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Efficacy and durability of response of belantamab mafodotin plus pomalidomide and dexamethasone treatment in patients with relapsed/refractory multiple myeloma: long-term follow-up of the phase 3 DREAMM-8 study

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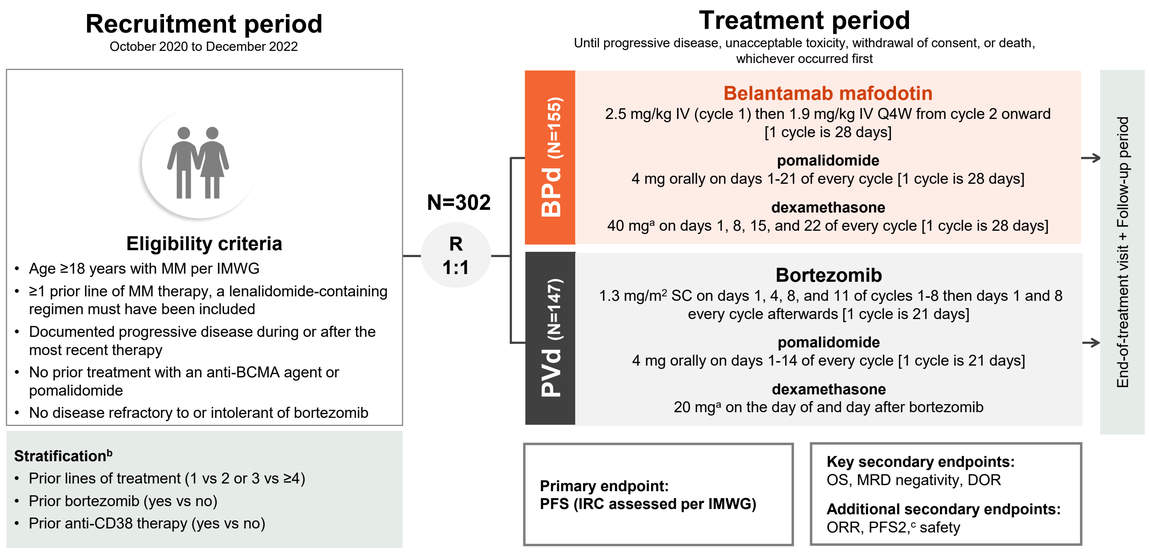
Background

- Targeting B-cell maturation antigen (BCMA) has transformed survival outcomes for patients with relapsed/refractory multiple myeloma (RRMM)[1,2]
- Belantamab mafodotin, an antibody-drug conjugate representing a unique BCMA-targeting modality, was recently approved in combination with pomalidomide and dexamethasone (BPd) as part of a triplet therapy for RRMM[3]
- At the primary analysis of DREAMM-8 (median follow-up, 21.8 months; data cutoff: January 29, 2024), BPd demonstrated significant improvement in progression-free survival (PFS) vs standard-of-care pomalidomide, bortezomib, and dexamethasone (PVd) in patients with RRMM who had ≥1 prior line of therapy (LOT) (hazard ratio [HR], 0.52; 95% CI 0.37-0.73; *P*<0.001)[4]
- To further characterize the durability of BPd treatment benefit in RRMM, we report longer follow-up of efficacy and safety outcomes from the DREAMM-8 trial (median follow-up, 35.8 months; data cutoff: July 7, 2025)

Methods

DREAMM-8 is a phase 3, open-label, randomized trial of BPd vs PVd in patients with RRMM treated with ≥1 prior line of therapy, including lenalidomide



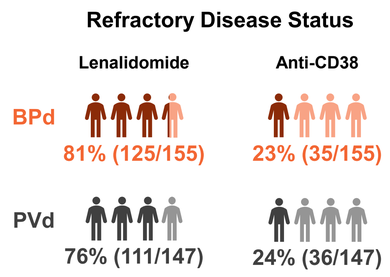
[a] Patients aged >75 years with comorbidities or intolerance of the 40-mg dose in arm A or 20-mg dose in arm B could have dose level reduced to half per investigator discretion. [b] Some patients were stratified by ISS stage (I vs II/III); the protocol was amended on April 20, 2021, to replace this randomization factor with prior anti-CD38 treatment (yes vs no). [c] PFS2 was defined as time from randomization to disease progression after initiation of new antimyeloma therapy or death from any cause, whichever was earliest.

