Preliminary Recommendations for Prevention and Management of Infections, Hypogammaglobulinemia, and Neutropenia During Treatment With Teclistamab Based on Experience From the MajesTEC-1 Study

Salomon Manier[1], Ajay K Nooka[2], Cesar Rodriguez[3], María-Victoria Mateos[4], Katherine Chastain[5], Arnob Banerjee[6], Rachel Kobos[5], Keqin Qi[7], Raluca Verona[6], Margaret Doyle[8], Thomas G Martin[9], Niels WCJ van de Donk[10]

[1]Lille University Hospital, Lille, France; [2]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [3]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [4]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [5]Janssen Research & Development, Raritan, NJ, USA; [6]Janssen Research & Development, Spring House, PA, USA; [7]Janssen Research & Development, Titusville, NJ, USA; [8]Janssen Sciences Ireland, Dublin, Ireland; [9]University of California, San Francisco, San Francisco, CA, USA; [10]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands

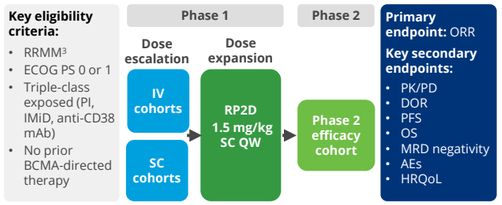
INTRODUCTION

- Patients with relapsed/refractory multiple myeloma (RRMM) are at an increased risk of infection,[1] which may be further increased by B-cell maturation antigen (BCMA)–targeting bispecific antibodies[2-4]
- Teclistamab is the only approved BCMA×CD3 bispecific antibody with a personalized, weight-based dosing schedule for the treatment of triple-class exposed RRMM, based on an overall response rate of 63.0%, median progression-free survival of 11.3 months, and median duration of response of 18.4 months[5-7]
- We provide preliminary recommendations for the prevention and management of potential infections, hypogammaglobulinemia, and neutropenia during teclistamab treatment

METHODS

- Full details of MajesTEC-1 (NCT03145181/NCT04557098) have been published[7,8]
- The MajesTEC-1 study design is shown in **Figure 1**
  - Patients must have had no evidence of serious bacterial, viral, or fungal infections to initiate treatment with teclistamab
  - Monitoring, prophylaxis, and management of infections, neutropenia, and hypogammaglobulinemia were per institutional guidelines

FIGURE 1: MajesTEC-1[a] study design



[a]NCT03145181, NCT04557098. AE, adverse event; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IMiD, immunomodulatory drug; IV, intravenous; mAb, monoclonal antibody; MRD, minimal residual disease; PD, pharmacodynamics; PI, proteasome inhibitor; PK, pharmacokinetics; QW, weekly; RP2D, recommended phase 2 dose; SC, subcutaneous.

MULTIPLE MYELOMA

RESULTS

- This analysis included 165 patients treated with the recommended phase 2 dose of teclistamab, with a median follow-up 22.8 months (range, 0.3–33.6)
- Infections were observed in 80.0% of patients overall (**Table 1**)

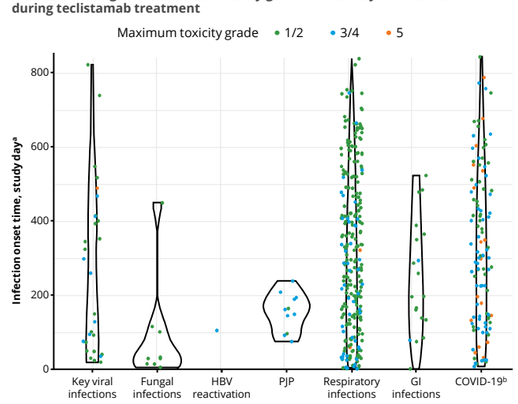
TABLE 1: Overall incidence and timing of infections during teclistamab treatment

	MajesTEC-1 study population (N=165)
Any-Grade infection, n (%)	132 (80.0)
Grade 3/4 infection, n (%)	91 (55.2)
Discontinuation due to infection, n (%)[a]	5 (3.0)
Death due to infection, n (%)[b]	21 (12.7)
Median time to first onset of infection, months (range) Any-Grade infection Grade ≥3 infection	 1.7 (0.0–24.7) 4.2 (0.0–34.6)

[a]Infections leading to teclistamab discontinuation were grade 3 adenoviral pneumonia (n=1), grade 3 COVID-19 (n=1), grade 4 COVID-19 (n=1), grade 3 *Pneumocystis jirovecii* pneumonia (n=1), grade 4 progressive multifocal leukoencephalopathy (n =1), and grade 4 sepsis (n=1). [b]Infections leading to death were COVID-19 (n=18), bilateral pneumonia (unknown pathogen; n=1), pneumococcal pneumonia (n=1), and progressive multifocal leukoencephalopathy (n=1).

