Overall survival with anti-BCMA therapies: indirect comparison of belantamab mafodotin/bortezomib/dexamethasone vs teclistamab/daratumumab in relapsed/refractory multiple myeloma

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In this MAIC, BVd demonstrated similar OS and lower odds of infection vs tec-dara after adjusting for key baseline differences, highlighting the benefit of BCMA targeting and offering clinically meaningful insights to inform benefit-risk considerations and broaden access to BCMA-directed therapies

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Background

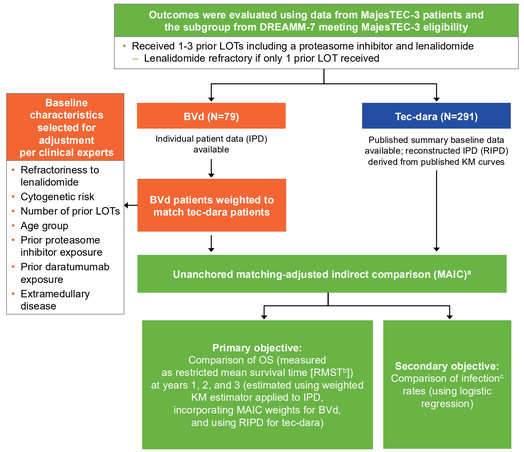
- Targeting BCMA has transformed outcomes in RRMM, with novel mechanisms of action, including ADCs and BsAbs[1,2]
- Both BsAb combinations and ADC combinations have demonstrated OS improvements compared with conventional anti-CD38–based triplet regimens in randomized trials; however, both have different AE profiles, including CRS and ICANS for BsAbs and ocular events for ADCs. Infection risks and treatment access can vary significantly between the two[1,2]

Aims

Compare OS and infections between BCMA-targeting ADC- and BsAb-based regimens by evaluating outcomes in matched patients with RRMM from DREAMM-7 (BVd) and MajesTEC-3 (tec-dara) using an indirect treatment comparison

Methods

Figure 1: Study Design



[a] An unanchored approach was selected for comparison, as DREAMM-7 and MajesTEC-3 lacked a common comparator arm. Specifically, DREAMM-7 analyzed BVd vs comparator DVd, whereas MajesTEC-3 analyzed tec-dara vs comparator DVd or DPd. [b] Given the immaturity of OS in MajesTEC-3 and the potential for nonproportional hazards, OS was compared using both differences and ratios of RMST to aid interpretation. RMST is defined as the area under the survival curve up to a specified time horizon and represents the average survival time up to that time point. [c] Throughout the poster, "infection" refers to infections and infestations.

Results

Table 1: Summary of Key Prognostic Factors

Variable, %[a]	Unadjusted DREAMM-7 BVd (N=79)	Adjusted DREAMM-7 BVd (ESS=47)[b]	MajesTEC-3 tec-dara (N=291)
Refractory to lenalidomide	74.7	82.5	82.5
High cytogenetic risk	25.3	45.2	45.2
No. of prior LOTs			
1	26.6	37.1	37.1
2	43.0	46.0	46.0
3	30.4	16.8	16.8
Age ≥75 years	17.7	10.7	10.7
Age ≤64 years	36.7	50.0	50.0
Prior daratumumab	1.3	5.2	5.2
Prior exposure to a proteasome inhibitor	94.9	99.7	99.7
Extramedullary disease present	7.6	4.8	4.8
International Staging System stage			
II	54.4	62.8	29.2
III	3.8	5.6	8.2
Race			
White	88.6	88.2	65.3
Asian	10.1	10.9	23.4
Other	1.3	1.0	11.3
ECOG PS			
0	41.8	45.4	57.4
1	51.9	50.6	37.1
2	6.3	4.0	5.5
1 or 2	58.2	54.6	42.6

[a] Factors that were matched are shown in bold. [b] ESS represents the sample size after population weighting.

- After matching, the highest priority prognostic factors were equal between tec-dara– and BVd-treated patients
- ISS stage and ECOG PS were biased against BVd
- OS RMST at 1, 2, and 3 years was comparable between treatments, with no statistically significant difference in the RMST ratio at any time point
- Although the OS curve for BVd fell below the tec-dara curve around 22 months, the overall relative effect favored BVd; at 3 years, the RMST still numerically favored BVd
- The absolute risk of any-grade treatment-emergent infection was 15% lower for BVd, resulting in a statistically significant odds ratio in favor of BVd
  - This result is aligned with the substantially lower rate of IVIG use with BVd in DREAMM-7 (8%) vs tec-dara in MajesTEC-3 (87.3%)[2,3]; despite this higher rate of IVIG use, tec-dara had a higher rate of infections
  - A sensitivity analysis performed using all (not just treatment-emergent) infections from DREAMM-7 retained the significant difference
- BVd and tec-dara provided similar risk for grade 3/4 infections
  - Similarly, there were no significant differences in grade ≥3 infections up to 6 months

