Longer-Term Follow-Up of Patients Receiving Prophylactic Tocilizumab for the Reduction of Cytokine Release Syndrome in the Phase 1/2 MajesTEC-1 Study of Teclistamab in Relapsed/Refractory Multiple Myeloma

Niels WCJ van de Donk[1], Alfred L Garfall[2], Lotfi Benboubker[3], Katarina Uttervall[4], Kaz Groen[1], Laura Rosiñol[5], Jeffrey Matous[6], Deeksha Vishwamitra[7], Caroline Hodin[8], Tara Stephenson[7], Keqin Qi[9], Athena Zuppa[7], Katherine Chastain[10], María-Victoria Mateos[11]

[1]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [2]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [3]Hôpital Bretonneau, Centre Hospitalier Régional Universitaire, Tours, France; [4]Karolinska University Hospital, Stockholm, Sweden; [5]Hospital Clínic de Barcelona, IDIBAPS, Barcelona, Spain; [6]Colorado Blood Cancer Institute and Sarah Cannon Research Institute, Denver, CO, USA; [7]Janssen Research & Development, Spring House, PA, USA; [8]Janssen Research & Development Beerse, Antwerp, Belgium; [9]Janssen Research & Development, Titusville, NJ USA; [10]Janssen Research & Development, Raritan, NJ, USA; [11]Hospital Universitario de Salamanca, Instituto de Investigación Biomédica de Salamanca (IBSAL), Centro de Investigación del Cáncer (IBMCC-USAL,CSIC), Salamanca, Spain

Presented by NWCJ van de Donk at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA & Virtual

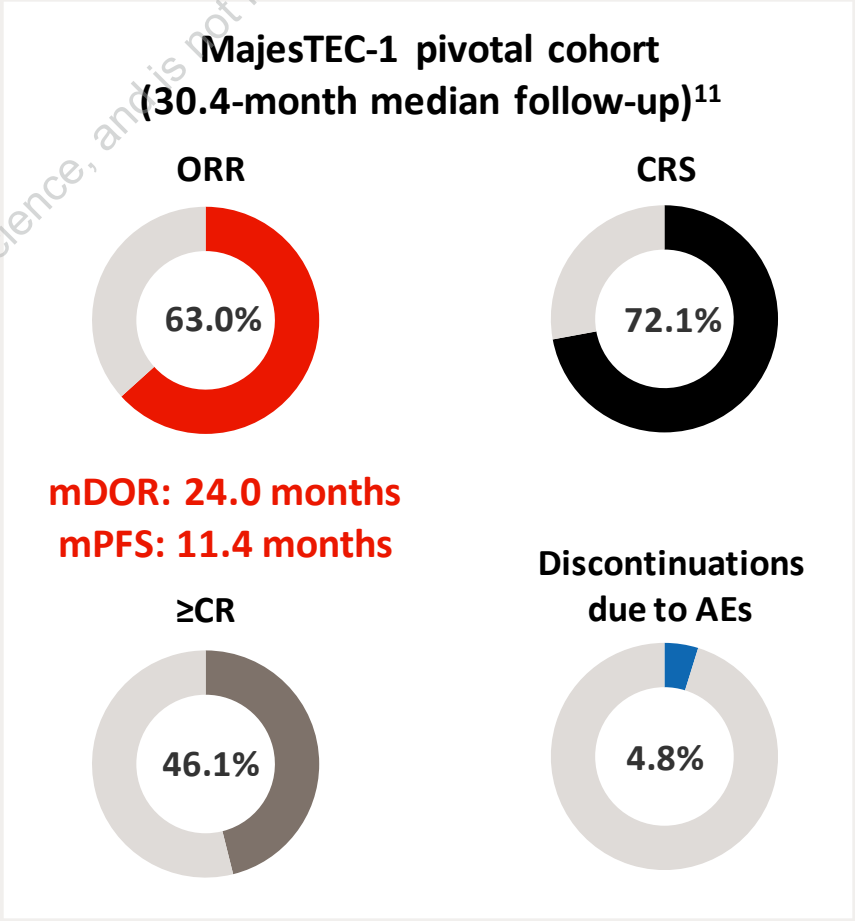
MajesTEC-1 Prophylactic Tocilizumab Cohort: Takeaway Message

Prophylactic tocilizumab reduced the overall incidence of CRS with teclistamab by 65% relative to the pivotal MajesTEC-1 population, with no new safety signals or impact on response

CRS, cytokine release syndrome.