- The timing and severity of clinically relevant infections (ie, those typically seen in patients with RRMM) during teclistamab treatment are shown in **Figure 2**
- **Table 2** summarizes the incidence, management, and key recommendations for infections, hypogammaglobulinemia, and neutropenia based on experience from MajesTEC-1

FIGURE 2: Timing and maximum toxicity grade of clinically relevant infections during teclistamab treatment



Infections were selected based on categories of clinically relevant infections typically occurring in patients with RRMM using MedDRA v24.0. Each point on the plot represents an individual infection (ie, patients were included for every infection event they experienced within these categories), colored according to maximum toxicity grade (1/2, 3/4, or 5). Key viral infections included parvovirus B19 infection, adenovirus infection and reactivation, adenoviral pneumonia, oral herpes, herpes zoster virus infection, cytomegalovirus viremia and reactivation, BK virus infection, and progressive multifocal leukoencephalopathy. [a]Relative to each patient based on their individual treatment start date. Days 200, 400, 600, and 800 correspond with 6.6, 13.2, 19.7, and 26.3 months, respectively. [b]Most patients were enrolled before COVID-19 vaccines were available; 99 (60.0%) patients received at least 1 COVID-19 vaccination dose during the study, including 12 of the 18 patients who died from COVID-19.
GI, gastrointestinal; HBV, hepatitis B virus; MedDRA, Medical Dictionary for Regulatory Activities; PJP, *Pneumocystis jirovecii* pneumonia.

TABLE 2: Incidence, management, and key recommendations for infections, hypogammaglobulinemia, and neutropenia during teclistamab treatment

	Severity (Gr 1/2 / Gr 3/4 / Gr 5)	Prophylaxis and management in MajesTEC-1	Key recommendations
Key viral infections[a]	12.1% overall 7.9% / 3.6% / 0.6%	• Antivirals for prophylaxis and management per institutional guidelines • Teclistamab interruption	• HSV/HZV prophylaxis recommended • Prophylaxis and management per institutional guidelines and working group recommendations • Consider teclistamab interruption • Consider monitoring for EBV, HHV6, and CMV
HBV reactivation	0.6% overall 0.6%		• Prophylaxis and management per institutional guidelines and working group recommendations • Consider teclistamab interruption
COVID-19 infection	29.1% overall 7.3% / 10.9% / 10.9%	• Glucocorticoids, monoclonal antibodies, hyperimmune plasma • Teclistamab interruption • Vaccinations (including booster doses)	• Up-to-date with COVID-19 vaccinations • Management per institutional guidelines • Consider teclistamab interruption
Fungal infections[b]	5.5% overall 5.5%	• Prophylaxis and management per institutional guidelines • Teclistamab interruption	• Prophylaxis (for high-risk patients) and management per institutional guidelines and working group recommendations • Consider teclistamab interruption
PJP infections	4.2% overall 4.2%		• PJP prophylaxis recommended • Prophylaxis and management per institutional guidelines and working group recommendations • Consider teclistamab interruption
Respiratory infections	57.6% overall 38.2% / 18.2% / 1.2%		• Antibacterial prophylaxis (for high-risk patients) and management per institutional guidelines and working group recommendations • Consider teclistamab interruption
GI infections	9.1% overall 7.9% / 1.2%		• Prophylaxis and management per institutional guidelines and working group recommendations • Consider teclistamab interruption
Hypogammaglobulinemia	71.5% overall 21.2% AE / 70.9% IgG <400 mg/dL Median time to IgG <400 mg/dL, 1.2 months (range, 0.2–19.8)	• Prophylaxis and management with IVIG per institutional guidelines	• IVIG to maintain serum IgG levels ≥400 mg/dL • IVIG per institutional guidelines prophylactically, for life-threatening infections and for serious or recurrent infections
Neutropenia	71.5% overall 6.0% / 65.5% Median time to grade ≥3 neutropenia or febrile neutropenia, 2.3 months (range, 0.0–18.1)	• Prophylaxis and management with G-CSF per institutional guidelines	• Consider G-CSF for grade ≥3 neutropenia with infection/fever and grade 4 neutropenia • Avoid growth factors during step-up dosing and CRS where possible[c]

