Long-Term Follow-Up From MajesTEC-1 of Teclistamab, a BCMA×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma

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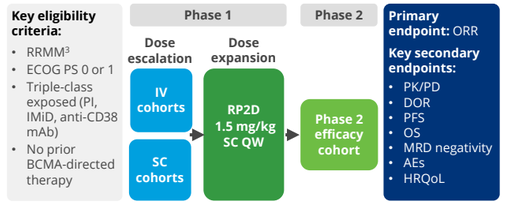
INTRODUCTION

- Teclistamab is the only approved B-cell maturation antigen (BCMA) × CD3 bispecific antibody with a personalized, weight-based dosing schedule for the treatment of triple-class exposed relapsed/refractory multiple myeloma (RRMM)[1]
- In the pivotal phase 1/2 MajesTEC-1 study, rapid, deep, and durable responses were observed in patients with triple-class exposed RRMM[2]
  - At median follow-up of 14.1 months, overall response rate (ORR) was 63.0% (complete response [CR] or better, 39.4%)
  - Median duration of response (mDOR), 18.4 months; median progression-free survival (mPFS), 11.3 months; median overall survival (mOS), 18.3 months
- Here, we present updated results from MajesTEC-1 at an extended median follow-up of ~2 years

METHODS

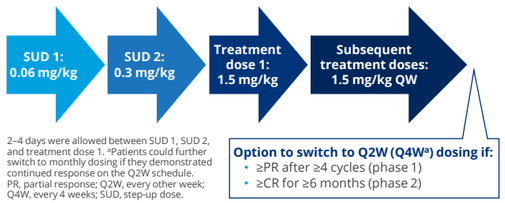
- The MajesTEC-1 study design was previously described[2] (**Figure 1** and **Figure 2**)

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.

FIGURE 2: Teclistamab dosing schedule



2–4 days were allowed between SUD 1, SUD 2, and treatment dose 1. [a]Patients could further switch to monthly dosing if they demonstrated continued response on the Q2W schedule. PR, partial response; Q2W, every other week; Q4W, every 4 weeks; SUD, step-up dose.

MULTIPLE MYELOMA

RESULTS

Study population

- At median follow-up of ~2 years (23 months; data cut-off January 4, 2023), 165 phase 1/2 patients had received teclistamab at the RP2D (**Table 1**)
  - A phase 2 efficacy subset (enrolled on or before March 18, 2021) was also evaluated (median follow-up, 22 months)
- In the overall population, 47 patients remain on treatment, 42 of whom have switched to Q2W dosing (9 on Q4W); 41 switched and maintained a deep response (Poster #MM-162)

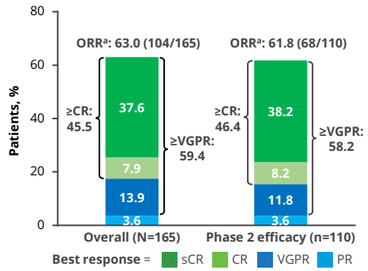
TABLE 1: Baseline characteristics

Characteristic	Overall (N=165)	Phase 2 efficacy (n=110)
Age (years), median (range)	64.0 (33–84)	66.0 (33–82)
Male, n (%)	96 (58.2)	62 (56.4)
Race, n (%)		
White	134 (81.2)	100 (90.9)
Black/African American	21 (12.7)	5 (4.5)
Asian	3 (1.8)	3 (2.7)
Other	7 (4.2)	1 (0.9)
EMD,[a] n (%)	28 (17.0)	19 (17.3)
High-risk cytogenetics, n/N (%)	38/148 (25.7)	24/96 (25.0)
ISS stage, n/N (%)		
I	85/162 (52.5)	55/109 (50.5)
II	57/162 (35.2)	41/109 (37.6)
III	20/162 (12.3)	13/109 (11.9)
Time since diagnosis (years), median (range)	6.0 (0.8–22.7)	6.4 (1.1-22.7)
Number of prior LOT, median (range)	5 (2–14)	5 (2–14)
Prior stem cell transplant, n (%)	135 (81.8)	89 (80.9)
Exposure status, n (%)		
Triple-class[b]	165 (100)	110 (100)
Penta-drug[c]	116 (70.3)	77 (70.0)
Refractory status, n (%)		
Anti-CD38 mAb	148 (89.7)	97 (88.2)
Triple-class[b]	128 (77.6)	84 (76.4)
Penta-drug[c]	50 (30.3)	28 (25.5)

[a]Includes patients who had ≥1 soft tissue plasmacytoma not associated with bone. [b]≥1 PI, ≥1 IMiD, and 1 anti-CD38 mAb. [c]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 mAb. EMD, extramedullary disease; ISS, International Staging System; LOT, line of therapy.

