Updated Results From Phase 3 DREAMM-8 Study of Belantamab Mafodotin Plus Pomalidomide and Dexamethasone vs Pomalidomide Plus Bortezomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma

Digital poster

Poster recording

Meletios A. Dimopoulos,[1,2] Meral Beksac,[3] Ludek Pour,[4] Sosana Delimpasi,[5] Vladimir Vorobyev,[6] Hang Quach,[7] Ivan Spicka,[8] Jakub Radocha,[9] Paweł Robak,[10] Kihyun Kim,[11] Michele Cavo,[12] Kazuhito Suzuki,[13] Kristin Morris,[14] Amy Phillips-Jones,[15] Ianire Garrobo-Calleja,[16] Giulia Fulci,[17] Elisabet E. Manasanch,[18] Brandon Kremer,[18] Joanna Opalinska,[18] María-Victoria Mateos,[19] Suzanne Trudel[20]

[1]Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [2]Department of Medicine, Korea University, Seoul, Republic of Korea; [3]Department of Hematology, Ankara Liv Hospital, İstinye University, Ankara, Turkey; [4]Department of Internal Medicine, Hematology, and Oncology, University Hospital Brno, Brno, Czech Republic; [5]General Hospital Evangelismos, Athens, Greece; [6]Leningrad Regional Clinical Hospital, Saint Petersburg, Russian Federation; [7]University of Melbourne, St Vincent's Hospital Melbourne, Melbourne, VIC, Australia; [8]First Faculty of Medicine, Charles University and General Hospital, Prague, Czech Republic; [9]4th Department of Internal Medicine-Hematology, University Hospital Hradec Králové, Charles University, Faculty of Medicine in Hradec Králové, Hradec Králové, Czech Republic; [10]Medical University of Łódź, Łódź, Poland; [11]Sungkyunkwan University, Samsung Medical Center, Seoul, Republic of Korea; [12]Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy; [13]Division of Clinical Oncology/Hematology, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan; [14]GSK, Durham, NC, USA; [15]GSK, Stevenage, UK; [16]GSK, London, UK; [17]GSK, Waltham, MA, USA; [18]GSK, Collegeville, PA, USA; [19]Hematology Department, University Hospital of Salamanca/IBSAL/Cancer Research Center-IBMCC (USAL-CSIC), Salamanca, Spain; [20]Department of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada

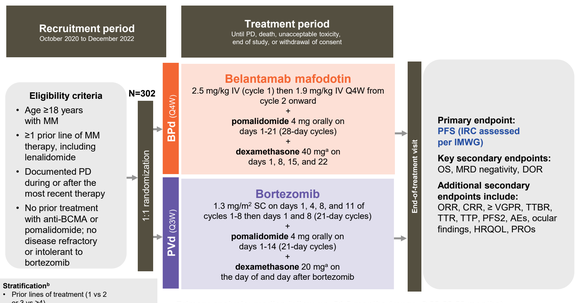
Background

- Most patients with MM experience progression on first-line treatments, which typically include triplet or quadruplet combination regimens of proteasome inhibitors, immunomodulators, and anti-CD38 monoclonal antibodies.[1,2] Therefore, novel treatment combinations are needed at first relapse
- The pivotal, phase 3 DREAMM-8 trial (NCT04484623) is assessing the efficacy and safety of BPd vs PVd in patients with RRMM who received ≥1 prior LOT, including lenalidomide (**Figure 1**)[3]
- Previous results demonstrated that treatment with BPd resulted in statistically significant and clinically meaningful PFS benefit compared with PVd (HR, 0.52; 95% CI, 0.37-0.73; *P*<.001)[3]
- In this post hoc analysis, we report updated efficacy and safety results from DREAMM-8 with an additional 8 months of study follow-up

Methods

- DREAMM-8 is a phase 3, open-label, randomized, multicenter trial evaluating the efficacy and safety of BPd vs PVd in patients with RRMM who received ≥1 prior LOT, including lenalidomide
- Patients were randomized 1:1 to BPd (28-day cycles) or PVd (21-day cycles)
- Treatment continued until progressive disease, unacceptable toxicity, or death
- Efficacy assessments occurred every 4 weeks
- Descriptive statistics were used to summarize the results, along with 95% exact CIs. HRs for PFS were estimated using the Cox model, with 95% CIs based on the Brookmeyer-Crowley method

Figure 1: **DREAMM-8 Study Design**

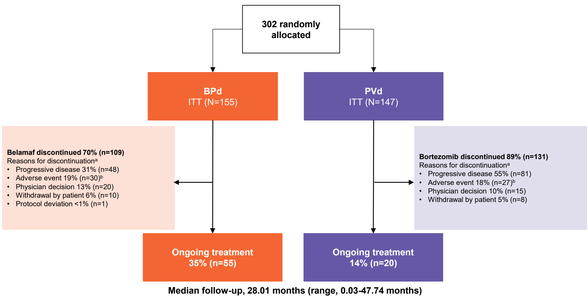


[a] *Patients aged >75 years with comorbidities or intolerance of the 40-mg dose in arm A or 20-mg dose in arm B could have dose level reduced to half per investigator discretion.* [b] *Some patients were stratified by ISS stage (I vs II/III); the protocol was amended on April 20, 2021, to replace this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