Infections were selected based on categories of clinically relevant infections typically occurring in patients with RRMM using MedDRA v24.0. Patients were counted once for any given event, regardless of the number of times they experienced the event. If toxicity grade was missing for a specific infection, the patient was only counted in the total percentage for that infection. [a]Excluding COVID-19. [b]Excluding PJP. [c]Where possible, growth factors should not be given during the step-up dosing schedule or during CRS, based on the theoretical potential for increased CRS severity due to temporal myeloid cell stimulation.[5,9,10] AE, adverse event; CMV, cytomegalovirus; CRS, cytokine release syndrome; EBV, Epstein-Barr virus; G-CSF, granulocyte colony-stimulating factor; Gr, grade; HHV6, human herpesvirus 6; HSV, herpes simplex virus; HZV, herpes zoster virus; IgG, immunoglobulin G; IVIG, intravenous immunoglobulin G.

KEY TAKEAWAY

Patients should be closely monitored for a range of infection types throughout teclistamab treatment to facilitate prompt investigation and intervention

CONCLUSIONS

- Before starting teclistamab, patients should be up-to-date with all vaccinations (including COVID-19) and screened for hepatitis B and C and HIV
- Teclistamab should not be given in patients with any active infections
- Prophylaxis for PJP and HSV/HZV is recommended during teclistamab treatment; other prophylactic antimicrobials should be administered per institutional guidelines (antibacterial and antifungal prophylaxis can be considered for patients at high risk of these infections)
- IVIG should be administered prophylactically, for life-threatening infections, and for serious or recurrent infections per institutional guidelines. Growth factors should be considered for grade ≥3 neutropenia with infection/fever and grade 4 neutropenia

ACKNOWLEDGMENTS

We thank the patients who participated in the study and their families and caregivers, the physicians and nurses who cared for patients and supported this clinical trial, staff members at the study sites, and staff members involved in data collection and analyses. This study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Emily Bell, BSc, of Eloquent Scientific Solutions, and funded by Janssen Scientific Affairs, LLC. This abstract was previously presented at the 9th World Congress on Controversies in Multiple Myeloma (COMy); May 11–14, 2023; Paris, France & Virtual.

DISCLOSURES

SM is a consultant for AbbVie, Adaptive Biotechnology, Amgen, Celgene/BMS, GSK, Janssen, Novartis, Oncopeptide, Regeneron, Roche, Sanofi and Takeda. **AKN** has received honoraria and has served in a consulting/advisory role for Adaptive Biotechnologies, Amgen, BeyondSpring Pharmaceuticals, BMS, Cellectar, Genzyme, GSK, Janssen, Karyopharm Therapeutics, Oncopeptides, QNK Therapeutics, Pfizer, Secura Bio, and Takeda; reports travel, accommodations, and expenses from GSK; has received research funding from Amgen, Arch Oncology, BMS/Celgene, Cellectar, GSK, Janssen, Pfizer, and Takeda. **CR** has served in a consulting/advisory role for Amgen, BMS, Janssen, Karyopharm Therapeutics and Takeda. **M-VM** has served in a consulting/advisory role for AbbVie, Amgen, Celgene, GSK, Janssen-Cilag, Pfizer, Regeneron, Roche/Genentech, and Takeda; and received honoraria from AbbVie/Genentech, Amgen, Celgene, GSK, Janssen-Cilag, Sanofi, and Takeda. **KC**, **AB**, **RK**, **KQ**, **RV**, and **MD** are employed by and own stock in Janssen. **TGM** has served in a consulting/advisory role for GSK and Legend Biotech; and has received research funding from Amgen, Janssen, and Sanofi. **NWCJvdD** has served in a consulting/advisory role for 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 Haematol* 2022;9:e143-61. 2. Mohan M, et al. *Blood Adv* 2022;6:2466-70. 3. Lancman G, et al. *Blood Cancer Discov* 2021;2:423-33. 4. Cliff ERS, et al. *J Clin Oncol* 2023;41:1949-51. 5. TECVAYLI (teclistamab). Summary of product characteristics. Leiden, Netherlands: Janssen Biologics BV; 2022. 6. TECVAYLI (teclistamab-cqyv). Prescribing information. Horsham, PA: Janssen Biotech, Inc; 2022. 7. Moreau P, et al. *N Engl J Med* 2022;387:495-505. 8. Usmani SZ, et al. *Lancet* 2021;398:665-74. 9. Gaut D, et al. *Int J Cancer* 2021;148:1192-6. 10. Miller KC, et al. *Blood Cancer J* 2022;12:146.

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