The 11th World Congress on CONTROVERSIES IN MULTIPLE MYELOMA (COMy)

Belantamab Mafodotin + Bortezomib + Dexamethasone Versus 2L+ Relapsed/Refractory Multiple Myeloma Regimens: Lenalidomide-Exposed, Lenalidomide-Refractory, High-Risk Cytogenic, and 2L-Only Subpopulations: A Network Meta-analysis

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KEY TAKEAWAY

- BVd demonstrates PFS benefit versus other PI-based regimens for patients with RRMM previously treated with ≥1 prior therapy who are lenalidomide-exposed/refractory, have received only 1 prior LOT, or have high-risk cytogenetic profiles.

INTRODUCTION

- The increase in early-line treatment options available for patients with MM, such as combination therapies based on PIs, immunomodulatory drugs, and monoclonal antibodies,[1] is likely to lead to an increase in patients becoming refractory to these therapies earlier in disease treatment.[2-4]
- Belantamab mafodotin, an afucosylated anti–B-cell maturation (BCMA) antibody-drug conjugate with multiple mechanisms of action[5,6] has shown PFS and OS survival benefits in combination with bortezomib and dexamethasone (BVd) over daratumumab with bortezomib and dexamethasone (DVd) in the Phase III DREAMM-7 study (NCT04246047) in patients with 2L+ RRMM.[7,8]
  - After a median (range) follow-up of 28.2 (0.1–40.0) months, median PFS (95% CI) was 36.6 months (28.4–not reached) versus 13.4 months (11.1–17.5; HR [95% CI] 0.41 [0.31–0.53], P<0.001), for BVd versus DVd, respectively.[7]
- In the absence of head-to-head trials (other than the comparison to DVd in DREAMM-7),[7] it is important to understand the relative efficacy of BVd against alternative regimens for patients with RRMM who had received at least one prior LOT, particularly in subpopulations with unmet clinical needs (e.g., refractory/high cytogenic risk to prior regimens).

AIMS

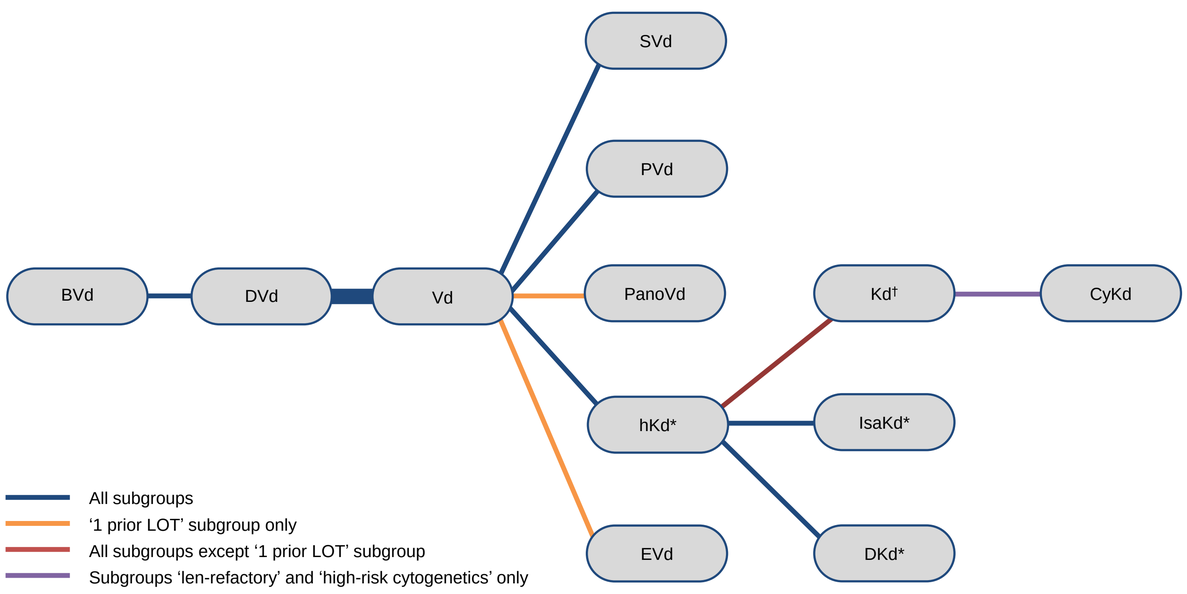
- To indirectly compare the relative efficacy of BVd versus other approved or likely to be approved 2L+ RRMM regimens by conducting a Bayesian NMA of outcomes from RCTs, identified by SLR, in adult patients with RRMM who are lenalidomide-exposed, lenalidomide-refractory, who have received 1 prior LOT only, or who are cytogenetically high-risk.

