Characterization of ophthalmic examination findings and impact on reading and driving in patients with relapsed/refractory multiple myeloma treated with belantamab mafodotin

Despite experiencing ocular events, most patients receiving belamaf-containing regimens did not have a clinically meaningful change in visual acuity and were able to continue their daily activities

Digital poster

Poster recording

Roman Hájek,[1] Meletios A. Dimopoulos,[2,3] Vania Hungria,[4] Paweł Robak,[5] Marek Hus,[6] Kihyun Kim,[7] Vera Zherebtsova,[8] Sergey Voloshin,[9] Esther Gonzalez Garcia,[10] Hanlon Sia,[11] Chang-Ki Min,[12] Marcelo Pitombeira de Lacerda,[13] Anna Sureda Balarí,[14] Ivan Spicka,[15] Sosana Delimpasi,[16] Christopher Ward,[17] P. Joy Ho,[18] Ana Carolina de Almeida,[19] Sebastian Grosicki,[20] Eric Lewis,[21] Julie Byrne,[22] Benga Kazeem,[23] Ianire Garrobo-Calleja,[24] Elisabet E. Manasanch,[22] Hena Baig,[25] Nick Pirooz,[22] Sybil Varghese,[22] Lydia Eccersley,[24] Joe Lee,[24] Meral Beksac,[26] Ludek Pour[27]

[1]Department of Hematooncology, University Hospital Ostrava, Ostrava and Department of Hematooncology, University of Ostrava, Ostrava, Czech Republic; [2]Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [3]Korea University, Seoul, Republic of Korea; [4]Clínica São Germano, São Paulo, Brazil; [5]Medical University of Łódź, Łódź, Poland; [6]Medical University of Lublin, Lublin, Poland; [7]Sungkyunkwan University, Samsung Medical Center, Seoul, Republic of Korea; [8]Gorodskaya Klinicheskaya Bol'nitsa Im. S.p. Botkina, Moscow, Russia; [9]Leningrad Regional Clinical Hospital, Saint Petersburg, Russia; [10]Hospital Universitario de Cabuerles, Gijón, Spain; [11]Pindara Private Hospital, Gold Coast, QLD, Australia; [12]Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Republic of Korea; [13]Universidade da Região de Joinville and Centro de Hematologia e Oncologia, Joinville, Santa Catarina, Brazil; [14]Institut Català d'Oncologia-L'Hospitalet, Institut de Ciències Biomèdiques de Bellvitge (IDIBELL), Universitat de Barcelona, Barcelona, Spain; [15]First Faculty of Medicine, Charles University and General Hospital, Prague, Czech Republic; [16]General Hospital Evangelismos, Athens, Greece; [17]The Royal North Shore Hospital, Sydney, NSW, Australia; [18]Royal Prince Alfred Hospital and University of Sydney, Camperdown, NSW, Australia; [19]Centro de Pesquisa e Ensino em Saúde de Santa Catarin, Florianópolis, Brazil; [20]Medical University of Silesia, Katowice, Poland; [21]GSK, Research Triangle Park, NC, USA; [22]GSK, Collegeville, PA, USA; [23]GSK, Stevenage, UK; [24]GSK, London, UK; [25]GSK, Mississauga, ON, Canada; [26]Liv Hospital Ankara, Istinye University, Ankara, Turkey; [27]Hematology and Oncology, University Hospital Brno, Brno, Czech Republic

Background

- In the phase 3, randomized DREAMM-7 and DREAMM-8 trials, belamaf plus standard therapies demonstrated significant PFS benefit in patients with RRMM after ≥1 line of therapy; significant OS benefit was observed in DREAMM-7[1-3]
- In DREAMM-7 and DREAMM-8, in patients treated with belamaf-based regimens, eye-related side effects were managed and reversed with appropriate dose modifications and follow-up; efficacy was maintained in these patients despite extended dose delays[1,2]
- Ocular events with belamaf, including ophthalmic examination findings (OEFs) and ocular adverse reactions (ARs), are due to off-target uptake of the ADC and intracellular release of the MMAF payload, which causes apoptosis of corneal epithelial cells[4]
- **Aim:** A post hoc analysis to better characterize the profile of ocular events and their impact on reading and driving in patients receiving belamaf-based regimens in DREAMM-7 (data cutoff: October 2, 2023) and DREAMM-8 (January 29, 2024)

