Impact of baseline ocular conditions on belantamab mafodotin (belamaf)–related corneal events in patients with relapsed or refractory multiple myeloma

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Disclosures

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- GSK: consultancy, honoraria, research funding, travel expenses
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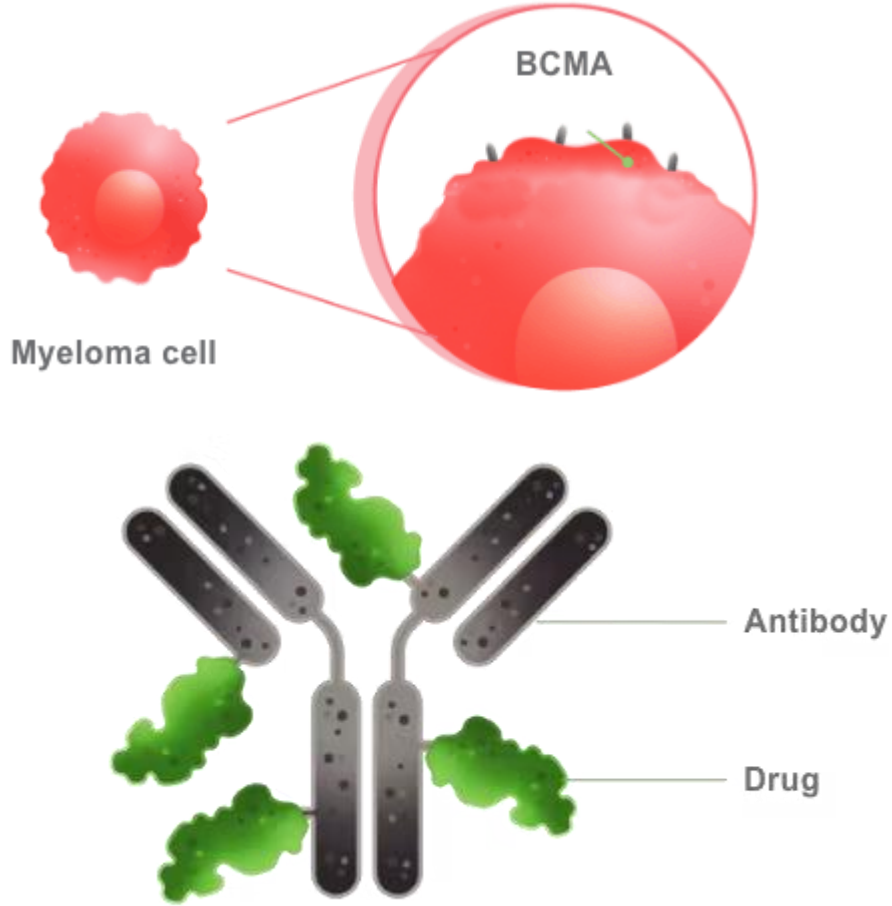
- Janssen and Bristol Myers Squibb: travel expenses

Belantamab mafodotin

Overview

- Belantamab mafodotin (belamaf) is a B-cell maturation antigen (BCMA)–targeting antibody-drug conjugate that is approved for the treatment of patients with relapsed or refractory multiple myeloma (RRMM) who have received ≥4 prior therapies[1]

- Belamaf has demonstrated activity in patients with triple-class refractory RRMM[2,3]
  - ORR was 32% in patients treated with belamaf 2.5 mg/kg in the ***D***riving ***E***xcellence in ***A***pproaches to ***M***ultiple ***M***yeloma (DREAMM)-2 study[a,3]



