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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Teclistamab Demonstrates Clinical Activity in Real-World Patients Ineligible for the Pivotal Majestec-1 Trial

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Introduction Treatment options for relapsed/refractory multiple myeloma (RRMM) are limited and associated with a poor median overall survival (OS) of 12.4 months (m) (Mateos et al. Leukemia 2022). The MajesTEC-1 trial demonstrated promising clinical activity of teclistamab (Tec), a BCMAxCD3 bispecific antibody, with an overall response rate (ORR) of 63%, complete response rate (CR) of 39.4%, median progression-free survival (PFS) of 11.3 m, and OS of 18.3 m. Here we present the results of a multicenter, retrospective study examining real-world patient characteristics and outcomes in patients with RRMM receiving Tec outside of a clinical trial, including those who would have been ineligible for the registrational study.

Methods An IRB-approved retrospective study of patients with RRMM treated with Tec at 4 academic centers was performed. Patient demographics, prior treatments, clinical outcomes and toxicities with special attention to cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and infection were extracted from the electronic patient record. Response rate was compared using Fisher's exact test. Median PFS and OS were estimated by Kaplan-Meier and compared using the log-rank test. Trial eligibility was evaluated using the MajesTEC-1 eligibility criteria.

Results A total of 45 patients, who received at least 1 dose of Tec, were evaluated. Of these 39% were derived from under-represented minorities (25% Black, 14% Hispanic). Patient characteristics and comparison to the MajesTEC-1 population are summarized, Table 1. High-risk cytogenetic features were present in 42.2% of patients, and 46.7% had extra-medullary disease (EMD). All patients were triple class exposed and 80% were penta-class exposed. Most patients (84.4%) would have been ineligible for MajesTEC-1 due to cytopenias (44.4%), prior BCMA-directed therapy (42.2%), inadequate washout (42.2%), and poor performance status (PS) (26.7%). Therapy was delivered according to protocol with no increased rate of infections or bleeding, even in the group of patients with low blood counts and poor PS. CRS/ICANS events of any grade were observed in 55% and 13% of patients, respectively, during step-up dosing. Most CRS/ICANS events were mild-moderate in severity (CRS 42.2% grade 1, 11.1% grade 2; ICANS 4.4% grade 1, 0% grade 2) and were managed conservatively with antipyretics, tocilizumab (37.8%), and steroids (13.3%). Grade 4 CRS and ICANS were only seen in 1 patient; a separate individual experienced grade 5 ICANS after the third step up dose.

The overall response rate (ORR) was 48.9% (95% CI 33.7-64.2) with 22.2% (95% CI 11.2-37.1) achieving at least a very-good partial response (VGPR). On univariate analysis prior anti-BCMA exposure was associated with an adverse ORR (23% vs 61%; p=0.02). Ineligibility for enrollment in MajesTEC-1, the presence of high-risk cytogenetics or EMD were not associated with ORR or depth of response. Updated follow up time, median PFS and OS will be presented at the meeting to allow time for data to mature. The presence of high-risk cytogenetics was associated with worse PFS (median NR vs 2.1 m, HR 2.32; p=0.041). Receipt of prior BCMA therapy and MajesTEC-1 ineligibility were not associated with PFS or OS. At the time of data cut-off,

19 (42.2%) patients remained on Tec; reasons for discontinuation included disease progression, infections, and CRS/ICANS in 19 (42.2%), 4 (8.8%), and 3 (6.7%) patients, respectively.

Conclusion Overall, Tec demonstrated significant clinical activity even in a group of heavily pre-treated real-world patients comprising high-risk and extramedullary disease populations. The overall toxicity profile was similar to prior reports demonstrating that side effects can be readily managed using simple approaches with only limited patients needing more intensive interventions. These results also suggest Tec may be used in patients previously excluded from clinical trials because of adverse clinical characteristics with high ORR being seen and an absence of increased toxicity. In the BCMA-naive population ORR were similar to MajesTEC-1, but were lower in the previously BCMA-exposed population. High-risk cytogenetics and EMD remain adverse prognostic features with Tec despite similar ORR.

