Efficacy Outcomes by Minimal Residual Disease Negativity in Patients With Relapsed or Refractory Multiple Myeloma Treated With Belantamab Mafodotin Plus Bortezomib and Dexamethasone vs Daratumumab, Bortezomib, and Dexamethasone: Analysis From the DREAMM-7 Trial

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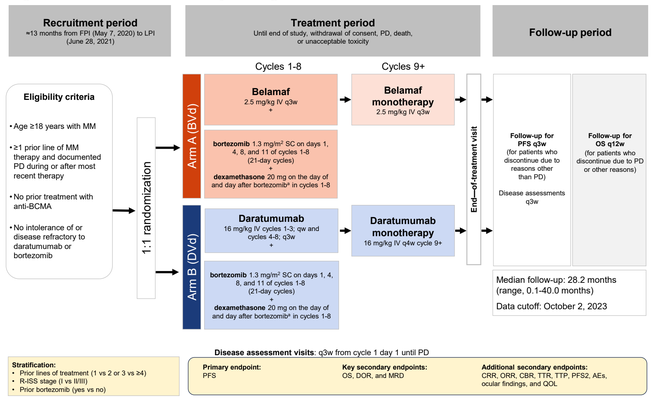
Background

- In DREAMM-7 (NCT04246047), BVd demonstrated a statistically significant and clinically meaningful PFS benefit vs the standard-of-care triplet DVd in patients with relapsed or refractory multiple myeloma who had received ≥1 prior line of treatment (**Figure 1**)[1]
- In the DREAMM-7 ITT, depth of response was greater in the BVd vs the DVd arm, including more than double the rate of MRD-negative status (**Figure 2 and Table 1**)[1]
  - In the prespecified subgroups with disease refractory to lenalidomide and ≥1 high-risk cytogenetic abnormality, responses were similar to those in the ITT population[2]
- MRD negativity has been shown to be a predictor of PFS and OS in multiple myeloma[3,4] and is becoming increasingly important to analyze since the April 2024 FDA ODAC decision to consider MRD as an endpoint for accelerated approval in multiple myeloma[5]
- Here, we sought to assess outcomes by MRD-negative status in the DREAMM-7 trial

Methods

- In DREAMM-7, patients with ≥1 prior line of treatment were randomized (1:1) to BVd or DVd (**Figure 1**)[1]
  - Enrolled patients were primarily male (55%), White (83%), and had an ECOG PS of ≤1 (96%)
- High cytogenetic risk was defined by the presence of ≥1 high-risk abnormality
  - These included t(4;14), t(14;16), and del(17p13)
- Patients achieving ≥ CR were tested for MRD-negative status by next-generation sequencing with 10^{-5} sensitivity; follow-up testing was performed every 6 months thereafter until progressive disease
  - An exploratory analysis of MRD status was also performed at the same sensitivity in patients who achieved a ≥ VGPR
- Post hoc subgroup analyses of PFS (IRC assessed) and OS were performed based on IRC-assessed response (≥ CR or ≥ VGPR) and MRD-negative status and evaluated using the Kaplan-Meier method; CIs were estimated using the Brookmeyer-Crowley method

Figure 1: **DREAMM-7 study design**



Hungria V, et al. N Engl J Med. 2024;391(5):393-407.
AE, adverse event; BVd, belantamab mafodotin, bortezomib, and dexamethasone; CBR, clinical benefit rate; CRR, complete response rate; DOR, duration of response; BCMA, B-cell maturation antigen; belamaf, belantamab mafodotin; DVd, daratumumab, bortezomib, and dexamethasone; FPI, first patient in; IV, intravenous; LPI, last patient in; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS2, time to progression on next line of therapy; PD, progressive disease; PFS, progression-free survival; q3w, every 3 weeks; q4w, every 4 weeks; q12w, every 12 weeks; QOL, quality of life; qw, once weekly; R-ISS, Revised International Staging System; SC, subcutaneous; TTP, time to progression; TTR, time to response.
[a] Reduce starting dose of dexamethasone to 10 mg for patients who are aged >75 years, have a body mass index of <18.5 kg/m², had previous unacceptable adverse events associated with glucocorticoid therapy, or are unable to tolerate the starting dose.