Belamaf

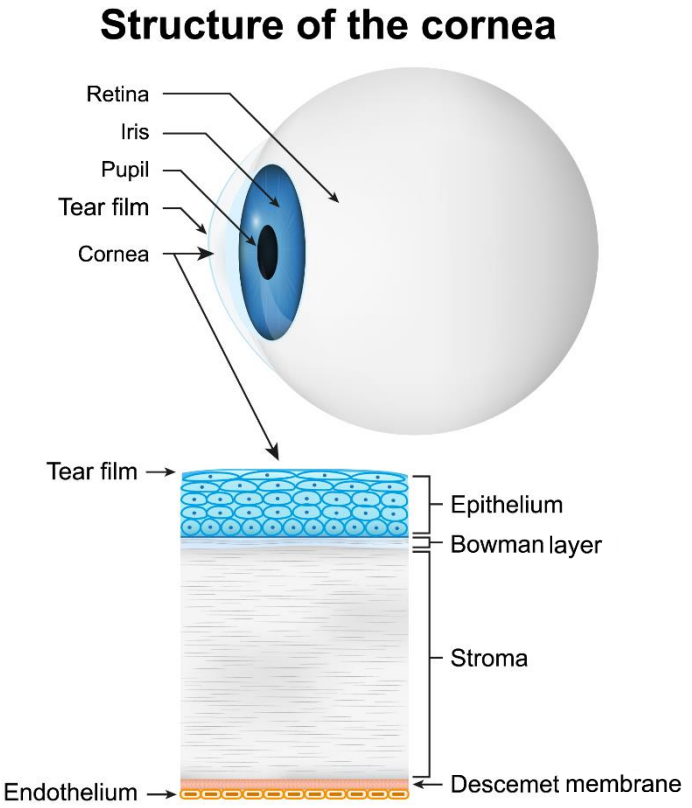
[a] ORR = sCR + CR +VGPR + PR as of January 31, 2020.

BCMA, B-cell maturation antigen; CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent CR; VGPR, very good PR.

1. BLENREP (belantamab mafodotin-blmf) [package insert]. GSK. Research Triangle Park, NC. 2022. 2. Lonial S, et al. *Lancet Oncol.* 2020;21:207-221. 3. Lonial S, et al. *Cancer.* 2021;127:4198-4212.

Rationale for analyzing the associations between baseline ocular conditions, belamaf treatment duration, and resulting ocular symptoms

- Corneal events and ocular symptoms were associated with the MMAF payload of belamaf in the DREAMM-2 study[1,2]
  - Patients with corneal epithelial disease were excluded from participation, except those with mild punctate keratopathy
  - No other baseline ocular conditions were excluded from the study
- Patients may present with ocular conditions as a result of comorbidities and/or previous treatment with antimyeloma therapies[3,4]
- Understanding the relationship between baseline ocular conditions and ocular symptoms reported during the DREAMM-2 study is important for appropriate patient counseling and healthcare provider benefit/risk assessment



MMAF, monomethyl auristatin F.

1. Popat R, et al. *Blood.* 2020;136(suppl 1):27-28. Poster presented at ASH 2020 [abstract 2278]. 2. Lonial S, et al. *Lancet Oncol.* 2020;21:207-221. 3. Wang F, et al. *J Med Econ.* 2022;25:182-192. 4. Pinazo-Durán MD, et al. *Biomed Res Int.* 2016;2016:6215745.

DREAMM-2 (NCT03525678): Open-label, phase 2 study

Key inclusion criteria

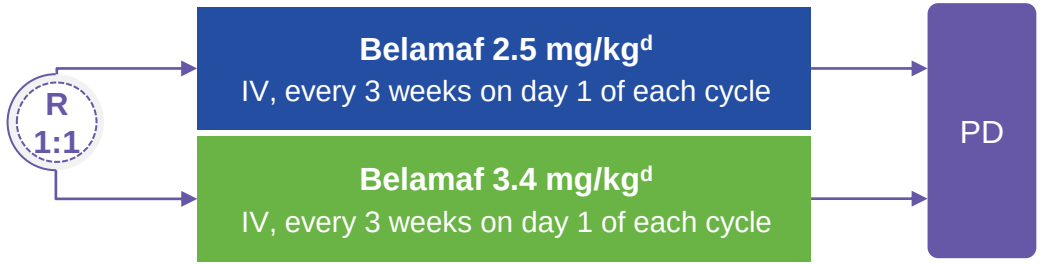
- Age ≥18 years with a histologically or cytologically confirmed diagnosis of MM[a]
- Disease progression after ≥3 prior LOT including an anti-CD38 antibody and disease refractory to an immunomodulatory agent and a PI
- ECOG PS score of 0 to 2

Key exclusion criteria

- Prior allogenic stem cell transplant
- **Current corneal epithelial disease except mild punctate keratopathy**
- Systemic antimyeloma therapy ≤14 days[b] or plasmapheresis ≤7 days prior to the first dose of study drug
- Systemic treatment with high dose steroids[c] for ≤14 days