Methods

- DREAMM-7 (NCT04246047) compared BVd vs DVd and DREAMM-8 (NCT04484623) compared BPd vs PVd[1,2]
- OEFs, graded per the KVA scale, comprised 2 components:
  (1) Corneal examination findings (CEFs) by slit lamp examination
  (2) Changes in BCVA measured by Snellen or equivalent assessments (**Table 1**)
- Grade ≥2 OEFs required protocol-recommended belamaf dose modifications; a grade ≥2 OEF may have included CEFs and/or BCVA changes
  - Dose modifications: dose delays until resolution (either OEF component [DREAMM-7] or both OEF components [DREAMM-8] decreasing to grade ≤1) and dose reductions
- Ocular ARs were reported in the eCRF and graded per CTCAE version 5.0
- Grade ≥2 OEFs and ocular ARs were assessed in patients with normal baseline BCVA (20/25 or better in ≥1 eye) who had either of the following at some point on treatment (until data cutoff):
  - No bilateral BCVA change to ≥20/50 (ie, no clinically meaningful change in visual acuity)
  - Bilateral BCVA change from ≥20/50 to <20/200 (ie, clinically meaningful change in visual acuity). Patients with >20/200 were excluded from the analysis due to small patient numbers
- The duration of the first 5 occurrences of grade ≥2 OEFs, as applicable, were assessed
- The ability of patients to perform daily activities (reading and driving) was also reported by an eye care professional at the time of the ocular examination
- We further investigated the impact of dose delays due to AEs, including ocular events, on treatment responses
- Descriptive statistics were used to summarize results

Table 1. **Grading of OEFs**

OEF graded per KVA[a,b]	Grade 1	Grade 2	Grade 3	Grade 4
Corneal examination finding (slit lamp examination)	Mild superficial punctate keratopathy (documented worsening from baseline, with or without symptoms)	Any or a combination of: • Moderate superficial punctate keratopathy • Patchy microcyst-like deposits • Peripheral subepithelial haze • New peripheral stromal opacity	Any or a combination of: • Severe superficial punctate keratopathy • Diffuse microcyst-like deposits • Central subepithelial haze • New central stromal opacity	Corneal epithelial defect such as corneal erosion(s) or corneal ulcers[c]
Change in BCVA[d] (Snellen or equivalent assessment)	Decline from baseline of 1 line on Snellen Visual Acuity	Decline from baseline of 2 or 3 lines (and Snellen Visual Acuity not worse than 20/200)	Decline from baseline of >3 lines (and Snellen Visual Acuity not worse than 20/200)	Snellen Visual Acuity worse than 20/200

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AE, adverse event; BCVA, best-corrected visual acuity; KVA, Keratopathy and Visual Acuity; OEF, ophthalmic examination finding.
[a] Examination findings were reported as AEs prior to implementation of the KVA scale. [b] Dose modification should be based on the most severe finding. If eyes differ in severity, the dose modification guideline should be applied based on the more severe eye. [c] Corneal ulcer is defined as an epithelial defect with underlying stromal infiltration. [d] Changes in visual acuity due to treatment-related corneal findings.

Results

OEFs leading to dose modifications were common but transient, with consistent and predictable median duration of occurrences across both DREAMM-7 and DREAMM-8

- Most patients (304 of 348 [87%]) across DREAMM-7 and DREAMM-8 with normal baseline BCVA had ≥1 grade ≥2 OEF
- Recurrences of OEFs were common, with or without clinically meaningful vision changes. In patients with multiple occurrences, the median duration of each occurrence was consistent and predictable across groups, ranging from 12 to 13 weeks in patients with no bilateral BCVA change to ≥20/50 and 11 to 16 weeks in patients with BCVA changes from ≥20/50 to <20/200
- In belamaf-treated patients in DREAMM-7 and DREAMM-8, 995 of 1192 (83%) grade ≥2 OEF occurrences had resolved. Ocular occurrences that had not resolved at the data cutoff were mainly in patients who were still on treatment or in follow-up (12%) or those who died or withdrew consent before resolution could be documented (5%)

