Efficacy and safety of teclistamab (tec), a B-cell maturation antigen (BCMA) x CD3 bispecific antibody, in patients (pts) with relapsed/refractory multiple myeloma (RRMM) after exposure to other BCMA-targeted agents

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INTRODUCTION

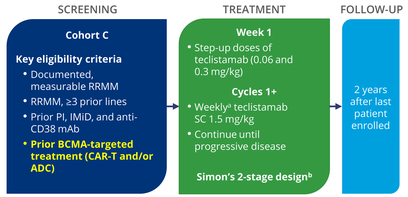
- B-cell maturation antigen (BCMA) represents an established target for the treatment of patients with multiple myeloma (MM)
- Three classes of BCMA-targeting agents have emerged in recent years, including chimeric antigen receptor T cell (CAR-T) therapies, antibody drug conjugates (ADCs; eg, belantamab mafodotin), and bispecific antibodies[1]
- Teclistamab (JNJ-64007957) is an off-the-shelf, BCMA x CD3 bispecific antibody that redirects CD3+ T cells to mediate T-cell activation and subsequent lysis of BCMA-expressing myeloma cells[2]
- The multicohort phase 1/2 MajesTEC-1 study is investigating teclistamab in patients with relapsed/refractory (RR) MM who previously received ≥3 lines of therapy[3,4]
- In the cohort of patients without prior BCMA-targeted treatment, weekly teclistamab 1.5 mg/kg (following step-up doses of 0.06 and 0.3 mg/kg) was well tolerated with a high response rate (oral presentation, Nooka #8007, Sunday, June 5, 2022, 10:00–11:00 AM, CDT)
- Here we present efficacy and safety results from cohort C of MajesTEC-1, which enrolled patients previously exposed to BCMA-targeted treatment

METHODS

Study design and key eligibility criteria

- MajesTEC-1 is a first-in-human, phase 1/2 (NCT03145181; NCT04557098), open-label, multicohort, multicenter study in patients with RRMM who were triple-class exposed
- Patients with prior exposure to BCMA-targeted treatment were enrolled in cohort C (**Figure 1**)

FIGURE 1: MajesTEC-1 phase 2 study design



Primary endpoint: ORR

Key secondary endpoints: DOR, ≥VGPR, ≥CR, sCR, TTR, MRD[c] status, PFS, OS, safety, PK, immunogenicity, patient-reported outcomes

[a]Patients could transition to Q2W dosing after maintaining CR/sCR for ≥6 months. [b]In cohort C, a Simon's 2-stage design was used to test the null hypothesis that the ORR was ≤15% vs ≥35%. [c]Baseline clones were obtained for all patients. All MRD assessments were done by NGS. CR, complete response; DOR, duration of response; IMiD, immunomodulatory drug; mAb, monoclonal antibody; MRD, minimal residual disease; NGS, next generation sequencing; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; sCR, stringent CR; SC, subcutaneous; TTR, time to response; VGPR, very good partial response

MULTIPLE MYELOMA

RESULTS

Patients

- As of March 16, 2022, 40 patients in cohort C had received teclistamab; 17 (42.5%) patients remain on treatment
- Median (range) follow-up was 12.5 months (0.7–14.4) and median duration of treatment was 5.2 months (0.2–13.6)
- Baseline characteristics are shown in **Table 1**

TABLE 1: Baseline characteristics

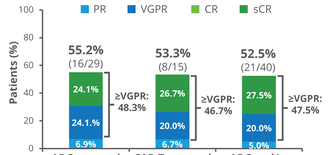
Characteristic	Cohort C n=40
Age (years), median (range)	63.5 (32–82)
Male, n (%)	25 (62.5)
Race, n (%) White Black or African American Asian Not reported	 35 (87.5) 3 (7.5) 1 (2.5) 1 (2.5)
Bone marrow plasma cells ≥60%[a], n (%)	4 (10.0)
Extramedullary plasmacytomas ≥1[b], n (%)	12 (30.0)
High-risk cytogenetics[c], n (%)	12 (33.3)[c]
Time since diagnosis (years), median (range)	6.5 (1.1–24.1)
Prior lines of therapy, n, median (range)	6 (3–14)
Prior stem cell transplantation, n (%)	36 (90.0)
Exposure status, n (%) Triple-class[d] Penta-drug[e] BCMA-targeted ADC BCMA-targeted CAR-T	 40 (100) 32 (80.0) 29 (72.5)[f] 15 (37.5)[f]
Refractory status, n (%) Triple-class[d] Penta-drug[e] To last line of therapy	 34 (85.0) 14 (35.0) 34 (85.0)

[a]Includes bone marrow biopsy and aspirate. [b]Includes soft-tissue plasmacytomas not associated with bone. [c]del(17p), t(4:14), and/or t(14;16); percentage calculated from n=36. [d]≥1 PIs, ≥1 IMiDs, and ≥1 anti-CD38 mAbs. [e]≥2 PI, ≥2 IMID, and ≥1 anti-CD38 antibody. [f]4 patients had previously received both ADC and CAR-T.
ADC, antibody drug conjugates; BCMA, B-cell maturation antigen; CAR- T, chimeric antigen receptor T cell; D/C, discontinued; PD, progressive disease

