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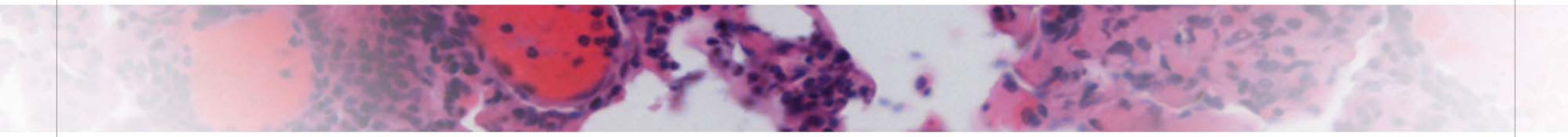

DREAMM-2: Single-Agent Belantamab Mafodotin (Belamaf) Effects on Patient-Reported Outcome (PRO) Measures in Patients with Relapsed/Refractory Multiple Myeloma (RRMM)

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Background

Aims:
To understand the impact of single-agent belantamab mafodotin (belamaf; BLENREP) at 2.5 mg/kg Q3W (the approved dose) on disease and treatment-related symptoms, functioning, and HRQoL in the DREAMM-2 study

In the heavily pre-treated RRMM patient population, extending survival while maintaining HRQoL is an important treatment goal[1]

Typically these patients have poor HRQoL; maintenance of, rather than improvement in, HRQoL has been reported as a benefit of commonly used treatments[1]

Belamaf is a first-in-class BCMA-binding, humanized, afucosylated, monoclonal MMAF-containing ADC with a multi-modal MoA[2,3]

In the pivotal DREAMM-2 study (NCT03525678), single-agent belamaf demonstrated deep and durable responses in patients with heavily pre-treated RRMM, and had a manageable safety profile[4,5]

Corneal events are commonly reported with MMAF-containing ADCs, such as belamaf[6]

In DREAMM-2, corneal events including keratopathy (MECs, an eye examination finding with/without symptoms), change in BCVA, or symptoms (blurred vision and dry eye) were the most common AEs reported during belamaf treatment[5,6]

MECs led to dose delays in 47% of patients in the 2.5 mg/kg arm, however most events improved, and dose delays did not impact efficacy[7]

DREAMM-2 included PROs to assess HRQoL and ocular symptoms and vision-related function

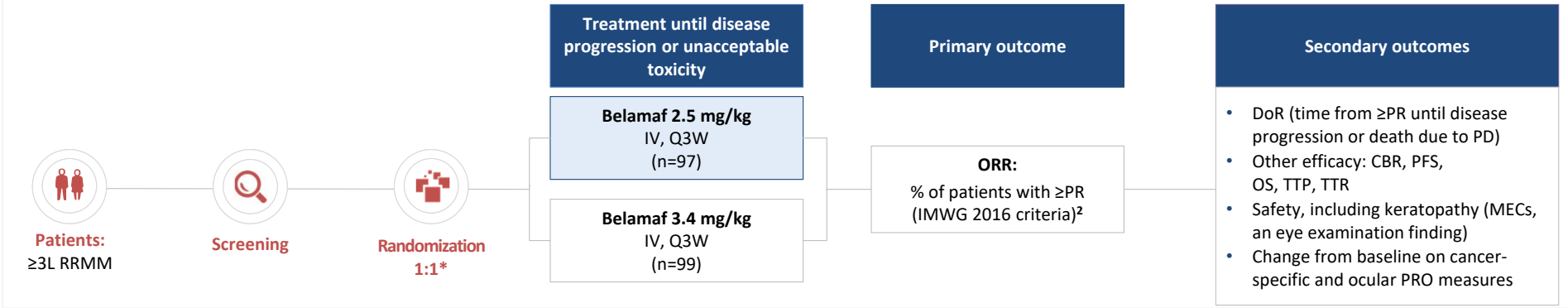
ADC, antibody-drug conjugate; ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent phagocytosis; AE, adverse event; BCMA, B-cell maturation antigen; BVCA, best-corrected visual acuity; HRQoL, health-related quality of life; ICD, immunogenic cell death; MECs, microcyst-like epithelial changes; MM, multiple myeloma; MMAF, monomethyl auristatin F; MoA, mechanism of action; PRO, patient-reported outcome; Q3W, every 3 weeks; RRMM, relapsed/refractory multiple myeloma.