Summary of BCVA changes and symptoms

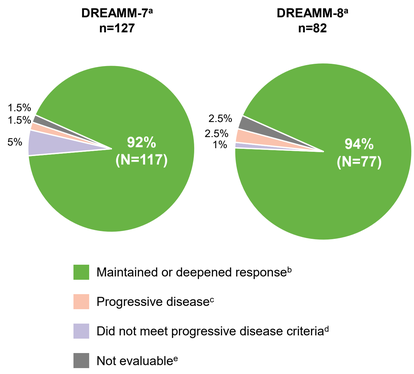
- Of the 392 patients treated with belamaf-containing regimens across DREAMM-7 (N=242) and DREAMM-8 (N=150), 348 (89%) had normal BCVA at baseline; 62% of these patients did not experience a bilateral BCVA change to ≥20/50 (ie, no clinically meaningful change in visual acuity) (**Figure 2**)
- In many cases, grade ≥2 OEFs were accompanied by no symptoms or mild/moderate symptoms without any impact on vision

Reading and driving

- The majority of patients evaluated for reading and driving at the time of their ocular examination did not report having to stop these activities
- Of the patients who reported having to stop reading or driving, this was transient. They had a median of 1 occurrence (IQR: 1.0-3.0 [reading]; 1.0-2.0 [driving]) and this comprised ≈10% to 12% of their median time on treatment
- Almost all returned to normal baseline reading (56/58; 97%) and driving (46/50; 92%)

The majority of patients, 92% and 94% in DREAMM-7 and DREAMM-8, respectively, maintained or deepened their response during their first extended dose delay (Figure 1)

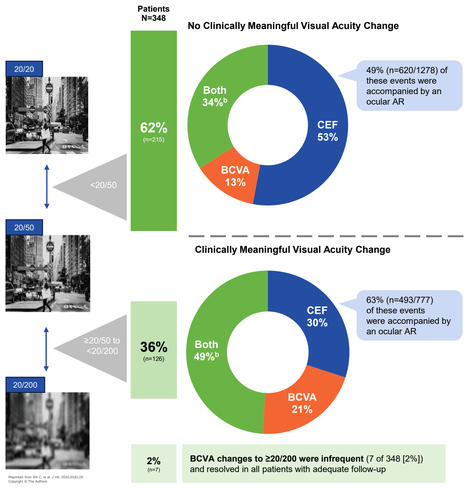
Figure 1. **Last Assessed Response During First Extended Belamaf Dose Delay of >9 weeks**



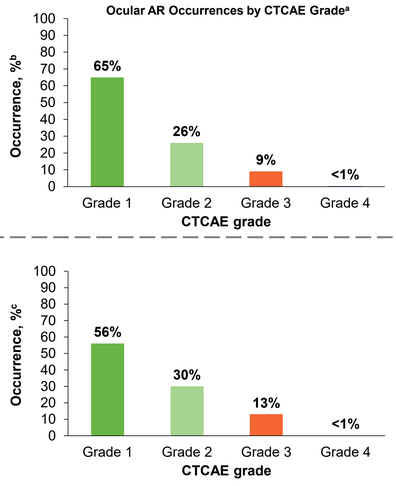
belamaf, belantamab mafodotin; CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response. [a] Percentages were rounded so the total adds up to 100%. [b] Response category was maintained or deepened; patients in a CR/sCR response category maintained a response of ≥VGPR. [c] Developed progressive disease. [d] Defined as patients who moved from a higher response category to a PR. [e] Not evaluable as the response assessment was not available or incomplete.

