Belantamab mafodotin for relapsed or refractory multiple myeloma: a real-world observational study update

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Background

Belantamab mafodotin (belamaf), an antibody-drug conjugate targeting B-cell maturation antigen (BCMA), induces cell death by direct cell killing and immune-mediated mechanisms.[1,2]

In the pivotal Phase II DREAMM-2 study (NCT03525678), single-agent belamaf demonstrated efficacy and a manageable safety profile in patients with relapsed/refractory multiple myeloma (RRMM).[1,2]

This is an addendum to the original study reporting real-world use of belamaf in patients with RRMM and the occurrence of ocular events in routine clinical practice in the US using national electronic medical records[3]; 6 months' additional follow-up data are presented.

Objective

To characterize patients with RRMM, including triple-class refractory patients, treated with belamaf in the US to better understand the real-world management of these patients, including the occurrence and management of ocular adverse events, as well as the efficacy of belamaf in the real world.

Methods

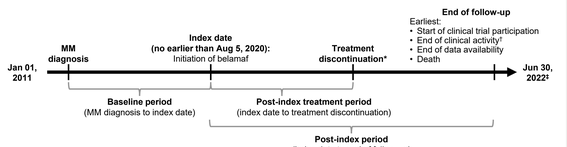
This retrospective, longitudinal, observational study analyzed de-identified US electronic health record data derived from the Flatiron Health database for the period from January 1, 2011, to June 30, 2022 (6 months additional follow-up from the previously presented cutoff of December 31, 2021).

Flatiron Health is a longitudinal database, comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction.[4] Data on belamaf dosing, derived response, ocular exams, and ocular adverse events of special interest (AESI) were extracted from unstructured fields of patient charts via a Flatiron Spotlight project.

Eligible patients had a confirmed MM diagnosis, initiated belamaf after August 5, 2020 (date of US approval; first dose=index date), were ≥18 years old at index, and had chart abstraction data for ocular safety and treatment efficacy.

Patients who participated in an interventional clinical trial during baseline or on the index date were excluded (**Figure 1**).

Figure 1. Study design



*Treatment discontinuation was defined as the earliest permanent discontinuation of belamaf treatment (recorded as clinician decision), the confirmed date of a new line of treatment, or the date of the end of follow-up. †Clinical activity was defined from the date of the first recorded interaction to the date of the last recorded interaction, where a recorded interaction between the patient and a healthcare provider included visits, use of therapies or lab tests, vital assessments, ECOG assessments, or comorbidity diagnoses. ‡Belamaf was pulled from the US market in November 2022 but remains approved as a monotherapy in other countries.

Demographic characteristics were assessed on the index date; disease and treatment history, and other clinical variables were described during the baseline period.

Belamaf treatment patterns (including duration of treatment and reasons for discontinuation) and ophthalmic monitoring (including frequency/timing of visits) were assessed during the post-index treatment period. Ocular AESIs and clinical efficacy of belamaf (i.e., overall response rate [ORR], overall survival [OS], and progression-free survival [PFS]) were also assessed during the post-index period.

- ORR consisted of partial response (PR) and very good partial response (VGPR), which were defined using International Myeloma Working Group criteria.[5]
- OS was defined as the time from the index date to the date of death due to any cause.
- Real-world PFS was defined as the time from index date to the earliest documented disease progression or death. Patients with no event were censored at the end of follow-up. Progression was derived from abstracted M-spike and structured free light chain lab values in the Flatiron database.

Kaplan–Meier analyses were conducted to evaluate OS, PFS, and ORR.

Ocular AESIs were identified using prespecified terms for belamaf-related ocular AESIs, including keratopathy, blurred vision, dry eye, and keratitis, which were abstracted from patient charts.

Keratopathy severity was defined as mild, moderate, or severe based on the first slit lamp examination occurring on or after the AE onset date during the post-index period.

Data on ocular AESIs were reported separately for all patients and for patients with ≥4 months of follow-up, to allow sufficient time post-index to evaluate incidence of ocular AEs and treatment mitigations.