Overview of study design[1,2]

N=221



Ophthalmic examinations at baseline and pre-dose every 3 weeks

Dose modification guidelines for belamaf-related corneal events[e]

- **Grade 1** – continue treatment with current dose, consider ophthalmology consult
- **Grade 2/3** – hold belamaf treatment and consult ophthalmology
  - Grade <1 within 14 days – consider restarting same dose
  - Grade <1 after 14 days – consider 25% dose reduction
- **Grade 4** – stop treatment and consult ophthalmology

Endpoints

Primary:

- ORR by independent review committee

Key Secondary:

- DOR
- TTR
- PFS
- OS
- Proportion achieving clinical benefit
- AEs, SAEs, AESIs

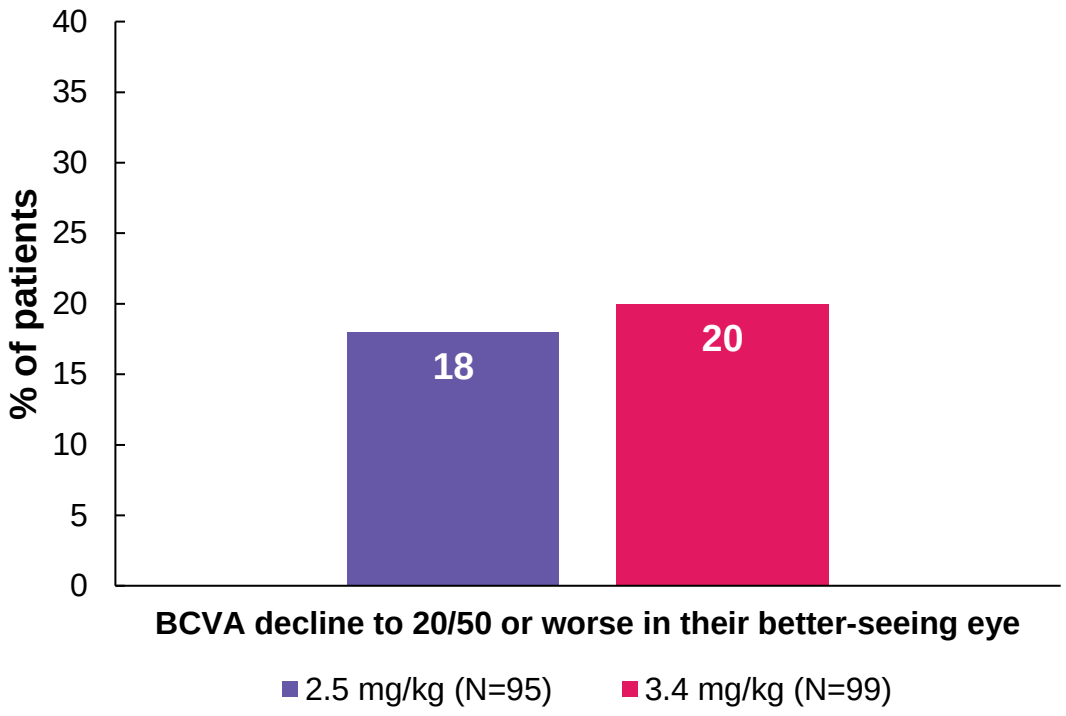
[a] Measurable disease with additional criteria: ≥1 of the following: serum M-protein ≥0.5 g/dL (≥5 g/L); urine M-protein ≥200 mg/24h; serum free light chain (FLC) assay: Involved FLC level ≥10 mg/dL (≥100 mg/L) and an abnormal serum FLC ratio (<0.26 or >1.65). [b] Or 5 half-lives, whichever is shorter. [c] ≥60 mg prednisone daily for ≥4 days. [d] Corticosteroid eye drops and preservative-free artificial tears were used in both eyes to mitigate corneal events. [e] Corneal toxicity was graded according to GSK scale for corneal events.

