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Teclistamab Plus Daratumumab (Tec-Dara) Versus Real-World Physician's Choice of Therapy for Relapsed/Refractory Multiple Myeloma: Comparative Effectiveness Based on an Indirect Treatment Comparison

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Key Takeaway

Tec-Dara was associated with an 88% risk reduction in progression or death and a 49% risk reduction in death versus rwPC and consistently outperformed a broad range of traditional rwPC regimens

Conclusions

Tec-Dara was associated with significantly improved PFS, OS, and TTNT versus rwPC in patients with RRMM after 1 to 3 pLOTs in this adjusted comparison against contemporary real-world treatment patterns

Results were consistent across base-case and full-model adjustment and sensitivity analyses, which supports the robustness of the findings

These data provide important real-world context for MajesTEC-3 and reinforce Tec-Dara as a highly effective SOC treatment option for RRMM as early as second line, while acknowledging that indirect comparisons may not replace randomized clinical trials

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Poster

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Introduction

- Teclistamab (Tec), with extensive real-world experience, is a standard-of-care (SOC) B-cell maturation antigen (BCMA)×CD3 bispecific antibody approved in combination with daratumumab (Tec-Dara) for the treatment of patients with relapsed/refractory multiple myeloma (RRMM) and ≥1 prior lines of therapy (pLOTs)[1-5]
- In the phase 3 MajesTEC-3 trial (NCT05083169), Tec-Dara significantly improved progression-free survival (PFS) and overall survival (OS) and deepened responses versus SOC (daratumumab plus dexamethasone and pomalidomide or bortezomib [DPd/DVd]) in patients with RRMM and 1 to 3 pLOTs, including a proteasome inhibitor (PI) and lenalidomide[6]
  - At a median follow-up of 34.5 months, Tec-Dara significantly reduced the risk of disease progression or death by 83% (*P*<0.0001) and the risk of death by 54% (*P*<0.0001) and significantly increased the rate of complete response or better (81.8% vs 32.1%)[6,7]
  - Tec-Dara benefits were maintained across all prespecified and clinically relevant subgroups, including high-risk cytogenetics and functional high-risk RRMM[7,8]
- It is important to contextualize results of MajesTEC-3 against traditional SOC therapies used in real-world practice settings
- Using data from MajesTEC-3, we performed an indirect adjusted treatment comparison to assess the comparative effectiveness of Tec-Dara versus real-world physician's choice (rwPC) of SOC therapy for the treatment of RRMM from a real-world US database

Methods

Data sources

- Individual patient-level data from MajesTEC-3 (clinical cut-off: August 1, 2025) included patients randomized to receive Tec-Dara (n=291)
- An external cohort was generated using the US Flatiron Health database, including patients who met key MajesTEC-3 eligibility criteria (**Table 1**) from January 2016 to October 2025
  - A total of 4224 observations were captured from 2959 patients

Table 1: Key MajesTEC-3 eligibility criteria

Inclusion	Exclusion
• ≥18 years of age • Received 1-3 pLOTs, including a PI and lenalidomide • Lenalidomide-refractory if received only 1 pLOT • Documented evidence of progressive disease based on investigator's determination of response by IMWG criteria on or after their last regimen • ECOG PS score of 0, 1, or 2 at screening and prior to the start of study treatment	• Received any prior BCMA-directed therapy • Disease that is considered refractory to an anti-CD38 monoclonal antibody per IMWG

BCMA, B-cell maturation antigen; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; PI, proteasome inhibitor; pLOT, prior line of therapy.

Comparison

- The primary analysis used inverse probability of treatment weighting (IPTW), with an average treatment effect in the treated (ATT) population to adjust for imbalances
- Treatment-effect modifiers were a priori selected and ranked by importance based on systematic literature reviews and clinical expert feedback
  - Base-case (most important factors): refractory status, cytogenetic risk, International Staging System disease stage, time to progression on pLOT, Eastern Cooperative Oncology Group performance status score, and age
  - Full-model (in addition to above): hemoglobin, number of pLOTs, time since diagnosis, prior transplant, race, sex, type of MM, and creatinine clearance

Statistical analysis

- Comparative effectiveness was determined for PFS, OS, and time to next treatment (TTNT)
- 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% confidence interval (CI)
- Patients who were included multiple times in different LOTs and fulfilled all MajesTEC-3 criteria at each LOT were grouped as "all observations" and used for the primary analysis

