Comparative Effectiveness of Teclistamab Versus Real-World Physician's Choice of Therapy for Patients With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma

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INTRODUCTION

- Teclistamab is the first approved B-cell maturation antigen × CD3 bispecific antibody, with precision dosing for the treatment of patients with triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM)[1,2]
- In the pivotal phase 1/2 MajesTEC-1 study (NCT03145181/NCT04557098), teclistamab demonstrated rapid, deep, and durable responses in patients with TCE RRMM[3,4]
  - At median follow-up of 22.8 months, overall response rate was 63.0% (complete response or better [≥CR], 45.5%)[4]
  - Median duration of response was 21.6 months, median progression-free survival (PFS) was 11.3 months, and median overall survival (OS) was 21.9 months[4]

OBJECTIVE

- Indirect adjusted comparisons were performed to assess the comparative effectiveness of teclistamab using data from MajesTEC-1 vs physician's choice of therapy from a real-world database for the treatment of patients with TCE RRMM

METHODS

Data sources

- Individual patient data from MajesTEC-1 included patients (N=165) who received subcutaneous teclistamab 1.5 mg/kg weekly or less-frequent dosing at a clinical cut-off of January 4, 2023
  - Patients could switch to every-other-week (Q2W) dosing if they achieved a partial response or better after ≥4 cycles (phase 1) or ≥CR for ≥6 months (phase 2) and could switch to monthly dosing if they demonstrated sustained response on the Q2W schedule
- An external control arm was created (**Figure 1**) using data from patients in the nationwide deidentified electronic health record–derived Flatiron Health multiple myeloma (MM) cohort database, including patients who met key MajesTEC-1 eligibility criteria from January 2016–August 2021, and followed until December 2022
- Selection of eligible lines of therapy (LOT) from the real-world physician's choice (RWPC) cohort was based on the earliest LOT initiated after all key eligibility criteria were met to provide the most statistical efficiency compared with using only the first or last eligible LOT
  - Patients in the RWPC cohort who received multiple subsequent LOT after meeting eligibility criteria contributed to multiple observations in the current analysis

Comparison

- Key MajesTEC-1 eligibility criteria were applied (**Figure 1**)
- The primary analysis used inverse probability of treatment weighting (IPTW) with average treatment effect in the treated (ATT) to adjust for imbalances in refractory status, time to progression on last LOT, cytogenetic risk, International Staging System stage, number of prior LOT, time since diagnosis, age, and hemoglobin
- A fully adjusted model additionally weighted patients on prior stem cell transplant, Eastern Cooperative Oncology Group performance status (ECOG PS), race, sex, and type of MM

Statistical analysis

- The comparative effectiveness of teclistamab vs RWPC was determined for PFS, time to next treatment (TTNT), and OS
- Outcomes were analyzed as time-to-event data using IPTW-adjusted Kaplan-Meier estimates and a weighted Cox proportional hazards model to estimate the hazard ratio (HR) and 95% CI
- A sensitivity analysis, including additional covariates, was used for the fully adjusted model
- A significance level of 0.05 was used for all comparisons with no adjustment for multiplicity

FIGURE 1: Key patient eligibility criteria

Patient eligibility criteria	MajesTEC-1 (N=165)	RWPC (N_{obs}=766 eligible LOT, corresponding to N=420 patients)
	• TCE • ≥3 prior LOT • ECOG PS 0 or 1 • Creatinine ≤1.5 mg/dL • Hemoglobin >8 g/dL • Progression within ≤12 months of most recent LOT	• TCE • ≥1 treatment after triple-class exposure • ≥3 prior LOT • ECOG PS 0 or 1 • Creatinine ≤1.5 mg/dL • Hemoglobin >8 g/dL • Progression within ≤12 months of most recent LOT • Available data for TTNT, PFS, and OS

N_{obs}, number of observations.

