DREAMM-7 update: subgroup analyses from a phase 3 trial of belantamab mafodotin + bortezomib and dexamethasone vs daratumumab, bortezomib, and dexamethasone in relapsed/refractory multiple myeloma

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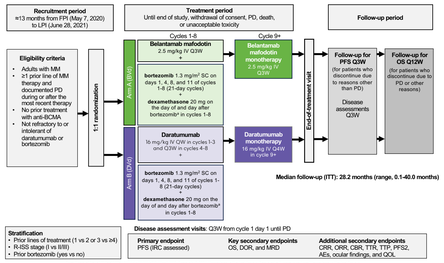
Background

- The results from the DREAMM-7 trial (NCT04246047) showed that belantamab mafodotin (belamaf) in combination with bortezomib and dexamethasone (BVd) led to a significant improvement in progression-free survival (PFS) and a strong trend toward improved overall survival (OS) vs daratumumab in combination with bortezomib and dexamethasone (DVd), an established standard of care (SOC), in patients (pts) with ≥1 prior line of therapy (LOT)[1]
  - BVd demonstrated a statistically significant and clinically meaningful PFS benefit, with a median PFS that was 23 months longer than that with DVd (median, 36.6 vs 13.4 mo; HR, 0.41; 95% CI, 0.31-0.53; *P*<.00001)[1]
- The safety profile of BVd was consistent with those of the individual components of the regimen. Notably, ocular adverse events, a known risk with belamaf treatment, were generally manageable and resolved through dose modification[1]
- The presence of certain features, including disease refractory to prior lenalidomide and the presence of ≥1 high-risk cytogenetic abnormality, is associated with worse prognosis and response to treatment in pts with relapsed/refractory multiple myeloma (RRMM); this underscores the high medical need in these pts[2-4]

The aim of this study was to further analyze the DREAMM-7 study data to better understand efficacy in key pt subgroups: pts refractory to lenalidomide and pts with high-risk cytogenetic features

Study design

Figure 1: DREAMM-7: study design



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[a] Starting dose of dexamethasone may be reduced to 10 mg for pts aged >75 years who have a body mass index of <18.5, previous unacceptable side effects associated with glucocorticoid therapy, or inability to tolerate the starting dose.

- In DREAMM-7, eligible pts were randomized 1:1 to receive BVd (n=243) or DVd (n=251). See **Figure 1** for study details
- Efficacy and safety were evaluated in prespecified pt subgroups based on lenalidomide refractory status and presence of high-risk cytogenetic features
  - Pts with high-risk cytogenetics had ≥1 of t(4;14), t(14;16), or del(17p13). Pts with standard risk were negative for all of these
  - Cytogenetic abnormalities were assessed by interphase fluorescent in situ hybridization with central laboratory thresholds of t(4;14) cut off at 2%, t(14;16) cut off at 2%, and del(17p13) cut off at 5%

Results

Figure 2: DREAMM-7: patients refractory to lenalidomide

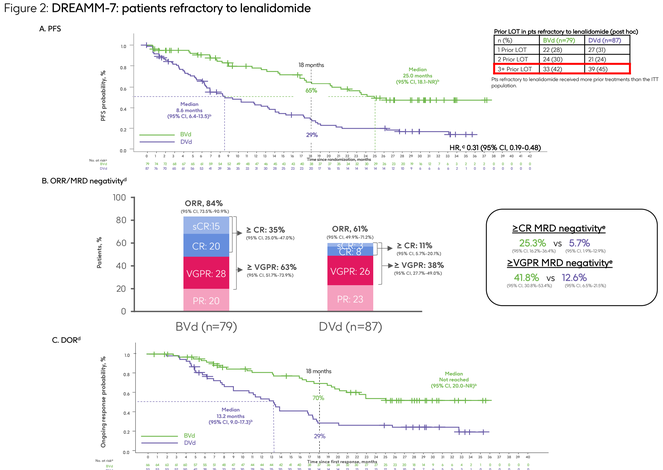
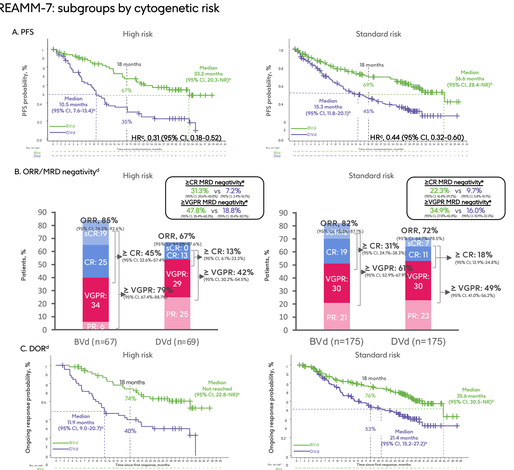