Sensitivity analysis

- A sensitivity analysis was also conducted using "first observations" only, defined as patients whose first LOT satisfied the inclusion criteria (excluding patients with multiple eligible LOTs) to assess the robustness of results

Results

Patient demographic characteristics

- After IPTW, baseline characteristics were comparable between Tec-Dara and rwPC cohorts (**Table 2**)
- The most common real-world regimen in the rwPC cohort was DPd (640/4224 [15.2%]; **Table 3**)

Table 2: Baseline characteristics before and after weighting

Characteristic	Tec-Dara (n=291)	rwPC before weighting (n=4224)	rwPC cohort after weighting			
			Base-case (ESS=1350)	SMD[a]	Full-model (ESS=995)	SMD[a]
Double refractory (PI+IMiD), n (%)	99 (34.0)	2034 (48.2)	101.0 (35.3)	0.025	103.4 (38.4)	0.090
Cytogenetic risk, n (%)						
High risk	104 (35.7)	801 (19.0)	101.7 (35.5)	0.01	92.9 (34.5)	0.03
Standard risk	126 (43.3)	2451 (58.0)	125.0 (43.7)	–0.01	119.1 (44.2)	–0.02
Unknown	61 (21.0)	972 (23.0)	59.7 (20.8)	0.00	57.2 (21.2)	–0.01
ISS stage, n (%)						
I	182 (62.5)	1747 (41.4)	176.1 (61.5)	0.02	164.7 (61.2)	0.03
II	85 (29.2)	1458 (34.5)	86.1 (30.1)	–0.02	81.0 (30.1)	–0.02
III	24 (8.2)	1019 (24.1)	24.2 (8.5)	–0.01	23.5 (8.7)	–0.01
Progression on pLOT ≥16 months, n (%)[b]	192 (66.0)	1285 (30.4)	186.3 (65.0)	0.02	166.9 (62.0)	0.09
ECOG PS score, n (%)						
0	167 (57.4)	1512 (35.8)	162.4 (56.7)	0.01	149.6 (55.6)	0.04
1	108 (37.1)	2103 (49.8)	107.6 (37.6)	–0.01	103.0 (38.2)	–0.02
2	16 (5.5)	609 (14.4)	16.4 (5.7)	–0.01	16.7 (6.2)	–0.02
Age category, n (%)						
≤65 years	147 (50.5)	1480 (35.0)	144.0 (50.3)	0.01	134.0 (49.8)	0.02
65 to ≤74 years	113 (38.8)	1462 (34.6)	111.0 (38.7)	0.00	102.5 (38.1)	0.02
≥75 years	31 (10.7)	1282 (30.4)	31.5 (11.0)	–0.01	32.7 (12.2)	–0.04
Hemoglobin ≥100 g/L, n (%)	226 (77.7)	3417 (80.9)	248.0 (86.6)[c]	–0.22	203.5 (75.6)	0.05
pLOTs, n (%)						
1	108 (37.1)	834 (19.7)	41.3 (14.4)[c]	0.51	80.8 (30.0)	0.16
2	134 (46.0)	2192 (51.9)	169.4 (59.1)[c]	–0.26	137.5 (51.1)	–0.10
3	49 (16.8)	1198 (28.4)	75.8 (26.5)[c]	–0.23	50.9 (18.9)	–0.05
Time from diagnosis to index ≥4 years, n (%)	133 (45.7)	1080 (25.6)	111.4 (38.9)[c]	0.15	124.0 (46.0)	–0.01
Received prior transplant, n (%)	210 (72.2)	1924 (45.5)	175.5 (61.3)[c]	0.23	182.2 (67.7)	0.09
White, n (%)	190 (65.3)	2776 (65.7)	183.0 (63.9)[c]	0.03	161.5 (60.0)	0.11
Female, n (%)	135 (46.4)	1913 (45.3)	131.1 (45.8)[c]	0.01	121.1 (45.0)	0.03
Type of MM, n (%)						
IgA	54 (18.6)	846 (20.0)	54.3 (19.0)[c]	–0.01	47.3 (17.6)	0.02
IgG	158 (54.3)	2599 (61.5)	180.1 (62.9)[c]	–0.17	146.4 (54.4)	–0.00
Other	79 (27.1)	779 (18.4)	52.0 (18.2)[c]	0.22	75.6 (28.1)	–0.02
CrCl >60 mL/min	235 (80.8)	2876 (68.1)	213.8 (74.6)[c]	0.14	215.9 (80.2)	0.01

CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group performance status; ESS, effective sample size; Ig, immunoglobulin; IMiD, immunomodulatory drug; ISS, International Staging System; MM, multiple myeloma; PI, proteasome inhibitor; pLOT, prior line of therapy; rwPC, real-world physician's choice; SMD, standardized mean difference; Tec-Dara, teclistamab plus daratumumab.
[a]An SMD ≥0.25 indicated a significant difference between cohorts.
[b]Given that the duration of time from progression on pLOT was quite long, a median duration (in this case, 16 months) was taken from the population to generate a suitable category.
[c]Not adjusted for in the base-case model.

Table 3: Most common[a] treatment regimens in the rwPC cohort

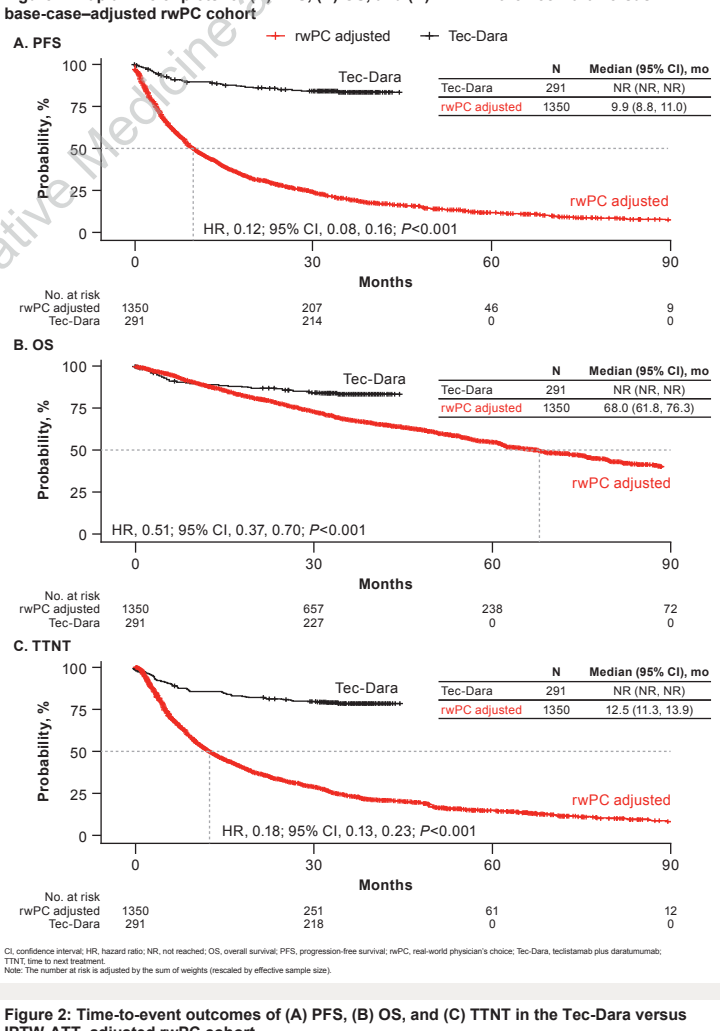
Treatment regimen, n (%)	Frequency (N=4224)
Anti-CD38–based combination[b]	2289 (54.2)
Monotherapy[c,d]	343 (15.0)
Doublet[c,d,e]	57 (2.5)
Triplet[c,f]	1605 (70.1)
Quadruplet[c]	284 (12.4)
Other MM combination[b]	1935 (45.8)
Doublet[e,g]	1005 (51.9)
Triplet[g]	611 (31.6)
Other[g,h]	319 (16.5)

MM, multiple myeloma; rwPC, real-world physician's choice.
[a]Most common is defined as those treatments used in ≥5% of the rwPC cohort. The most common treatment regimens were daratumumab based.
[b]Percentage calculated using the total number (N=4224) as the denominator.
[c]Percentage calculated using the total number of anti-CD38–based combinations (n=2289) as the denominator.
[d]Daratumumab monotherapy only with or without dexamethasone.
[e]Doublets in general include ≥1 core MM drug with or without dexamethasone.
[f]Triplets include daratumumab/pomalidomide/dexamethasone (640/4224 [15.2%]), daratumumab/bortezomib/dexamethasone (266/4224 [6.3%]), daratumumab/carfilzomib/dexamethasone (255/4224 [6.0%]), and daratumumab/lenalidomide/dexamethasone (236/4224 [5.6%]).
[g]Percentage calculated using the total number of other MM combinations (n=1935) as the denominator.
[h]Dexamethasone, cyclophosphamide, clinical study drugs, etoposide, melphalan, prednisone, and other non-MM drugs.