Results

Patient characteristics

A total of 246 patients with a confirmed MM diagnosis and with ≥1 administration of belamaf were identified, of which 62 were excluded due to participation in an interventional clinical trial (during the baseline period or on the index date) or lack of chart abstraction data.

Overall, 184 patients were included in the study (**Table 1**).

- Mean age was 68.7 years and 46.7% of patients were female.
- Median (interquartile range [IQR]) time between MM diagnosis and index was 5 (3–7) years.
- Eastern Cooperative Oncology Group (ECOG) performance status was ≥2 in 28.3%.
- Median (IQR) number of agents per line of therapy (LOT) was 3.0 (2.6–3.3), 62.0% received at least 5 prior LOTs, and 82.1% of patients were triple-class refractory.

Table 1. Baseline patient demographics and disease characteristics

Characteristic	Belamaf (N=184)
Patient demographics	
Age, years, mean (SD)	68.7 (10.0)
Female, n (%)	86 (46.7)
Race, n (%)	
White	117 (63.6)
Black or African American	23 (12.5)
Hispanic or Latino	12 (6.5)
Other*	32 (17.4)
Disease characteristics	
Extramedullary disease, n (%)	39 (21.2)
ECOG performance status, n (%)	
0	34 (18.5)
1	79 (42.9)
2	43 (23.4)
3	8 (4.3)
4	1 (0.5)
Unknown	19 (10.3)
ISS stage n (%)	
I	42 (22.8)
II	40 (21.7)
III	50 (27.2)
Unknown	52 (28.3)
Cytogenetic risk, n (%)†	
High	73 (39.7)
Standard	81 (44.0)
Unknown	30 (16.3)
Pre-existing comorbidities, n (%)	
Cardiovascular disease	97 (52.7)
Renal disease	71 (38.6)
Bone disease	58 (31.5)
Cardiac disease	42 (22.8)
Peripheral neuropathy	36 (19.6)
Pulmonary disease	34 (18.5)
Eye disease	26 (14.1)
Diabetes	26 (14.1)
Cardiovascular toxicity	1 (0.5)
Refractory status, n (%)	
Triple‡	151 (82.1)
Quad§	59 (32.1)
Penta¶	58 (31.5)
Refractory to CD38 mAb	173 (94.0)
Refractory to lenalidomide only**	1 (0.5)
Treatment history	
Number of prior LOTs, n (%)††	
1	4 (2.2)
2	12 (6.5)
3	15 (8.2)
4	39 (21.2)
5	41 (22.3)
6	22 (12.0)
7	23 (12.5)
8+	28 (15.2)
Median (IQR)	5 (4–7)

*Number of patients in each race subgroup categorized was too low to be reported separately without risking de-identification of patients. †High-risk cytogenetics were defined as presence of del(17p), t(4;14), t(14;16), t(14;20), or 1q21 gains/amplifications identified by FISH or karyotyping. Standard-risk cytogenetics were defined as evidence of genetic testing but no documented presence of high-risk identifiers. ‡Triple-class-refractory MM was defined as MM that does not respond to treatment with any of the following drug classes: immunomodulatory agent (lenalidomide, pomalidomide, thalidomide), PI (bortezomib, carfilzomib, ixazomib), or mAb (daratumumab, isatuximab). §Quad-refractory MM was defined as MM that does not respond to treatment with bortezomib, carfilzomib, lenalidomide, or pomalidomide. ¶Penta-refractory MM was defined as MM that does not respond to treatment with bortezomib, carfilzomib, lenalidomide, pomalidomide, or daratumumab. **Refractory to lenalidomide AND not refractory to other immunomodulatory drugs, PI, or mAb. ††LOT was oncologist-defined by the rule-based Flatiron Health algorithm specific to MM.