STUDY DESIGN

- RCTs of adults with RRMM who have been previously treated with ≥1 prior therapy and who have documented disease progression on/after most recent therapy were identified in an SLR (2008–January 2024) performed in December 2021 and updated most recently in January 2024.
- RCTs included only those that evaluated PFS in regimens that were approved for RRMM by the US FDA or the EMA, were considered likely to be approved at the time of study initiation, or were of interest for health technology assessment.
- Trials were linked together by the treatment(s) they shared to form connected networks of evidence, and Bayesian NMAs[6] were conducted.
  - Trials/regimens that were not part of the connected evidence networks were excluded from the NMAs.
- A fixed effects model was employed for the NMA using:
  - Normal likelihood and the identity link function for PFS and OS; HRs and 95% credible intervals (CrIs) were computed for BVd, relative to each comparator.
- Primary analyses examined PFS in the ITT population and have been reported previously;[9] here we report secondary analyses which examined PFS in the lenalidomide-exposed and lenalidomide-refractory populations, and subgroup network analyses, which were carried out to explore outcomes according to patient characteristics (high-risk cytogenetics and 1 prior LOT).[9,10]

RESULTS

Figure 1. Connected network of evidence based on studies identified in the SLR comprised 8 RCTs (lenalidomide-exposed/lenalidomide-refractory) and 10 RCTs (1 prior LOT/high-risk cytogenetics) including DREAMM-7 for PFS. All comparator regimens included in the NMA included a PI.

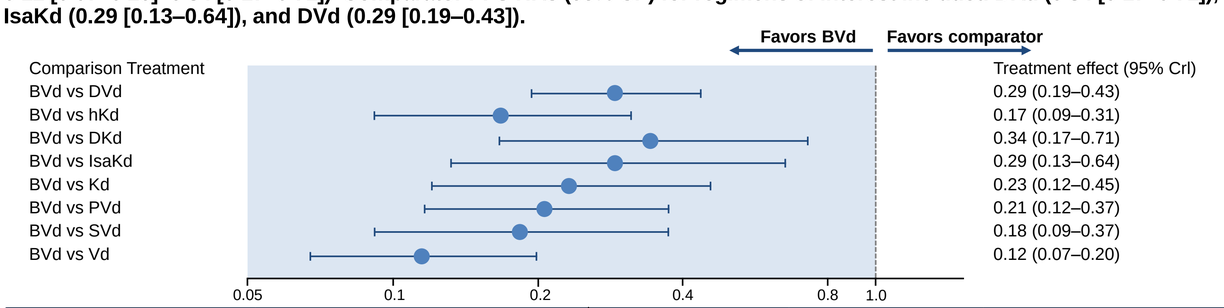


*High-dose carfilzomib. †All networks other than patients with 1 prior LOT also included an alternative dosage of Kd.
Bolded line indicates 2 studies in the network (CASTOR and LEPUS). To facilitate inclusion of the ARROW and GEM KyCyDex studies in the network, equivalence of the twice-weekly 27 mg/m^2 carfilzomib and dexamethasone regimen in the ARROW study and the 56 mg/m^2 carfilzomib and dexamethasone regimen in the ENDEAVOR and CANDOR studies was assumed. This is not expected to materially impact results.

Acronym	Total number of patients per regimen, N	Trial	ITT, n	Len-exposed, n (%)*	Len-refractory, n (%)*	1 Prior line, n (%)*	High-risk cytogenetics, n (%)*
BVd	243	DREAMM-7[7]	243	127 (52)	79 (33)	125 (51)	67 (28)
DVd	643	DREAMM-7	251	130 (52)	87 (35)	125 (50)	69 (27)
		LEPUS[11–12]	141	NA	NA	41 (29)	46 (33)
		CASTOR[13–16]	251	89 (35)	60 (24)	122 (49)	40 (16)
Vd	1723	LEPUS	70	NA	NA	19 (27)	27 (39)
		CASTOR	247	120 (49)	81 (33)	113 (46)	35 (14)
		OPTIMISMM[17–19]	278	278 (100)	191 (69)	115 (41)	49 (18)
		BOSTON[20–22]	207	77 (37)	53 (26)	99 (48)	71 (34)
		PANORAMA-1[23,24]	381	NA	NA	174 (46)	NA
		NCT01478048[25]	75	NA	NA	51 (68)	NA
		ENDEAVOR[26–29]	465	177 (38)	122 (26)	229 (49)	113 (24)
EVd	77	NCT01478048	77	NA	NA	50 (65)	NA
hKd	979	ENDEAVOR	464	177 (38)	113 (24)	231 (50)	97 (21)
		CANDOR[30–32]	154	74 (48)	55 (36)	67 (44)	26 (17)
		ARROW[33]	238	194 (82)	170 (71)	NA	47 (20)
		IKEMA[34,35]	123	59 (48)	42 (34)	55 (45)	31 (25)
PanoVd	387	PANORAMA-1	387	NA	NA	178 (46)	NA
PVd	281	OPTIMISMM	281	281 (100)	200 (71)	111 (40)	61 (22)
SVd	195	BOSTON	195	77 (39)	53 (27)	99 (51)	70 (36)
DKd	312	CANDOR	312	123 (39)	99 (32)	133 (43)	48 (15)
IsaKd	179	IKEMA	179	72 (40)	57 (32)	80 (45)	42 (23)
Kd	340	ARROW	240	207 (86)	186 (78)	NA	34 (14)
		GEM-KyCyDex[36]	100	NA	46 (46)	NA	28 (28)
CyKd	94	GEM-KyCyDex	97	NA	43 (44)	NA	24 (25)