Introduction

- Teclistamab is the first approved BCMA×CD3 BsAb for TCE RRMM, with weight-based dosing and longest study follow-up of any BsAb in MM[1-3]
- In the phase 1/2 MajesTEC-1 study, 72.1% of patients experienced CRS (all grade 1/2 except 1 grade 3 event in 1 patient)[3,4]
- Teclistamab has been given successfully in the outpatient setting, with prophylactic tocilizumab used to manage CRS[5-9]
- In a separate cohort of MajesTEC-1, prophylactic tocilizumab prior to step-up dose 1 reduced CRS to 26% (all grade 1 and 2) at 2.6-month median follow-up[10]
  - Here, we present data with a longer median follow-up of 8.1 months in the prophylactic tocilizumab cohort (n=24) in MajesTEC-1

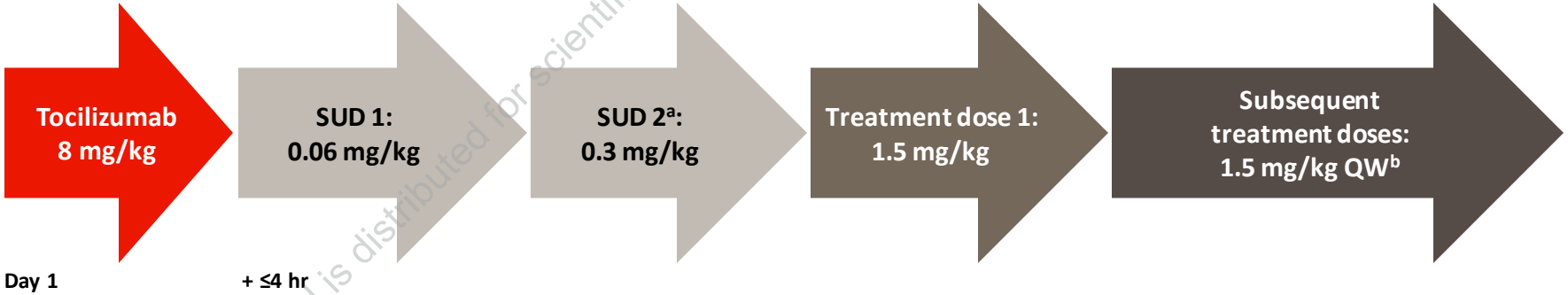


BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CD3, cluster of differentiation 3; CRS, cytokine release syndrome; mDOR, median duration of response; MM, multiple myeloma; mPFS, median progression-free survival; RRMM, relapsed/refractory multiple myeloma; TCE, triple-class exposed.

1. TECVAYLI (teclistamab). Summary of Product Characteristics. Leiden, The Netherlands. Janssen Biologics BV; 2022. 2. TECVAYLI (teclistamab-cqyv). Prescribing Information. Horsham, PA: Janssen Biotech, Inc; 2022. 3. Moreau P, et al. *NEJM* 2022;387:495-505. 4. Martin TG, et al. *Cancer* 2023;129(13):2035-2046. 5. Trudel S, et al. *Blood* 2022;140(Suppl 1):1363-5. 6. Kauer J, et al. *J Immunother Cancer* 2020;8:e000621. 7. Scott, S et al. *Blood Cancer J* 2023;13(1):191. 8. Kowalski A, et al. Blood (2023) 142 (Supplement 1): 4709. 9. Varshavsky-Yanovsky AN, et al. *Hemasphere* 2023;7(Suppl):e605007f. 10. van de Donk NWCJ, et al. Presented at ASCO; June 2-6, 2023; Chicago, IL, USA. Poster #8033. 11. Garfall AL, et al. Presented at ASCO; May 31-June 4, 2024; Chicago, IL, USA. Poster #7540.