Disclosures Monge: *Janssen:* Consultancy. **Parmar:** *Sanofi:* Consultancy, Honoraria; *Cellectar Biosciences:* Consultancy, Honoraria. **Siegel:** *Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Celularity Scientific:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Karyopharm:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *BMS:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau. **Biran:** *Boehringer Ingelheim:* Other: spouse of employee; *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Honoraria; *Genomic Testing Cooperative:* Divested equity in a private or publicly-traded company in the past 24 months; *GSK:* Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Merck:* Research Funding; *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Karyopharm:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Amgen:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding. **Davies:** *Janssen:* Membership on an entity's Board of Directors or advisory committees; *sanofi:* Membership on an entity's Board of Directors or advisory committees; *pfizer:* Membership on an entity's Board of Directors or advisory committees; *BMS / Celgene:* Membership on an entity's Board of Directors or advisory committees; *Regeneron:* Membership on an entity's Board of Directors or advisory committees; *Amgen:* Membership on an entity's Board of Directors or advisory committees; *Takeda:* Membership on an entity's Board of Directors or advisory committees.

Table 1: Patient Baseline Characteristics

Characteristic	Real-World (n = 45)	MajesTEC-1 (n = 165)
Age at C1D1		
Median (range)	66 (45-88)	64 (33-84)
≥75 years n (%)	9 (20)	24 (14.5)
Sex - n (%)		
Male	21 (46.7)	96 (58.2)
Female	24 (53.3)	68 (41.8)
Race - n (%)		
White, Non-Hispanic	24 (53.3)	134 (81.2)
Hispanic	6 (13.6)	
Black	11 (25)	21 (12.7)
Other	4 (9)	
URM	21 (46.7)*	31 (18.4)**
Median Time Since Diagnosis (range)	4.9 (1.1-25.8)	6.0 (0.8-22.7)
Extramedullary Disease - n (%)	21 (46.7)	28 (17.0)
ECOG PS - n (%)		
0	14 (31.1)	55 (33.3)
1	19 (42.2)	110 (66.7)
≥2	12 (26.7)	NA
ISS - n (%)		
I	11 (24.4)	85/162 (52.5)
II	13 (28.9)	57/162 (35.2)
III	12 (26.7)	20/162 (12.3)
Unknown	9 (20)	0/162 (0)
High-Risk Cytogenetics - n (%)	19 (42.2)	38/148 (25.7)
del(17p)	15 (33.3)	23/148 (15.5)
t(4;14)	7 (15.6)	16/148 (10.8)
t(14;16)	5 (11.1)	4/148 (2.7)
Median Prior Lines of Therapies (Range)	6 (2-14)	5 (2-14)
Prior AutoSCT - n (%)	33 (73.3)	135 (81.8)
Prior AlloSCT - n (%)	2 (4.4)	0 (0)
Previous therapy exposure - n (%)		
Triple-class***	45 (100)	165 (100)
Penta-drug****	36 (80)	116 (70.3)
Ineligible for MajesTEC-1 - n (%)	**38 (84.4)**	**0 (0)**
Cytopenias (Hgb <8, Plt <75, ANC <1000)	20 (44.4)	NA
Prior BCMA	19 (42.2)	NA
Belantamab	12 (26.7)	NA
CAR-T	11 (24.4)	NA
Inadequate Washout (<3 weeks)	19 (42.2)	NA
ECOG >1	12 (26.7)	NA
Renal Dysfunction	9 (20)	NA
Plasma Cell Leukemia, Amyloidosis	6 (13.3)	NA

*Black, Hispanics, American Indians or Alaska Natives, Asian, Native Hawaiians, and Pacific Islanders
**Black (21), Asian (3), Other (7).
***anti-CD38 antibody, IMiD, and PI
****Daratumumab or Isatuximab, lenalidomide, pomalidomide, bortezomib, and carfilzomib

Figure 1

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