Figure 3: DREAMM-7: subgroups by cytogenetic risk



[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] CIs were estimated using the Brookmeyer-Crowley method. 95% CIs were not adjusted for multiplicity and cannot be used for hypothesis testing. [c] HRs were estimated using a Cox proportional hazards model stratified by the number of lines of prior therapy (1 vs 2 or 3 vs ≥4), prior bortezomib, and R-ISS stage at screening (I vs II/III), with a covariate of treatment. [d] Post hoc analyses. [e] MRD negativity rate was defined as percentage of patients who were MRD negative by NGS based on sensitivity of 10-5.

Table 1: DREAMM-7: post hoc analysis of grade ≥3 AEs of special interest in lenalidomide-refractory patients
Occurring in ≥5% of patients

Preferred term, n (%)	BVd (n=242)		DVd (n=246)	
	Lenalidomide refractory (n=79)	Total (n=242)	Lenalidomide refractory (n=87)	Total (n=246)
Any	65 (82)	198 (82)	55 (63)	120 (49)
Thrombocytopenia	41 (52)	134 (55)	40 (46)	87 (35)
Platelet count decreased	19 (24)	44 (18)	13 (15)	26 (11)
Vision blurred	18 (23)	53 (22)	1 (1)	2 (1)
Visual impairment	6 (8)	13 (5)	0	1 (<1)
Dry eye	4 (5)	17 (7)	0	0
Eye irritation	4 (5)	12 (5)	0	0

according to NCI-CTCAE version 5.0

Table 2: DREAMM-7: post hoc analysis of grade ≥3 AEs of special interest by cytogenetic risk status
Occurring in ≥5% of patients in any subgroup

Preferred term, n (%)	BVd (N=242)			DVd (N=246)		
	Cytogenetic risk[a]		Total	Cytogenetic risk[a]		Total
	High (n=66)	Standard (n=175)	N=242	High (n=68)	Standard (n=171)	N=246
Any	53 (80)	144 (82)	198 (82)	35 (51)	82 (48)	120 (49)
Thrombocytopenia	34 (52)	99 (57)	134 (55)	26 (38)	58 (34)	87 (35)
Platelet count decreased	14 (21)	30 (17)	44 (18)	9 (13)	17 (10)	26 (11)
Vision blurred	16 (24)	37 (21)	53 (22)	1 (1)	1 (<1)	2 (1)
Visual impairment	2 (3)	11 (6)	13 (5)	0	1 (<1)	1 (<1)
Dry eye	3 (5)	14 (8)	17 (7)	0	0	0
Eye irritation	1 (2)	11 (6)	12 (5)	0	0	0

[a] Cytogenetic risk in the BVd arm and 7 patients in the DVd arm missing or nonevaluable for cytogenetic risk.
according to NCI-CTCAE version 5.0