Figure 2. **Bilateral BCVA Change and Composite of Grade ≥2 Components of OEFs[a]**

A. Grade ≥2 OEFs frequently comprised corneal examination findings (CEFs) alone, without changes in BCVA



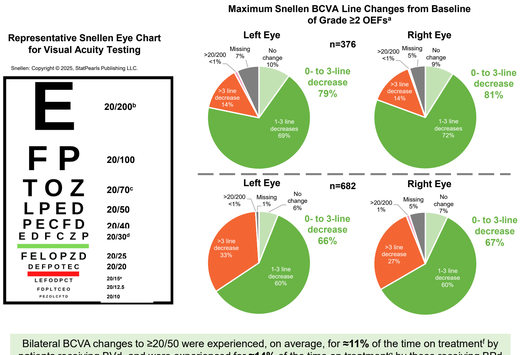
C. Regardless of BCVA change, most ocular ARs were mild/moderate (CTCAE grading)



AR, adverse reaction; BCVA, best-corrected visual acuity; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; BVd, belantamab mafodotin, bortezomib, and dexamethasone; OEF, ophthalmic examination finding.
[a] Post hoc pooled analysis (BVd and BPd) in patients with normal baseline BCVA (20/25 or better in ≥1 eye). [b] Percentage has been rounded so that the total adds up to 100% in the graph.

AR, adverse reaction; BCVA, best-corrected visual acuity; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; BVd, belantamab mafodotin, bortezomib, and dexamethasone; CTCAE, Common Terminology Criteria for Adverse Events.
[a] Post hoc pooled analysis (BVd and BPd) in patients with normal baseline BCVA (20/25 or better in ≥1 eye). No grade 5 ocular ARs occurred. [b] Percentages are based on 1672 total occurrences. [c] Percentages are based on 2294 total occurrences.

B. Most grade ≥2 OEFs that included BCVA changes were accompanied by 0-3 Snellen line decreases, which for a patient with baseline 20/20 vision is no more than 20/40



Bilateral BCVA changes to ≥20/50 were experienced, on average, for **≈11%** of the time on treatment[f] by patients receiving BVd, and were experienced for **≈14%** of the time on treatment[g] by those receiving BPd

BCVA, best-corrected visual acuity; belamaf, belantamab mafodotin; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; BVd, belantamab mafodotin, bortezomib, and dexamethasone; OEF, ophthalmic examination finding.
[a] Post hoc pooled analysis (BVd and BPd) in patients with normal baseline BCVA (20/25 or better in ≥1 eye). Percentages may not add up to 100% due to rounding. [b] Snellen assessment used in DREAMM-7 and DREAMM-8 included worse than 20/160, 20/150, or 20/160, and 20/125. [c] Included 20/70 or 20/80 and 20/60 or 20/63. [d] Included 20/30 or 20/32. [e] Included 20/15 to 20/16. [f] In DREAMM-7: Time on belamaf treatment was (last dose + 21) – first dose + 1. [g] In DREAMM-8: Time on belamaf treatment was (last dose + 28) – first dose + 1.

Conclusions

- OEFs leading to dose modifications were common but transient, with consistent and predictable median duration of occurrences across both DREAMM-7 and DREAMM-8
- While dose modifications, including dose delays, were common, the vast majority of patients (92%-94%) maintained or deepened their responses during their first extended dose delay
- Of patients with normal BCVA at baseline who received belamaf-containing regimens in DREAMM-7 and DREAMM-8, almost two-thirds did not experience a clinically meaningful change in visual acuity
  - Clinically meaningful visual acuity changes were transient and generally reversible with appropriate dose modifications and follow-up
- Grade ≥2 OEFs were often accompanied by no symptoms or mild/moderate symptoms without any impact on vision
- Regardless of BCVA change, most ocular ARs were mild/moderate
- Overall, patients were able to continue reading and driving, and discontinuation rates due to ocular events were low, as previously reported[1,2]

Abbreviations

ADC, antibody-drug conjugate; AE, adverse event; AR, adverse reaction; BCVA, best-corrected visual acuity; belamaf, belantamab mafodotin; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; BVd, belantamab mafodotin, bortezomib, and dexamethasone; CEF, corneal examination finding; CTCAE, Common Terminology Criteria for Adverse Events; DVd, daratumumab, bortezomib, and dexamethasone; eCRF, electronic case report form; KVA, Keratopathy and Visual Acuity; MMAF, Monomethyl auristatin F; OEF, ophthalmic examination finding; OS, overall survival; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone; RRMM, relapsed/refractory multiple myeloma.

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