Evaluating Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma Following Exposure to Other B-Cell Maturation Antigen (BCMA)-Targeted Agents

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Presented at the European Hematology Association (EHA) 2022 Hybrid Congress; June 9–12, 2022; Vienna, Austria.

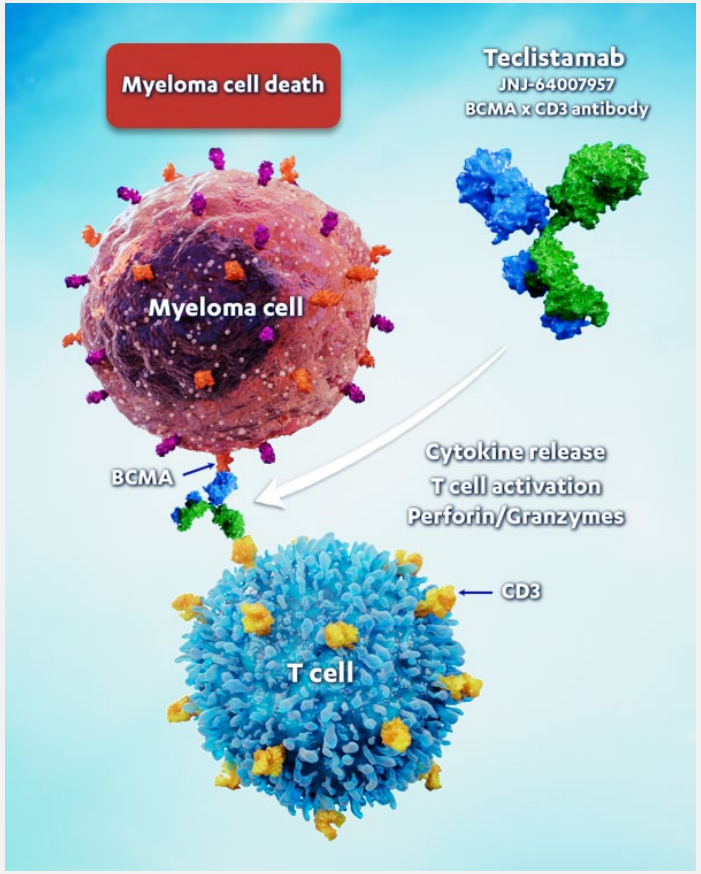
Disclosures

Dr. Touzeau declares the following:

- Janssen (advisory board and honoraria)
- Amgen (advisory board and honoraria)
- BMS (advisory board and honoraria)
- Takeda (advisory board and honoraria)
- AbbVie (advisory board and honoraria)
- Pfizer (advisory board and honoraria)
- GSK (research funding)
- Sanofi (research funding)

Teclistamab Treatment After Other BCMA-Targeted Agents

- **BCMA** represents an established target for treatment of patients with MM
- **Three classes of BCMA-targeted agents** have emerged in recent years, including CAR-T, ADCs (eg, belantamab mafodotin), and bispecific antibodies[1]
- **Teclistamab (JNJ-64007957)** is a full size, fully humanized, 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 RRMM who previously received ≥3 lines of therapy[3,4]
- In Cohort A (patients without prior BCMA-targeted treatment), weekly teclistamab (following step-up doses) was well tolerated with a high response rate[4]
- **Here we present efficacy and safety results from Cohort C of MajesTEC-1, which enrolled patients previously exposed to BCMA-targeted treatment**



ADC, antibody drug conjugate; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; MM, multiple myeloma; RRMM, relapsed/refractory MM