DREAMM-7: patients refractory to lenalidomide

- In both arms of the intent-to-treat (ITT) population, approximately one-third of pts (BVd=79, DVd=87) had disease refractory to prior lenalidomide
- BVd led to a clinically meaningful risk reduction in progression or death in lenalidomide-refractory pts (median PFS, 25.0 vs 8.6 mo; HR, 0.31; **Figure 2A**)
- In lenalidomide-refractory pts, BVd led to greater depth of response vs DVd, including a nearly 5-fold increase in MRD negativity in those with ≥ CR (**Figure 2B**)
- BVd led to a greater response duration vs DVd, with early and sustained separation of Kaplan-Meier curves in lenalidomide refractory pts (**Figure 2C**)
- The rates of grade ≥3 AEs of special interest in lenalidomide refractory pts in the BVd arm were consistent with those reported in the overall population (**Table 1**)

DREAMM-7: subgroups by cytogenetic risk

- In the BVd arm, 67 pts (28%) had high-risk cytogenetic abnormalities
  - t(4;14) n=41 (61%), t(14;16) n=8 (12%), and del(17p13) n=30 (45%)[a,b]
- In the DVd arm, 69 pts (27%) had high-risk cytogenetic abnormalities
  - t(4;14) n=42 (61%), t(14;16) n=6 (9%), and del(17p13) n=35 (51%)[a,b]
- BVd led to a strong PFS benefit (more than double to triple the median PFS) regardless of cytogenetic risk status vs DVd (**Figure 3A**)
  - In the BVd arm, median PFS was similar between pts with high-risk cytogenetics (33.2 months) and those with standard risk (36.6 months)
- Regardless of cytogenetic risk, BVd was associated with a higher ORR and substantially greater response depth and MRD negativity compared with DVd (**Figure 3B**)
- Pts treated with BVd had greater response durability than those receiving DVd regardless of cytogenetic risk status (**Figure 3C**)
- The rates of grade ≥3 AEs of special interest in the BVd arm were consistent with those reported in the overall population regardless of cytogenetic risk status (**Table 2**)

[a] Post hoc exploratory analyses. [b] Pts may have ≥1 cytogenetic abnormality.

Conclusions

In the ITT population, BVd led to a statistically significant and clinically meaningful improvement in PFS vs DVd (median PFS, 36.6 vs 13.4 mo; HR, 0.41; 95% CI, 0.31-0.53; *P*<.00001) and showed a strong and clinically meaningful OS benefit (HR, 0.57; *P*=.00049[a])[1]

Analysis of key subgroups associated with poor prognosis, including pts with disease refractory to lenalidomide and those with high-risk cytogenetic abnormalities, showed that:

- In pts with poor prognostic features, BVd was associated with pronounced benefit vs DVd, including:
  - Clinically meaningful risk reduction in PFS
  - Higher ORR, greater depth of response (≥ CR and ≥ VGPR), and MRD-negative status
  - Increased response durability
- The safety profile of BVd in these subgroups was consistent with that in the overall trial population and with the known safety profile of belamaf and the constituent therapies

These results demonstrate efficacy benefit and a consistent safety profile in key subgroups with a high unmet need and support BVd as a potential new standard of care in pts with RRMM at first relapse or later

[a] The *P* value has not yet reached criteria for statistical significance (*P*≤.00037) at this interim analysis. Follow-up for OS is ongoing

Abbreviations

AE, adverse event; BCMA, B-cell maturation antigen; BVd, belantamab mafodotin, bortezomib, and dexamethasone; CBR, clinical benefit rate; CR, complete response; CRR, complete response rate; DOR, duration of response; DVd, daratumumab, bortezomib, and dexamethasone; FPI, first patient in; HR, hazard ratio; IRC, independent review committee; ITT, intent to treat; IV, intravenous; LPI, last patient in; MM, multiple myeloma; MRD, minimal residual disease; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NGS, next-generation sequencing; NR, not reached; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; pt, patient; 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; sCR, stringent complete response; SOC, standard of care; TTP, time to progression; TTR, time to response; VGPR, very good partial response.

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Disclosures

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