Persistence on belamaf

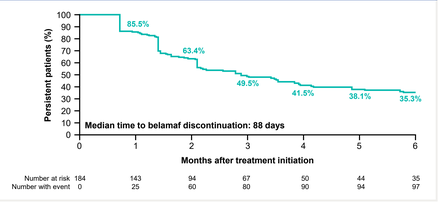
Median (IQR) treatment period was 2.0 (1.1–4.5) months and follow-up time was 4.1 (1.9–8.5) months.

At 3 and 6 months after starting therapy, 49.5% and 35.3% of patients, respectively, were still on treatment with belamaf (**Figure 2**).

- Mean (SD) number of belamaf doses received by those still on belamaf at 3 and 6 months was 3.5 (1.2) and 5.6 (2.0), respectively.

Reason for discontinuation was reported for 104 patients; the most common reasons listed were disease progression (34.6%), treatment toxicity (17.3%), or both (16.3%).

Figure 2. Proportion of patients who continued on belamaf



Ocular AESI

In total, 91.8% of patients had a record for an ophthalmic examination prior to the first administration of belamaf.

Among patients with ≥4 months of follow-up (94 patients), 74.5% had at least 1 ocular AESI, of which keratopathy (61.7%) and blurred vision (48.9%) were the most common (**Table 2**).

- Mean (SD) time to first ocular AESI was 39.4 (33.9) days, with a mean (SD) of 2.1 (1.2) belamaf doses received prior to first ocular AESI.

Among patients with a keratopathy event, ≥4 months of follow-up, and available severity information (n=48), 52.1% had mild and 47.9% had moderate/severe keratopathy (determined by most recent slit lamp examination occurring on or after the onset date).

Most ocular AEs were managed by therapy hold (68.6%; of which 72.9% restarted belamaf) and/or AE treatment (62.9%) (**Table 3**).

Table 2. Occurrence of ocular AEs during post-index period

	Post-index period* (N=184)	Patients with ≥4 months of post-index period (N=94)
Patients with ≥1 ocular AE,† n (%)	92 (50.0)	70 (74.5)
Time to first ocular AE, days, mean (SD)	39.4 (31.6)	39.4 (33.9)
Number of belamaf doses prior to first ocular AE, mean (SD)	2.1 (1.1)	2.1 (1.2)
Number of ocular AEs, median (IQR)	2.0 (1.0–2.0)	2.0 (1.0–2.0)
1 ocular AE, n (%)	44 (47.8)	28 (40.0)
2 ocular AEs, n (%)	34 (37.0)	28 (40.0)
≥3 ocular AEs, n (%)	14 (15.2)	14 (20.0)
Type of ocular AE, n (%)		
Keratopathy	76 (41.3)	58 (61.7)
Blurred vision	52 (28.3)	46 (48.9)
Dry eye	32 (17.4)	26 (27.7)
Keratitis	18 (9.8)	16 (17.0)
Patients with ≥1 keratopathy event, n (%)	76 (41.3)	58 (61.7)
Patients with ≥1 ocular exam result recorded on or following the first event in the post-index period, n (%)	72 (94.7)	56 (96.6)
Patients with a BCVA score assessment‡	63 (87.5)	48 (85.7)
Patients with a slit lamp examination‡	71 (98.6)	55 (98.2)
Mild keratopathy	38 (61.3)	25 (52.1)
Moderate/severe keratopathy§	24 (38.7)	23 (47.9)

*The post-index period is defined as the period from the index date to the end of follow-up (i.e., start of participation in a clinical trial, end of clinical activity, end of data availability, or death). †Ocular AESIs were keratitis, keratopathy, blurred vision, and dry eye events. ‡Patients received ophthalmic monitoring via BCVA assessment or slit lamp examination following an AESI for compliance with the REMS program, which requires ophthalmic examination promptly for worsening symptoms. §Number of patients with severe keratopathy was too low to be reported separately without risking de-identification of patients.