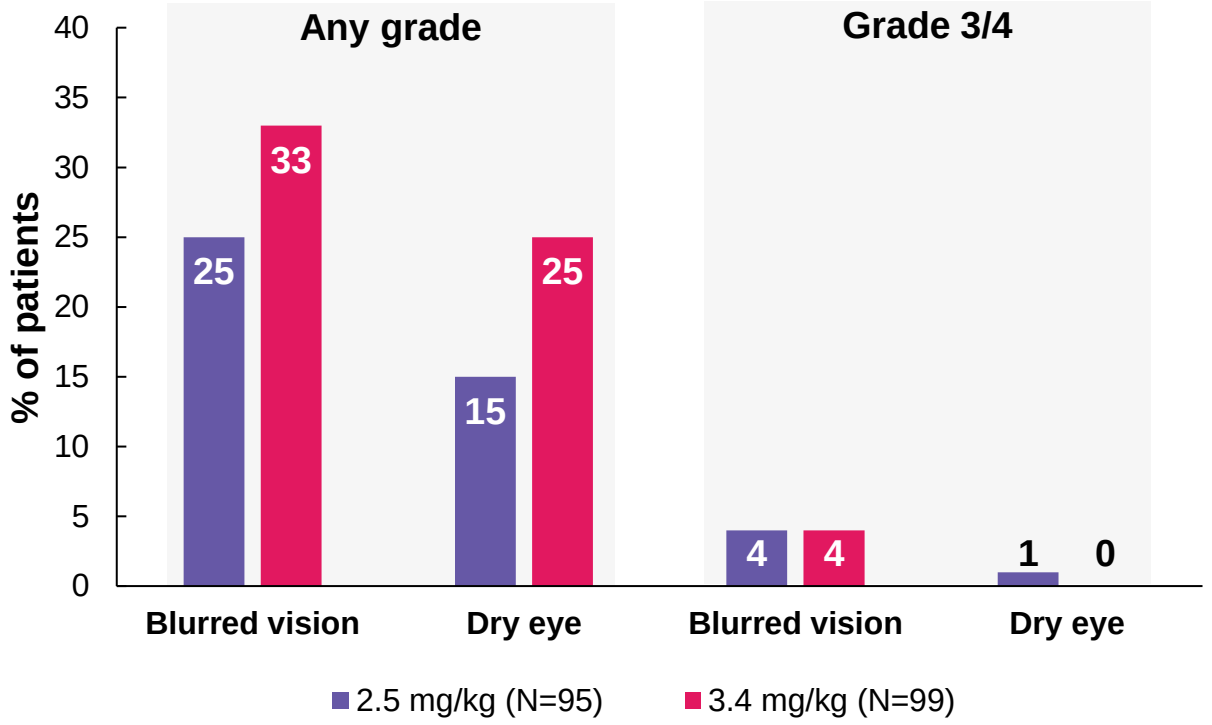
AE, adverse event; AESI, AE of special interest; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; LOT, lines of therapy; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PI, proteasome inhibitor; RRMM, relapsed or refractory multiple myeloma; SAE, serious AE; TTR, time-to-response.

1. ClinicalTrials.gov. Accessed July 25, 2022. https://clinicaltrials.gov/ct2/show/NCT03525678. 2. Lonial S, et al. *Lancet Oncol.* 2020;21:207-221.

Blurred vision, decline in BCVA, and dry eyes were the most commonly reported ocular symptoms in the DREAMM-2 study

13-month follow-up[1,2]





Both doses were assessed in DREAMM-2 and included in this analysis, but 2.5 mg/kg is the approved dose for belamaf[3]

BCVA, best corrected visual acuity.

1. Lonial S, et al. *Cancer.* 2021;127:4198-4212. 2. Lonial S, et al. Poster presented at EHA 2020 [abstract EP970]. 3. BLENREP (belantamab mafodotin-blmf) [package insert]. GSK, Research Triangle Park, NC. 2022.

Methods: DREAMM-2 post-hoc analysis of ocular symptoms in patients based on baseline ocular conditions

Collection of patient-reported ocular symptoms

Analysis of ocular symptoms via the presence or absence of the most common baseline ocular conditions

Stratification based on belamaf treatment duration to assess impact of drug exposure

Differences were defined as ≥20 percentage point difference in ocular symptoms between patients with and without each baseline ocular condition

Limitation: *DREAMM-2 was not powered for this post-hoc analysis; thus, results presented here could only be descriptive*

≥20 percentage point difference in ocular symptoms, present vs absent

Baseline ocular conditions

Cornea	Lens	Retina
– Keratopathy – Dry eye	– Cataract	– Age-related macular degeneration