MajesTEC-1 Prophylactic Tocilizumab Cohort: Study Design

- Patients received teclistamab 1.5 mg/kg weekly (phase 1 exploratory cohort) or a comparable fixed dose after a single dose of tocilizumab and SUD
  - Tocilizumab 8 mg/kg was administered intravenously ≤4 hours before the first teclistamab SUD
  - Dexamethasone, acetaminophen, and diphenhydramine were given as premedications during the teclistamab SUD schedule
  - Hospitalization was required for 48 hours after each SUD and after the first treatment dose
- Tocilizumab treatment was permitted for grade 1 CRS and recommended for grade ≥2
- CRS as an AE was graded per Lee et al[1]



[a]2–4 days were allowed between SUD 1, SUD 2, and treatment dose 1. [b]Less frequent dosing (e.g., Q2W) starting cycle 3.
CRS, cytokine release syndrome; IV, intravenous; PR, partial response; QW, weekly; Q2W, every other week; RP2D, recommended phase 2 dose; SC, subcutaneous; SUD, step-up dose.
1. Lee DW, et al. *Blood* 2014;124:188-95.

MajesTEC-1 Prophylactic Tocilizumab Cohort: Baseline Characteristics

- 24 patients received prophylactic tocilizumab prior to SUD 1 of teclistamab
  - Median follow-up: 8.1 months (range, 0.9–13.2)
- Patient demographics and disease characteristics were generally consistent with the MajesTEC-1 pivotal population[1]

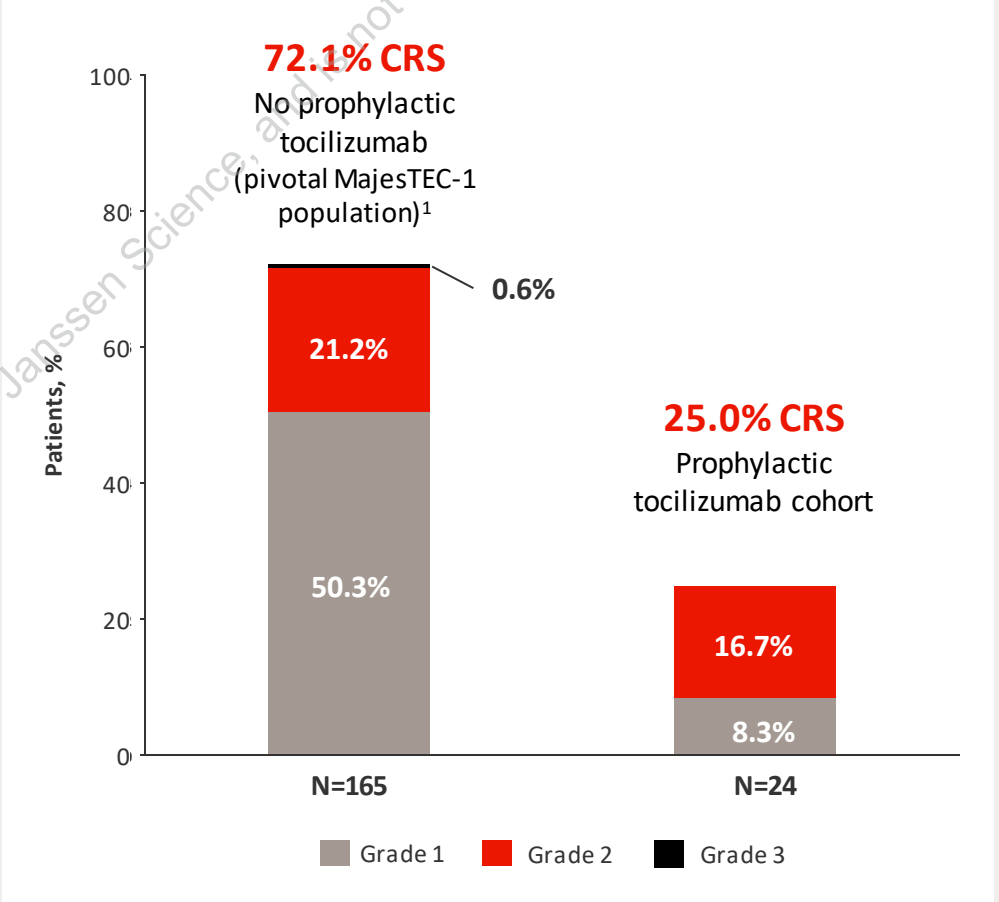
Characteristic	All patients (N=24)
Median age, years (range)	72 (50–82)
Male, n (%)	14 (58.3)
Race, n (%)	
White	19 (79.2)
Other	2 (8.3)
Not reported	3 (12.5)
ECOG PS score, n (%)	
0	13 (54.2)
1	11 (45.8)
Extramedullary plasmacytomas,[a] n (%)	
0	19 (79.2)
≥1	5 (20.8)
High-risk cytogenetics,[b] n (%)	6 (26.1)
ISS stage, n (%)	
I	16 (66.7)
II	7 (29.2)
III	1 (4.2)
Median prior lines of therapy, n (range)	4 (2–9)
Triple-class refractory,[c] n (%)	14 (58.3)
% BMPCs (biopsy or aspirate), n (%)	
<30	16 (66.7)
30–59	3 (12.5)
≥60	5 (20.8)

