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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Teclistamab Induces Favorable Responses in Patients with Relapsed and Refractory Multiple Myeloma after Prior BCMA-Directed Therapy

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Introduction: Teclistamab (TEC) received regulatory approval for the treatment of patients with Relapsed/Refractory Multiple Myeloma (RRMM) after ≥ 3 prior lines of therapy based on the results of the pivotal MajesTEC-1 trial in which such patients achieved an overall response rate (ORR) of 63%, ≥ complete response (CR) of 39%, and median progression free survival (PFS) of 11.3 months (Moreau et al. *N Engl J Med* 2022). Patients who had received a prior B-cell maturation antigen-targeted therapy (BCMA-TT) were excluded from MajesTEC-1 trial. Data on the efficacy of TEC in patients who have received and relapsed after prior BCMA targeted therapy is lacking. Several studies have shown reduced efficacy of both FDA approved BCMA targeted chimeric antigen receptor T cell therapies (CAR-T) for myeloma, idecabtagene vicleucel (ide-cel) and cilta-cabtagene autoleucel (cilta-cel), when administered after BCMA targeted bi-specific antibodies. There is a paucity of data on the efficacy of TEC when administered in patients who progress after ide-cel or cilta-cel. We evaluated the real-world outcomes of patients treated with standard of care (SOC) TEC after having previously received a BCMA-TT.

Methods We performed a retrospective chart review to find patients treated at our center that were > 30 days from first dose of commercial TEC, received at least one prior BCMA-targeted therapy, and were consented to an IRB approved registry protocol. Cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS) were graded per ASTCT consensus criteria, while responses were graded based on the International Myeloma Working Group (IMWG) response criteria.

Results: A total of 22 patients who had received prior BCMA-TT and TEC were evaluable for response, safety, and survival analyses. Median age was 66 years (range 48-81), 59% were male, and 13% had an ECOG PS ≥2. Beside prior BCMA-TT, other exclusion to MajesTEC-1 would have been cytopenias (27%), performance status ≥2 (9%), creatinine clearance <40 mL/min (5%), and plasma cell leukemia (5%). Eleven pts (50%) had high risk cytogenetics (defined as del17, t(4;14), t(14;16)), and 13 pts (59%) had gain 1q.

Patients were heavily pretreated with a median of 8 (5-13) prior lines of therapy, 45% had R-ISS III, 14% had extramedullary disease (EMD), 27% had a high marrow burden (≥60% PCs in the marrow) and 11 (50%) were penta-class refractory.

Sixty-eight percent (n=15) had received prior Chimeric Antigen Receptor T-cell Therapy (CAR-T), 9% (n=2) prior Antibody Drug Conjugate (ADC), and 23% (n= 5) both CAR-T and ADC, all BCMA-TT. Median time from prior BCMA-TT to TEC was 12.3 (1.3-33.5) months.

With a median follow up of 4.16 (1.07-7.27) months, the best overall and ≥ CR response rates were 63% and 36% (N=8), respectively. Of those who had achieved a ≥ CR, 3 were MRD negative by clonoSEQ® (10^{-6}). Thirteen (57%) pts received TEC as the next line of therapy from prior BCMA-TT. Thirteen of 14 pts tested for BCMA expression were positive by IHC, with 9 expressors responding to TEC; the non-expressor responded to TEC.

Toxicity was comparable to that seen in MajesTEC-1. Cytokine release syndrome (CRS) of any grade occurred in 16 (73%) pts. All events occurred during step-up and cycle 1 doses. All events of CRS were grade 1 (n=13; 59%) and 2 (n=3; 14%). The median time to onset of CRS was 3 (1-12) days after the most recent dose, and the median duration was 3 (1-9) days. Tocilizumab was administered to 4 (18%) pts. Only 1 patient had ICANS, grade 3 and requiring steroids. Infections were seen in 12 (55%) pts, including viral (10), bacterial (1), and fungal (1). 6 (50%) infections were deemed severe and required hospitalization. Prior to TEC, 13 (59%) pts had hypogammaglobulinemia (IgG< 400). After TEC, 6 pts developed new hypogammaglobulinemia. 11 (50%) pts had treatment delays, mainly due to CRS and infections. Four pts died due to progression of disease.
Conclusions: This single center study in patients with heavily pretreated and prior BCMA-TT demonstrated favorable ORR (63%) and CR (36%) rates, comparable to pts in the MajesTEC-1 trial, without prior BCMA-TT exposure. No new safety signals were identified. Results on progression free survival (PFS) and overall survival (OS) will be reported with continued follow up and will be presented in the meeting.

