Patient-reported outcomes in patients with relapsed/refractory multiple myeloma (RRMM) treated with belantamab mafodotin (belamaf) vs pomalidomide/low dose dexamethasone (Pd) in the DREAMM-3 study

Poster No. MM-510

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Background

Belantamab mafodotin (belamaf) is a first-in-class humanized antibody-drug conjugate targeting B cell maturation antigen (BCMA), a surface marker found on all malignant plasma cells.[1,2]

The DREAMM-2 Phase II study showed that single-agent belamaf produced durable responses, with a well-defined and manageable safety profile, and stable or improved patient-reported outcomes (PRO) in relapsed/refractory MM (RRMM).[3–5]

In many countries, the doublet of pomalidomide plus low-dose dexamethasone (Pd) is a common treatment option for patients with RRMM who have received ≥2 prior lines of therapy and have progressive disease.

The Phase 3, open-label, randomized, multicenter DREAMM-3 trial (NCT04162210; GSK study 207495) was designed to show single-agent belamaf progression-free survival superiority compared with Pd in adult patients with RRMM at second relapse (3L+) or later; this poster presents results from PRO measures administered in DREAMM-3 (efficacy and safety are reported in abstract S199: the primary endpoint was not met).

Objective

To evaluate changes in patient-reported health-related quality of life (HRQoL), pain, and vision-related functioning (VRF) as well as trends in patient-reported treatment tolerability of the DREAMM-3 trial.

Methods

Patients were randomized (2:1) to receive belamaf or Pd.

PRO measures were collected electronically at baseline and at 3-week intervals during treatment. This analysis was based on data available at the time of primary analysis.

Key domains of HRQoL, including fatigue, physical functioning, and global health status, were evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 30-item Core module (EORTC-QLQ-C30).

Disease-related pain was evaluated with the disease symptoms domain of the EORTC Multiple Myeloma 20-item module (EORTC-QLQ-MY20).

The impact of potential treatment-associated ocular adverse events (AEs) of special interest on VRF was evaluated with the Ocular Surface Disease Index (OSDI).

Patient-reported symptomatic AEs were assessed using PRO-Common Terminology Criteria for Adverse Events (CTCAE) and bother associated with treatment side effects was assessed with Functional Assessment of Cancer Therapy – General Population item 5 (FACT-GP5).

Mean changes from baseline were reported by visit for continuous PRO variables; mixed model repeated measures (MMRM) analysis was used to identify between-treatment differences in mean EORTC scores over time.

Proportions of patients with meaningful improvement from baseline in EORTC scores (≥10-point change)[6,7] and meaningful deteriorations in VRF scores (≥12.5-point change) were assessed.[8,9]

Results

Patient Population

The intent-to-treat (ITT) population included 325 patients with RRMM randomized to belamaf (n=218) or Pd (n=107) between June 09, 2020, and April 18, 2022.

Baseline patient characteristics were well-matched between treatment arms; median age was 68 years, 57% were male, 78% were White, 25% had ISS stage III disease, and 18% had extramedullary disease (**Table 1**).

Patients received a median of 4 and 3 prior lines of therapy in the belamaf and Pd arms, respectively; 50% in each arm received >3 prior lines (**Table 1**). The belamaf arm included more heavily pre-treated patients (≥6 lines of therapy) (15%) compared with the Pd arm (7%).

Table 1. Baseline demographics and clinical characteristics*

Characteristic, n (%)	Belamaf (N=218)	Pd (N=107)
Age, median (range), years	68 (43–86)	68 (38–90)
Sex		
Male	118 (54)	66 (62)
Race	212	104
White – Caucasian / European Heritage	162 (76)	84 (81)
Asian – East Asian Heritage	30 (14)	14 (13)
Asian – Japanese Heritage	12 (6)	5 (5)
Asian – South-East Asian Heritage	4 (2)	0
Black or African American	3 (1)	1 (<1)
Mixed Asian Race	1 (<1)	0
Unknown	6	3
ISS disease stage at screening		
Stage I	76 (35)	37 (35)
Stage II	89 (41)	41 (38)
Stage III	52 (24)	28 (26)
Unknown	1 (<1)	1 (<1)
Extramedullary disease	39 (18)	19 (18)
Prior lines of therapy†		
Median (range)	4 (2–12)	3 (2–13)
≤3 lines	108 (50)	54 (50)
>3 lines	110 (50)	53 (50)
≥6 lines	33 (15)	8 (7)