Data cut-off: Nov 1, 2023. [a]≥1 soft-tissue plasmacytoma not associated with bone. [b]n=23; high-risk cytogenetics included del(17p), t(4;14), t(14;16). [c]≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and an anti-CD38 monoclonal antibody. BMPC, bone marrow plasma cell; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; SUD, step-up dose.

1. Moreau P, et al. *N Engl J Med* 2022;387:495-505.

MajesTEC-1 Prophylactic Tocilizumab Cohort: CRS Incidence and Severity

- CRS with prophylactic tocilizumab (25%)
  - Grade 1 (n=2); grade 2 (n=4); no grade 3 events
  - 3 patients each had 1 recurrent event
  - Median time to onset: 2 days (range, 1–3)
  - Median duration: 2 days (range, 2–4)
  - All events resolved
- All initial events occurred during teclistamab SUD 1 and SUD 2



Data cut-off: Nov 1, 2023.
CRS, cytokine release syndrome; SUD, step-up dosing.
1. Martin TG, et al. *Cancer* 2023;129:2035-46.

MajesTEC-1 Prophylactic Tocilizumab Cohort: CRS and Baseline Characteristics

- No disease characteristic was associated with CRS, consistent with the pivotal cohort[1]; however, small sample size precludes clinically meaningful conclusions

Prophylactic tocilizumab cohort (N=24)			
Characteristic	**No CRS (n=18)**	**CRS Grade 1 (n=2)**	**CRS Grade 2 (n=4)**
% BMPCs			
Median	8.0	19.0	62.5
Range	0–80	8–30	30–80
ISS stage,[a] %			
I	72.2	50	50
II	22.2	50	50
III	5.6	0	0
No. of EMPs			
Median	0	0	0
Range	0–4	0	0–2

Data cut-off: Nov 1, 2023.. [a]Derived based on the combination of serum β_2-microglobulin and albumin.
BMPC, bone marrow plasma cell; CRS, cytokine release syndrome; EMP, extramedullary plasmacytoma; ISS, International Staging System.
1. Martin TG, et al. *Cancer* 2023;129:2035-46.

MajesTEC-1 Prophylactic Tocilizumab Cohort: Safety Generally Consistent with MajesTEC-1 Pivotal Cohort[1]

- Grade 3/4 infections occurred in 25% of patients and included:
  - Pneumonia (n=4)
  - Bacterial infection (n=1)
  - Diverticulitis (n=1)
  - CMV infection (n=1)
  - Sepsis (n=1)
  - Septic shock (n=1)
- 5 patients had 10 neurotoxicity[a] events including:
  - Headache, ICANS, myoclonus, dizziness, and insomnia
  - All events were grade 1–2
  - All events resolved except for grade 2 headache
- Grade 5 pulmonary embolism occurred 20 days after the last teclistamab dose