- Efficacy assessments occurred every 4 weeks in the intention-to-treat (ITT) population
- Patients achieving a confirmed ≥ VGPR per IMWG criteria and IRC assessment were tested for MRD negativity using NGS with a sensitivity of 10^{-5}
- Descriptive statistics were used to summarize the updated results
  - HRs were estimated using the Cox model, stratified by number of lines of prior therapy (1 vs 2 or 3 vs ≥4) and prior bortezomib use (yes or no)
  - 95% CIs were calculated based on the Brookmeyer-Crowley method

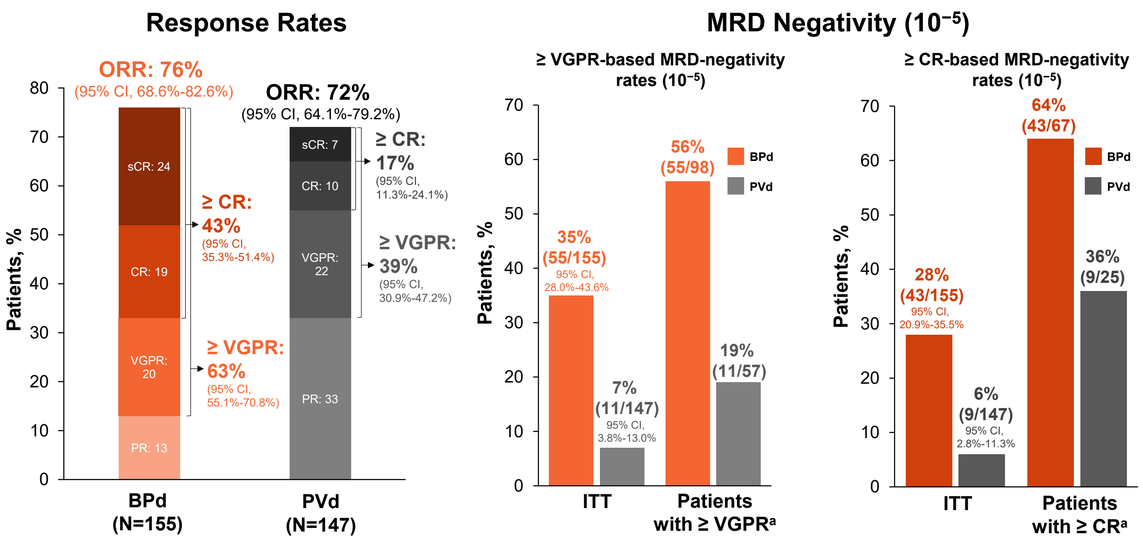
Results

Most patients had lenalidomide-refractory disease, and a quarter had disease refractory to anti-CD38 monoclonal antibodies[4]

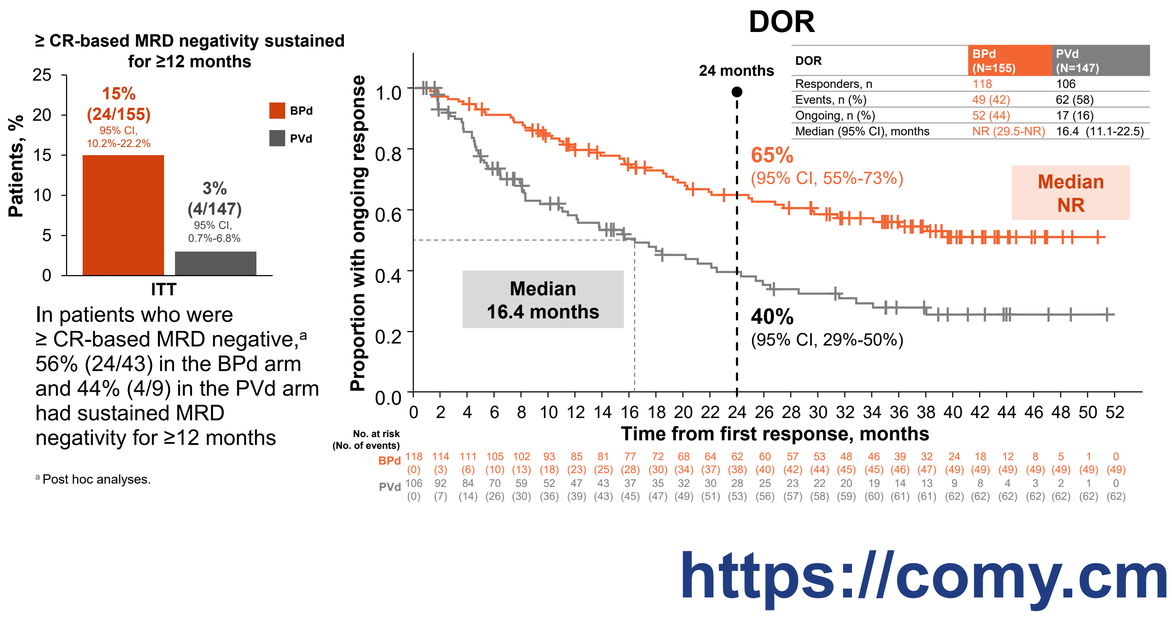
- Overall, 159 patients (53%) had received 1 prior line of therapy, 102 (34%) had received 2 or 3, and 41 (14%) had received ≥4
- All patients had previously received lenalidomide; 25% (38/155) in the BPd arm had previously received anti-CD38 antibodies vs 29% (42/147) in the PVd arm
- Approximately one-quarter of patients in each arm were triple-class exposed: 22% (34/155) in the BPd arm and 27% (39/147) in the PVd arm