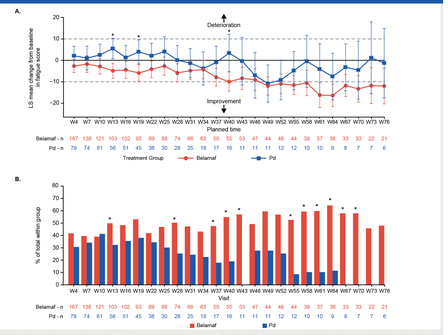
*ITT population was defined as all randomized patients whether or not they received study treatment. †The number of prior lines of therapy is derived as the number of prior anti-cancer regimens received by a patient as reported on the electronic case report form. Combination therapy containing multiple components was counted as one regimen.
ISS, International Staging System

Similar proportions of patients achieved meaningful improvement in physical functioning (~20–30%) and global health status (~20–35%) through Week 19 in both arms. A larger proportion (6–21%) of patients treated with belamaf had meaningful improvement in these domains compared to Pd from Week 22 to 31.

Pain (Disease Symptoms Domain - EORTC QLQ-MY20)

Both treatment arms had small improvements from baseline in disease pain early on in treatment; though no statistically significant difference was noted between arms, mean improvements in pain continued to increase for those receiving belamaf across later visits (**Figure 4A**). Approximately 27–58% of patients receiving belamaf and 14–50% receiving Pd achieved meaningful improvement across visits (**Figure 4B**).

Figure 1. A) LS mean (95% CI) change from baseline in EORTC QLQ-C30 Fatigue domain and B) Proportions of patients achieving meaningful improvement in mean fatigue scores



A) Statistical significance determined using 95% CIs generated from MMRM analysis, with covariates of treatment group, visit baseline value, treatment by visit interactions and baseline value by visit interactions. Statistics were only calculated for time points where the total number of patients with analyzable data across both groups was ≥10. *LS Mean Difference (95% CI) belamaf vs Pd: Week 13, −10.4 (−16.4, −4.4); Week 19, −9.9 (−16.7, −3.0); Week 40, −13.4 (−23.3, −3.5).
B) *Statistical significance determined using Fisher's exact test where significance threshold was p<0.05.
CI, confidence interval; LS, least squares

Figure 2. A) Mean change from baseline and CIs for EORTC QLQ-C30 Physical Functioning domain and B) Proportions of patients achieving meaningful improvement in physical functioning

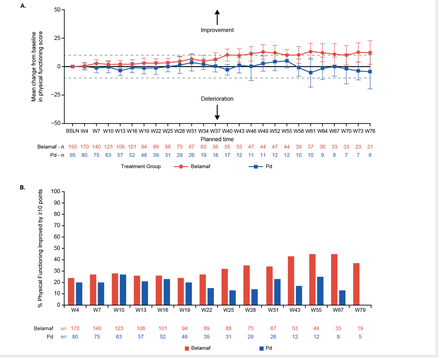


Figure 3. A) Mean change from baseline and CIs of EORTC QLQ-C30 Global Health Status domain and B) Proportions of patients achieving meaningful improvement in global health status

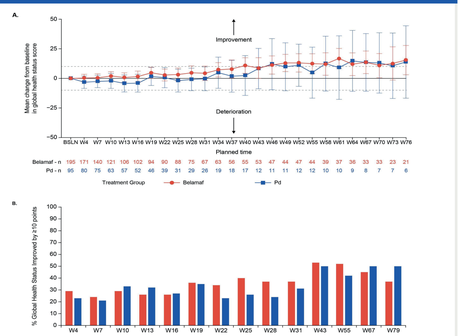
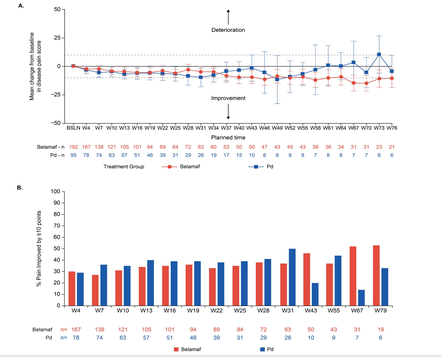


Figure 4. A) Mean change from baseline and CIs for EORTC QLQ-MY20 Pain domain and B) Proportions of patients achieving meaningful improvement in disease-related pain



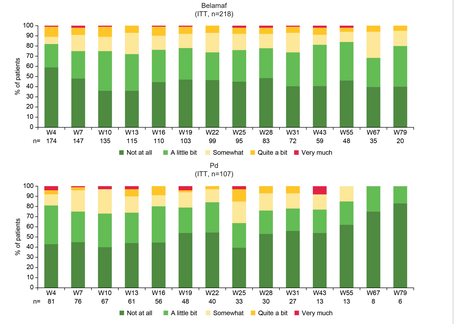
Vision impairments (OSDI)

OSDI data indicated that deterioration in mean VRF scores became notable by Week 7 for the belamaf arm. Among patients with baseline OSDI scores and ≥1 post-baseline assessment (n=177; belamaf, n=85; Pd, n=92), 67% of patients receiving belamaf had ≥1 instance of meaningful deterioration in VRF (≥12.5-point decline of OSDI score) compared with 49% of patients on Pd.