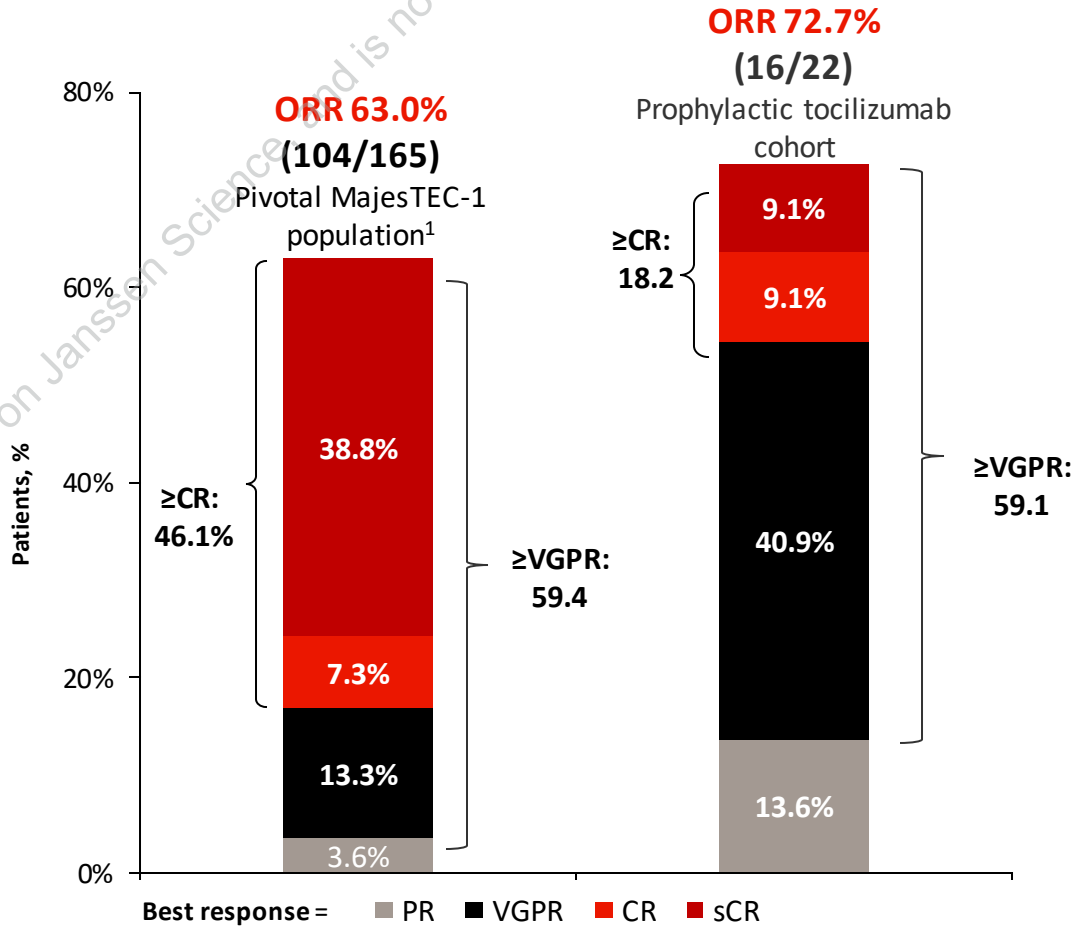
Prophylactic tocilizumab cohort (N=24)		
TEAE, n[b] (%)	Any Grade	Grade 3/4
Infections[c]	19 (79.2)	6 (25.0)
Neutropenia	15 (62.5)	15 (62.5)
Anemia	14 (58.3)	6 (25.0)
Thrombocytopenia	12 (50.0)	6 (25.0)
Lymphopenia	9 (37.5)	9 (37.5)
Leukopenia	6 (25.0)	5 (20.8)
Increased lipase	6 (25.0)	5 (20.8)

[a]Neurotoxicity is defined as a neurological adverse event considered related by investigator. [b]TEAEs are listed if occurring at grade 3/4 in ≥20% of patients. [c]Rate of any grade infections and grade 3/4 in the MajesTEC-1 pivotal was 63.0% and 30.9%, respectively, at 7.2 months median follow-up.
CMV, cytomegalovirus; ICANS, immune effector cell–associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event.
1. Garfall AL, et al. Presented at ASCO; May 31–June 4, 2024; Chicago, IL, USA & Virtual. Poster #7540.