Figure 2: KM Plot of Survival Probability per RMST

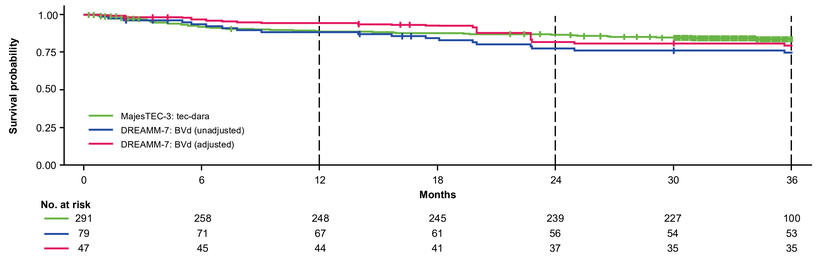


Table 2: OS RMST

	Adjusted DREAMM-7 BVd (ESS=47)	MajesTEC-3 tec-dara (N=291)
OS		
RMST at 1 year (SE), months	11.6 (0.25)	11.2 (0.15)
RMST ratio (95% CI); *P* value	1.04 (0.99-1.09); 0.141	
RMST at 2 years (SE), months	22.5 (0.67)	21.7 (0.37)
RMST ratio (95% CI); *P* value	1.04 (0.97-1.11); 0.277	
RMST at 3 years (SE), months	32.2 (1.3)	31.9 (0.60)
RMST ratio (95% CI); *P* value	1.01 (0.93-1.10); 0.801	

Table 3: Infection Rates in the Base Case Analyses[a]

	Adjusted DREAMM-7 BVd (ESS=47)	MajesTEC-3 tec-dara (N=283)
Base case		
Treatment-emergent infections of any grade, %	81.3	96.5
Odds ratio (95% CI); *P* value	0.16 (0.06-0.43); <0.001	
Treatment-emergent grade 3/4 infections, %	46.7	54.1
Odds ratio (95% CI); *P* value	0.75 (0.40-1.40); 0.363	
Treatment-emergent grade ≥3 infections up to 6 months, %	27.9	35.3
Odds ratio (95% CI); *P* value	0.71 (0.36-1.40); 0.320	

[a] Sensitivity analyses that compared all BVd infections (not just treatment emergent) to treatment-emergent infections on tec-dara produced similar results that still numerically favored BVd: any-grade odds ratio = 0.24 (95% CI, 0.10-0.61); grade 3/4 odds ratio = 0.92 (95% CI, 0.49-1.72); grade ≥3 up to 6 months odds ratio = 0.90 (95% CI, 0.45-1.81).

Figure 3: OS RMST Difference

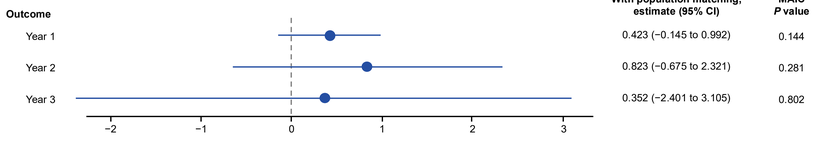
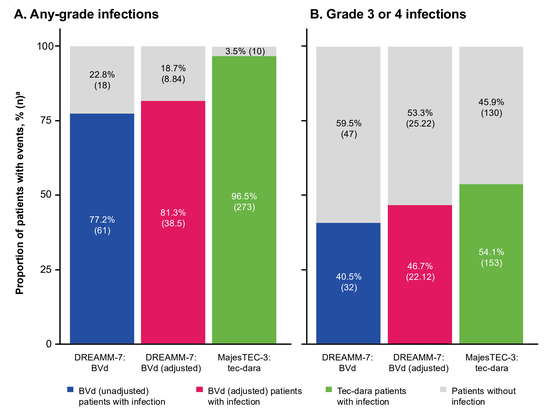


Figure 4: Treatment-Emergent Infections of (A) Any Grade and (B) Grade 3 or 4



[a] Colored bars indicate the proportion (number) of patients with an event.

Limitations

- The reduction in ESS that occurs after weighting on multiple factors means that it is not feasible to adjust for a large number of prognostic factors. Consequently, variables not included in the matching model may show residual imbalance after weighting
- Only published aggregate data were available for MajesTEC-3, and RIPD derived from published KM curves were used for the tec-dara arm
- As DREAMM-7 had a longer follow-up than MajesTEC-3 (42.3 vs 34.5 months), OS comparisons at specific landmark time points were used to aid interpretation
- OS maturity was low for both MajesTEC-3 (15.5% for tec-dara) and DREAMM-7 (22.8% for BVd), which may affect the precision and reliability of RMST estimates

Conclusions

There is a need for accessible BCMA-directed therapies that demonstrate high efficacy with a tolerable safety profile for patients

BVd demonstrated similar OS and lower odds of infection vs tec-dara when adjusting for differences in key baseline patient characteristics (within the assumptions/ limitations of unanchored MAICs)

These results highlight the transformative benefit of targeting BCMA and offer clinically meaningful insights to inform benefit-risk considerations and broaden access to BCMA-directed therapies, particularly in healthcare settings and patient populations where intensive infection management/hospitalization are impractical

Abbreviations

ADC, antibody-drug conjugate; AE, adverse event; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; BVd, belantamab mafodotin with bortezomib plus dexamethasone; CRS, cytokine release syndrome; DPd, daratumumab with pomalidomide plus dexamethasone; DVd, daratumumab plus bortezomib and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; ESS, effective sample size; ICANS, immune effector cell–associated neurotoxicity syndrome; IPD, individual patient data; ISS, International Staging System; IVIG, intravenous immunoglobulin; KM, Kaplan-Meier; LOT, line of therapy; MAIC, matching-adjusted indirect comparison; OS, overall survival; RIPD, reconstructed individual patient data; RMST, restricted mean survival time; RRMM, relapsed/refractory multiple myeloma; tec-dara, teclistamab plus daratumumab.

References

1. Hungria V, et al. *Lancet Oncol*. 2025;26(8):1067-1080.
2. Costa LJ, et al. *N Engl J Med*. 2025;94(8):739-752.
3. Hungria V, et al. *N Engl J Med*. 2024;391(5):393-407.

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Disclosures

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