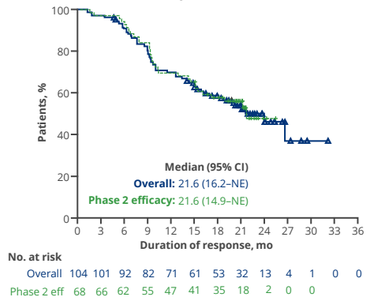
- 81.0% (34/42) of MRD-evaluable patients (at day 100) were MRD negative (10^{-5} threshold)
  - 81.5% (44/54) MRD-evaluable patients (as of Mar 2022[4]) were MRD negative at any point

FIGURE 3: Overall response rate



[a]ORR assessed by independent review committee. sCR, stringent CR; VGPR, very good partial response.

FIGURE 4: Duration of response



NE, not estimable.

Efficacy

- ORR: overall, 63.0%; phase 2 efficacy subset, 61.8% (**Figure 3**)
  - Responses continued to deepen and were durable (**Figure 3, Figure 4,** and **Table 2**)
  - 45.5% achieved ≥CR overall; phase 2 efficacy subset, 46.4%
  - ORR for patients with high-risk cytogenetics and/or EMD: 53.3% (32/60)
- Median time to ≥CR: 4.6 months (range, 1.6–18.5)
- Patients with ≤3 LOT
  - ORR, 74.4% (32/43); ≥CR, 58.1%; ≥VGPR, 72.1%
  - mPFS (95% CI),18.1 mo (13.8–26.9)
  - mOS (95% CI), 25.9 mo (18.3–NE)

TABLE 2: DOR, PFS, and OS

	Overall		Phase 2 efficacy (n=110)
	All patients (N=165)	≥CR (n=75)	
mDOR, mo (95% CI)	22 (16–NE)[a]	27 (22–NE)	22 (15–NE)[b]
mPFS, mo (95% CI)	11 (9–16)	27 (23–NE)	11 (7–16)
mOS, mo (95% CI)	22 (15–NE)	Not reached (NE–NE)	22 (13–NE)

[a]n=104; [b]n=68.

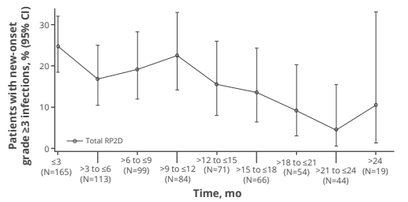
Safety

- The most common AEs remained cytopenias, infections, and cytokine release syndrome (**Table 3**)
- Immune effector cell–associated neurotoxicity syndrome (n=5, all grade 1/2 and resolved) and CRS unchanged since previous report[2]
- Infections occurred in 132 (80.0%) patients overall (grade 3/4, 55.2%)
- Onset of new grade ≥3 infections decreased over time, corresponding with the timing of switch to less frequent dosing (**Figure 5**)
- AEs leading to dose reduction (n=1) or discontinuation (n=8, including 5 due to infection) were infrequent
- 7 treatment-related deaths occurred (4 due to COVID-19)
- No new safety signals were reported

TABLE 3: AEs in MajesTEC-1

AEs ≥20%, n (%)	N=165	
	Any Grade	Grade 3/4
Hematologic		
Neutropenia	118 (71.5)	108 (65.5)
Anemia	90 (54.5)	62 (37.6)
Thrombocytopenia	70 (42.4)	37 (22.4)
Lymphopenia	60 (36.4)	57 (34.5)
Leukopenia	33 (20.0)	15 (9.1)
Nonhematologic		
Infections	132 (80.0)	91 (55.2)
Cytokine release syndrome	119 (72.1)	1 (0.6)
Diarrhea	56 (33.9)	6 (3.6)
Pyrexia	52 (31.5)	1 (0.6)
Fatigue	48 (29.1)	4 (2.4)
COVID-19	48 (29.1)	35 (21.2)
Nausea	45 (27.3)	1 (0.6)
Cough	44 (26.7)	0
Injection site erythema	43 (26.1)	0
Arthralgia	42 (25.5)	1 (0.6)
Headache	40 (24.2)	1 (0.6)
Constipation	36 (21.8)	0
Hypogammaglobulinemia	34 (20.6)	3 (1.8)

FIGURE 5: New-onset grade ≥3 infections over time



KEY TAKEAWAY

With ~2-year median follow-up, responses to teclistamab continued to deepen and were durable, even in patients who switched to Q2W or Q4W dosing schedules