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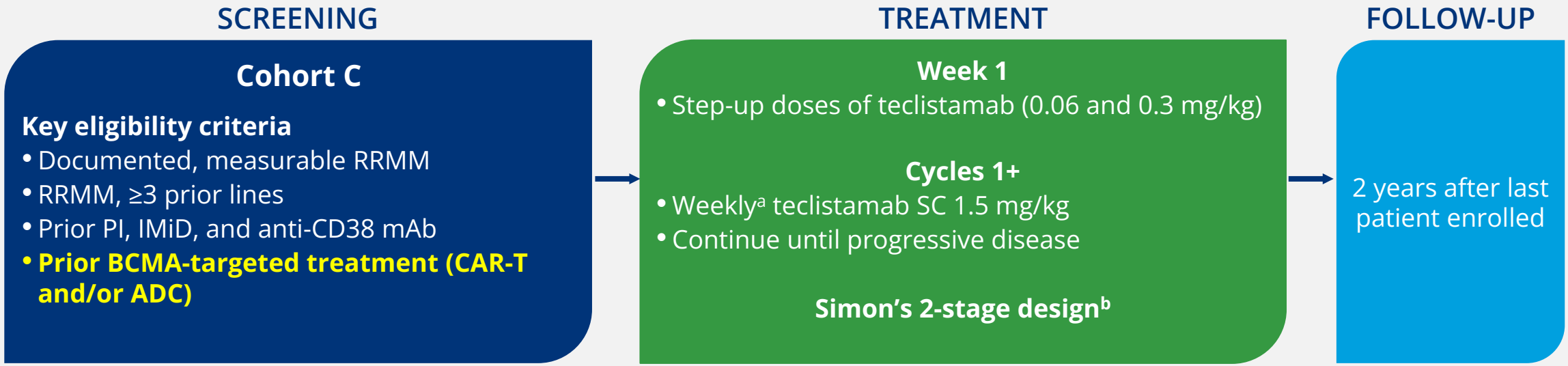
MajesTEC-1 Cohort C: Study Design

- First-in-human, phase 1/2 (NCT03145181; NCT04557098), open-label, multicohort, multicenter study in patients with RRMM who were triple-class exposed
- Cohort C enrolled patients with prior exposure to BCMA-targeted treatment



Primary endpoint: ORR

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

[a]Patients could transition to Q2W dosing after maintaining CR/sCR for ≥6 months. [b]In cohort C, 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. ADC, antibody drug conjugate; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; 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; PK, pharmacokinetics; PRO, patient-reported outcome; Q2W, every other week; RRMM, relapsed/refractory multiple myeloma; sCR, stringent CR; SC, subcutaneous; TTR, time to response; VGPR, very good partial response

MajesTEC-1 Cohort C: Patients

Characteristic		N=40
Age (years), median (range)		63.5 (32–82)
Male, n (%)		25 (62.5)
Race, n (%)	White	35 (87.5)
	African American/Black	3 (7.5)
	Asian	1 (2.5)
	Not reported	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)
ISS stage, n (%)	I	21 (52.5)
	II	9 (22.5)
	III	10 (25.0)
Time since diagnosis (years), median (range)		6.5 (1.1–24.1)