Efficacy

- The ORR was 52.5% (21/40; 95% CI: 36.1–68.5) in patients with prior BCMA-targeted treatment (**Figure 2**)
  - Among the 29 ADC-exposed patients, ORR was 55.2% (95% CI: 35.7–73.6) and 48.3% had VGPR or better
  - In the 15 CAR-T–exposed patients, ORR was 53.3% (95% CI: 26.6–78.8) and 46.7% had VGPR or better
  - 3 of the 4 patients with prior ADC and CAR-T had a response
- MRD negativity (10^{-5}) rate was 17.5% (95% CI: 7.3–32.8)
  - 7 of 11 patients (63.6%) with CR or better were MRD negative
- Responses occurred early, deepened over time, and were durable (**Figure 3**)

FIGURE 2: ORR[a] in cohort C



[a]PR or better, IRC assessed, per IMWG 2016 criteria.
ADC, antibody drug conjugates; CAR- T, chimeric antigen receptor T cell; CR, complete response; IMWG, International Myeloma Working Group; IRC, independent review committee; ORR, overall response rate; PR, partial response; sCR,stringent CR; VGPR, very good partial response

- Median (range) time to first and best response was 1.2 months (0.2–4.9) and 2.9 months (1.1–9.5), respectively
- Responses deepened over time in 15 (71.4%) of 21 patients with response
- Median DOR was not reached (95% CI: 10.5 months to NE)
- At data cutoff, 15 (71.4%) of 21 responders maintained response

Safety

- Teclistamab was well tolerated, with no dose reductions or discontinuations due to adverse events (AEs)
- The most common AEs are summarized in **Table 2**
- All cytokine release syndrome (CRS) events were grade 1/2 and resolved without treatment discontinuation
- Infections occurred in 26 patients (65.0%; grade 3/4: 30.0%)
- There were 6 deaths due to AEs, one of which was considered possibly related to treatment (cardiac arrest)
- The most common neurotoxic event was headache (12.5%)
- Four patients had immune effector cell-associated neurotoxicity syndrome (ICANS) events; all ICANS events were grade 1/2, except grade 3 ICANS in 1 patient that resolved in 2 days with supportive care

TABLE 2: Safety profile

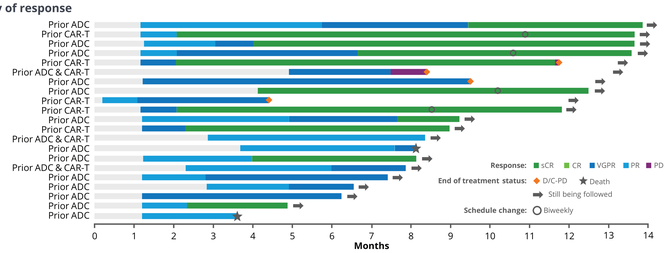
	Cohort C n=40	
AEs ≥20%, n (%)	Any Grade	Grade 3/4
Hematologic		
Neutropenia	27 (67.5)	25 (62.5)
Anemia	20 (50.0)	14 (35.0)
Lymphopenia	18 (45.0)	17 (42.5)
Thrombocytopenia	18 (45.0)	12 (30.0)
Nonhematologic		
CRS	26 (65.0)	0
Constipation	14 (35.0)	0
Diarrhea	14 (35.0)	1 (2.5)
Injection site erythema	13 (32.5)	0
Pyrexia	13 (32.5)	0
Arthralgia	10 (25.0)	0
Dyspnea	9 (22.5)	1 (2.5)
Headache	9 (22.5)	0
Asthenia	8 (20.0)	2 (5.0)
Bone pain	8 (20.0)	1 (2.5)

AE, adverse events; CRS, cytokine release syndrome

Pharmacokinetics, immunogenicity, and baseline BCMA tumor expression

- Serum concentrations of teclistamab in patients with prior BCMA-targeted treatment were comparable to those observed in BCMA treatment-naive patients
- As of September 7, 2021, no patients had developed anti-teclistamab antibodies
- Baseline BCMA expression was comparable in patients with and without prior exposure to BCMA-targeted treatments

FIGURE 3: Durability of response



ADC, antibody drug conjugates; CAR- T, chimeric antigen receptor T cell; CR, complete response; D/C, discontinued; ORR, overall response rate; PD, progressive disease; PR, partial response; sCR,stringent CR; VGPR, very good partial response

KEY TAKEAWAY

Serial targeting of BCMA with teclistamab following treatment with an ADC or CAR-T resulted in a promising response rate in patients with heavily pretreated RRMM

CONCLUSIONS

- Responses to teclistamab occurred early and deepened over time, with comparable response rates in patients previously treated with an ADC and/or CAR-T
- Teclistamab was well tolerated in patients with prior exposure to BCMA-targeted agents, with a safety profile similar to that observed in BCMA treatment-naive patients
- These data support teclistamab as a promising new, off-the-shelf, T-cell redirecting therapy for patients with RRMM and prior exposure to BCMA-targeted agents

ACKNOWLEDGMENTS

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