MM-1485

DREAMM-8 study of belantamab mafodotin plus pomalidomide and dexamethasone (BPd) vs pomalidomide plus bortezomib and dexamethasone (PVd) in relapsed/refractory multiple myeloma: a subgroup analysis in patients with high-risk cytogenetic features

BPd showed PFS benefit and deep responses in patients with ≥1 HRCA

Digital poster

Poster recording

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Introduction

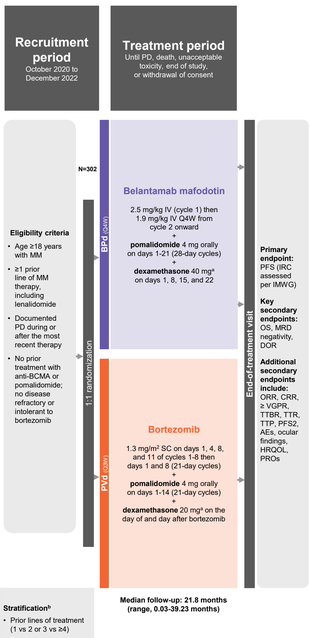
- In the pivotal phase 3 DREAMM-8 (NCT04484623) trial, BPd led to a statistically significant lower risk of disease progression or death compared with PVd (HR, 0.52; 95% CI, 0.37-0.73; *P*<.001) in patients with RRMM after ≥1 prior line of therapy, including lenalidomide (**Figure 1**)[1]
- PFS benefit was maintained in patients exposed to anti-CD38 therapies +/- lenalidomide as well as those with disease refractory to either anti-CD38 agents or lenalidomide[1]
- Patients with MM with high-risk cytogenetic abnormalities (HRCA), including t(4;14), t(14;16), del(17p13), and amp1q, have a poor prognosis and need more efficacious treatments[2,3]
- In this updated post hoc analysis, we present efficacy outcomes in patients with ≥1 HRCA, including t(4;14), t(14;16), del(17p13), and amp1q

Methods

- Patients were randomized 1:1 to receive BPd (28-day cycles) or PVd (21-day cycles). Patients were treated until disease progression, unacceptable toxicity, or death (**Figure 1**)
- Efficacy assessments occurred every 4 weeks
- Cytogenetic abnormalities were assessed by interphase FISH with the following central laboratory thresholds: t(4;14) cutoff at 2%; t(14;16) cutoff at 2%; del(17p13) cutoff at 5%; amp1q[a] cutoff at 7%. Local laboratory thresholds were based on local standards
- Descriptive statistics were used to summarize the results, along with 95% exact CIs. Cox models were used to estimate HRs for PFS, with 95% Brookmeyer-Crowley CIs for the median estimated using the Kaplan-Meier method

[a] *At the time of DREAMM-8 study design and subsequent data collection, amp1q was considered a secondary genetic event in the IMWG consensus guidelines.*[4] *In the 2024 IMWG update, the presence of amp1q is considered high risk.*[5]

Figure 1: **DREAMM-8 Study Design**[6]



AE, adverse event; BCMA, B-cell maturation antigen; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CRR, complete response rate; DOR, duration of response; HRQOL, health-related quality of life; IMWG, International Myeloma Working Group; IRC, independent review committee; ISS, International Staging System; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival on subsequent line of therapy; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; Q4W, every 4 weeks; QW, every 1 week; QW, every 3 weeks; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; sCR, stringent complete response; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.

[a] *Patients aged >75 years who had comorbidities or were intolerant of 40-mg dose in arm A or 20-mg dose in arm B could have dose level reduced to half per investigator discretion.* [b] *Some patients were stratified by ISS stage (I vs II/III); the protocol was amended on April 20, 2021, to replace this randomization factor with prior anti-CD38 therapy (yes vs no).*

Results

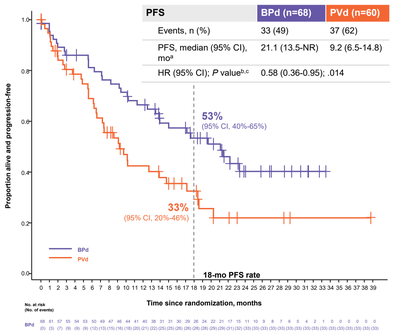
- The ITT population included 302 patients randomized to the BPd (N=155) arm or the PVd (N=147) arm
  - HRCAs were observed in 68 patients (44%) in the BPd arm and 60 patients (41%) in the PVd arm (**Table 1**)
- Similarly to previously published results in the ITT population, PFS benefit favored BPd (median PFS, 21.1 months; 95% CI, 13.5 months-NR) vs PVd (median PFS, 9.2 months; 95% CI, 6.5-14.8 months) in patients with ≥1 HRCA (HR, 0.58; 95% CI, 0.36-0.95) (**Figure 2**)
- PFS benefit was maintained across HRC subgroups (**Figure 3**). Results for t(14;16) HRCA were not presented due to a low number of patients in each arm (BPd, n=7; PVd, n=11)
- In patients with ≥1 HRCA, responses were more frequent and deeper with BPd vs PVd (**Figure 4**); benefit was maintained across HRC subgroups (**Table 2**)

Table 1: **Summary of HRCAs Observed in Each Treatment Arm**

Patients, n (%)	BPd (N=155)	PVd (N=147)
≥1 HRCA[a]	68 (44)	60 (41)
t(4;14)	23 (15)	20 (14)
t(14;16)	7 (5)	11 (7)
del(17p13)	32 (21)	26 (18)
amp1q[b]	40 (26)	33 (22)

