MM-1484

DREAMM-7 study of belantamab mafodotin plus bortezomib and dexamethasone (BVd) vs daratumumab plus bortezomib and dexamethasone (DVd) in relapsed/ refractory multiple myeloma (RRMM): a subgroup analysis in patients with high-risk cytogenetic features

BVd showed PFS and OS benefits as well as higher response rates vs DVd in patients with ≥1 high-risk cytogenetic abnormality

Digital poster

Poster recording

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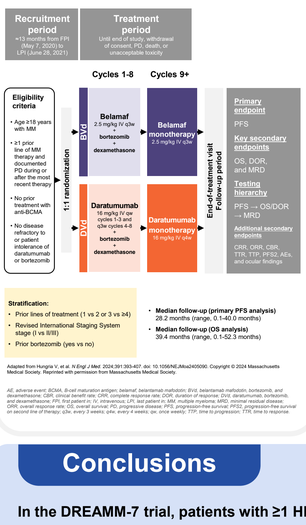
Background

- In the pivotal phase 3 DREAMM-7 (NCT04246047) trial, BVd demonstrated significant PFS (HR, 0.41; 95% CI, 0.31-0.53; *P*<.001) and OS benefit (HR, 0.58; 95% CI, 0.43-0.79; *P*=.00023) vs DVd in patients with RRMM who had ≥1 prior line of treatment[1,2]
- In a post hoc analysis in patients with ≥1 HRCA, including t(4;14), t(14;16), and del(17p13), more patients had deep responses (≥CR) with BVd (45%; 95% CI, 32.6%-57.4%) than with DVd (13%; 95% CI, 6.1%-23.3%)[3]
- Up to 70% of patients with RRMM have amp1q genetic abnormality at early relapse, which confers an increased risk of disease progression[4-6]
- In this updated post hoc analysis, we present efficacy outcomes in patients with ≥1 HRCA, now including amp1q in addition to the 3 HRCAs previously reported

Methods

- As previously reported, patients with ≥1 prior line of treatment were randomized (1:1) to BVd or DVd (**Figure 1**)[1]
- Efficacy assessments occurred every 3 weeks
- High cytogenetic risk was defined by the presence of ≥1 HRCA
  - These included t(4;14), t(14;16), t(14;20), del(17p13), and amp1q for this post hoc analysis
- Cytogenetic abnormalities were assessed by interphase fluorescence in situ hybridization with the following central laboratory thresholds: t(4;14) cutoff at 2%; t(14;16) cutoff at 2%; del(17p13) cutoff at 5%; amp1q cutoff at 4%. Local laboratory thresholds were based on local standards
- Descriptive statistics were used to summarize results, with 95% exact CI. Cox models were used to estimate HRs for PFS (data cutoff, October 2, 2023) and OS (data cutoff, October 7, 2024), with 95% Brookmeyer-Crowley CIs for the median estimated using the Kaplan-Meier method

Figure 1: **DREAMM-7 Study Design**



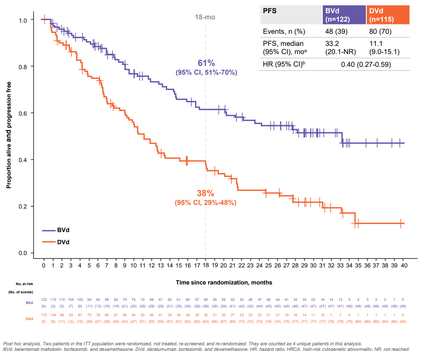
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AE, adverse event; BCMA, B-cell maturation antigen; belamaf, belantamab mafodotin; BVd, belantamab mafodotin, bortezomib, and dexamethasone; CBR, clinical benefit rate; CRR, complete response rate; DOR, duration of response; DVd, daratumumab, bortezomib, and dexamethasone; FPI, first patient in; IV, intravenous; LPI, last patient in; MM, multiple myeloma; MRD, minimal residual disease; ocular TTR, ocular time to first response; PD, progressive disease; PFS2, progression-free survival on second line of therapy; q2w, every 2 weeks; q4w, every 4 weeks; qw, once weekly; TTP, time to progression; TTR, time to response.

