson & Johnson/Janssen; and has received patents or royalties from Janssen. **MDS** is an employee of Amgen and Janssen; and may own stock in Amgen and Johnson & Johnson/Janssen. **NWCJvdD** has served in a consulting or advisory role with Adaptive Biotechnologies, Amgen, Bayer, BMS, Celgene, Janssen, Novartis, Roche, Servier, and Takeda; and has received research funding from Amgen, BMS, Celgene, Cellectis, Janssen, and Novartis.

REFERENCES:

1. Raje NS, et al. *Lancet Hematol* 2022;9:e143-61. 2. Mohan M, et al. *Blood Adv* 2022;6:2466-70. 3. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 4. Kodama T, et al. *Mol Cancer Ther* 2019;18:1555-64. 5. Chari A, et al. Presented at ASH; December 10–13, 2022; New Orleans, LA. 6. Moreau P, et al. *N Engl J Med* 2022;387:495-505.

Presented at the 11th Annual Meeting of the Society of Hematologic Oncology (SOHO); September 6–9, 2023; Houston, TX, USA