Corneal Epithelial Findings in Patients with Multiple Myeloma Treated with Antibody-Drug Conjugate Belantamab Mafodotin in the Pivotal, Randomized, Phase II, DREAMM-2 Study

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The infographic represents the opinions of the authors. For a full list of declarations, including funding and author disclosure statements, please see the full text online.

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Background

Belantamab mafodotin (belamaf; BLENREP) is a first-in-class ADC targeting BCMA on multiple myeloma cells[1–3]

Single-agent belamaf has shown clinically meaningful anti-myeloma activity in patients with heavily pretreated RRMM who typically have a poor prognosis[1–6]

In patients receiving belamaf, microcyst-like epithelial changes (MECs), with or without symptoms, were common, which is a novel AE for hematologist/oncologists to manage in patients with RRMM[1–3]

Aim

To better characterize the MECs observed in patients receiving belamaf and provide eye care professionals with guidance on how to report these events to the treating hematologist/oncologist

1. MECs and corneal events in the long-term follow-up of DREAMM-2 (NCT03525678)

72% experienced MECs

25% had blurred vision

15% had subjective dry eye

18% experienced a clinically meaningful change in BCVA (20/50 or worse)

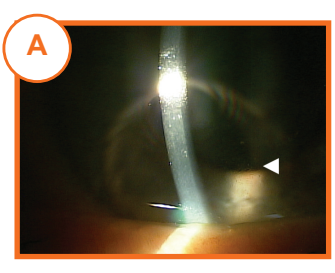
47% had dose delays and **25%** had dose reductions, but only **3%** discontinued due to MECs or other corneal events

77% recovered from the first MEC event

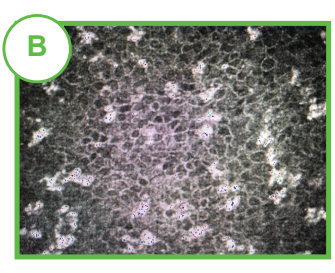
82% recovered as of the last follow-up

There have been no reports of permanent vision loss to date

2. MEC images



MECs were described as small, bilateral, diffuse lesions observed on slit lamp microscopy in the corneal periphery and mid-periphery (**Figure A**, arrowhead). In some patients, centrally-located MECs tended to correlate with blurred vision compared with mid-peripheral changes.



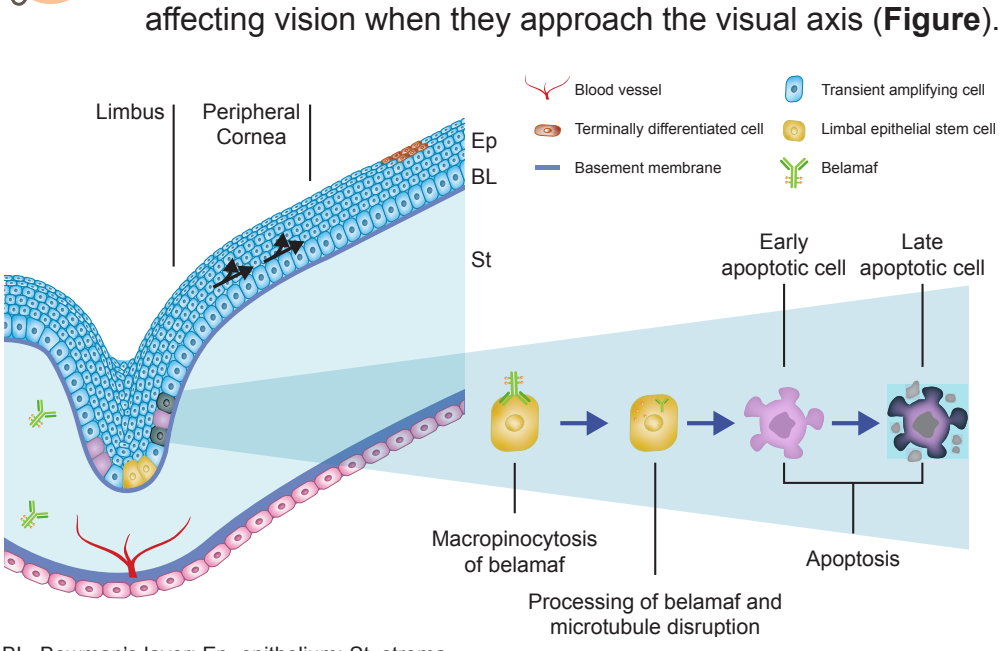
MECs appeared as hyperreflective deposits, rather than microcyst-like lesions, on in vivo confocal microscopy (**Figure B**).