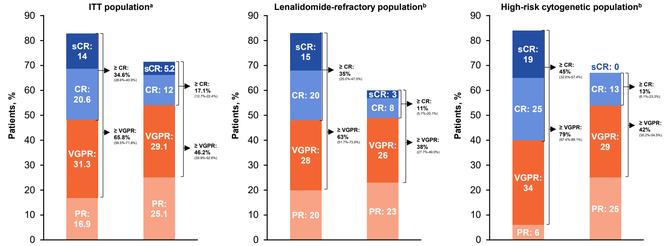
Results

- As previously reported, BVd was associated with a greater depth of response and higher rates of MRD negativity than DVd; benefit was maintained in patients with positive lenalidomide refractory status and those with high-risk cytogenetic features (**Figures 2 and Table 1**)[1,2]
- Patients with CR-based MRD negativity had durable PFS with few events reported regardless of treatment arm (**Figure 3**)
- In patients who did not achieve CR-based MRD negativity, median PFS was 15.3 months (95% CI, 12.7-18.0 months; BVd, 25.0 months; DVd, 11.8 months; **Figure 3**)
- Similar results were observed in patients based on VGPR-based MRD-negative status (**Figure 4**)
  - Durable PFS was observed in patients achieving VGPR-based MRD negativity (18-month PFS rates >90%)
  - In those who did not achieve VGPR-based MRD negativity, median PFS was 21.3 months in the BVd arm vs 10.5 months in the DVd arm
- Durable OS was observed in patients with CR-based MRD negativity regardless of treatment arm, with few events reported (**Figure 5**)
- In patients who did not achieve CR-based MRD negativity, 18-month OS rates were 79% and 70% in the BVd and DVd arms, respectively (**Figure 5**)
- Overall, OS results were similar when assessing MRD negativity based on ≥ VGPR (**Figure 6**)

Conclusions

- **In the DREAMM-7 trial, patients in the BVd arm achieved MRD negativity at more than double the rate observed in the DVd arm, regardless of lenalidomide-refractory status or the presence of ≥1 high-risk cytogenetic features**
- **MRD negativity was associated with durable PFS and OS benefits even in patients not achieving confirmed CR, which is consistent with the literature**
  - In patients that did not achieve MRD negativity, BVd was still associated with prolonged PFS and OS
- **These results highlight the importance of the greater response depth achieved with BVd in the DREAMM-7 trial**

Figure 2: **Response in the ITT population and prespecified subgroups[1]**



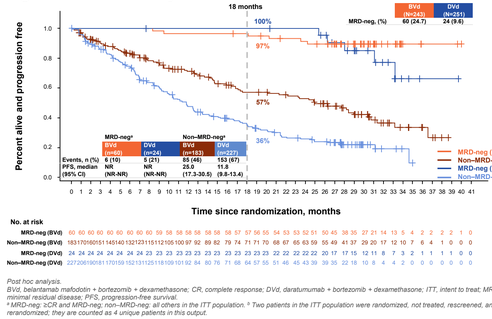
BVd, belantamab mafodotin + bortezomib + dexamethasone; CR, complete response; DVd, daratumumab + bortezomib + dexamethasone; ITT, intent to treat; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
[a] Two patients in the ITT population were randomized, not treated, rescreened, and rerandomized; they are counted as 4 unique patients in this output. [b] Post hoc analysis.

Table 1: **Response** and **MRD negativity in the ITT population and prespecified subgroups**

	ITT[1,a]		Lenalidomide refractory[2,d]		High-risk cytogenetics[2,d]	
	BVd (N=243)	DVd (N=251)	BVd (n=79)	DVd (n=87)	BVd (n=67)	DVd (n=69)
≥CR (sCR + CR), n (%)	84 (34.6)	43 (17.1)	28 (35)	10 (11)	30 (45)	9 (13)
≥VGPR (sCR + CR + VGPR), n (%)	160 (65.8)	116 (46.2)	50 (63)	33 (38)	53 (79)	29 (42)
MRD-negativity rate, n (%) [95% CI][b,c]						
Patients with sCR or CR	60 (24.7) [19.4-30.6]	24 (9.6) [6.2-13.9]	20 (25.3) [16.2-36.4]	5 (5.7) [1.9-12.9]	21 (31.3) [20.6-43.8]	5 (7.2) [2.4-16.1]
Patients with sCR, CR, or VGPR	94 (38.7) [32.5-45.1]	43 (17.1) [12.7-22.4]	33 (41.8) [30.8-53.4]	11 (12.6) [6.5-21.5]	32 (47.8) [35.4-60.3]	13 (18.8) [10.4-30.1]
MRD negativity (≥CR) sustained for ≥12 months, n (%) [95% CI][c]	24 (9.9) [6.4-14.3]	6 (2.4) [0.9-5.1]	7 (8.9) [3.6-17.4]	1 (1.1) [0-6.2]	11 (16.4) [8.5-27.5]	2 (2.9) [0.4-10.1]

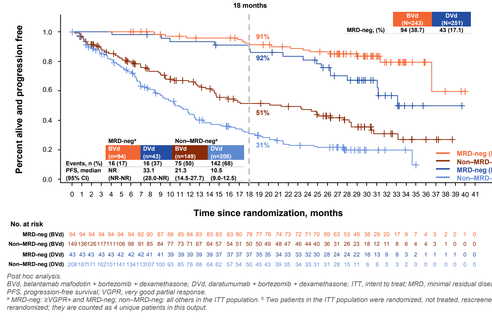
BVd, belantamab mafodotin + bortezomib + dexamethasone; CR, complete response; DVd, daratumumab + bortezomib + dexamethasone; ITT, intent to treat; MRD, minimal residual disease; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
[a] Two patients in the ITT population were randomized, not treated, rescreened, and rerandomized; they are counted as 4 unique patients in this output. [b] MRD-negativity rate was defined as the percentage of patients who were MRD negative by next-generation sequencing based on a sensitivity of 10^{-5}; all percentages are calculated out of N per treatment arm. [c] The CIs have not been adjusted for multiplicity and cannot be used in place of hypothesis testing. [d] Post hoc analysis.