Adapted from Richter J, et al. *Am J Hematol*. 2025[9].
*Percentage of total number of patients per regimen in each trial.

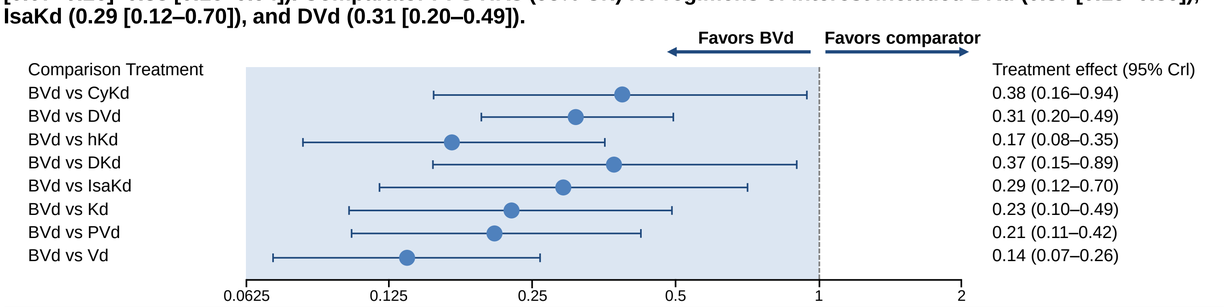
Figure 2. For the lenalidomide-exposed subpopulation, NMA results of PFS for BVd versus RCT treatment regimens showed PFS of BVd was the longest compared with all therapies included in the fixed-effect NMA (HR [95% CrI] range: 0.12 [0.07–0.20]–0.34 [0.17–0.71]). Comparator PFS HRs (95% CrI) for regimens of interest included DKd (0.34 [0.17–0.71]), IsaKd (0.29 [0.13–0.64]), and DVd (0.29 [0.19–0.43]).



Analysis	Total residual deviance	DIC	pD	Data points
Fixed effect	8.00	15.99	8.00	8

Richter J, et al. *Am J Hematol*. 2025.[9]

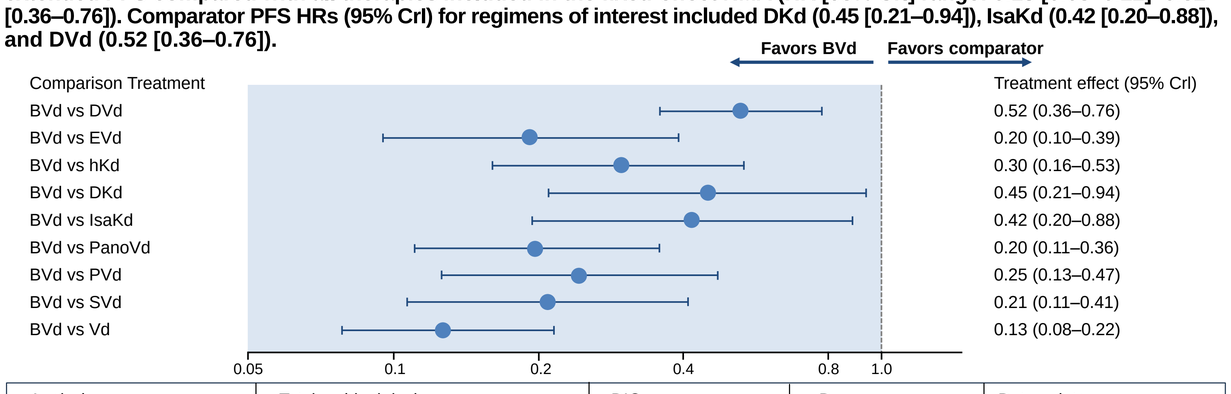
Figure 3. For the lenalidomide-refractory subpopulation, NMA results of PFS for BVd versus RCT treatment regimens showed BVd improved PFS compared with all therapies included in the fixed-effect NMA (HR [95% CrI] range: 0.14 [0.07–0.26]–0.38 [0.16–0.94]). Comparator PFS HRs (95% CrI) for regimens of interest included DKd (0.37 [0.15–0.89]), IsaKd (0.29 [0.12–0.70]), and DVd (0.31 [0.20–0.49]).