Among patients who completed ≥1 post-baseline PRO-CTCAE questionnaire (belamaf n=204; Pd n=93), blurry vision (of any severity level) was reported by 79% of belamaf-treated patients at some point during treatment compared with 66% of patients treated with Pd. While treated with belamaf, 31% of patients reported ≥1 instance of "severe" or "very severe" blurred vision versus 8% on Pd (PRO-CTCAE). Belamaf was well tolerated overall with >80% of patients reporting either none, mild, or infrequent AE concepts across visits. Similar PRO-CTCAE results were seen for Pd with some minor exceptions.

A majority of patients in both treatment arms (>70%) reported being "not at all" or only "a little bit" bothered by treatment side effects across most study visits (FACT-GP5) (**Figure 5**).

Figure 5. Patient-reported tolerability related to treatment side effects (FACT-GP5)



Conclusions

The DREAMM-3 PRO results build on and were consistent with PRO data on single-agent belamaf from the DREAMM-2 study.

In this randomized controlled study, a greater proportion of patients receiving belamaf compared with Pd experienced meaningful improvement in fatigue, a common and difficult-to-manage symptom in RRMM.

Other than fatigue, no statistically significant differences were observed for other HRQoL domains.

Despite the high prevalence of blurry vision reported by patients, mean physical functioning and global health status remained stable early in treatment and even improved over time for patients on belamaf.

VRF declines were common in patients treated with belamaf (67%) and were also seen in patients on Pd (49%), suggesting that there may be additional factors (e.g. age-related changes in vision) other than treatment impacting visual function in this patient population.

Overall, the DREAMM-3 PRO data demonstrate that single-agent belamaf is a well-tolerated treatment, with a positive impact on important health outcomes for patients with third-line or greater RRMM.

Disclosures

VH has received fees for consulting from AbbVie, Amgen, BMS, Celgene, Janssen, Sanofi, and Takeda; **KW** has received honoraria from Abbvie, Amgen, Adaptive Biotech, Astra Zeneca, BMS/Celgene, Janssen, GSK, Karyopharm, Novartis, Oncopeptides, Pfizer, Roche Pharma, Sanofi, Stemline, and Takeda; consulting or advisory fees from Abbvie, Amgen, Adaptive Biotech, BMS/Celgene, Janssen, GSK, Karyopharm, Oncopeptides, Pfizer, Roche Pharma, Sanofi, and Takeda; and research funding from Abbvie, Amgen, BMS/Celgene, Janssen, GSK, and Sanofi; **BC**, **SP**, **SS**, **LN**, **JB**, and **KD** are employees of and hold stocks and shares in GSK; **AM** is an employee of GSK and holds stocks and shares in AstraZeneca, GSK, Haleon, and Novartis. **NS** is an employee of GSK and holds stocks and shares in GSK, Pfizer, and BMS; **WH** was an employee of GSK at the time this analysis was completed and holds stocks and shares in GSK; **ML** is an employee of GSK and holds stocks and shares in GSK and Astra Zeneca; **SB** and **KP** are employees of GSK; **MAD** has received fees from speaker's bureau participation from Amgen, Beigene, BMS, Janssen, and Takeda.

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References

1. Lee L, et al. *Br J Haematol*. 2016;174(6):911–22
2. O'Connor BP, et al. *J Exp Med*. 2004;199(1):91–8
3. Lonial S, et al. *Lancet Oncol*. 2020;21(2):207–221
4. Lonial S, et al. *Cancer*. 2021;127(22):4198–4212
5. Popat R, et al. *Blood*. 2020; 136(Supplement 1):27–28
6. Cocks K. *Eur J Cancer*. 2012;48(11):1713–21
7. Osoba D. *J Clin Oncol*. 1998;16(1):139–44
8. Schiffman R, et al. *Arch Ophthalmology*. 2000; 118:615–621
9. Eliason L, et al. Value in Health. 2020;23:S477

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