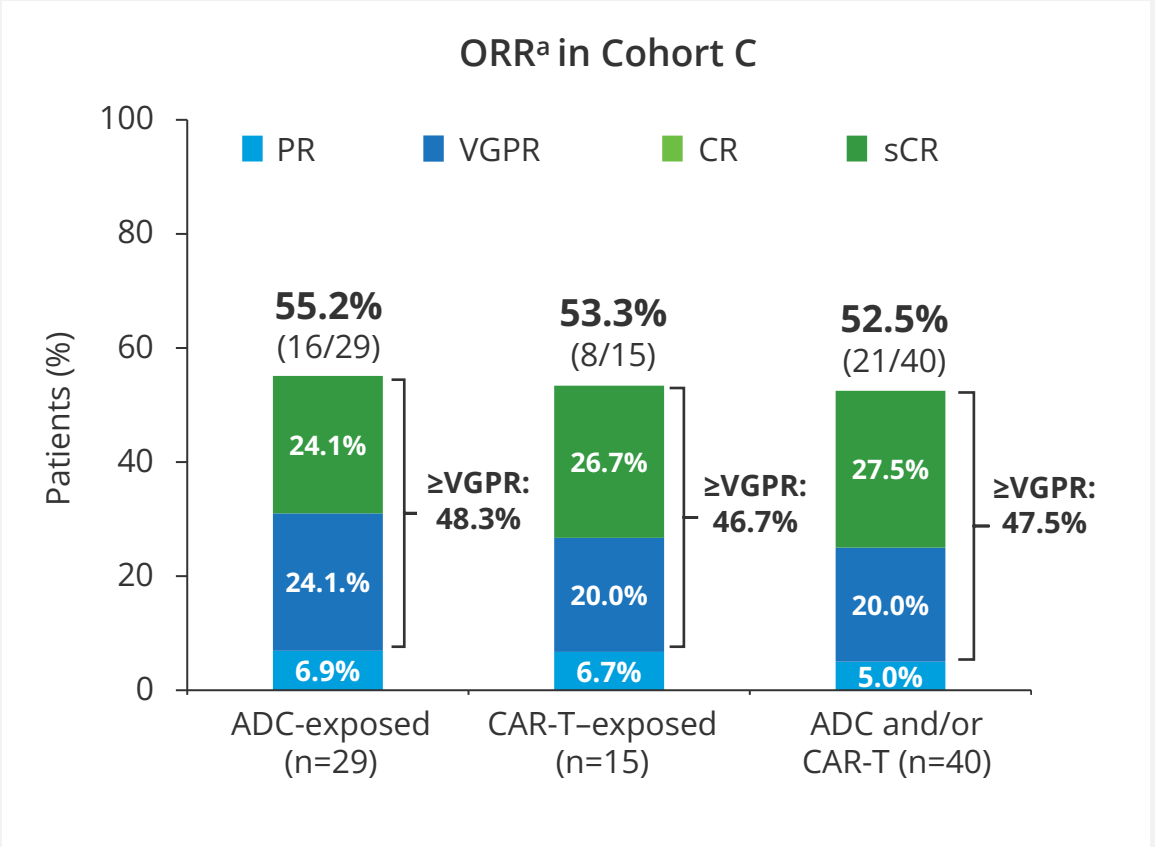
Characteristic	N=40
Prior lines of therapy, median (range)	6 (3–14)
Prior stem cell transplantation, n (%)	36 (90.0)
Exposure status, n (%)	
Triple-class[d]	40 (100)
Penta-drug[e]	32 (80.0)
BCMA-targeted treatment	40 (100)[f]
ADC	29 (72.5)
CAR-T	15 (37.5)
Refractory status, n (%)	
Triple-class[d]	34 (85.0)
Penta-drug[e]	14 (35.0)
To last line of therapy	34 (85.0)

- **Median follow-up** was 12.5 months (range: 0.7–14.4); 17 of 40 patients (42.5%) remain on treatment
- Median duration of treatment was 5.2 months (range: 0.2–13.6)
- Baseline BCMA expression and soluble BCMA levels were comparable in patients with and without prior BCMA-targeted treatment

Data analysis cutoff date: March 16, 2022.
[a]Includes bone marrow biopsy and aspirate. [b]Soft-tissue plasmacytomas not associated with bone were included. [c]del(17p), t(4:14), and/or t(14;16) (n=36). [d]≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody. [e]≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb. [f]4 patients had received both ADC and CAR-T.
ADC, antibody drug conjugate; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; IMiD, immunomodulatory drug; ISS, International Staging System; PI, proteasome inhibitor