Optic nerve	External / eyelid	Vision (BCVA)
– Glaucoma	– Blepharitis	– Visual acuity 20/30 or better – Visual acuity worse than 20/30 to 20/50 or better – Visual acuity worse than 20/50

Time on therapy

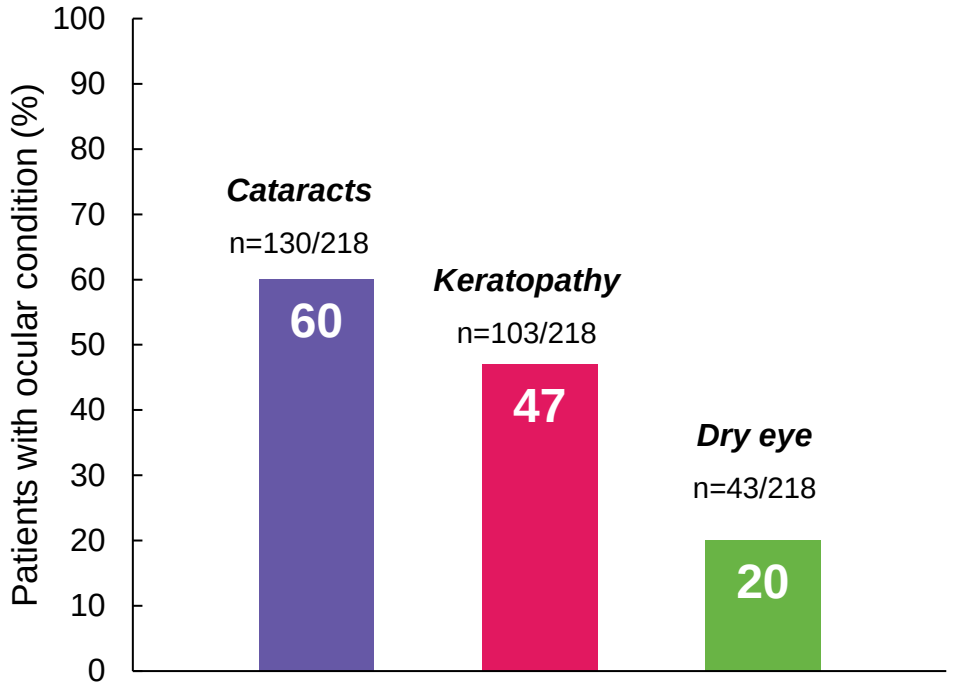
- **Any duration**
- **≤ 3 months**
- **> 3 months**

BCVA, best corrected visual acuity.

90% of patients in DREAMM-2 had baseline ocular conditions

	Baseline ocular conditions and BCVA for DREAMM-2 pooled analysis group (N=218)			
		Present	**Absent**	**Missing**
	Any of the below ocular conditions, n (%)	196 (89.9)	22 (10.1)	0
	Ocular conditions by area of the eye effected, n (%)			
Cornea	– Keratopathy	103 (47.2)	115 (52.8)	0
Cornea	– Dry eye	43 (19.7)	175 (80.3)	0
Lens	– Cataract	130 (59.6)	82 (37.6)	6 (2.8)
Retina	– Age-related macular degeneration	8 (3.6)	49 (22.5)	161 (73.9)
Optic nerve	– Glaucoma	26 (11.9)	192 (88.1)	0
External / eyelid	– Blepharitis	45 (20.6)	169 (77.5)	4 (1.8)
	BCVA, n (%)			
Vision	– 20/30 or better	174 (79.8)	44 (20.2)	0
Vision	– Worse than 20/30 to 20/50 or better	28 (12.8)	190 (87.2)	0
Vision	– Worse than 20/50	16 (7.3)	202 (92.7)	0

- The most commonly reported baseline ocular conditions included cataracts, keratopathy, and dry eye



BCVA, best corrected visual acuity.

