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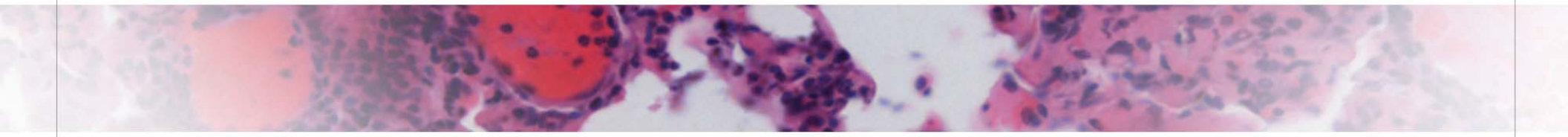

Recovery of Ocular Events with Longer-term Follow-up in the DREAMM-2 Study of Single-Agent Belantamab Mafodotin (Belamaf) in Patients with Relapsed or Refractory Multiple Myeloma (RRMM)

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Background

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]

Figure: Slit-lamp eye exam showing MECs

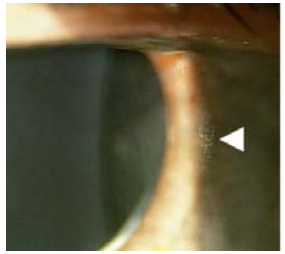


Figure reproduced from Farooq et al. 2020[8] under Creative Commons License

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

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

1. Gandhi UH, et al. *Leukemia.* 2019;33:2266–75; **2.** Chari A, et al. *N Engl J Med.* 2019;381:727–38; **3**. Tai Y-T, et al. *Blood*. 2014; 123:3128; **4.** Lonial S, et al. ASCO 2020, Poster 436; **5**. Lonial S, et al. *Lancet Oncol.* 2020;21:207–21; **6**. BLENREP PI: GlaxoSmithKline plc; 2020; **7.** BLENREP 100 mg powder SmPC: GlaxoSmithKline plc; 2020; **8.** Farooq AV, et al. *Ophthal Ther*. 2020; https://doi.org/10.1007/s40123-020-00280-8; **9.** Eaton JS, et al. J *Ocul Pharmacol Ther*. 2015;31:589–604.

Methods

Ocular event identification and management

Ocular events

AEs reported by patients

- Ocular symptoms including blurred vision and dry eye collected by the hematologist/oncologist
- Events were graded by investigator per CTCAE v4.03

Recovery

- Recovery was defined as full recovery or return to baseline

AEs identified by eye-care professionals

- 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
- *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*
- 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)

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

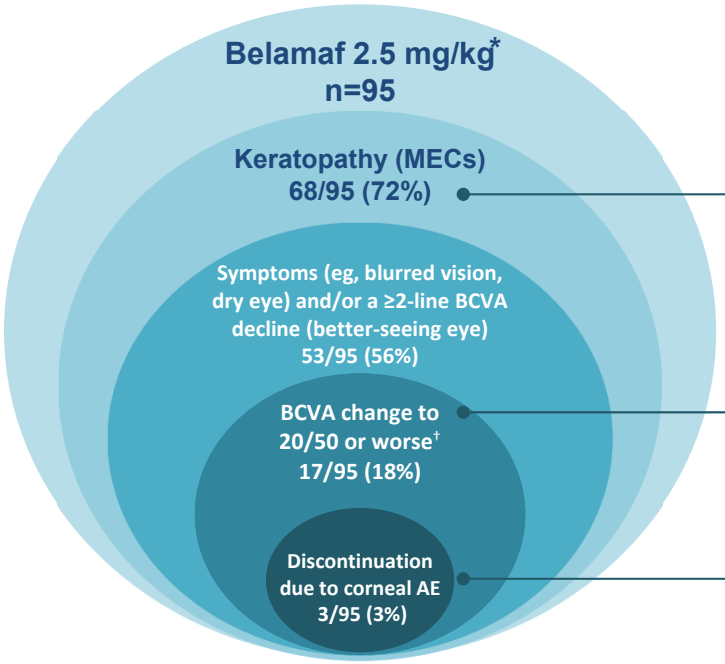
Previous analysis has found that dose modifications did not impact efficacy; of 31 patients receiving belamaf 2.5 mg/kg who were on a dose hold >63 days, 88% maintained or deepened their response[1]

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

1. Cohen et al, SOHO 2020 Poster No. MM-250.

Results

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



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¶

*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[1]; ‡20/200, the threshold for legal blindness in many countries[1]; ¶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

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

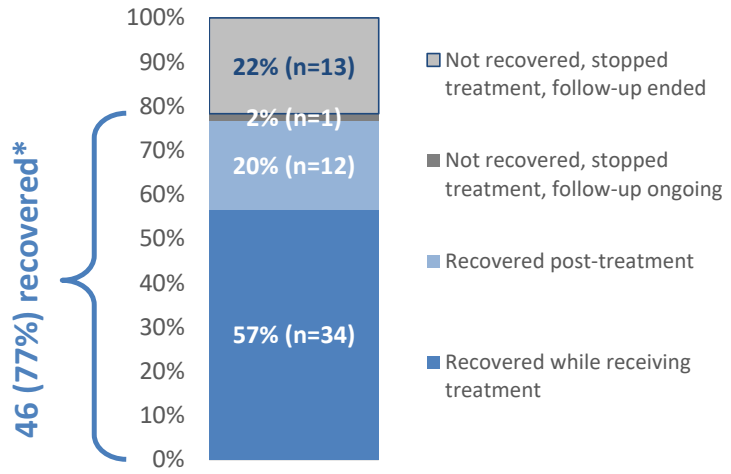
Data on File. Study 205678. GSK Study Register. Available at: https://www.gsk-studyregister.com. 1. Bron AM, et al. *Clin Ophthalmol*. 2010;4:1361–9.7