3. Proposed mechanism of belamaf-associated MECs

A literature review revealed that similar MECs are reported with other MMAF-containing ADCs[7,8]

ADC payload (MMAF or other) may contribute to the cytotoxic effects on corneal epithelial cells[7–10]

Belamaf may enter the cornea and become internalized by basal corneal epithelial cells; before these cells undergo apoptosis they may migrate centrally and anteriorly, potentially affecting vision when they approach the visual axis (**Figure**).



BL, Bowman's layer; Ep, epithelium; St, stroma

4. Diagnosis, monitoring, and management of belamaf-associated MECs

Conduct eye examinations (visual acuity and slit lamp microscopy) at baseline, prior to each treatment cycle, and promptly for worsening symptoms.

The treating hematologist/oncologist should determine the recommended dose modification of belamaf based on the most severe finding in the worst affected eye per KVA scale (**Figure**).

Advise patients to use preservative-free lubricant eye drops at least 4 times a day throughout treatment and to avoid use of contact lenses unless directed by an eye care professional. Ophthalmic steroids have not been demonstrated to be beneficial for reducing the incidence of MECs and symptoms.

Patients should also be advised to exercise caution when driving and operating machinery.

Figure. Recommended belamaf dose modifications (per US label[11]) based on eye examination findings per the KVA scale

Grade	Corneal Adverse Reaction*	Recommended Dosage Modifications
1	**Corneal examination finding(s):** Mild superficial keratopathy, documented worsening from baseline, with or without symptoms **Change in BCVA:** Decline from baseline of 1 line on Snellen Visual Acuity	Continue belamaf at current dose.
2	**Corneal examination finding(s):** Moderate superficial keratopathy, with or without patchy microcyst-like deposits, involving the central corneal, sub-epithelial haze (peripheral), or a new peripheral stromal opacity **Change in BCVA:** Decline from baseline of 2 or 3 lines on Snellen Visual Acuity and not worse than 20/200	Withhold belamaf until improvement in both corneal examination findings and change in BCVA to Grade 1 or better and resume at same dose.
3	**Corneal examination finding(s):** Severe superficial keratopathy, with or without diffuse microcyst-like deposits, sub-epithelial haze (central), or a new central stromal opacity **Change in BCVA:** Decline from baseline by more than 3 lines on Snellen Visual Acuity and not worse than 20/200	Withhold belamaf until improvement in both corneal examination findings and change in BCVA to Grade 1 or better and resume at reduced dose.
4	**Corneal examination finding(s):** Corneal epithelial defect, such as corneal ulcers **Change in BCVA:** Snellen Visual Acuity worse than 20/200	Consider permanent discontinuation of belamaf. Based on a benefit:risk assessment, if continuing treatment, withhold belamaf until improvement in both corneal examination findings and change in BCVA to Grade 1 or better and resume at reduced dose.

*For corneal examination findings, the worst grade for each finding is to be used.

Proactive management of corneal changes should minimize the burden of these AEs on the patient, enabling patients to continue with treatment, and allow better anti-myeloma outcomes in patients treated with belamaf.

ADC, antibody-drug conjugate; AE, adverse event; BCVA, best corrected visual acuity; BCMA, B-cell maturation antigen; DREAMM, DRiving Excellence in Approaches to Multiple Myeloma; KVA scale, Keratopathy and Visual Acuity Scale; MECs, microcyst-like epithelial changes; MMAF, monomethyl auristatin F; RRMM, relapsed/refractory multiple myeloma.

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