Table 3. Assessment and management of keratopathy events during the post-index period

	Patients with keratopathy event (N=76)	Patients with keratopathy event and ≥4 months of follow-up (N=58)
Patients with ≥1 ocular exam on keratopathy onset date or following the keratopathy event during the post-index period, n (%)	72 (94.7)	56 (96.6)
Severity of first keratopathy* event (among patients with keratopathy severity information), n (%)†	N=62	N=48
Mild	38 (61.3)	25 (52.1)
Action taken, n (%)‡	27 (71.1)	20 (80.0)
Therapy hold§	19 (70.4)	16 (80.0)
Patients with subsequent belamaf administration	17 (89.5)	15 (93.8)
Patients with therapy hold >28 days	5 (29.4)	5 (33.3)
Treatment for ocular AESI¶	19 (70.4)	13 (65.0)
Therapy dose or schedule change**	7 (25.9)	6 (30.0)
Therapy discontinuation	3 (11.1)	2 (10.0)
Moderate/severe††	24 (38.7)	23 (47.9)
Action taken, n (%)‡	23 (95.8)	22 (95.7)
Therapy hold§	19 (82.6)	18 (81.8)
Patients with subsequent belamaf administration	14 (73.7)	13 (72.2)
Patients with subsequent therapy hold >28 days	12 (85.7)	12 (92.3)
Treatment for ocular AESI¶	12 (52.2)	11 (50.0)
Therapy dose or schedule change**	7 (30.4)	7 (31.8)
Therapy discontinuation	5 (21.7)	5 (22.7)

*Keratopathy severity is based on the most recent slit lamp examination findings occurring on or after the keratopathy onset date. †Of the 76 patients with keratopathy in the full cohort and the 58 patients in the cohort with ≥4 months of follow-up, there were 10 and 8 patients without severity information recorded, respectively. ‡Patients may have had multiple actions taken following the keratopathy event; therefore, the categories presented are not mutually exclusive. §Defined as any treatment interruption/delay due to an AE with a gap of ≥28 days and <90 days from the previous to the subsequent belamaf administration. ¶Treatment for the AE is defined as any treatment (does not have to be pharmacological) that is recommended, prescribed, or administered by the clinician to treat the AE. **Defined as dose modifications to the given LOT as a result of the AE or if the AE caused a change in treatment schedule. ††Number of patients with severe keratopathy was too low to be reported separately without risking de-identification of patients.

Efficacy

Tumor response was observed in 39 patients (ORR at 6 months: 25.5%). Of those with an overall response, a best response of PR was achieved in 19 (48.7%) patients, and 20 (51.3%) patients achieved a best response of VGPR.

Median OS and real-world PFS were 7.9 months and 4.5 months, respectively (**Figure 3**).

Limitations

Unlike in clinical trial settings, the assessment of outcomes in real-world clinical practice may not be consistent across patients or across physicians; it is not possible to implement the consistent monitoring and homogenous evaluation criteria that are inherent to clinical trial design.

Excluding patients who have participated in clinical studies could potentially confound the data and may have resulted in low patient numbers for inclusion, especially in academic settings. Additionally, the Flatiron Health database is not comprehensive of all US oncology centers.

Baseline comorbidities of patients from the study sample were identified by diagnostic codes in electronic health records, which may be incomplete, particularly if a patient was diagnosed in a non-Flatiron medical center. Therefore, identification of comorbidities may be underestimated and misclassification due to miscoding of these conditions may occur.

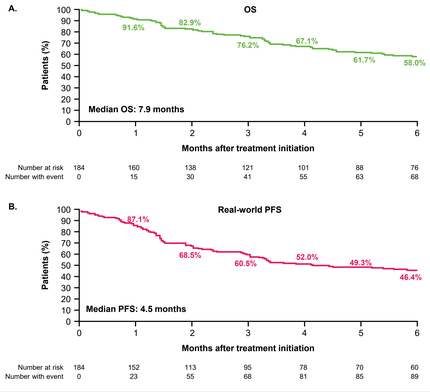
Ophthalmic monitoring and associated dose reductions may be underreported, as patients may seek care at different practices or hospitals, which may not always be captured in the Flatiron Health database.

Outcome measures such as treatment response are clinician-assessed in the real-world setting and may differ from the prespecified definitions used in clinical trials, complicating comparisons between clinical trials and real-world data.

