PA-301

Matching-Adjusted Indirect Treatment Comparison of Teclistamab With Daratumumab (Tec-Dara) vs Belantamab With Bortezomib and Dexamethasone (BVd) for Early-Line Relapsed/Refractory Multiple Myeloma

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Key Takeaway

Tec-Dara demonstrated improved PFS and OS and deeper, clinically meaningful responses over BVd in a DREAMM-7–like patient population, per unanchored MAIC

Conclusions

Tec-Dara was associated with a 78% reduction in the risk of progression or death, 52% reduction in risk of death, and twice the probability of achieving ≥CR compared with BVd, after adjusting for differences in baseline characteristics, suggesting deeper and greater efficacy with Tec-Dara

Adjustment for IMiD-refractory status was limited due to high prevalence of IMiD-refractory patients in MajesTEC-3; nonetheless, the comparative benefit of Tec-Dara over BVd persisted after MAIC adjustment across base-case, full-model, and subgroup analyses, demonstrating robust results and effectiveness of Tec-Dara regardless of refractory status

These findings support Tec-Dara as a highly effective, fully immunotherapy-based, steroid-sparing, standard-of-care regimen in RRMM as early as first relapse, expanding upon that observed in MajesTEC-3

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Disclosure

WS is a current employee of Johnson & Johnson and may hold stock in Johnson & Johnson.

Introduction

- Teclistamab (Tec), a standard-of-care B-cell maturation antigen (BCMA)×CD3 bispecific antibody, combined with daratumumab (Dara; Tec-Dara), is approved in multiple countries for the treatment of relapsed or refractory multiple myeloma (RRMM) with ≥1 prior line of therapy (pLOT)[1-5]
- In the phase 3 MajesTEC-3 study (NCT05083169; median follow-up, 34.5 months), Tec-Dara significantly improved progression-free survival (PFS) and overall survival (OS) and increased the rate of complete response or better (≥CR) versus standard-of-care daratumumab plus dexamethasone and pomalidomide or bortezomib (DPd/DVd) in patients with RRMM and 1 to 3 pLOTs[6,7]
  - Benefits were observed despite 83.6% of patients having lenalidomide-refractory disease[6]
- Other off-the-shelf BCMA-directed therapies are available in early-line RRMM, including belantamab mafodotin plus bortezomib and dexamethasone (BVd), which is approved for RRMM with ≥1 (EU)[8] or ≥2 pLOTs (USA)[9]
  - In the phase 3 DREAMM-7 study (NCT04246047; median follow-up, 28.2 months), BVd significantly improved PFS versus DVd in patients with RRMM and ≥1 pLOT; 34% were lenalidomide-refractory[10]
- In the absence of head-to-head studies, matching-adjusted indirect treatment comparisons (MAICs) can be used to indirectly compare treatments and contextualize efficacy given varying patient populations
- We conducted an unanchored MAIC to compare the relative treatment effectiveness of Tec-Dara versus BVd in early-line RRMM

Methods

Data sources

- Individual patient-level data (IPD) for MajesTEC-3, Tec-Dara
  - PFS/OS and overall response rate (ORR)/very good partial response or better (≥VGPR)/≥CR: Costa LJ, et al. *N Engl J Med* 2026[6] (median follow-up, 34.5 months; data cut-off, August 1, 2025)
- Aggregated data for DREAMM-7, BVd
  - PFS: Hungria V, et al. *N Engl J Med* 2024[10] (median follow-up, 28.2 months; data cut-off, October 2, 2023)
  - OS and ORR/≥VGPR/≥CR: Hungria V, et al. *Lancet Oncol* 2025[11] (median follow-up, 39.4 months; data cut-off, October 7, 2024)
  - 1 pLOT, lenalidomide-refractory: Hungria V, et al. International Myeloma Society 2025[12] (median follow-up, 39.4 months; data cut-off, October 7, 2024)