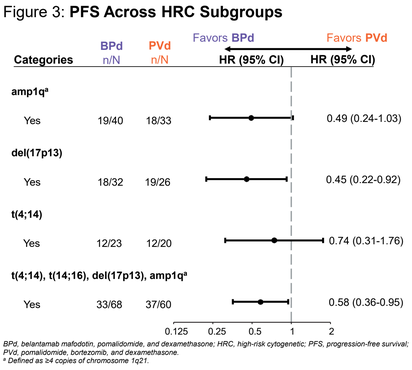
BPd, belantamab mafodotin, pomalidomide, and dexamethasone; HRCA, high-risk cytogenetic abnormality; PVd, pomalidomide, bortezomib, and dexamethasone.
[a] *Patients with HRCAs were defined as having ≥1 of the following: t(4;14), t(14;16), del(17p13), and amp1q.*
[b] *Defined as ≥4 copies of chromosome 1q21.*

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



BPd, belantamab mafodotin, pomalidomide, and dexamethasone; HRCA, high-risk cytogenetic abnormality; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone.
[a] *CIs estimated using Brookmeyer-Crowley method.* [b] *HR was estimated using the Cox proportional hazards model stratified by number of lines of prior therapy and prior bortezomib use with a covariate of treatment.* [c] *Nominal P value.*

Figure 3: **PFS Across HRC Subgroups**



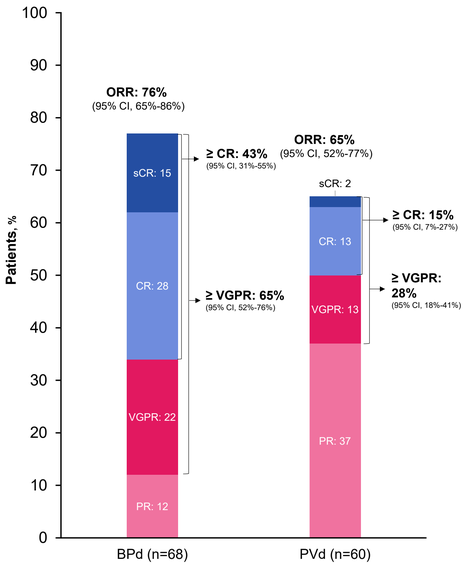
BPd, belantamab mafodotin, pomalidomide, and dexamethasone; HRC, high-risk cytogenetic; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone.
[a] *Defined as ≥4 copies of chromosome 1q21.*

Conclusions

In the DREAMM-8 trial, BPd demonstrated PFS benefit and was associated with higher rates of deep responses vs PVd in patients with ≥1 HRCA

- Efficacy benefit was maintained across HRC subgroups
- These data support the potential use of BPd as a standard-of-care regimen in this key patient population with a high unmet need

Figure 4: **ORR in Patients With ≥1 HRCA**[a,b]



BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CR, complete response; HRCA, high-risk cytogenetic abnormality; ORR, overall response rate; PR, partial response; PVd, pomalidomide, bortezomib, and dexamethasone; sCR, stringent complete response; VGPR, very good partial response.
[a] *Post hoc analysis.* [b] *CIs are based on the exact method.*

Table 2: **Response Rates in HRC Subgroups**

Response rates in HRC subgroups n/N (%)	BPd	PVd
t(4;14)		
≥ CR	9/23 (39)	5/20 (25)
95% CI, %[a]	19.7-61.5	8.7-49.1
≥ VGPR	12/23 (52)	8/20 (40)
95% CI, %[a]	30.6-73.2	19.1-63.9
t(14;16)		
≥ CR	3/7 (43)	2/11 (18)
95% CI, %[a]	9.9-81.6	2.3-51.8
≥ VGPR	3/7 (43)	5/11 (45)
95% CI, %[a]	9.9-81.6	16.7-76.6
del(17p13)		
≥ CR	11/32 (34)	0/26
95% CI, %[a]	18.6-53.2	0.0-13.2
≥ VGPR	20/32 (63)	4/26 (15)
95% CI, %[a]	43.7-78.9	4.4-34.9
amp1q[b]		
≥ CR	17/40 (43)	3/33 (9)
95% CI, %[a]	27.0-59.1	1.9-24.3
≥ VGPR	23/40 (58)	6/33 (18)
95% CI, %[a]	40.9-73.0	7.0-35.5

BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CR, complete response; HRC, high-risk cytogenetic; PVd, pomalidomide, bortezomib, and dexamethasone; VGPR, very good partial response.
[a] *CIs are based on the exact method.* [b] *Defined as ≥4 copies of chromosome 1q21.*

Abbreviations

AE, adverse event; BCMA, B-cell maturation antigen; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CD, cluster of differentiation; CR, complete response; CRR, complete response rate; DOR, duration of response; FISH, fluorescence in situ hybridization; HR, hazard ratio; HRC, high-risk cytogenetic; HRCA, high-risk cytogenetic abnormality; HRQOL, health-related quality of life; IMWG, International Myeloma Working Group; IRC, independent review committee; ISS, International Staging System; ITT, intention to treat; IV, intravenous; MM, multiple myeloma; MRD, minimal residual disease; NR, not reached; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival on subsequent line of therapy; PR, partial response; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; Q3W, every 3 weeks; Q4W, every 4 weeks; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; sCR, stringent complete response; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.

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