Treatment with BPd led to higher rates of deep and durable responses compared with PVd

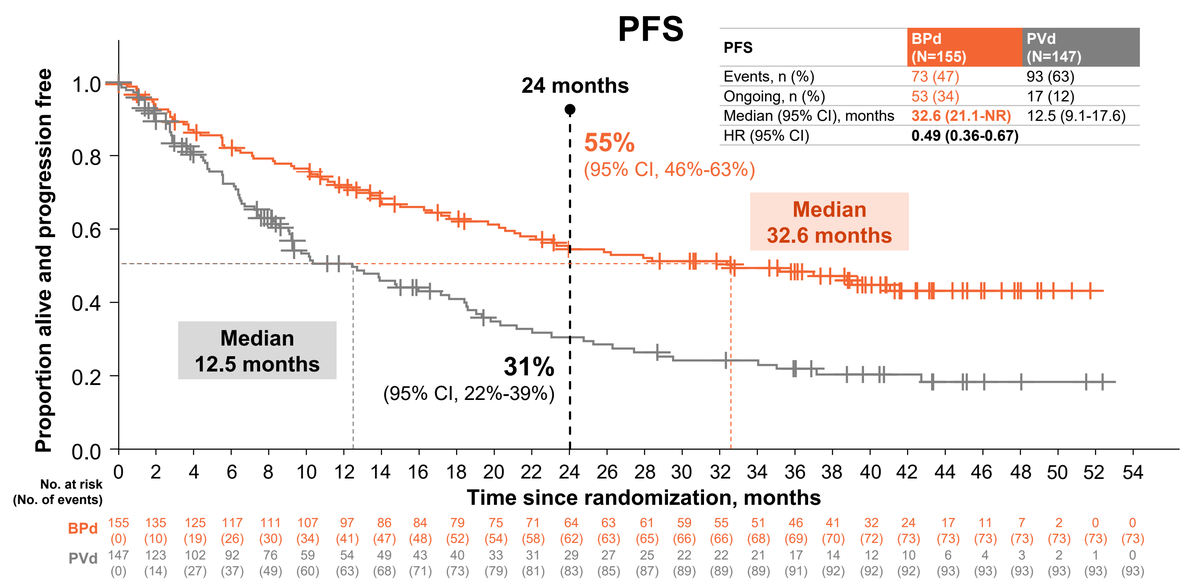


[a] Post hoc analyses.

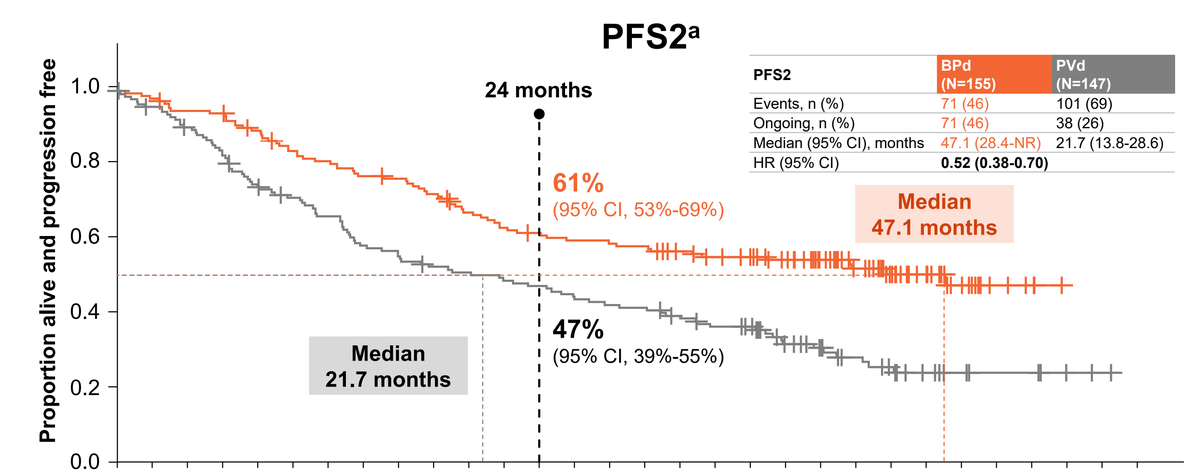


[a] Post hoc analyses.