MULTIPLE MYELOMA

RESULTS

Patient demographics and baseline characteristics
- After IPTW, baseline characteristics were comparable between the teclistamab cohort and the RWPC cohort (**Table 1**)
- The most common treatment regimens in the RWPC cohort are shown in **Table 2**

Efficacy outcomes
- In the primary analysis, patients treated with teclistamab had significantly greater PFS (**Figure 2A**) and TTNT (**Figure 2B**) and numerically improved OS (**Figure 2C**) vs RWPC
- Outcomes for the fully adjusted model were consistent with results from the primary analysis (**Table 3**)

TABLE 1: Baseline characteristics

Characteristic	Teclistamab (N=165)	RWPC cohort before ATT weighting (N=766)	RWPC cohort after ATT weighting: Primary analysis (N=326)	RWPC cohort after ATT weighting: Fully adjusted (N=195)
Refractory status,[a] n (%)				
Triple- or quad-class	78 (47.3)	301 (39.3)	107 (32.7)	91 (46.8)
Penta-drug[b]	50 (30.3)	211 (27.5)	151 (46.4)	62 (31.7)
Other	37 (22.4)	254 (33.2)	68 (20.9)	42 (21.5)
High-risk cytogenetics,[c] n (%)	38 (23.0)	163 (21.3)	74 (22.6)	41 (21.2)
ISS stage, n (%)				
I	88 (53.3)	297 (38.8)	169 (51.8)	102 (52.1)
II	57 (34.5)	245 (32.0)	119 (36.4)	70 (36.0)
III	20 (12.1)	224 (29.2)	38 (11.8)	23 (12.0)
Number of prior LOT				
≤4	78 (47.3)	347 (45.3)	143 (44.0)	86 (43.9)
>4	87 (52.7)	419 (54.7)	183 (56.0)	109 (56.1)
Age (years), n (%)				
<65	86 (52.1)	274 (35.8)	169 (51.9)	101 (51.6)
65–74	55 (33.3)	279 (36.4)	108 (33.2)	62 (32.0)
≥75	24 (14.5)	213 (27.8)	49 (14.9)	32 (16.4)
ECOG PS, n (%)				
0	55 (33.3)	239 (31.2)	112 (34.3)	74 (38.2)
1	110 (66.7)	527 (68.8)	214 (65.7)	121 (61.8)
Race, n (%)				
White	134 (81.2)	559 (73.0)	226 (69.3)	156 (80.0)
Black/African American	21 (12.7)	87 (11.4)	51 (15.6)	27 (14.0)
Not reported/other	10 (6.1)	120 (15.7)	49 (15.1)	12 (6.0)
Male, n (%)	96 (58.2)	384 (50.1)	174 (53.5)	109 (56.1)

[a]Refractoriness was defined as drug discontinuation or switch within 60 days. [b]Refractory to 2 IMiDs + 2 PIs + anti-CD38 monoclonal antibody. [c]At least 1 of del17p, t(14;16), or t(4;14). IMiD, immunomodulatory drug; PI, proteosome inhibitor; SMD, standardized mean difference.

SMD 0.0–0.1 | SMD >0.1–0.2 | SMD >0.2

TABLE 2: Treatment regimens in the RWPC cohort (≥2% of patients)

