

Ocular Health of Patients with Relapsed/Refractory Multiple Myeloma (RRMM): Baseline Data from the DREAMM-2 Trial of Belantamab Mafodotin (Belamaf)

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Introduction: The treatment paradigm for RRMM is characterized by continuous treatment to suppress the malignant plasma cell clone. Some treatments may affect the eye, leading to a broad spectrum of ocular disorders, from dry eye to glaucoma, causing impaired quality of life. Therefore, we examined the baseline eye health of patients with RRMM receiving single-agent belamaf in the DREAMM-2 study (NCT03525678) and compared the findings to those of age-matched individuals in the general population. A better understanding of baseline ocular status is important as patients may have existing, undiagnosed eye conditions that may affect future treatment options.

Methods: DREAMM-2 investigated belamaf, a B-cell maturation antigen–targeted antibody–drug conjugate in patients with RRMM. Eligible patients had received ≥ 3 prior therapies and were refractory to an immunomodulatory agent, a proteasome inhibitor, and refractory and/or intolerant to an anti-CD38 monoclonal antibody. Prior to receiving belamaf, patients underwent systematic ocular history collection and eye examination and completed the eye-specific National Eye Institute Visual Function Questionnaire 25 (NEI-VFQ-25). We report pretreatment eye-related findings to describe the baseline ocular status of patients with RRMM in DREAMM-2

Results: Of 221 patients enrolled, 100 (45%) were female and 121 (55%) were male, with a median age (range) of 66 years (34–89), median time from diagnosis of 5.4 years (1.1–12.1), and median 6 (3–21) prior lines of therapy; 98% patients had received bortezomib. Previous ocular history reported by patients were cataract (60%), intraocular surgery and/or laser treatment (35%), dry eye (20%), and glaucoma (6%), and history of ocular disease requiring medical treatment (12%). On examination, the mean best corrected visual acuity (BCVA) Snellen score was worse than 20/50 in one or both eyes in 20 and 4 of 218 patients with data, respectively. Blepharitis (anterior) was

evident in approximately 20% and the corneal epithelium was abnormal (mainly mild-grade keratopathy) in 43% of patients. Impaired tear film production was reported with meibomian gland dysfunction (MGD) in 33% of patients, and evidence of dry eye (Schirmer's test, median 8.2 mm [normal ≥ 15 mm] in the worse eye. Median worse-eye tear break up time was 8.6 sec [normal > 10 sec]). Slit-lamp examination revealed a cataract in approximately 50% of patients. Ten (8%) patients had evidence of prior cataract surgery with an implanted lens (pseudophakia). Dilated funduscopy identified an abnormal optic nerve in 10% of patients in either eye; of these, glaucomatous cupping was noted in 43% (right eye) to 50% (left eye) of patients. Median (range) overall composite vision score by NEI-VFQ-25 was 95.3 (28–100).

Conclusions: There was a 60% prevalence of cataract in the study cohort and an increased prevalence of glaucoma (6% vs expected 3% in patients > 65 years old; Kreft et.al. *BMC Public Health* 2019) in RRMM patients treated in the DREAMM-2 study. Both conditions can be associated with corticosteroids, often used in MM treatments, although cataract is also an age-related phenomenon. We noted a significant number of patients with blepharitis (anterior), dry eye, and MGD, which may be associated with prior bortezomib treatment. Forty-three percent of patients had an abnormal corneal epithelium at baseline, which may be related to dry eye. This is relevant as belamaf is associated with keratopathy (microcyst-like epithelial changes visible on slit-lamp examination, with or without symptoms). Overall NEI-VFQ-25 scores were comparable to those reported in patients > 65 years old (Nickels et al. *Health Qual Life Outcomes* 2017).

Patients with RRMM may have a number of baseline ocular abnormalities suggesting a need for regular ophthalmic examinations in this vulnerable population to identify and manage underlying conditions and treatment-related complications. Specifically, attention should be paid to patients who may have ocular conditions associated with prior treatment with corticosteroids or bortezomib. The optimization of ocular health in this population is particularly relevant given that emerging RRMM therapies such as belamaf are associated with significant ocular side effects