Results

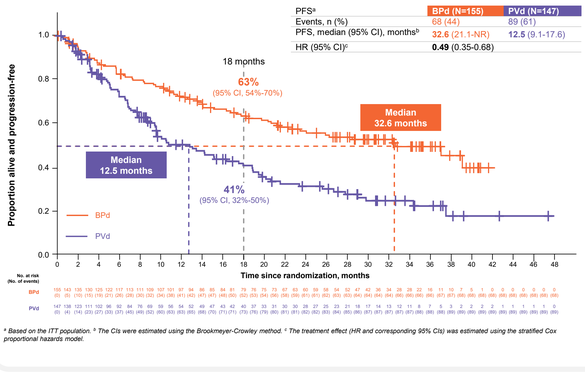
- In the ITT population, 155 patients were randomized to the BPd arm and 147 to the PVd arm
- As of the data cutoff of October 7, 2024, treatment was ongoing in 55 patients (35%) in the BPd arm and 20 patients (14%) in the PVd arm (**Figure 2**)
- With an additional 8 months of study follow-up (median, 28.01 months; range, 0.03-47.74 months), the PFS benefit demonstrated by BPd vs PVd was maintained (**Figure 3**)
  - Median PFS was 32.6 months (95% CI, 21.1 months-NR) with BPd vs 12.5 months (95% CI, 9.1-17.6 months) with PVd (HR, 0.49; 95% CI, 0.35-0.68)
- PFS benefit was maintained across subgroups, including patients with high-risk cytogenetics (unadjusted HR, 0.55; 95% CI, 0.33-0.90), lenalidomide-refractory disease (unadjusted HR, 0.43; 95% CI, 0.30-0.60), anti-CD38–refractory disease (unadjusted HR, 0.64; 95% CI, 0.36-1.15), 1 prior LOT (unadjusted HR, 0.47; 95% CI, 0.29-0.77), and ≥2 prior LOTs (unadjusted HR, 0.51; 95% CI, 0.33-0.77) (**Figure 4**)

Figure 2: **Treatment Status**



[a] *Patients may have only 1 primary reason for discontinuation. Reasons are reported for patients who were randomized and not dosed.* [b] *Treatment discontinuation due to adverse event includes discontinuations due to death where no decision was made to discontinue treatment prior to death.*

Figure 3: **BPd Maintained PFS Benefit vs PVd**



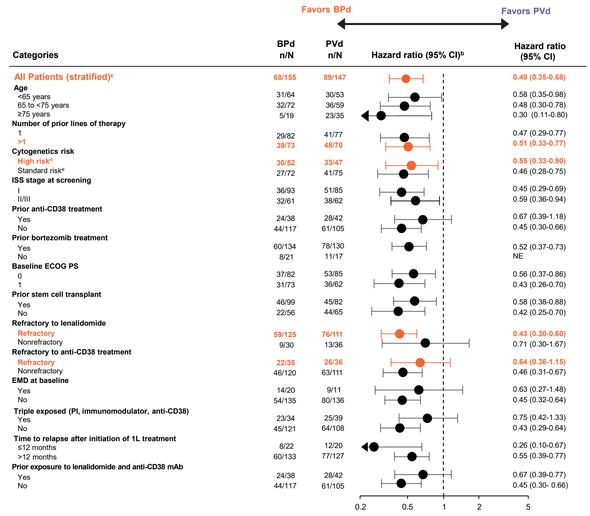
[a] *Based on the ITT population.* [b] *The CIs were estimated using the Brookmeyer-Crowley method.* [c] *The treatment effect (HR and corresponding 95% CIs) was estimated using the stratified Cox proportional hazards model.*

Conclusions

With a median PFS of 32.6 months (HR, 0.49), BPd continued to demonstrate clinically meaningful PFS benefit in patients with RRMM with ≥1 prior LOT

- PFS benefit was maintained across key subgroups, including patients with high-risk cytogenetics and those with anti-CD38– and lenalidomide-refractory disease
- The safety profile of BPd was manageable and consistent with the known safety profiles of the individual agents
- These data further support BPd as a potential standard-of-care option at first relapse or later due to robust efficacy, manageable safety, and ease of administration

Figure 4: **PFS Benefit Was Maintained Across Subgroups[a]**



[a] *Based on ITT population.* [b] *Hazard ratios for subgroups were estimated using Cox proportional hazards models, without adjustment for stratification variables.* [c] *Stratified by the number of lines of prior therapy (1 vs 2/3 vs ≥4) and prior bortezomib (yes vs no), with a covariate of treatment.* [d] *Patients were considered high risk if they had any of the following: t(4;14), t(14;16), or del(17p13).* [e] *Patients were considered standard risk if they were negative for all high-risk abnormalities: t(4;14), t(14;16), and del(17p13).*