Deep and durable responses with BPd were associated with substantial PFS benefit that was maintained following subsequent antimyeloma therapy



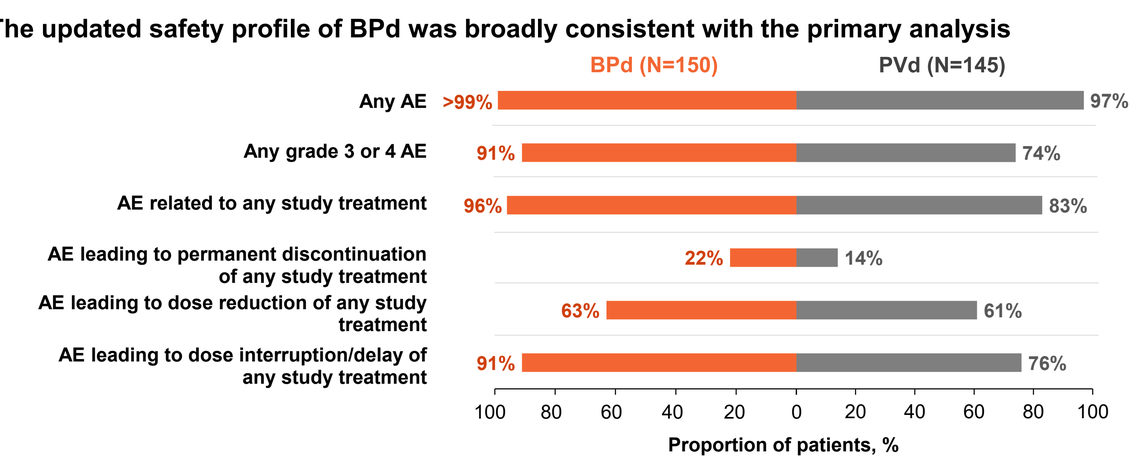
PFS	BPd (N=155)	PVd (N=147)
Events, n (%)	73 (47)	93 (63)
Ongoing, n (%)	53 (34)	17 (12)
Median (95% CI), months	32.6 (21.1-NR)	12.5 (9.1-17.6)
HR (95% CI)	**0.49 (0.36-0.67)**	



PFS2	BPd (N=155)	PVd (N=147)
Events, n (%)	71 (46)	101 (69)
Ongoing, n (%)	71 (46)	38 (26)
Median (95% CI), months	47.1 (28.4-NR)	21.7 (13.8-28.6)
HR (95% CI)	**0.52 (0.38-0.70)**	

[a] PFS2 is defined as the time from randomization to disease progression after initiation of new antimyeloma therapy or death from any cause, whichever is earlier. If disease progression after new antimyeloma therapy cannot be measured, a PFS event is defined as the date of discontinuation of new antimyeloma therapy or death from any cause, whichever is earlier.

The updated safety profile of BPd was broadly consistent with the primary analysis



Conclusions

BPd led to a 5-fold increase in MRD negativity and sustained MRD negativity vs PVd in patients with RRMM, most of whom had lenalidomide-refractory disease and a quarter of whom had disease refractory to anti-CD38 monoclonal antibodies

BPd was associated with an approximately 3-fold greater median PFS vs PVd (increase of >20 months), with greater than double the benefit following subsequent antimyeloma therapy (median PFS2); follow-up for OS is ongoing

Longer follow-up from the DREAMM-8 trial demonstrated that BPd maintained superiority over PVd across all efficacy endpoints, including PFS, MRD negativity, sustained MRD negativity, and DOR. Importantly, benefit was maintained following subsequent antimyeloma therapy

Collectively, these findings support BPd as an accessible, outpatient anti-BCMA agent for treatment of MM at first relapse across all sites of care

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; HR, hazard ratio; 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; NGS, next-generation sequencing; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; Q3W, every 3 weeks; Q4W, every 4 weeks; R, randomization; 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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