Baseline ocular conditions in the cornea appear to have more impact on likelihood of ocular symptoms, specifically blurred vision, compared with those affecting other parts of the eye

		Ocular symptom(s)		
		Any duration of belamaf treatment		
	Baseline ocular condition	Present, n	Absent, n	≥20 percentage point difference in ocular symptoms
Cornea	– Keratopathy	103	115	– Any[a] (52% vs 30%)
Cornea	– Dry eye	43	175	– Any[b] (58% vs 36%) – Blurred vision (44% vs 21%)
Lens	– Cataract	130	82	– Not met
Retina	– Age-related macular degeneration	8	49	– Any[c] (63% vs 29%) – Blurred vision (38% vs 14%) – Diplopia (25% vs 0%)
Optic nerve	– Glaucoma	26	192	– Not met
External / eyelid	– Blepharitis	45	169	– Not met
	BCVA	Present, n	Absent, n	≥20 percentage point difference in ocular symptoms
Vision	– 20/30 or better	174	44	– Not met
Vision	– Worse than 20/30 to 20/50 or better	28	190	– Not met
Vision	– Worse than 20/50	16	202	– Not met

[a] ≥20 percentage point difference mostly driven by blurred vision (35% vs 17%) and dry eye (24% vs 10%). [b] ≥20 percentage point difference mostly driven by blurred vision (44% v 21%) and reduced visual acuity (12% vs 3%). [c] ≥20 percentage point difference mostly driven by blurred vision (38% vs 14%), dry eye (25% vs 12%), and diplopia (25% vs 0%).

BCVA, best corrected visual acuity.

Analysis performed by time on treatment to adjust for drug exposure shows comparable patterns, with more defined differences for corneal- and vision-related baseline ocular conditions

		Ocular symptom(s)					
		≤3 months of belamaf treatment			>3 months of belamaf treatment		
	Baseline ocular condition	Present, n	Absent, n	≥20 percentage point difference in ocular symptoms	Present, n	Absent, n	≥20 percentage point difference in ocular symptoms
Cornea	– Keratopathy	55	68	– Any[a] (36% vs 9%)	48	47	– Blurred vision (56% vs 36%)
Cornea	– Dry eye	20	103	– Not met	23	72	– Any[b] (83% vs 60%) – Blurred vision (65% vs 40%)
Lens	– Cataract	78	42	– Not met	52	40	– Not met
Retina	– Age-related macular degeneration	5	34	– Any[c] (60% vs 12%) – Diplopia (20% vs 0%)	3	15	– Blurred vision (67% vs 33%)
Optic nerve	– Glaucoma	15	108	– Not met	11	84	– Dry eye (9% vs 30%)[d]
External / eyelid	– Blepharitis	24	97	– Not met	21	72	– Not met
	BCVA	Present, n	Absent, n	≥20 percentage point difference in ocular symptoms	Present, n	Absent, n	≥20 percentage point difference in ocular symptoms
Vision	– 20/30 or better	99	24	– Not met	75	20	– Blurred vision (51% vs 30%)
Vision	– Worse than 20/30 to 20/50 or better	15	108	– Not met	13	82	– Any[e] (46% vs 68%)[d]
Vision	– Worse than 20/50	9	114	– Not met	7	88	– Not met

[a] ≥20 percentage point difference mostly driven by blurred vision (16% vs 4%) and dry eye (15% vs 4%). [b] ≥20 percentage point difference mostly driven by blurred vision (65% vs 40%) and photophobia (22% vs 11%). [c] ≥20 percentage point difference mostly driven by blurred vision (20% vs 6%), dry eye (20% vs 6%), and diplopia (20% vs 0%). [d] Presence of condition shows an inverse relationship, but analysis is limited by small number of "present" conditions. [e] ≥20 percentage point difference mostly driven by blurred vision (31% vs 49%) and photophobia (8% vs 15%).

BCVA, best corrected visual acuity.

Conclusions

- Baseline ocular conditions were very common in the DREAMM-2 patient population, with 90% of patients having at least one baseline ocular condition
- Some ocular symptoms were more common in patients with cornea-related baseline ocular conditions, such as keratopathy and dry eye
  - Patients with baseline age-related macular degeneration experienced an increased number of symptoms; however, this may be confounded by the small number of patients
- There was little evidence that baseline ocular conditions not related to the cornea, such as cataracts, glaucoma, or blepharitis, had any effect on treatment-emergent ocular symptoms
- These findings inform risk/benefit decision-making with belamaf and indicate that belamaf can be a treatment option for patients with RRMM despite the presence of baseline ocular conditions

RRMM, relapsed or refractory multiple myeloma.

Disclosures and Acknowledgments

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