Results

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

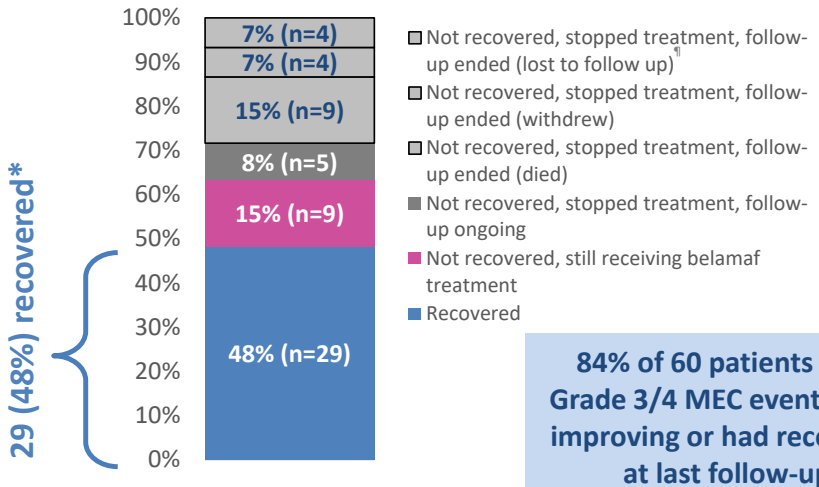
The majority of patients recovered from their first event while receiving treatment†

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



Among the 31 patients who did not recover from their last event, 9 patients are still receiving treatment, 5 are in follow-up, and 17 did not complete follow-up

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



84% of 60 patients with Grade 3/4 MEC events were improving or had recovered at last follow-up

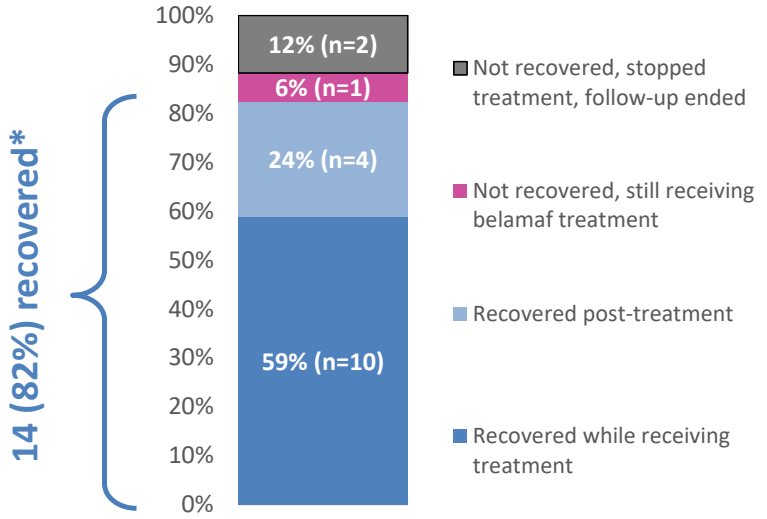
*Represents patients with events that recovered either prior to end of treatment or after the end of study treatment; recovery was defined as any Grade 1 exam finding or no exam finding compared with baseline; †Note that these patients may have experienced dose modifications, see Cohen et al, SOHO 2020 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.
Farooq AV, et al. *Ophthal Ther 2020*; doi.org/10.1007/s40123-020-00280-8.

Results

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

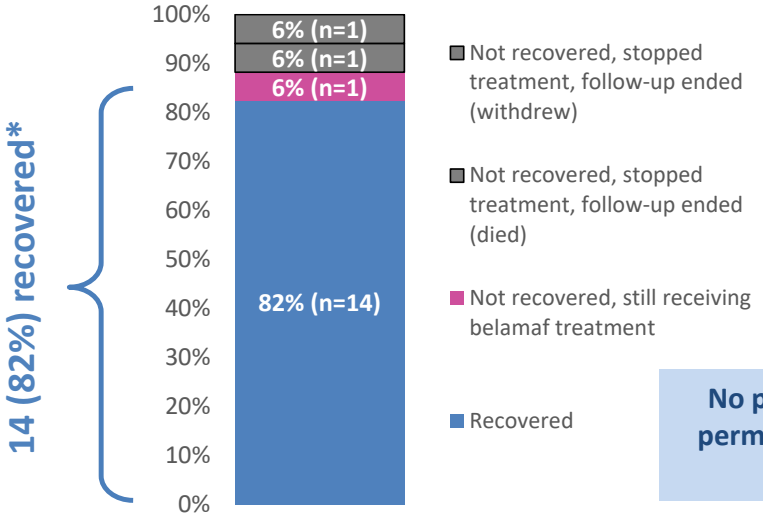
The majority of patients recovered from their first event while receiving treatment‡

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



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)



No patients had permanent vision loss

*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.

Farooq AV, et al. *Ophthal Ther 2020*; doi.org/10.1007/s40123-020-00280-8.

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[1]

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[2-4]

BCVA, best-corrected visual acuity; belamaf, belantamab mafadotin; MECs, microcyst-like epithelial changes.

1. Lonial S, et al. *Lancet Oncol.* 2020;21:207–21; **2**. Cohen AD, et al. SOHO 2020 poster MM-250; **3.** BLENREP PI: GlaxoSmithKline plc; 2020; **4.** BLENREP 100 mg powder SmPC: GlaxoSmithKline plc; 2020.

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