Safety

- The median treatment duration was 18.97 months (range, 0.92-43.47 months) across all components in the BPd arm and 8.51 months (range, 0.26-48.13 months) in the PVd arm
- Updated safety results were consistent with the primary analysis and did not change the safety profile of BPd, as presented previously[3]
  - Exposure-adjusted AE rates were generally similar or lower in the BPd vs the PVd arm, and overall rates of AEs leading to treatment discontinuation were balanced between arms (**Table 1**)

Table 1: **Safety Overview**

Event	Safety population	
	BPd (N=150)	PVd (N=145)
Any AE, n (%)	149 (>99)	140 (97)
Grade 3/4 AE, n (%)[a]	136 (91)	108 (74)
Exposure-adjusted, patients/100 person-years[b]	55	70
AEs leading to interruption/delay, n (%)	137 (91)	110 (76)
Exposure-adjusted, patients/100 person-years[b]	55	72
AEs leading to dose reduction, n (%)	94 (63)	88 (61)
Exposure-adjusted, patients/100 person-years[b]	38	57
AEs leading to permanent discontinuation of any study treatment, n (%)	28 (19)	21 (14)
Exposure-adjusted, patients/100 person-years[b]	11	14
Any SAE, n (%)	101 (67)	68 (47)
Exposure-adjusted, patients/100 person-years[b]	41	44
Fatal SAEs, n (%)	19 (13)[c]	18 (12)

[a] *Includes any patient with a grade 3 or 4 AE.* [b] *Exposure-adjusted incident rates were calculated as the total number of patients with an event divided by the total exposure time in person-years (per 100 person-years). Total person-years is the sum of all patient exposure calculated as (last dose − first dose + 1) / 365.25.* [c] *Fatal SAEs of pneumonia, meningoencephalitis herpetic, and metastatic gastrointestinal cancer were considered related to treatment in 1 patient each in the BPd group.*

- The safety profile of BPd was broadly consistent with the known profiles of the individual components of the regimen (**Table 2**)
  - Exposure-adjusted rates of thrombocytopenia, neutropenia, and infections were similar
- Ocular events (KVA/CTCAE) were managed by dose holds (83%) and dose reductions (59%) and led to a low rate of treatment discontinuations (11%)

Table 2: **AEs of Clinical Interest**

Grouped term	Safety population			
	BPd (N=150)		PVd (N=145)	
	n (%)	Patients/ 100 person-years	n (%)	Patients/ 100 person-years
Thrombocytopenia[a]				
Any event	81 (54)	33	60 (41)	39
Grade ≥3	57 (38)	23	42 (29)	27
Neutropenia[b]				
Any event	97 (65)	39	69 (48)	45
Grade ≥3	87 (58)	35	60 (41)	39
Infections[c]				
Any event	124 (83)	50	101 (70)	66
Grade ≥3	78 (52)	31	39 (27)	25
Ocular AESIs (by CTCAE) preferred terms, n (%) ≥30% of patients in either treatment group				
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any event	133 (89)	66 (44)	46 (32)	3 (2)
Vision blurred	120 (80)	26 (17)	23 (16)	0
Dry eye	92 (61)	13 (9)	14 (10)	0
Foreign body sensation in eye	91 (61)	9 (6)	11 (8)	0
Eye irritation	77 (51)	6 (4)	14 (10)	0
Photophobia	69 (46)	5 (3)	6 (4)	0
Eye pain	49 (33)	3 (2)	8 (6)	0

[a] *Thrombocytopenia included events identified by site or preferred terms thrombocytopenia or platelet count decreased.* [b] *Neutropenia includes preferred terms febrile neutropenia, neutropenia, and neutrophil count decreased.* [c] *Infections are based on all preferred terms included in the system organ class of infections and infestations.*

Abbreviations

1L, first line; AE, adverse event; AESI, adverse event of special interest; BCMA, B-cell maturation antigen; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CD, cluster of differentiation; CRR, complete response rate; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; EMD, extramedullary disease; 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; KVA, keratopathy and visual acuity; LEN, lenalidomide; LOT, line of therapy; mAB, monoclonal antibody; MM, multiple myeloma; MRD, minimal residual disease; ORR, objective response rate; NR, not reached; OS, overall survival; PI, proteasome inhibitor; 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; RRMM, relapsed/refractory multiple myeloma; SAE, serious adverse event; SC, subcutaneous; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.

References

1. Dimopoulos MA, et al. *Ann Oncol*. 2021;32(3):309-322.
2. Kurtin SE, Bilotti E. *J Adv Pract Oncol*. 2013;4(5):307-321.
3. Dimopoulos MA, et al. *N Engl J Med*. 2024;391:308-421

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Disclosures

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