Figure 3: **PFS rate by CR-based MRD status[a,b]**



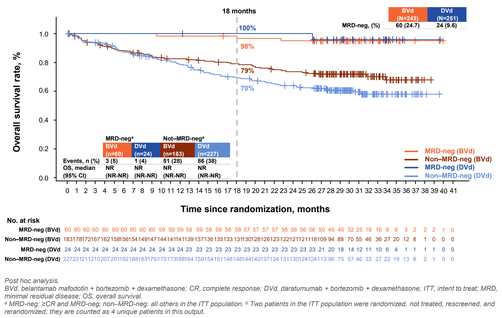
Post hoc analysis.
BVd, belantamab mafodotin + bortezomib + dexamethasone; CR, complete response; DVd, daratumumab + bortezomib + dexamethasone; ITT, intent to treat; MRD, minimal residual disease; PFS, progression-free survival.
[a] MRD-neg: ≥CR and MRD-neg; non–MRD-neg: all others in the ITT population. [b] Two patients in the ITT population were randomized, not treated, rescreened, and rerandomized; they are counted as 4 unique patients in this output.

Figure 4: **PFS rate by VGPR-based MRD status[a,b]**



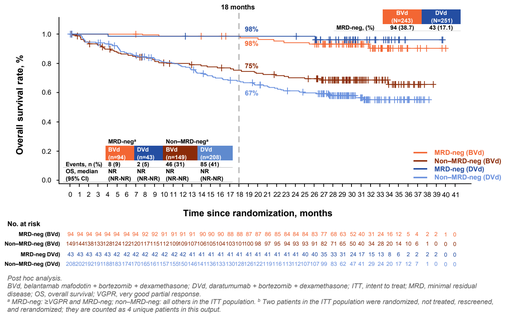
Post hoc analysis.
BVd, belantamab mafodotin + bortezomib + dexamethasone; DVd, daratumumab + bortezomib + dexamethasone; ITT, intent to treat; MRD, minimal residual disease; PFS, progression-free survival; VGPR, very good partial response.
[a] MRD-neg: ≥VGPR+ and MRD-neg; non–MRD-neg: all others in the ITT population. [b] Two patients in the ITT population were randomized, not treated, rescreened, and rerandomized; they are counted as 4 unique patients in this output.

Figure 5: **OS rate by CR-based MRD status[a,b]**



Post hoc analysis.
BVd, belantamab mafodotin + bortezomib + dexamethasone; CR, complete response; DVd, daratumumab + bortezomib + dexamethasone; ITT, intent to treat; MRD, minimal residual disease; OS, overall survival.
[a] MRD-neg: ≥CR and MRD-neg; non–MRD-neg: all others in the ITT population. [b] Two patients in the ITT population were randomized, not treated, rescreened, and rerandomized; they are counted as 4 unique patients in this output.

Figure 6: **OS rate by VGPR-based MRD status[a,b]**



Post hoc analysis.
BVd, belantamab mafodotin + bortezomib + dexamethasone; DVd, daratumumab + bortezomib + dexamethasone; ITT, intent to treat; MRD, minimal residual disease; OS, overall survival; VGPR, very good partial response.
[a] MRD-neg: ≥VGPR and MRD-neg; non–MRD-neg: all others in the ITT population. [b] Two patients in the ITT population were randomized, not treated, rescreened, and rerandomized; they are counted as 4 unique patients in this output.

Abbreviations

BVd, belantamab mafodotin + bortezomib + dexamethasone; CR, complete response; DVd, daratumumab + bortezomib + dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; FDA, US Food and Drug Administration; IRC, independent review committee; ITT, intent-to-treat population; MRD, minimal residual disease; ODAC, Oncologic Drugs Advisory Committee; OS, overall survival; PFS, progression-free survival; VGPR; very good partial response.

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Acknowledgments

We thank the patients and their families and caregivers, investigators, and investigational site staff of DREAMM-7 (NCT04246047)
DREAMM-7 was funded by GSK (Study #207503)
Drug-linker technology was licensed from Seagen Inc.; monoclonal antibody was produced using POTELLIGENT Technology, licensed from BioWa
Medical writing support was provided by Jocelyn Steinfeld, PhD (Nucleus Global, an Inizio company), and was funded by GSK

National Community of Oncology Dispensing Association Spring Forum | April 23-25, 2025 | Denver, CO, USA
Previously presented at 66th ASH Annual Meeting & Exposition | December 7-10, 2024 | San Diego, CA, USA

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