Short observation periods and small sample size limit the generalizability of findings in this study.

Data are from patient charts, and so specific events such as details of comorbid conditions (including ophthalmic history) may be missing, and inconsistencies may occur between charts.

Figure 3. Real-world time to OS (A) and PFS (B)



Conclusions

These findings provide important insights into the real-world use of belamaf in patients with RRMM.

Compared with the belamaf 2.5 mg/kg cohort in DREAMM-2, patients in this study were slightly older, had fewer prior LOTs, and had a shorter time between MM diagnosis and belamaf treatment initiation, suggesting that patients in this study may have had slightly more severe disease, requiring initiation of belamaf treatment earlier in their course of therapy.[3]

ORR in this real-world study was consistent with the DREAMM-2 study (25.5% vs 32.0%); however, PFS was longer (4.5 vs 2.8 months) and OS shorter (7.7 vs 13.7 months) than in DREAMM-2.[4]

Real-world compliance with ocular monitoring was high, with >90% of patients having a record for an ophthalmic examination prior to the first administration of belamaf. Keratopathy was one of the most common ocular AESI reported in patients receiving belamaf treatment.[3]

Overall, patients with RRMM treated with belamaf in the clinical real-world setting experienced similar outcomes to those who received belamaf in the DREAMM-2 study.[3] Ocular events were managed with therapy holds, and patients generally remained on treatment.

Our findings suggest that belamaf may help to fill the unmet treatment need in patients with RRMM, supporting ongoing studies investigating belamaf in combination with standard and novel agents.

Disclosures

MH has received consultancy fees from Curio Science LLC, GSK, Intellisphere LLC; participated in advisory committees for GSK and BMS; and received research funding from Amgen, Daiichi Sankyo, GSK, and SpringWorks Therapeutics; **DK** has ownership interests in Calm Water Therapeutics LLC; has received consultancy fees from GSK and Triphase Accelerator Corp; and participated in advisory committees for Calm Water Therapeutics LLC; **RV** has received honoraria from Adaptive Biotech, BeiGene, BMS, GSK, Janssen, Oncopeptides, Sanofi, and Takeda; and grant support from BMS, Sanofi, and Takeda; **FE** has participated in advisory boards for Amgen, BMS, GSK, Janssen, Sanofi, and Takeda; **MD** has received honoraria from Amgen, BMS, Janssen, GSK, Sanofi, and Menarini Stemline; **NK, JB, NB, LCO,** and **LPH** are employees of and hold stocks/shares in GSK; **GG, MSD, FL, MM** and **AU** are employees of Analysis Group, which received funding from GSK to conduct the study; **HL** has received consulting fees from BMS, Celgene, Genentech, Karyopharm, Legend Biotech, GSK, Sanofi, Pfizer, Monte Rosa Therapeutics, Oncopetides, Takeda Pharmaceuticals, and Allogene Therapeutics; and research funding from Amgen, BMS, Janssen, GSK, Regeneron, and Takeda Pharmaceuticals.

Abbreviations

AE, adverse event; AESI, adverse event(s) of special interest; BCMA, B-cell maturation antigen; BCVA, best corrected visual acuity; belamaf, belantamab mafodotin; ECOG, Eastern Cooperative Oncology Group; FISH, fluorescence in situ hybridization; IQR, interquartile range; ISS, International Staging System; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PR, partial response; REMS, risk evaluation and mitigation strategy; RRMM, relapsed or refractory multiple myeloma; SD, standard deviation; VGPR, very good partial response.

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References

1. Lonial S, et al. *Lancet Oncol*. 2020;21:207–11.
2. Lonial S, et al. *Cancer*. 2021;127:4198–212.
3. Hultcrantz M, et al. *Blood*. 2022;140(Supplement 1):10124-10126.
4. medRxiv. https://arxiv.org/abs/2001.09765. Accessed November 2022.
5. Durie BGM, et al. *Leukemia*. 2006;20(9):1467–73.

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