Disclosures Grajales-Cruz: *Janssen:* Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Amgen:* Speakers Bureau; *Cellectar:* Membership on an entity's Board of Directors or advisory committees. **Castaneda:** *Adaptive Biotechnologies:* Speakers Bureau; *Moffitt Cancer Center:* Current Employment. **Hansen:** *Janssen:* Consultancy; *Bristol Myers Squibb:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Karyopharm:* Consultancy, Research Funding; *International Myeloma Society Young Investigator Award:* Research Funding; *Pfizer:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Pentecost Family Myeloma Research Center:* Research Funding; *OncLive:* Honoraria; *Survivorship:* Honoraria. **Blue:** *Sanofi:* Consultancy; *Oncopeptides:* Consultancy; *AbbVie:* Consultancy; *Pfizer:* Consultancy; *Kite Pharmaceuticals:* Consultancy; *Janssen:* Consultancy. **Liu:** *BioLineRx:* Membership on an entity's Board of Directors or advisory committees. **Freeman:** *Celgene:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria, Research Funding; *ONK Therapeutics:* Consultancy, Honoraria; *Bristol Myers Squibb:* Consultancy, Honoraria, Research Funding. **Locke:** *Cowen:* Consultancy; *BioPharma Communications CARE Education:* Other: Institutional; *Takeda:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Emerging Therapy Solutions:* Consultancy, Other; *CERo Therapeutics:* Other: (Institutional); *ASH:* Other: Travel Support; *Aptitude Health:* Other: Travel Support; *Cellular Medicine Group:* Consultancy; *Allogene:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Institutional ; *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Institutional , Research Funding; *Caribou:* Consultancy; *Calibr:* Consultancy; *Umoja:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Wugen:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Iovance:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Bluebird Bio:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Institutional; *Amgen:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *GammaDelta Therapeutics:* Consultancy; *EcoR1:* Consultancy; *Daiichi Sankyo:* Consultancy; *Janssen:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Legend Biotech:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Sana:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *Kite, a Gilead Company:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Institutional , Research Funding; *Leukemia and Lymphoma Society:* Other; *Society for Immunotherapy of Cancer:* Other; *National Cancer Institute:* Other; *Clinical Care Options Oncology:* Other; *Imedex:* Other; *Bristol Myers Squibb/ Celgene:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Institutional , Research Funding; *Gerson Lehrman Group (GLG):* Consultancy; *A2 Biotherapeutics:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: Travel support. **Nishihori:** *Medexus:* Speakers Bureau; *Moffitt Cancer Center:* Other: Personal fees from Karyopharm and Novartis outside the submitted work. **Shain:** *GlaxoSmithKline:* Honoraria; *Amgen:* Honoraria; *Amgen:* Honoraria; *Janssen:* Honoraria; *Bristol Myers Squibb:* Honoraria; *Karyopharm:* Research Funding; *Takeda:* Honoraria; *Sanofi:* Honoraria; *Adaptive:* Honoraria; *AbbVie:* Research Funding. **Baz:** *Karyopharm:* Research Funding; *BMS:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *AbbVie:* Research Funding; *Pfizer:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Janssen:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Curio Science:* Honoraria; *AHOMPR:* Honoraria; *GSK:* Honoraria; *Regeneron:* Research Funding; *HIKMA Cancer Network:* Honoraria; *ASH:* Honoraria. **Alsina:** *Genzyme:* Consultancy, Honoraria; *Bristol Myers Squibb:* Consultancy, Research Funding; *RevHealth LLC, Red Med LLC:* Honoraria; *Janssen Oncology:* Consultancy, Speakers Bureau.

Table 1. Comparison of patient characteristics and outcomes by intended SOC vs. MajesTEC-1 trial participants.

	Intended SOC, N=22	MajesTEC-1, N=165
Median age, yrs	66 (48-81)	64 (33-84)
ECOG PS 0 or 1	20 (91%)	165 (100%)
Extramedullary disease	3 (14%)	28 (17%)
High marrow burden	6 (27%)	18 (11%)
High-risk cytogenetics	11 (50%)	38 (26%)
Median prior regimens (range)	8 (5-13)	5 (2-14)
Penta-refractory disease	11 (50%)	50 (30%)
Grade ≥ 3 CRS and ICANS	0%/5%	0.6%/3%
Prior BCMA-TT		
CAR-T	15 (68%)	0%
ADC	2 (9%)	0%
Both CAR-T and ADC	5 (23%)	0%
Best ORR/≥CR	63%/36%	63%/39%

Figure 1

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