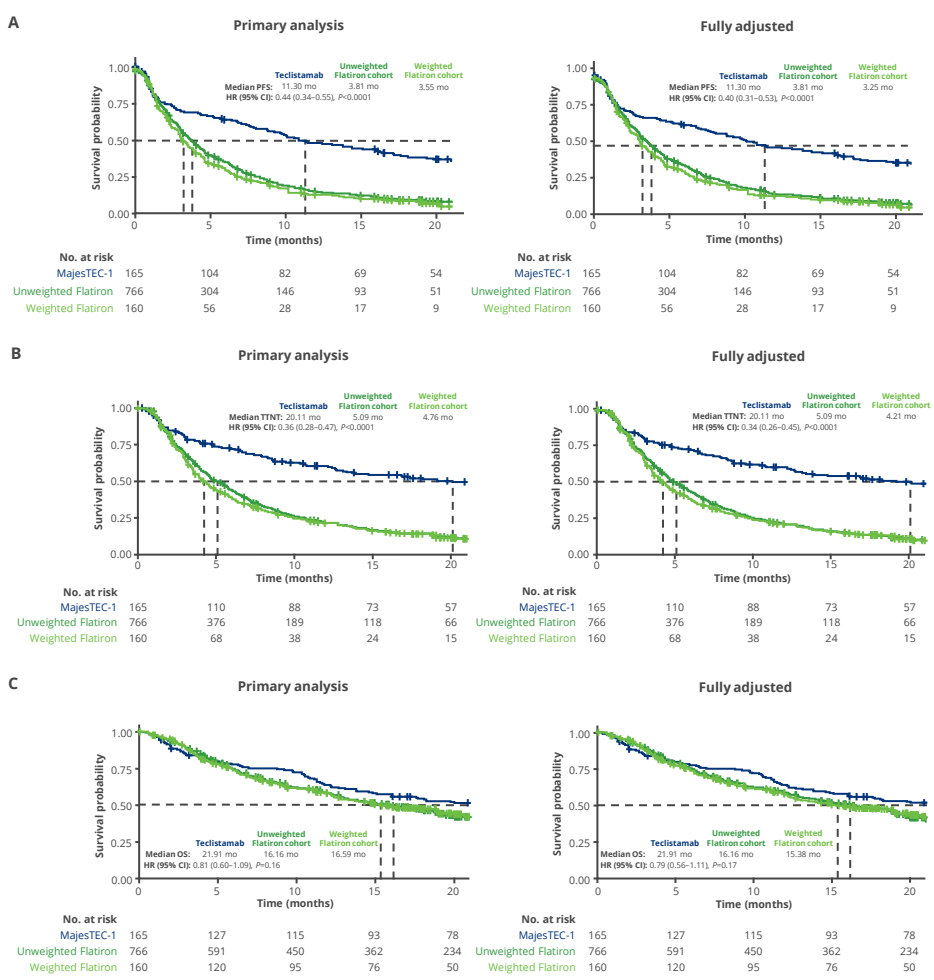
Treatment regimen, n (%)	Frequency (N=766)
Elotuzumab, pomalidomide, and dexamethasone	44 (5.7)
Daratumumab, pomalidomide, and dexamethasone	43 (5.6)
Carfilzomib and dexamethasone	37 (4.8)
Clinical study drug	37 (4.8)
Carfilzomib, pomalidomide, and dexamethasone	32 (4.2)
Carfilzomib, cyclophosphamide, and dexamethasone	30 (3.9)
Pomalidomide and dexamethasone	25 (3.2)
Daratumumab, carfilzomib, and dexamethasone	23 (3.0)
Daratumumab, bortezomib, and dexamethasone	15 (2.0)

TABLE 3: Primary analysis and fully adjusted sensitivity model for PFS, TTNT, and OS

Outcome/Analysis	Teclistamab	RWPC	HR (95% CI)	*P* value
PFS	**Median PFS, months (95% CI)**			
Unadjusted	11.30 (8.77–16.36)	3.81 (3.45–4.21)	0.43 (0.35–0.54)	<0.0001
Primary analysis	11.30 (8.77–16.36)	3.55 (3.09–4.37)	0.44 (0.34–0.55)	<0.0001
Fully adjusted model	11.30 (8.77–16.36)	3.25 (2.89–3.94)	0.40 (0.31–0.53)	<0.0001
TTNT	**Median TTNT, months (95% CI)**			
Unadjusted	20.11 (12.68–NR)	5.09 (4.60–5.68)	0.35 (0.27–0.45)	<0.0001
Primary analysis	20.11 (12.68–NR)	4.76 (4.11–6.01)	0.36 (0.28–0.47)	<0.0001
Fully adjusted model	20.11 (12.68–NR)	4.21 (3.52–5.09)	0.34 (0.26–0.45)	<0.0001
OS	**Median OS, months (95% CI)**			
Unadjusted	21.91 (15.08–NR)	16.16 (14.00–18.14)	0.77 (0.60–1.00)	0.05
Primary analysis	21.91 (15.08–NR)	16.59 (13.14–20.34)	0.81 (0.60–1.09)	0.16
Fully adjusted model	21.91 (15.08–NR)	15.38 (12.12–20.70)	0.79 (0.56–1.11)	0.17

NR, not reached.

