Recovery of Ocular Events with Longer-term Follow-up in the DREAMM-2 Study of Single-Agent Belantamab Mafodotin (Belamaf) in Patients with Relapsed or Refractory Multiple Myeloma (RRMM)

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Aim:
To report ocular event outcomes for patients receiving belamaf 2.5 mg/kg Q3W from a 13-month follow-up post-hoc analysis of the DREAMM-2 study

**Belamaf**
- Patients with heavily pre-treated RRMM have a poor prognosis (median OS: 6–9 months); novel, well-tolerated treatments that induce lasting responses are warranted\(^1,2\)
- Belamaf (BLENREP) is a first-in-class, BCMA-targeting ADC containing MMAF\(^3\)
- In the open-label, randomized Phase 2 DREAMM-2 study of single-agent belamaf (NCT03525678),\(^4\) patients with heavily pre-treated RRMM* who responded to belamaf maintained deep responses at 13-month follow-up, with a manageable safety profile\(^4\)
  - With belamaf 2.5 mg/kg Q3W, median DoR was 11.0 months, median OS estimate was 13.7 months\(^5\)
- Belamaf 2.5 mg/kg Q3W is approved in the US and EU for the treatment of patients with RRMM\(^6,7\)

**DREAMM-2 ocular events**
In patients receiving belamaf in DREAMM-2\(^4,7\):
- Common ocular events included symptoms such as blurred vision or dry eye, and changes to BCVA\(^5,8\)
- Keratopathy, or corneal MECs (observed on slit lamp microscopy with or without symptoms or changes in BCVA; Figure), are associated with MMAF-containing ADCs and were common in DREAMM-2\(^8,9\)

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\(*\) Refractory to an immunomodulatory agent and a proteasome inhibitor and refractory to/intolerant of an anti-CD38 monoclonal antibody. || ADC, antibody-drug conjugate; AE, adverse events; BCMA, b-cell maturation antigen; BCVA, best-corrected visual acuity; belamaf, belantamab mafodotin; DoR, duration of response; MECs, microcyst-like epithelial changes; MMAF, monomethyl auristatin F; OS, overall survival; Q3W, every 3 weeks; RRMM, relapsed or refractory multiple myeloma.

# Methods

Ocular event identification and management

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<table>
<thead>
<tr>
<th>AEs reported by patients</th>
<th>AEs identified by eye-care professionals</th>
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</thead>
<tbody>
<tr>
<td>• Ocular symptoms including blurred vision and dry eye collected by the hematologist/oncologist</td>
<td>• Patients underwent routine ophthalmic exams Q3W prior to each dose, which included, at minimum, an assessment of the cornea using a slit lamp and measurement of BCVA</td>
</tr>
<tr>
<td>• Events were graded by investigator per CTCAE v4.03</td>
<td>• A change to a BCVA 20/50 or worse (ie, limiting driving ability) in the better-seeing eye (in patients with BCVA better than 20/50 at baseline) was considered one definition of clinically meaningful VA decrease</td>
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**Recovery**

- Recovery was defined as full recovery or return to baseline
- Events were graded by investigator per the protocol-defined KVA scale

**Recovery**

- Recovery was defined as a clinically stable event, ie, KVA scale Grade 1 exam findings/no exam findings, and ≤1-line decline in Snellen VA vs baseline
- Recovery in BCVA was defined as improvement to better than 20/50 (better-seeing eye)

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Ocular events were managed by dose modifications in DREAMM-2

Dose modifications (dose reductions or delays) were based on the severity of eye exam findings and BCVA changes from baseline per KVA scale. Previous analysis has found that dose modifications did not impact efficacy; of 31 patients receiving belalaf 2.5 mg/kg who were on a dose hold >63 days, 88% maintained or deepened their response.1

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AEs, adverse events; BCVA, best-corrected visual acuity; belalaf, belantamab mafodotin; CTCAE, Common Terminology Criteria for Adverse Events; KVA, Keratopathy and Visual Acuity; Q3W, every 3 weeks; RRMM, relapsed or refractory multiple myeloma; VA, visual acuity.