Comparison

- Baseline characteristic imbalances were adjusted by applying propensity score weights to MajesTEC-3 IPD to match baseline DREAMM-7 characteristics
  - MajesTEC-3 had substantially more immunomodulatory drug (IMiD)-refractory patients than DREAMM-7 (Tec-Dara, 84.9%; BVd, 39%),[6,10] therefore adjusting for this would undermine any conclusion due to effective sample size (ESS) limitation and imprecision
  - 12% of BVd patients in DREAMM-7 had ≥4 prior LOTs[7] and thus were recategorized as "≥3 pLOTs" to account for the MajesTEC-3 population
- Unanchored MAIC adjusted for both prognostic factors and treatment-effect modifiers that were *a priori* identified and ranked based on systematic literature reviews and clinical expert feedback
  - Base case (primary analysis): proteasome inhibitor (PI)-refractory status, cytogenetic risk, revised International Staging System (ISS) disease stage, extramedullary disease, Eastern Cooperative Oncology Group performance status score, and age group
  - Full model (in addition to above): number of pLOTs, time since diagnosis, prior transplant, race, sex, and MM type

Statistical analysis

- Comparative effectiveness was estimated for PFS, OS, ORR, ≥VGPR, and ≥CR; outcome definitions were consistent across trials
- For time-to-event end points, hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using a weighted Cox proportional hazards model
- For ORR/≥VGPR/≥CR end points, relative effects were quantified using odds ratios (ORs) and risk ratios (RRs) with 95% CIs derived from a weighted logistic regression analysis

Subgroup analysis

- A subgroup analysis was also conducted in patients with 1 pLOT only who were lenalidomide-refractory; covariates adjusted for included cytogenetic risk, revised ISS stage, extramedullary disease, and age

Results

Patient demographic and baseline disease characteristics

- In total, 291 Tec-Dara and 243 BVd patients were included
  - Baseline characteristics were generally comparable; however, a higher proportion of patients in the Tec-Dara cohort were PI-refractory, had revised ISS disease stage III, and had high-risk cytogenetics; more patients in the BVd cohort had ≥3 pLOTs
- Tec-Dara ESS was 157 and 74 per base-case and full-model adjustment, respectively
  - All variables included in the model were well balanced after weighting (**Table 1**)

Table 1: Key baseline characteristics before and after adjustment

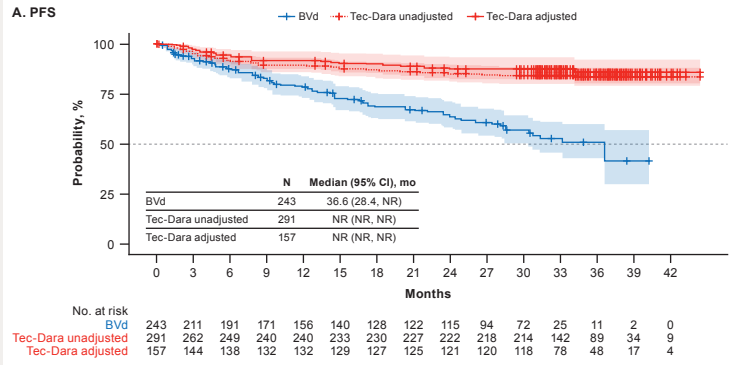
Characteristic, %	BVd (n=243)	MajesTEC-3 Tec-Dara IPD (n=291)	Tec-Dara IPD cohort after weighting	
			Base case (ESS=157)	Full model (ESS=74)
Refractory to a PI	9	40	9	9
High cytogenetic risk	28	36	28	28
Revised ISS disease stage				
I	42	29	42	42
II	54	66	54	54
III	4	6	4	4
Presence of EMD	5	5	5	5
ECOG PS score				
0	50	57	50	50
1	46	37	46	46
2	4	5	4	4
Age group				
<65 years	50	51	50	50
65-74 years	35	39	35	35
≥75 years	15	11	15	15
No. of pLOTs				
1	51	37	45[a]	51
2	22	46	40[a]	22
≥3	27	17	15[a]	27
Time since diagnosis, years	4.30	3.70	3.81[a]	4.27
Received prior transplant	67	72	74[a]	67
Race				
White	85	65	64[a]	85
Asian	12	23	20[a]	12
Female	47	46	45[a]	47
IgG MM	66	54	56[a]	66