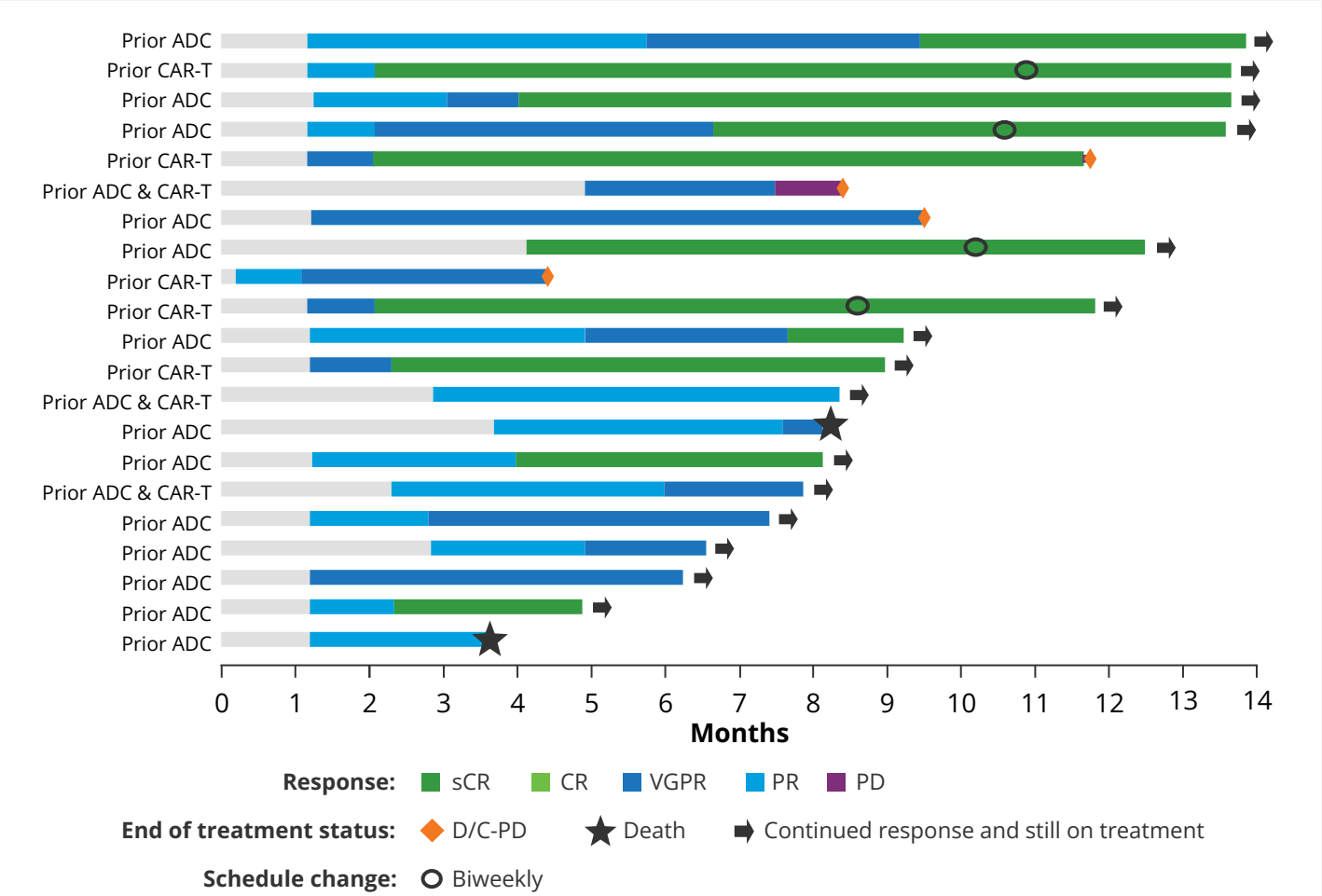
MajesTEC-1 Cohort C: Overall Response Rate

- The ORR was **52.5%** (21/40; 95% CI: 36.1–68.5) in patients with prior exposure to either class of BCMA-targeted treatment
  - ADC-exposed patients: **55.2%**
  - CAR-T–exposed patients: **53.3%**
  - Both ADC and CAR-T: 3 of 4 patients responded
- MRD negativity (10^{-5}) rate was 17.5%
  - Among ≥CR patients: **63.6%** (7/11)



Data analysis cutoff date: March 16, 2022.
[a]PR or better, IRC assessed, per IMWG 2016 criteria.
ADC, antibody drug conjugate; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; CR, complete response; IMWG, International Myeloma Working Group; IRC, independent review committee; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