MajesTEC-1 Prophylactic Tocilizumab Cohort: Efficacy Outcomes

Response to teclistamab (22 of 24 patients evaluable)[a]

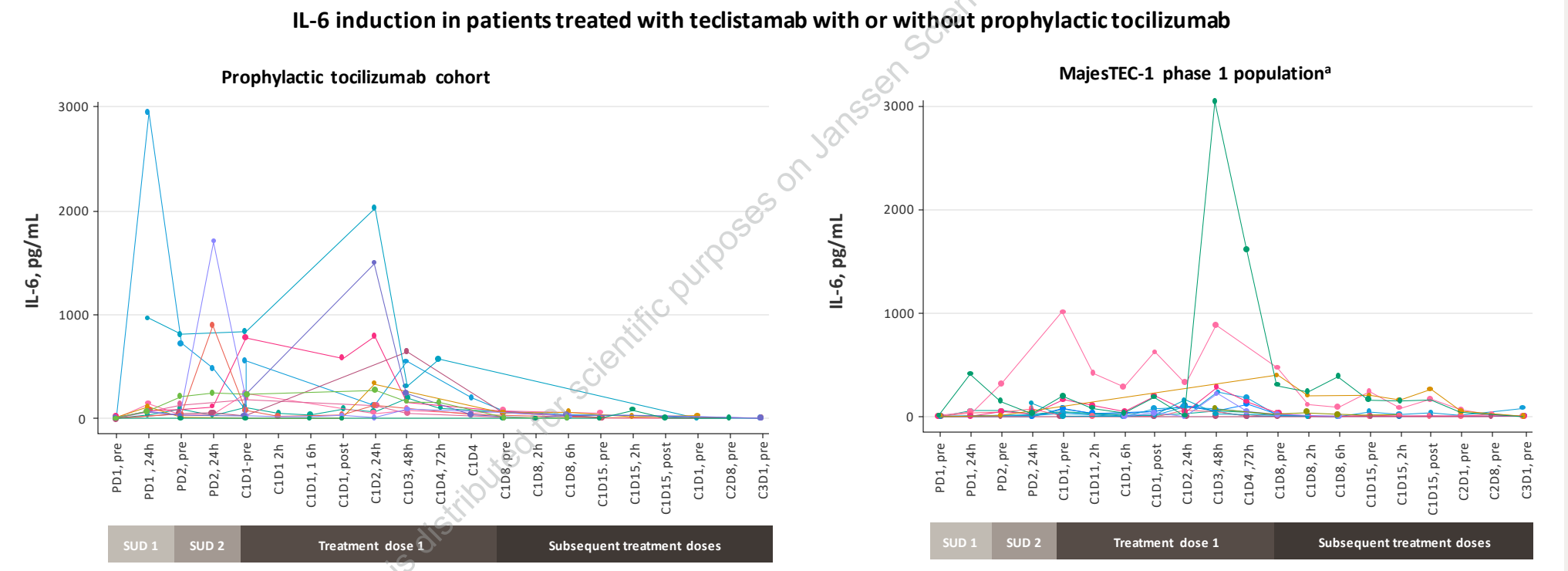
- Responses were generally consistent with the MajesTEC-1 pivotal population[1]
  - The lower ≥CR rate in the prophylactic tocilizumab cohort is likely due to limited availability of bone marrow samples to confirm CR and duration of follow-up
  - With 5.5 months of additional follow-up since the last published report,[2] prophylactic tocilizumab still does not appear to affect response to teclistamab



[a]Response evaluable patients received ≥ 1 study treatment and have ≥ 1 post-baseline response evaluation by the investigator.
CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
1. Garfall AL, et al. Presented at ASCO; May 31–June 4, 2024; Chicago, IL, USA & Virtual. Poster #7540. 2. van de Donk NWCJ, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. Poster #8033.