BVd, belantamab mafodotin plus bortezomib and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; EMD, extramedullary disease; ESS, effective sample size; IgG, immunoglobulin G; IMiD, immunomodulatory drug; IPD, individual patient-level data; ISS, International Staging System; MM, multiple myeloma; PI, proteasome inhibitor; pLOT, prior line of therapy; Tec-Dara, teclistamab plus daratumumab.
Note: The % values in the proportion variables were calculated based on the total sample size for the unadjusted data and on the ESS for the adjusted data.
[a]Variables were not adjusted for in the base-case model.

PFS and OS outcomes

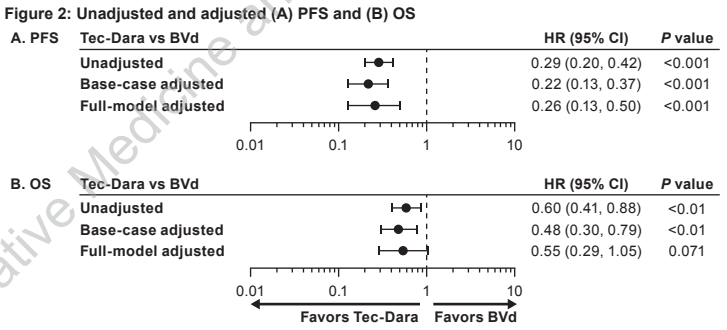
- Patients treated with Tec-Dara had a clinically significant 78% reduction in the risk of progression and death versus BVd (**Figure 1A**); PFS continued to significantly favor Tec-Dara will full-model adjustment (**Figure 2A**)
- Patients treated with Tec-Dara had a clinically significant 52% reduction in the risk of death versus BVd (**Figure 1B**)
  - The OS point estimate for the full model was consistent with the base-case analysis, while CIs were widened due to decreased ESS (**Figure 2B**)

Figure 1: Unadjusted and base-case–adjusted Kaplan-Meier plots for (A) PFS and (B) OS



BVd, belantamab mafodotin plus bortezomib and dexamethasone; CI, confidence interval; ESS, effective sample size; NR, not reached; OS, overall survival; PFS, progression-free survival; Tec-Dara, teclistamab plus daratumumab.
Note: The number at risk is adjusted by the sum of weights (rescaled by ESS).

Figure 2: Unadjusted and adjusted (A) PFS and (B) OS

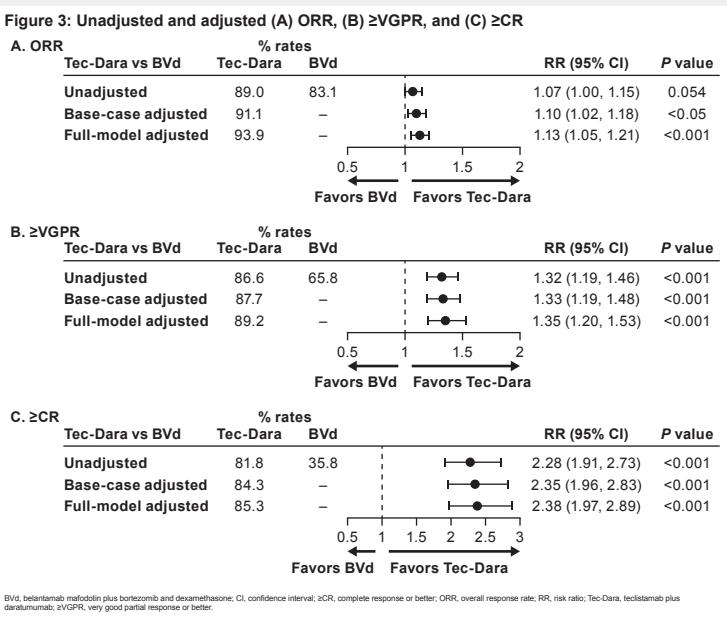


BVd, belantamab mafodotin plus bortezomib and dexamethasone; CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; Tec-Dara, teclistamab plus daratumumab.