Analysis	Total residual deviance	DIC	pD	Data points
Fixed effect	8.01	16.02	8.01	8

Richter J, et al. *Am J Hematol*. 2025.[9]

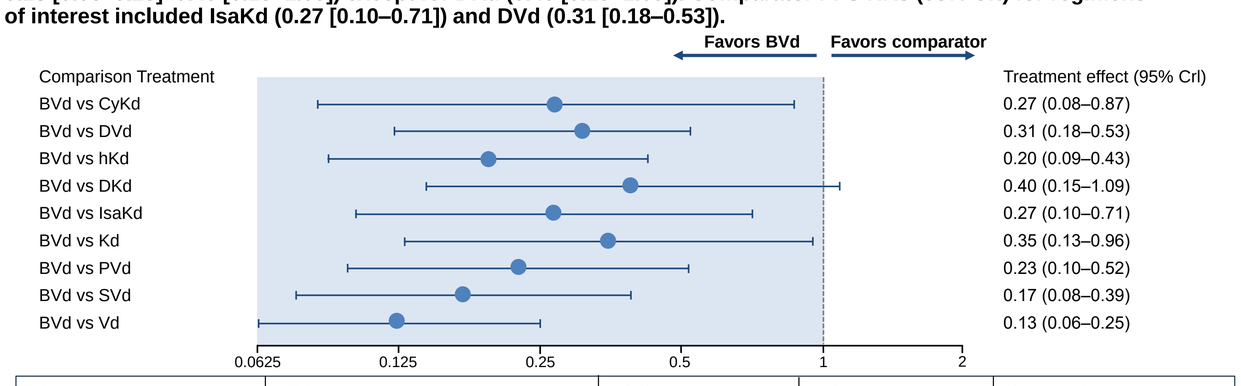
Figure 4. For the 1 prior LOT subpopulation, NMA results of PFS for BVd versus RCT treatment regimens showed BVd extended PFS compared with all therapies included in the fixed-effect NMA (HR [95% CrI] range: 0.13 [0.08–0.22]–0.52 [0.36–0.76]). Comparator PFS HRs (95% CrI) for regimens of interest included DKd (0.45 [0.21–0.94]), IsaKd (0.42 [0.20–0.88]), and DVd (0.52 [0.36–0.76]).



Analysis	Total residual deviance	DIC	pD	Data points
Fixed effect	11.44	20.45	9.01	10

Richter J, et al. *Am J Hematol*. 2025.[9]

Figure 5. For the high-risk cytogenetic subpopulation, NMA results of PFS for BVd versus RCT treatment regimens showed BVd improved PFS compared with all therapies included in the fixed-effect NMA (HR [95% CrI] range: 0.13 [0.06–0.25]–0.40 [0.15–1.09]) except for DKd (0.40 [0.15–1.09]). Comparator PFS HRs (95% CrI) for regimens of interest included IsaKd (0.27 [0.10–0.71]) and DVd (0.31 [0.18–0.53]).



Analysis	Total residual deviance	DIC	pD	Data points
Fixed effect	9.03	18.06	9.03	10

Richter J, et al. *Am J Hematol*. 2025.[9]

CONCLUSIONS

- In addition to the DREAMM-7 study findings, this NMA reinforces the important clinical benefits of BVd patients with RRMM, including those subgroups for whom there are limited effective treatment options.
- In the absence of direct comparison in head-to-head RCTs, this NMA found that BVd offered the highest PFS versus other PI-based regimens for patients with RRMM who are lenalidomide-exposed/refractory, had received only one prior LOT, or with high-risk cytogenetic profiles; the majority of comparisons suggested a high probability that the treatment effect consistently favored BVd.