Efficacy outcomes

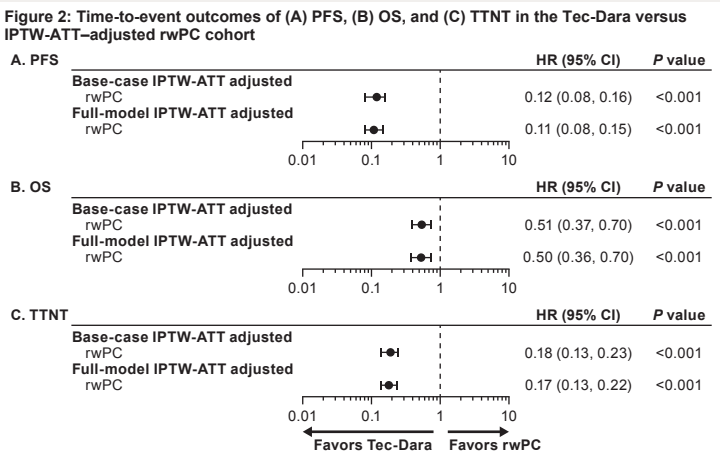
- Per base-case adjustment, patients treated with Tec-Dara had significantly improved PFS, OS, and TTNT versus rwPC as shown in **Figures 1A**, **1B**, and **1C**, respectively
- Similarly, full-model adjustment results significantly favored Tec-Dara for PFS (HR, 0.11 [95% CI, 0.08, 0.15]), OS (HR, 0.50 [95% CI, 0.36, 0.70]), and TTNT (HR, 0.17 [95% CI, 0.13, 0.22]; **Figure 2**)

Figure 1: Kaplan-Meier plots for (A) PFS, (B) OS, and (C) TTNT in the Tec-Dara versus base-case–adjusted rwPC cohort



CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival; rwPC, real-world physician's choice; Tec-Dara, teclistamab plus daratumumab; TTNT, time to next treatment.
Note: The number at risk is adjusted by the sum of weights (rescaled by effective sample size).

Figure 2: Time-to-event outcomes of (A) PFS, (B) OS, and (C) TTNT in the Tec-Dara versus IPTW-ATT–adjusted rwPC cohort



ATT, average treatment effect in the treated; CI, confidence interval; HR, hazard ratio; IPTW, inverse probability of treatment weighting; OS, overall survival; PFS, progression-free survival; rwPC, real-world physician's choice; Tec-Dara, teclistamab plus daratumumab; TTNT, time to next treatment.

Sensitivity analysis

- In a sensitivity analysis of first observations only, results were consistent with the primary analysis and consistently favored Tec-Dara across outcomes versus rwPC (**Table 4**)

Table 4: Sensitivity analyses per base-case–adjusted first observations only

	Tec-Dara		rwPC			
	Median (95% CI), mo	Est. 36-mo rates (95% CI), %	Median (95% CI), mo	Est. 36-mo rates (95% CI), %	HR (95% CI)	*P* value
PFS	NR (NR, NR)	83.4 (79.0, 88.0)	9.7 (8.7, 10.9)	18.6 (16.0, 21.5)	0.11 (0.08, 0.15)	<0.001
OS	NR (NR, NR)	83.3 (78.9, 87.8)	68.2 (62.0, 77.9)	67.4 (64.2, 70.8)	0.50 (0.36, 0.68)	<0.001
TTNT	NR (NR, NR)	78.7 (73.9, 83.7)	12.0 (10.9, 13.4)	21.8 (19.0, 24.9)	0.17 (0.13, 0.22)	<0.001

CI, confidence interval; Est, estimated; HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival; rwPC, real-world physician's choice; Tec-Dara, teclistamab plus daratumumab; TTNT, time to next treatment.

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