Results

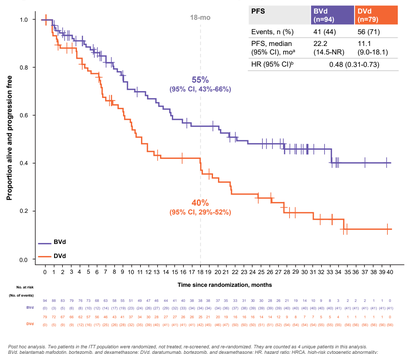
- The ITT population included 494 patients, of whom 243 were randomized to BVd and 251 to DVd
  - In the BVd arm, 122/243 (50%) patients had ≥1 HRCA, of whom 41 (17%) had t(4;14), 8 (3%) had t(14;16), 1 (0.4%) had t(14;20), 30 (12%) had del(17p13), and 94 (39%) had amp1q
  - In the DVd arm, 115/251 (46%) patients had ≥1 HRCA, of whom 42 (17%) had t(4;14), 6 (2%) had t(14;16), 1 (0.4%) had t(14;20), 35 (14%) had del(17p13), and 79 (31%) had amp1q
- As in the ITT population (data cutoff, October 2, 2023), PFS benefit favored BVd (median PFS, 33.2 months; 95% CI, 20.1 months-NR) vs DVd (median PFS, 11.1 months; 95% CI, 9.0-15.1 months) in patients with RRMM with ≥1 HRCA (HR, 0.40; 95% CI, 0.27-0.59; **Figure 2**)
  - The 18-month PFS rates were 61% and 38%, respectively
- PFS benefit favored BVd across subgroups with an HR of 0.36 (95% CI, 0.19-0.67) in patients with a t(4;14) HRCA, 0.25 (95% CI, 0.11-0.61) in those with del(17p13), and 0.48 (95% CI, 0.31-0.73) in those with amp1q (**Figures 3** and **4**). Patients with a t(14;16) or t(14;20) HRCA were not analyzed due to a low number of patients
- Among patients with ≥1 HRCA, the overall response rate was 81% (95% CI, 73.1%-87.7%) in patients treated with BVd (n/N=99/122) and 69% (95% CI, 59.4%-77.0%) in patients treated with DVd (n/N=79/115; **Figure 5**)
- More patients achieved ≥CR with BVd than with DVd, and this benefit was maintained across HRCA subgroups (**Table 1**)
- OS benefit (data cutoff, October 7, 2024) favored BVd (median OS, NR; 95% CI, NR-NR) vs DVd (median OS, 42.9 months; 95% CI, 30.4 months-NR) in patients with RRMM with ≥1 HRCA (HR, 0.59; 95% CI, 0.39-0.91; **Figure 6**)
  - The 18-month OS rates were 80% and 66%, respectively
- OS benefit favored BVd across subgroups with an HR of 0.54 (95% CI, 0.26-1.12) in patients with a t(4;14) HRCA, 0.31 (95% CI, 0.12-0.83) in those with del(17p13), and 0.58 (95% CI, 0.36-0.94) in those with amp1q (**Figures 7** and **8**). Patients with a t(14;16) or t(14;20) HRCA were not analyzed due to a low number of patients

Figure 2: **PFS in Patients With ≥1 HRCA**



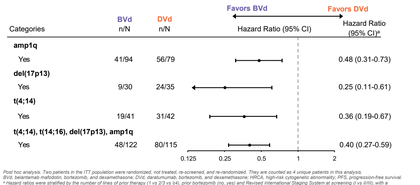
Post hoc analysis. Two patients in the ITT population were randomized, not treated, re-screened, and re-randomized. They are counted as 4 unique patients in this analysis.
PFS, progression-free survival; belamaf, belantamab mafodotin; bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; HRCA, high-risk cytogenetic abnormality; NR, not reached; PFS, progression-free survival.
[a] Confidence intervals were estimated using the Brookmeyer-Crowley method. [b] Hazard ratios were estimated using a Cox proportional hazards model stratified by the number of lines of prior therapy (1 vs 2/3 vs ≥4), prior bortezomib (no, yes), and Revised International Staging System at screening (I vs II/III), with a covariate of treatment.

Figure 3: **PFS in Patients With amp1q**



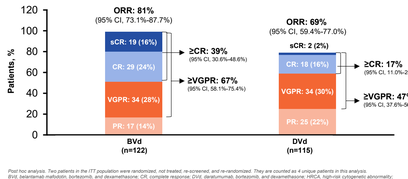
Post hoc analysis. Two patients in the ITT population were randomized, not treated, re-screened, and re-randomized. They are counted as 4 unique patients in this analysis.
BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; HRCA, high-risk cytogenetic abnormality; NR, not reached; PFS, progression-free survival.
[a] Confidence intervals were estimated using the Brookmeyer-Crowley method. [b] Hazard ratios were estimated using a Cox proportional hazards model stratified by the number of lines of prior therapy (1 vs 2/3 vs ≥4), prior bortezomib (no, yes) and Revised International Staging System at screening (I vs II/III), with a covariate of treatment.