ABBREVIATIONS

2L+, second line of therapy or later; BCMA, B-cell maturation antigen; BVd, belantamab mafodotin, bortezomib, and dexamethasone; CI, confidence interval; CrI, credible interval; CyKd, cyclophosphamide, carfilzomib, and dexamethasone; DIC, deviance information criterion; DKd, daratumumab, carfilzomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; EVd, elotuzumab, bortezomib, and dexamethasone; hKd, high-dose carfilzomib and dexamethasone; HR, hazard ratio; IsaKd, isatuximab, carfilzomib, and dexamethasone; ITT, intent to treat; IV, intravenous; Kd, carfilzomib and dexamethasone; LOT, line of therapy; MM, multiple myeloma; NMA, network meta-analysis; OR, odds ratio; OS, overall survival; PanoVd, panobinostat, bortezomib, and dexamethasone; pD, effective number of parameters as a measure of model complexity; PFS, progression-free survival; PI, proteasome inhibitor; PVd, pomalidomide, bortezomib and dexamethasone; RCT, randomized controlled trial; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; SLR, systematic literature review; SVd, Selinexor, bortezomib and dexamethasone; US FDA, United States Food and Drug Administration; Vd, bortezomib and dexamethasone.

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DISCLOSURES

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REFERENCES

1. Bhatt P, et al. *Curr Oncol*. 2023;30:2322–47.
2. Dhakal B, et al. *Blood Adv*. 2024;8(19):5062–71.
3. Facon T, et al. *Lancet Oncol*. 2021;22(11):1582–96.
4. de Arriba de la Fuente F, et al. *Cancers (Basel)*. 2022;15(1):155.
5. Tai YT, et al. *Blood*. 2014;123(20):3128–383.
6. Montes de Oca R, et al. *Mol Cancer Ther*. 2021;20(10):1941–55.
7. Hungria V, et al. *N Engl J Med*. 2024;391(5):393–407.
8. GSK press release 9 December 2024. https://www.gsk.com/media/11702/blenrep-dreamm-7-os-full-data-press-release_final.pdf (accessed: 25 Mar 2025)
9. Richter J, et al. *Am J Hematol*. 2025. Ahead of publication. https://doi.org/10.1002/ajh.27661.
10. Rodríguez-Otero P, et al. *Blood*. 2024;144(Suppl 1):7054.
11. Fu W, et al. *Clin Lymphoma Myeloma Leuk*. 2023;23(1):e51–e58.
12. Lu J, et al. *Clin Lymphoma Myeloma Leuk*. 2021;21(9):e699–e709.
13. Mateos M-V, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(8):509–18.
14. Sonneveld P, et al. *J Clin Oncol*. 2023;41(8):1600–9.
15. Weisel KC, et al. *Blood*. 2019;134(Suppl 1):3192.
16. Palumbo A, et al. *N Engl J Med*. 2016;375(8):754–66.
17. Kropff M, et al. *Ann Hematol*. 2017;96(11):1857–66.
18. Richardson PG, et al. *Lancet Oncol*. 2019;20(6):781–94.
19. Beksac M, et al. *Clin Lymphoma Myeloma Leuk*. 2023;23:S27–S28.
20. Grosicki S, et al. *Lancet*. 2020;396(10262):1563–73
21. Mateos M, et al. *Blood*. 2020;136:50–52.
22. Leleu X, et al. *J Clin Oncol*. 2021;39(Suppl 15):8024.
23. San-Miguel JF, et al. *Lancet Oncol*. 2014;15(11):1195–1206.
24. San-Miguel JF, et al. *Lancet Haematol*. 2016;3(11):e506–e515.
25. Jakubowiak A, et al. *Blood*. 2016;127(23):2833–40.
26. Dimopoulos MA, et al. *Lancet Oncol*. 2016;17(1):27–38.
27. Orlowski RZ, et al. *Clin Lymphoma Myeloma Leuk*. 2019;19(8):522–530.e1.
28. Siegel DS, et al. *Clin Lymphoma Myeloma Leuk*. 2017;17(1):e142.
29. Moreau P, et al. *Leukemia*. 2017;31(1):115–22.
30. Usmani SZ, et al. *Blood Adv*. 2023;7(14):3739–48.
31. Usmani SZ, et al. *Lancet Oncol*. 2022;23(1):65–76.
32. Dimopoulos M, et al. *Lancet*. 2020;396(10245):186–97.
33. Moreau P, et al. *Lancet Oncol*. 2018;19(7):953–64.
34. Martin T, et al. *Blood Cancer J*. 2023;13(1):72.
35. Moreau P, et al. *Lancet*. 2021;397(10292):2361–71.
36. Puertas B, et al. *Haematologica*. 2023;108(10):2753–63.

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