CONCLUSIONS

- Rapid, deep, and durable responses to teclistamab were observed, and the majority of patients are now on Q2W or Q4W dosing
- ORR was 63%, 45.5% had ≥CR, and >80% MRD-evaluable patients were MRD negative by day 100. mDOR increased to 22 months (all patients) and 27 months (patients in ≥CR); mPFS was 11 months (all patients) and 27 months (patients in ≥CR)
- Efficacy outcomes were consistent between the overall study population (phase 1/2 patients) and the phase 2 efficacy cohort
- Rates of new grade ≥3 infections decreased over time, corresponding to the time of switch to less frequent dosing, and no new safety signals were observed

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DISCLOSURES

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. **PM** has served in a consulting/advisory role and has received honoraria from AbbVie, Amgen, Celgene, GSK, Janssen, Oncopeptides, and Sanofi. **ALG** has served in a consulting/advisory role for Amgen, CDR-Life, GSK, and Janssen; has patents, royalties, other intellectual property in the field of CAR-T cell therapy; has stock/other ownership interests in Cabaletta Bio; and has received research funding from CRISPR Therapeutics, Janssen, Novartis, and Tmunity Therapeutics, Inc. **MB** has received research funding from Adaptive Biotechnologies, Amgen, Bluebird Bio, BMS/Celgene, Cellularity Inc., Cerecor, Janssen, Legend Biotech, MedImmune, and Takeda. **AO** has served in a consulting/advisory role for Amgen, BMS/Celgene, GSK, Janssen, and Sanofi; and has served on speakers' bureaus for Amgen, BMS/Celgene, GSK, Janssen, and Sanofi. **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, ONK Therapeutics, Pfizer, Secura Bio, and Takeda; reports travel, accommodations, and expenses from GlaxoSmithKline; and has received research funding from Amgen, Arch Oncology, BMS/Celgene, Cellectar, GlaxoSmithKline, Janssen, Pfizer, and Takeda. **TGM** has served in a consulting/advisory role for GSK and Legend Biotech; and has received research funding from Amgen, Janssen, and Sanofi. **LR** has served in a consulting/advisory role for Amgen, Celgene, Janssen-Cilag, and Sanofi; and has received honoraria from Amgen, Celgene, GSK, Janssen-Cilag, Sanofi, 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. **NB** has served in a consulting/advisory role for Amgen, Celgene, Janssen, Karyopharm Therapeutics, Pfizer, Sanofi, and Takeda; received honoraria from AbbVie, Amgen, Celgene, Genentech/Roche, GSK, Janssen, Karyopharm Therapeutics, Sanofi, and Takeda; and has received research funding from Celgene and Janssen. **RP** has served in a consulting/advisory role for BeiGene, Celgene, GSK, Janssen, and Roche; has received travel, accommodations, and expenses from GSK and Janssen; received honoraria from AbbVie, Celgene, GSK, Janssen, and Sanofi; and has received research funding from GSK. **BB** has received honoraria from Amgen, GSK, Janssen-Cilag, and Sanofi. **JM-L** has served in a consulting/advisory role for BMS, Janssen, and Novartis; has served on speakers' bureaus for BMS, Janssen-Cilag, and Roche; and has received research funding from Astellas and BMS. **AK** has served in a consulting/advisory role for Celgene, GSK, Janssen, Oncopeptides, Pfizer, and Regeneron; has served in a leadership role for Sutro Biopharma; has served on speakers' bureaus for Amgen, Celgene, and Takeda; has stock/other ownership interests in BMS; and has received research funding from Janssen. **MD** has served in a consulting/advisory role for Amgen, BMS, GSK, Janssen, Sanofi, Stemline Therapeutics, and Takeda; and has received research funding from Janssen. **DT** and **KC** are employed by and have stock/other ownership interests in Janssen. **RIV** and **TS** are employed by, own stock in, and have received travel, accommodations, and expenses from Janssen. **SS** has served in a consulting/advisory role for BMS/Celgene, Janssen, Mangenta Therapeutics, Oncopeptides, and Sanofi; and has received research funding from Allogene Therapeutics, BMS/Celgene, Janssen, and Magenta Therapeutics.

REFERENCES:

1. TECVAYLI (teclistamab-cqyv). Prescribing information. Horsham, PA: Janssen Biotech, Inc; 2022. 2. Moreau P, et al. *New Engl J Med* 2022;387:495-505.
3. Kumar S, et al. *Lancet Oncol* 2016;17:e328-46. 4. Nooka AK, et al. Presented at ASCO; June 3–7, 2022; Chicago, IL, USA. Oral #8007.

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