Figure 4: **PFS Across HRCA Subgroups**



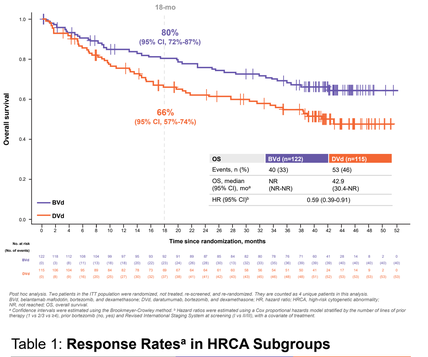
Post hoc analysis. Two patients in the ITT population were randomized, not treated, re-screened, and re-randomized. They are counted as 4 unique patients in this analysis.
BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; HRCA, high-risk cytogenetic abnormality; PFS, progression-free survival.
[a] Hazard ratios were stratified by the number of lines of prior therapy (1 vs 2/3 vs ≥4), prior bortezomib (no, yes), and Revised International Staging System at screening (I vs II/III), with a covariate of treatment.

Figure 5: **ORR in Patients With ≥1 HRCA[a]**



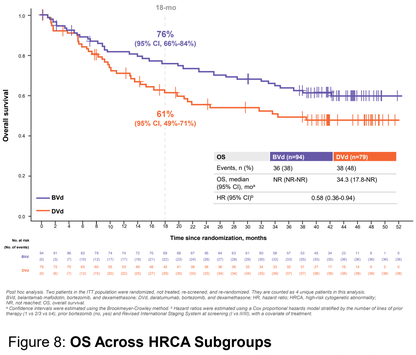
Post hoc analysis. Two patients in the ITT population were randomized, not treated, re-screened, and re-randomized. They are counted as 4 unique patients in this analysis.
BVd, belantamab mafodotin, bortezomib, and dexamethasone; CR, complete response; DVd, daratumumab, bortezomib, and dexamethasone; HRCA, high-risk cytogenetic abnormality; ORR, overall response rate; sCR, stringent complete response; VGPR, very good partial response.
[a] Confidence intervals were based on the exact method.

Figure 6: **OS in Patients With ≥1 HRCA**



Post hoc analysis. Two patients in the ITT population were randomized, not treated, re-screened, and re-randomized. They are counted as 4 unique patients in this analysis.
BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; HRCA, high-risk cytogenetic abnormality; NR, not reached; OS, overall survival.
[a] Confidence intervals were estimated using the Brookmeyer-Crowley method. [b] Hazard ratios were estimated using a Cox proportional hazards model stratified by the number of lines of prior therapy (1 vs 2/3 vs ≥4), prior bortezomib (no, yes) and Revised International Staging System at screening (I vs II/III), with a covariate of treatment.

Figure 7: **OS in Patients With amp1q**



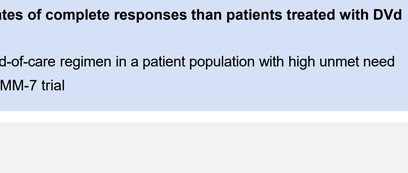
Post hoc analysis. Two patients in the ITT population were randomized, not treated, re-screened, and re-randomized. They are counted as 4 unique patients in this analysis.
BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; HRCA, high-risk cytogenetic abnormality; NR, not reached; OS, overall survival.
[a] Confidence intervals were estimated using the Brookmeyer-Crowley method. [b] Hazard ratios were estimated using a Cox proportional hazards model stratified by the number of lines of prior therapy (1 vs 2/3 vs ≥4), prior bortezomib (no, yes) and Revised International Staging System at screening (I vs II/III), with a covariate of treatment.

Table 1: **Response Rates[a] in HRCA Subgroups**

Response rates in HRCA groups n/N (%) [95% CI]	BVd	DVd
t(4;14)		
≥CR	20/41 (49) [32.9-64.9]	6/42 (14) [5.4-28.5]
≥VGPR	33/41 (80) [65.1-91.2]	21/42 (50) [34.2-65.8]
t(14;16)		
≥CR	1/8 (13) [0.3-52.7]	0/6 (0) [0-45.9]
≥VGPR	7/8 (88) [47.3-99.7]	3/6 (50) [11.8-88.2]
del(17p13)		
≥CR	11/30 (37) [19.9-56.1]	4/35 (11) [3.2-26.7]
≥VGPR	24/30 (80) [61.4-92.3]	13/35 (37) [21.5-55.1]
Amp1q[b]		
≥CR	31/94 (33) [23.6-43.4]	16/79 (20) [12.0-30.8]
≥VGPR	60/94 (64) [53.3-73.5]	41/79 (52) [40.4-63.3]

Post hoc analysis.
BVd, belantamab mafodotin, bortezomib, and dexamethasone; CR, complete response; DVd, daratumumab, bortezomib, and dexamethasone; HRCA, high-risk cytogenetic abnormality; VGPR, very good partial response.
[a] Confidence intervals were based on exact method. [b] Defined as ≥4 copies of chromosome amp1q.