MajesTEC-1 Cohort C: Durability of Response



- Responses occurred early, deepened over time, and were durable
- Median time to first response was 1.2 months (range: 0.2–4.9)
- Median time to best response was 2.9 months (range: 1.1–9.5)
- 15 (71.4%) of the 21 responders had responses that deepened over time
- Median DOR was not reached (95% CI: 10.5 months to NE)
- With a median follow-up of 11.8 months (range: 3.6–13.8) in responders, 71.4% of responders (15/21) maintained their response

Data analysis cutoff date: March 16, 2022.
ADC, antibody drug conjugate; CAR-T, chimeric antigen receptor T cell; CR, complete response; D/C, discontinued; DOR, duration of response; NE, not estimable; PD, progressive disease; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

MajesTEC-1 Cohort C: Overall 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)

- The safety profile was as expected based on the broader MajesTEC-1 data
- Teclistamab was well tolerated, with no dose reductions or discontinuations due to AEs
- The most common AEs were cytopenias and CRS
- Infections occurred in 26 patients (65.0%; grade 3/4: 30.0%)
- There were 6 deaths due to AEs, including 2 COVID-19 deaths
  - One death due to a teclistamab-related AE (cardiac arrest)

Data analysis cutoff date: March 16, 2022.
AE, adverse event; BCMA, B-cell maturation antigen; CRS, cytokine release syndrome

MajesTEC-1 Cohort C: Cytokine Release Syndrome

Parameter	Cohort C n=40
Patients with CRS, n (%)[a]	26 (65.0)
Grade 1	21 (52.5)
Grade 2	5 (12.5)
Grade ≥3	0
Patients with ≥2 CRS events	12 (30.0)
Time to onset (days), median (range)	2 (2–6)
Duration (days), median (range)	2 (1–4)
Received supportive measures[b] for CRS, n (%)	23 (57.5)
Tocilizumab	12 (30.0)
Low-flow oxygen by nasal cannula[c]	4 (10.0)
Intravenous fluids	2 (5.0)
Corticosteroids	1 (2.5)
Vasopressor	0

- All CRS events were grade 1/2 and all resolved without treatment discontinuation

Data analysis cutoff date: March 16, 2022.
[a]CRS was graded using ASTCT criteria in phase 2. [b]A patient could receive >1 supportive therapy. [c]≤6 L/min.
ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome

MajesTEC-1 Cohort C: Neurotoxic Events

Parameter	Cohort C n=40
Neurotoxic event[a], n (%)	10 (25.0)
Headache	5 (12.5)
ICANS	4 (10.0)
Dysgeusia	1 (2.5)
Peripheral sensory neuropathy	1 (2.5)
Insomnia	1 (2.5)
Grade ≥3 events, n (%)	1 (2.5)
Time to onset, median (range) days	2 (1–4)
Duration, median (range) days	2 (1–35)
Received supportive measures for neurotoxic events, n (%)[b]	7 (17.5)
Tocilizumab	2 (5.0)
Anakinra	1 (2.5)
Dexamethasone	1 (2.5)
Pregabalin	1 (2.5)

- The most common neurotoxic event was headache (12.5%)
- Four patients had ICANS events
- All ICANS events were grade 1/2, except grade 3 ICANS in 1 patient that resolved in 2 days with supportive care

Data analysis cutoff date: March 16, 2022.
[a]Neurotoxic events were defined as adverse events under the "nervous system disorder" or "psychiatric disorder" SOC that were judged by the investigator to be related to study drug, including ICANS events. [b]Tocilizumab, anakinra, and dexamethasone were used to treat ICANS events.
ICANS, immune effector cell–associated neurotoxicity syndrome; SOC, system organ class

MajesTEC-1 Cohort C: Conclusions

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

- 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

ADC, antibody drug conjugate; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; RRMM, relapsed/refractory multiple myeloma

MajesTEC-1 Cohort C Acknowledgements

- We thank the patients who are participating in this study and their caregivers, the physicians and nurses who took care of them, the staff at study sites and the staff involved in data collection and analyses

- This study was funded by Janssen Research & Development, LLC

- Medical writing support was provided by Lela Creutz, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC

- Previously presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting; June 3-7, 2022; Chicago, IL, USA & Virtual