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Results

Keratopathy (MECs), symptoms, BCVA changes, and discontinuations due to ocular AEs in DREAMM-2

<table>
<thead>
<tr>
<th>Event</th>
<th>Count</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Keratopathy (MECs)</td>
<td>68/95 (72%)</td>
<td></td>
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<tr>
<td>Symptoms (e.g., blurred vision, dry eye)</td>
<td>53/95 (56%)</td>
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<tr>
<td>BCVA change to 20/50 or worse</td>
<td>17/95 (18%)</td>
<td></td>
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<tr>
<td>Discontinuation due to corneal AE</td>
<td>3/95 (3%)</td>
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</tbody>
</table>

*Only data from the approved dose of 2.5 mg/kg are presented; †better seeing eye; ‡represents threshold at which activities of daily living may, eg, legal driving, become affected; ¶20/200, the threshold for legal blindness in many countries; ‡CTCAE scale event grading: 1 patient (with a history of cataract surgery in the right eye) developed a central corneal ulcer that resolved 9 days after onset with the use of topical antibiotics.


Belamaf 2.5 mg/kg

n=95

In patients with keratopathy (MECs) events Grade ≥2 per KVA, 48% (29/60) had >1 event

Of these patients, 76% (13/17) had 1 event and 24% (4/17) had 2 events (no patients had >2 events)

1 patient discontinued due to keratopathy (MECs), 1 due to blurred vision, and 1 due to reduced BCVA

1 patient experienced a worsening of BCVA to 20/200 in their better-seeing eye that recovered to baseline

1 patient developed a Grade 4 corneal ulcer

AE, adverse event; BCVA, best-corrected visual acuity; belamaf, belantamab mafodotin; KVA, Keratopathy and Visual Acuity; MECs, microcyst-like epithelial changes.
Results

Recovery* of Grade ≥2 keratopathy (MECs) in DREAMM-2

The majority of patients recovered from their first event while receiving treatment†

FIRST occurrence of keratopathy (MECs) Grade ≥2, belamaf 2.5 mg/kg (60/95 patients)‡

At LAST follow-up: keratopathy (MECs) Grade ≥2, belamaf 2.5 mg/kg (60/95 patients)

*Represents patients with events that recovered either prior to end of treatment or after the end of study treatment; recovery was defined as any Grade 1 exam finding or no exam finding compared with baseline; †Note that these patients may have experienced dose modifications, see Cohen et al, SOHO 2020 Poster No. MM‐250 for further information; ‡Median (range) time to event 37 (19–147) days §Patients in survival follow‐up but have confirmed they are not coming back to site for further corneal exams.

Belamaf, belantamab mafadotin; MECs, microcyst‐like epithelial changes.

Results

Recovery* of changes in BCVA worse than 20/50 in the better-seeing eye† in DREAMM-2

The majority of patients recovered from their first event while receiving treatment‡

FIRST occurrence of change to BCVA worse than 20/50 in the better-seeing eye, belamaf 2.5 mg/kg (17/95 patients)§

14 (82%) recovered*

- 12% (n=2) Not recovered, stopped treatment, follow-up ended
- 6% (n=1) Not recovered, still receiving belamaf treatment
- 59% (n=10) Recovered while receiving treatment
- 24% (n=4) Recovered post-treatment

The majority of patients had recovered at last follow-up

At LAST follow-up: change to BCVA worse than 20/50 in the better-seeing eye, belamaf 2.5 mg/kg (17/95 patients)

14 (82%) recovered*

- 82% (n=14) Recovered
- 6% (n=1) Not recovered, stopped treatment, follow-up ended (died)
- 6% (n=1) Not recovered, stopped treatment, follow-up ended (withdrew)

*Represents patients with events that recovered either prior to end of treatment or after the end of study treatment; recovery was defined as any Grade 1 exam finding or no exam finding compared with baseline; †In patients with better than 20/50 BCVA in their better-seeing eye at baseline; ‡Note that these patients may have experienced dose modifications, see Cohen et al, SOHO 2020 Poster No. MM-250 for further information. §Median (range) time to event 66 (20–442) days.

BCVA, best-corrected visual acuity; belamaf, belantamab mafadotin.

Conclusions

Long-term follow-up in this DREAMM-2 post-hoc analysis demonstrated that although ocular events were common, the majority of patients recovered while remaining on treatment. No new ocular safety signals were observed at 13-month follow-up.

Though keratopathy (MECs) were frequently observed on eye exam (72% of patients), 44% of patients did not experience symptoms such as a clinically meaningful BCVA decline, and treatment discontinuation was rare.

Most patients recovered from the first keratopathy (MECs) event (77%) or from clinically meaningful BCVA decline (82%).

With some patients lost to follow-up, it is not possible to obtain full recovery data for all events.

Implications for managing belamaf-treated patients

The recovery of most ocular events is consistent with the established safety profile of belamaf.

- Events can be asymptomatic so close monitoring by an eye care professional is important.
- Ocular events can be managed by dose modifications, without impacting efficacy.

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