ORR, ≥VGPR, and ≥CR outcomes

- Per RRs, patients treated with Tec-Dara were 1.1-, 1.3-, and 2.4-times more likely to achieve ORR, ≥VGPR, and ≥CR, respectively, compared with BVd (**Figure 3**); results were consistent per calculated ORs (**Table 2**)

Figure 3: Unadjusted and adjusted (A) ORR, (B) ≥VGPR, and (C) ≥CR



BVd, belantamab mafodotin plus bortezomib and dexamethasone; CI, confidence interval; ≥CR, complete response or better; ORR, overall response rate; RR, risk ratio; Tec-Dara, teclistamab plus daratumumab; ≥VGPR, very good partial response or better.

Table 2: Unadjusted and adjusted comparative analyses of ORR/≥VGPR/≥CR outcomes

Tec-Dara vs BVd	OR (95% CI)	*P* value
ORR		
Unadjusted	1.64 (1.00, 2.70)	0.051
Base case	2.09 (1.14, 3.83)	<0.05
Full model	3.11 (1.51, 6.43)	<0.01
≥VGPR		
Unadjusted	3.35 (2.18, 5.15)	<0.001
Base case	3.69 (2.13, 6.41)	<0.001
Full model	4.28 (1.95, 9.44)	<0.001
≥CR		
Unadjusted	8.05 (5.42, 11.97)	<0.001
Base case	9.63 (5.78, 16.05)	<0.001
Full model	10.43 (5.26, 20.66)	<0.001

BVd, belantamab mafodotin plus bortezomib and dexamethasone; CI, confidence interval; ≥CR, complete response or better; OR, odds ratio; ORR, overall response rate; Tec-Dara, teclistamab plus daratumumab; ≥VGPR, very good partial response or better.

Subgroup analysis

- In patients with 1 pLOT and lenalidomide-refractory disease (Tec-Dara, n=71; BVd, n=22), results were generally consistent with the primary analysis, but should be interpreted with caution given the lower ESS (Tec-Dara ESS, n=35)
  - PFS significantly favored Tec-Dara versus BVd (HR, 0.27; 95% CI, 0.10, 0.76; *P*<0.05)
  - ORR was comparable between treatments (RR, 1.01; 95% CI, 0.90, 1.13; OR, 1.26; 95% CI, 0.11, 14.73), ≥VGPR numerically favored Tec-Dara (RR, 1.16; 95% CI, 0.92, 1.45; OR, 3.49; 95% CI, 0.77, 15.90), and patients were significantly more likely to achieve a deeper, clinically meaningful ≥CR with Tec-Dara than BVd (RR, 1.64; 95% CI, 1.11, 2.43; *P*<0.05; OR, 11.13; 95% CI, 2.90, 42.78; *P*<0.001)

Strengths and Limitations

- Despite the ability to match on pLOT, PI refractoriness and other important factors, the extent of IMiD refractoriness was more extensive for Tec-Dara in the primary analyses; regardless, a clinical and statistically significant benefit with Tec-Dara versus BVd was observed
- With an imbalance between trials in IMiD-refractory patients, IMiD-refractoriness was not adjusted for to preserve a higher ESS; while this may have introduced bias against Tec-Dara, its clinical and statistically significant benefit persisted following unanchored MAIC
- With IPD available from MajesTEC-3 and published data from DREAMM-7, analyses of both primary and secondary end points were feasible in this MAIC
- Base-case and full-model results were consistent, and results of the subgroup analysis of patients with 1 pLOT and lenalidomide-refractory disease mirrored that of the intent-to-treat population, favoring Tec-Dara in both PFS and ≥CR

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Multiple Myeloma

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