FIGURE 2: Unadjusted and adjusted (ATT weighted) Kaplan-Meier plots for (A) PFS, (B) TTNT,[a] and (C) OS



The number of patients at risk is the sum of weights for the cohort-weighted RWPC of therapy cohort. Dashed lines indicate median values.
Adjusted HRs and adjusted curves reflect IPTW with ATT weights.
[a]TTNT defined as time to next treatment or death, whichever comes first.

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KEY TAKEAWAY

Long-term follow-up data from the pivotal MajesTEC-1 phase 1/2 trial demonstrate continued clinical benefits of teclistamab over RWPC in patients with TCE RRMM who received ≥3 prior LOT

CONCLUSIONS

Teclistamab continues to show improved effectiveness in PFS, TTNT, and OS compared with RWPC in patients with TCE RRMM who received ≥3 prior LOT

Results of the fully adjusted model were consistent with the primary analysis

These findings further support the clinical benefit of teclistamab in patients with TCE RRMM who have limited treatment options

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DISCLOSURES

AK reports leadership with Sutro Biopharma; has stock/other ownership interests with BMS; has served in a consulting/advisory role for BMS, GSK, Janssen, Pfizer, Regeneron, and Sanofi; has served on speakers' bureaus for BMS, GSK Canada, and Takeda; and has received research funding from Janssen. **AKN** has served in a consulting/advisory role for Adaptive Biotechnologies, Amgen, BeyondSpring Pharmaceuticals, BMS, Genzyme, GSK, Janssen Oncology, Karyopharm Therapeutics, Oncopeptides, Secura Bio, and Takeda; reports travel, accommodations, and expenses from GSK; has received honoraria from Adaptive Biotechnologies, Amgen, BeyondSpring Pharmaceuticals, BMS/Celgene, Genzyme, GSK, Janssen Oncology, Karyopharm Therapeutics, Oncopeptides, Secura Bio, and Takeda; and has received research funding from Amgen, Arch Oncology, BMS/Celgene, GSK, Janssen Oncology, and Takeda. **AC** has served in a consulting/advisory role for AbbVie, Amgen, Antengene, BMS/Celgene, Genentech, Genzyme, GSK, Janssen Oncology, Karyopharm Therapeutics, Oncopeptides, Seattle Genetics, Secura Bio, Shattuck Labs, and Takeda; and has received research funding from Celgene, Janssen, Pharmacyclics, Seattle Genetics, and Takeda. **ALG** has served in a consulting/advisory role for Amgen, GSK, and Janssen Oncology; has a patent in the field of CAR-T therapy; has stock/other ownership interests in Calbaletta Bio; and has received research funding from CRISPR Therapeutics, Janssen Oncology, Novartis, and Tmunity Therapeutics, Inc. **TGM** has served in a consulting/advisory role for GSK and Juno Therapeutics; and has received research funding from Amgen, Janssen Oncology, and Sanofi. **SN**, **XL**, **KQ**, **AL**, **EMA**, **TP**, and **AM** are employed by and have stock/other ownership interests in Janssen/Johnson & Johnson. **LP**, **KC**, and **MS** are employed by and have stock/other ownership interests in Janssen. **SZU** has served in a consulting/advisory role for AbbVie, Amgen, BMS/Celgene, Celgene, Genentech, Gilead Sciences, GSK, Janssen Oncology, Karyopharm Therapeutics, Merck, Oncopeptides, Seattle Genetics, SkylineDx, and Takeda; has served on speakers' bureaus for Amgen, BMS/Celgene, Janssen Oncology, Sanofi, and Takeda; and has received research funding from Amgen, Array BioPharma, BMS, Celgene, GSK, Janssen Oncology, Merck, Pharmacyclics, Sanofi, Seattle Genetics, and SkylineDx.