MajesTEC-1 Prophylactic Tocilizumab Cohort: Cytokine Profiles

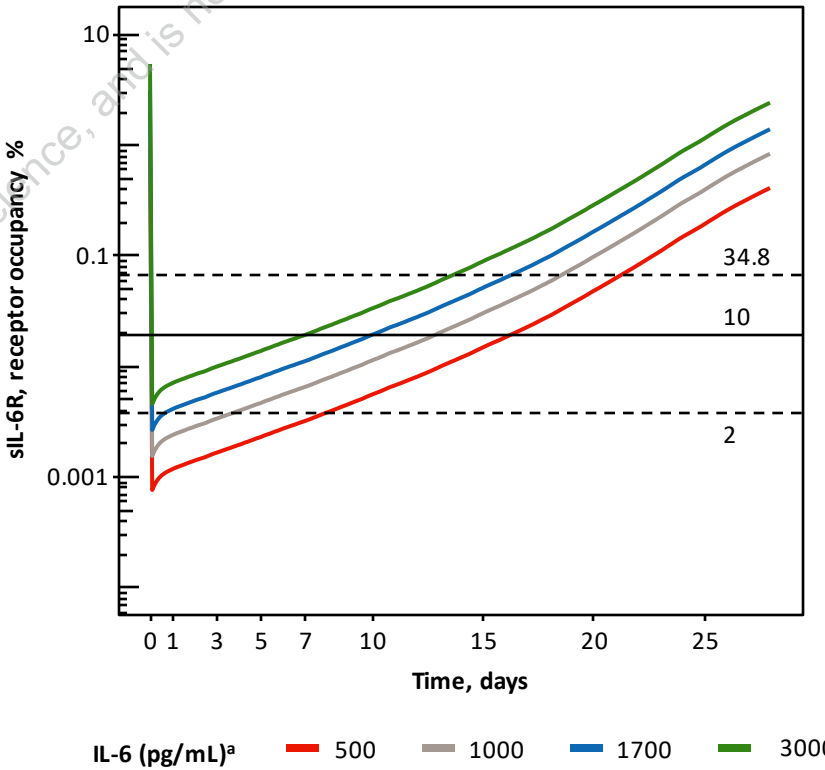
- Timing of IL-6 induction was consistent with phase 1 MajesTEC-1 population[1]
  - Magnitude of IL-6 induction was greater with prophylactic tocilizumab



[a]Treated with the recommended phase 2 dose of teclistamab (1.5 mg/kg weekly), without prophylactic tocilizumab.
C, cycle; D, day; IL, interleukin; IL-6R, IL-6 receptor; PD, priming dose; post, post dose; pre, pre dose.
1. van de Donk NWCJ, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. Poster #8033.

MajesTEC-1 Prophylactic Tocilizumab Cohort: IL-6 Pathway Activity

- Based on modeling data, a single dose of prophylactic tocilizumab blocks IL-6 receptor occupancy for ~10 days[1]
- Duration of IL-6 signaling blockade spans the teclistamab dosing schedule, supporting the approach for lowering overall risk of CRS during teclistamab SUD



[a]Curves indicate sIL-6R receptor occupancy % by IL-6 in the presence of tocilizumab at different IL-6 concentrations (500, 1000, 1700, and 3000 pg/mL). Horizontal lines indicate sIL-6R in the absence of tocilizumab at different IL-6 concentrations (2, 10, and 34.8 pg/mL). CRS, cytokine release syndrome; IL, interleukin; IL-6R, IL-6 receptor; sIL-6R, soluble IL-6 receptor; SUD, step-up dose.

1. Zhou J, et al. Presented at ASH; December 9–12, 2023; San Diego, CA, USA. Poster #4670.

MajesTEC-1 Prophylactic Tocilizumab Cohort: Conclusions

- Incidence of CRS with teclistamab was reduced from 72.1%, without prophylactic tocilizumab in the pivotal cohort of MajesTEC-1, to 25% in the prophylactic tocilizumab cohort (all events grade 1/2)
- There were no new safety signals or impact on response to teclistamab with longer follow-up
- Further data to inform potential risk factors for higher-grade CRS is needed
- Prophylactic tocilizumab may be considered to mitigate risk of CRS for outpatient dosing of teclistamab[1]
  - A single dose of prophylactic tocilizumab blocks IL-6 receptor occupancy for ~10 days, covering the teclistamab SUD schedule
  - Prophylactic tocilizumab is being evaluated prior to teclistamab SUD 1 in the phase 2, multicenter, prospective OPTec study[2] (Poster #7528, June 3, 9:00 AM – 12:00 PM CDT)[3]

Prophylactic tocilizumab reduced the incidence of CRS with teclistamab, with a 65% relative reduction in overall incidence vs the pivotal MajesTEC-1 population

CRS, cytokine release syndrome; IL-6, interleukin-6; SUD, step-up dose.

1. Rodriguez-Otero P, et al, *Lancet Oncol* 2024;25: e205-16. 2. ClinicalTrials.gov, NCT05972135. 3. Rifkin R. Presented at ASCO; May 31–Jun 4 2024; Chicago, IL, USA & Virtual. Poster #7528.