MM-1486

Minimal residual disease negativity in patients with relapsed or refractory multiple myeloma treated with belantamab mafodotin plus pomalidomide and dexamethasone vs pomalidomide, bortezomib, and dexamethasone: analysis from the DREAMM-8 trial

Digital poster

Poster recording

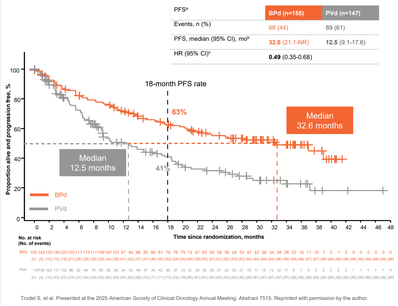
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Introduction

- Results from the primary analysis (data cutoff: January 29, 2024; median follow-up: 21.8 months [range, 0.03-39.23 months]) of the DREAMM-8 trial demonstrated statistically significant and clinically meaningful PFS benefit with BPd vs PVd (HR, 0.52; *P*<.001) in patients with RRMM after ≥1 prior line of therapy, including lenalidomide[1]
- In an updated analysis from the October 2024 data cutoff, with a median follow-up of 28.01 months (range, 0.03-47.74 months), median PFS with BPd vs PVd was 32.6 months vs 12.5 months (HR, 0.49; 95% CI, 0.35-0.68) (**Figure 1**)[2]
- In the primary analysis, BPd was associated with greater depth of response than PVd, with a 5 times higher rate of CR-based MRD negativity (23.9% vs 4.8%)[1]
- MRD negativity is predictive of PFS and OS in MM. As of 2024, MRD is considered an endpoint for accelerated approval in MM, based on an FDA ODAC decision[3]
- In this updated post hoc analysis, we present additional analyses of efficacy outcomes by MRD status in DREAMM-8

Figure 1: **Updated Interim PFS Results[2]**



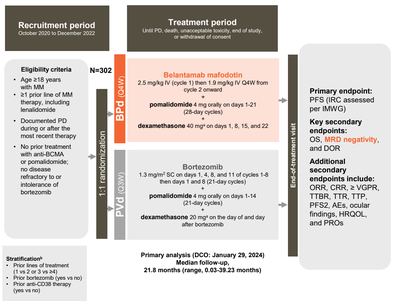
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BPd, belantamab mafodotin, pomalidomide, and dexamethasone; HR, hazard ratio; NR, not reached; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone; RRMM, relapsed/refractory multiple myeloma.
[a] Data cutoff: October 7, 2024. Median follow-up: 28.01 months (range, 0.03-47.74 months).[b] [c] The CIs were estimated using the Brookmeyer-Crowley method.
[c] The treatment effect (HR and corresponding 95% CIs) was estimated using the stratified Cox proportional hazards model.

Methods

- Patients were randomized 1:1 to receive BPd (28-day cycles) or PVd (21-day cycles). Patients were treated until progressive disease, unacceptable toxicity, or death (**Figure 2**)
- Efficacy assessments occurred every 4 weeks
- 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 2: **DREAMM-8 Study Design**

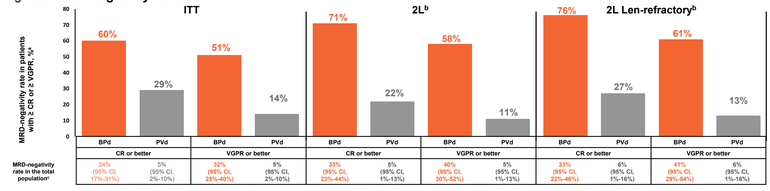


AE, adverse event; BCMA, B-cell maturation antigen; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CD, cluster of differentiation; CRR, complete response rate; DOR, duration of response; HRQOL, health-related quality of life; IMWG, International Myeloma Working Group; IRC, independent review committee; ISS, International Staging System; IV, intravenous; MM, multiple myeloma; MRD, minimal residual disease; ORR, objective 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; Q3W, every 3 weeks; Q4W, every 4 weeks; SC, subcutaneous; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.
** Patients aged >75 years, with comorbidities, or 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.*
** Some patients were stratified by ISS status (I vs II/III); the protocol was amended on 20 April 2021 to replace this randomization factor with prior anti-CD38 treatment (yes vs no).*

Results

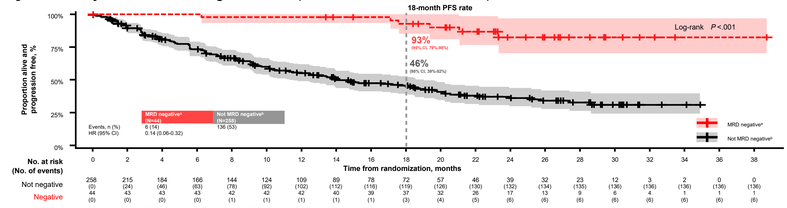
- Treatment with BPd was consistently associated with 5 to 7 times higher rates of ≥CR-based or ≥VGPR-based MRD negativity than PVd across patients in the ITT population and key subgroups (**Figure 3**)
  - In the ITT population, ≥CR-based MRD-negativity rates were 24% in the BPd arm and 5% in the PVd arm. ≥VGPR-based MRD-negativity rates were similar in the ITT population (32% vs 5%)
- When pooled across treatment arms, patients with CR-based MRD negativity (n=44) had a substantially lower risk of disease progression or death than patients who did not achieve MRD negativity (n=258) (HR, 0.14; 95% CI, 0.06-0.32) (**Figure 4**)
  - In patients who did not achieve CR-based MRD negativity, median PFS favored BPd vs PVd (19.6 vs 10.2 months; HR, 0.67; 95% CI, 0.47-0.94) (**Figure 5**)
- Patients with CR-based MRD negativity (n=44) had a substantially lower risk of death than patients who did not achieve MRD negativity (n=258) (HR, 0.18; 95% CI, 0.07-0.49) (**Figure 6**)
  - In the patients who achieved CR-based MRD-negative status, 18-month OS rates were 100% and 92% in PVd and BPd arms, respectively (**Figure 7**)
  - In patients who did not have MRD-negative status, 18-month OS rates were 72% and 67% in BPd and PVd arms, respectively (**Figure 7**)