Figure 8: **OS Across HRCA Subgroups**



Post hoc analysis. Two patients in the ITT population were randomized, not treated, re-screened, and re-randomized. They are counted as 4 unique patients in this analysis.
BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HRCA, high-risk cytogenetic abnormality; OS, overall survival.
[a] Hazard ratios were stratified by the number of lines of prior therapy (1 vs 2/3 vs ≥4), prior bortezomib (no, yes) and Revised International Staging System at screening (I vs II/III), with a covariate of treatment.

Conclusions

In the DREAMM-7 trial, patients with ≥1 HRCA treated with BVd had a PFS and OS benefit and achieved higher rates of complete responses than patients treated with DVd

- PFS and OS benefit and higher response rates with BVd vs DVd were maintained across HRCA subgroups
- Current outcomes in patients with RRMM and HRCA are suboptimal, and these results support BVd as a potential standard-of-care regimen in a patient population with high unmet need
- These results highlight the importance of the greater proportion of complete responses achieved with BVd in the DREAMM-7 trial

Abbreviations

BVd, belantamab mafodotin, bortezomib, and dexamethasone; CR, complete response; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; HRCA, high-risk cytogenetic abnormality; ITT, intention to treat; NR, not reached; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma.

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Disclosures

MVM reports a consulting or advisory role (may include participation on a data safety monitoring board or advisory board) for Amgen, BMS, GSK, Janssen, Sanofi, and Pfizer and honoraria from BMS, GSK, Janssen, Sanofi, AbbVie, Pfizer, Kite, and Stemline. **CW** reports honoraria from Alexion, AstraZeneca, Bayer, CSL, Drivetime Radio, and GSK and the leadership role of Education Chair for the International Society on Thrombosis and Haemostasis Annual Congress Planning Committee, 2024. **PJH** reports a consulting or advisory role (may include participation on a data safety monitoring board or advisory board) for the Australasian Leukaemia & Lymphoma Group trials, Antengene, Gilead, iTeos Therapeutics, Janssen, and Pfizer and research funding from Novartis. **RH** reports honoraria from Amgen, BMS, Celgene, Janssen, PharmaMar, and Takeda; a consulting or advisory role (may include participation on a data safety monitoring board or advisory board) for AbbVie, Amgen, BMS, Celgene, GSK, Janssen, Novartis, Oncopeptides, PharmaMar, Sanofi, and Takeda; research funding from Amgen, Celgene, Janssen, and Takeda; and grants or contracts from Amgen, BMS, Celgene, Janssen, Novartis, and Takeda. **KK** reports a consulting or advisory role (may include participation on a data safety monitoring board or advisory board) for BMS, GSK, Janssen, and AbbVie and research funding from BMS, Janssen, and Sanofi. **MAD** reports honoraria from Amgen, AstraZeneca, BeiGene, BMS, GSK, Janssen, Menarini, Regeneron, Sanofi, Swixx, and Takeda and a consulting or advisory role (may include participation on a data safety monitoring board or advisory board) for Amgen, AstraZeneca, BeiGene, BMS, GSK, Janssen, Menarini, Regeneron, Sanofi, Swixx, and Takeda. **CC** reports honoraria from AbbVie, Amgen, Astellas, BeiGene, BMS, Glycomimetics, GSK, Immunogen, Janssen, Jazz, Karyopharm, Menarini-Stemline, Oncopeptides, Pfizer, Sanofi, Servier, Stemline, and Takeda and stock or stock options in GSK. **NP**, **AM**, **HB**, **LE**, **SR-G**, and **JO** report employment and stock or stock options in GSK. **CPL** reports employment with GSK. **VH** reports honoraria from AbbVie, Amgen, BMS, GSK, Janssen, Pfizer, Sanofi, and Takeda and a consulting or advisory role (may include participation on a data safety monitoring board or advisory board) for BMS, GSK, Janssen, Kite, Regeneron, and Sanofi. **PR**, **MH**, **CF**, and **VZ** have nothing to disclose.

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