Figure 3: **MRD-Negativity Rates**



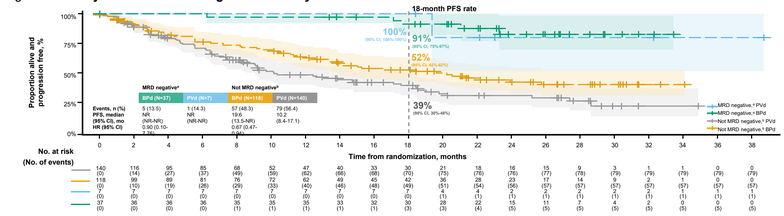
2L, second line (received 1 prior line); BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CR, complete response; ITT, intention to treat; len, lenalidomide; MRD, minimal residual disease; PVd, pomalidomide, bortezomib, and dexamethasone; sCR, stringent complete response; VGPR, very good partial response.
[a] Calculated as patients with a CR and MRD-negative status / patients with a CR or patients with a VGPR and MRD-negative status / patients with ≥ VGPR. [b] Post hoc analysis. [c] Calculated as patients with a CR or ≥ VGPR and MRD-negative status / total patients (ITT or subgroups).

Figure 4: **PFS by CR-Based MRD-Negative Status (Pooled Across Treatment Arms)**



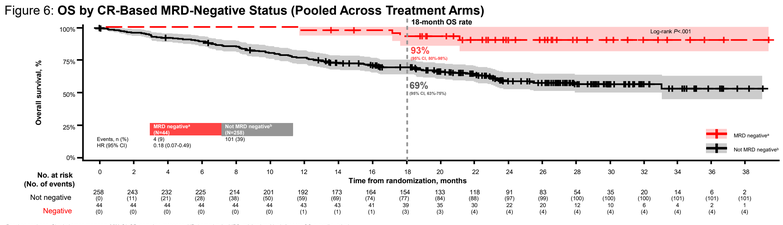
Post hoc analyses. Shaded areas represent 95% CI. CR, complete response; HR, hazard ratio; MRD, minimal residual disease; PFS, progression-free survival.
[a] Patients achieving a response of ≥ CR and MRD-negative status. [b] Not MRD negative" is defined as MRD positive, not assessable, or without assessment.

Figure 5: **PFS by CR-Based MRD-Negative Status by Treatment Arm**



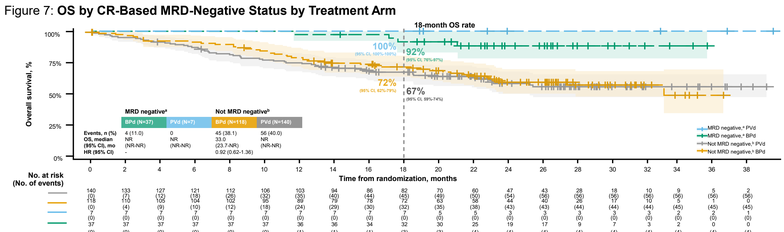
Post hoc analyses. Shaded areas represent 95% CI. BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CR, complete response; HR, hazard ratio; MRD, minimal residual disease; NR, not reached; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone.
[a] Patients achieving a response of ≥ CR and MRD-negative status. [b] Not MRD negative" is defined as MRD positive, not assessable, or without assessment.

Figure 6: **OS by CR-Based MRD-Negative Status (Pooled Across Treatment Arms)**



Post hoc analyses. Shaded areas represent 95% CI. CR, complete response; HR, hazard ratio; MRD, minimal residual disease; OS, overall survival.
[a] Patients achieving a response of ≥ CR and MRD-negative status. [b] Not MRD negative" is defined as MRD positive, not assessable, or without assessment.

Figure 7: **OS by CR-Based MRD-Negative Status by Treatment Arm**



Post hoc analyses. Shaded areas represent 95% CI. BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CR, complete response; HR, hazard ratio; MRD, minimal residual disease; NR, not reached; OS, overall survival; PVd, pomalidomide, bortezomib, and dexamethasone.
[a] Patients achieving a response of ≥ CR and MRD-negative status. [b] Not MRD negative" is defined as MRD positive, not assessable, or without assessment.

Conclusions

Although depth of response correlates with long-term outcomes, there seem to be additional durability benefits to long-term treatment with BPd that are not explained by MRD status

- Patients treated with BPd achieved a 5 to 7 times higher CR-based MRD-negativity rate vs those treated with PVd, with consistent benefit in key subgroups
- MRD negativity was associated with durable PFS and OS benefits
  - PFS HR (MRD negative vs not MRD negative): 0.14 (95% CI, 0.06-0.32)[a]
  - OS HR (MRD negative vs not MRD negative): 0.18 (95% CI, 0.07-0.49)[a]
- Clinically meaningful PFS benefit was observed with BPd vs PVd in patients who did not achieve CR-based MRD negativity

[a] Patients were pooled across treatment arms.

Abbreviations

BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CR, complete response; FDA, US Food and Drug Administration; HR, hazard ratio; MRD, minimal residual disease; ODAC, Oncologic Drugs Advisory Committee; OS, overall survival; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone; RRMM, relapsed/refractory multiple myeloma; VGPR, very good partial response.

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1. Dimopoulos MA, et al. N Engl J Med. 2024;391:408-421.
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Disclosures

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