1. Song KW, et al. *Haematologica.* 2015;100:e63–e67. **2**. Tai YT, et al. *Blood* 2014;123:3128–38. **3.** Tai YT, Anderson KC. *Immunotherapy* 2015;7:1187. 4. Lonial S, et al. *Lancet Oncol* 2020;21:207–21. **5**. Lonial S, et al. Poster 436 Presented at ASCO (Virtual) Meeting; May 29–31, 2020. **6**. Farooq AV, et al. *Ophthal Ther* 2020 https://doi.org/10.1007/s40123-020-00280-8. **7**. Cohen AD, et al. SOHO 2020 Poster MM-250

Methods

DREAMM-2 study design[1]

PROs are included as secondary outcomes in the ongoing DREAMM-2 study of single-agent belamaf



Eligibility Criteria

- Measurable disease†
- ECOG PS of 0–2
- ≥3 prior lines of therapy
- Refractory to immunomodulatory agents and PIs, and refractory and/or intolerant to an anti-CD38 mAb
- Not exposed to a prior BCMA-targeted therapy
- Prior ASCT allowed; allogeneic stem cell transplant excluded

*Patients stratified based on number of previous lines of therapy (≤4 vs. >4) and presence or absence of HR cytogenetic features; †defined as serum myeloma protein (M-protein) ≥0.5 g/dL; urine M-protein ≥200 mg/24 h; serum FLC assay: involved FLC level ≥10 mg/dL and an abnormal serum FLC ratio (<0.26 or >1.65).

3L, third line; ASCT, autologous stem cell transplant; CBR, clinical benefit rate; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FLC, serum free light chain assay; MEC, microcyst-like epithelial change; PD, progressive disease; PIs, proteasome inhibitors; PRO, patient-reported outcome; TTP, time to progression; TTR, time to response.

1. Lonial S, et al. *Lancet Oncol* 2020;21:207–21. **2**. Kumar S et al. *Lancet Oncol*. 2016;17:e328–46.

Methods

Collection of PROs in DREAMM-2

- Data on cancer- and treatment-related symptoms and impacts were collected as shown in the table[1,2]
- Patients used a tablet to complete PRO surveys electronically, ahead of clinical discussions at study visits[1]
- Group-level mean changes were evaluated over the course of the study[1]
- For EORTC-CLC-C30 and EORTC-MY20, we evaluated within-patient change across cancer-specific measures based on a **10-point** threshold for improvement[3]
- For OSDI, within-patient changes in vision-related function were based on thresholds of **≥12.5**[2] **and 16.67 points***

Collection of HRQoL and MM-related symptom data in DREAMM-2[1,2]

Instrument	Domains/purpose	Schedule
Global HRQoL measures		
EORTC-QLQ-C30	Multiple symptom and functioning domains, including pain, fatigue, and overall health status/QoL	Baseline and every 6 weeks
Disease symptom measures		
EORTC-QLQ-MY20	Disease symptoms, future perspective, body image, side effects	Baseline and every 6 weeks
Vision-related measures		
OSDI	Ocular symptoms, vision-related function, and environmental triggers related to dry eye	Baseline and every 3 weeks
NEI-VFQ-25	Ocular-related QoL and functioning	

*Threshold for OSDI based on an analysis that used recommended methods for establishing clinically meaningful change thresholds for ocular PROs that measure treatment-related corneal events in patients with RRMM receiving belamaf.
EORTC-QLQ, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (C30, core 30; MY20, Myeloma 20); HRQoL, health-related quality of life; MM, multiple myeloma; NEI-VFQ-25, National Eye Institute Visual Function Questionnaire-25 item; OSDI, Ocular Surface Disease Index; PRO, patient-reported outcome; QoL, quality of life.

1. Popat R, et al. EHA 2020; Poster EP1746. **2**. Eliason L et al, ISPOR EU 2020, poster PCN309. **3**. Osoba, D, et al. *J Clin Oncol.* 1998;16:139–44.

Results

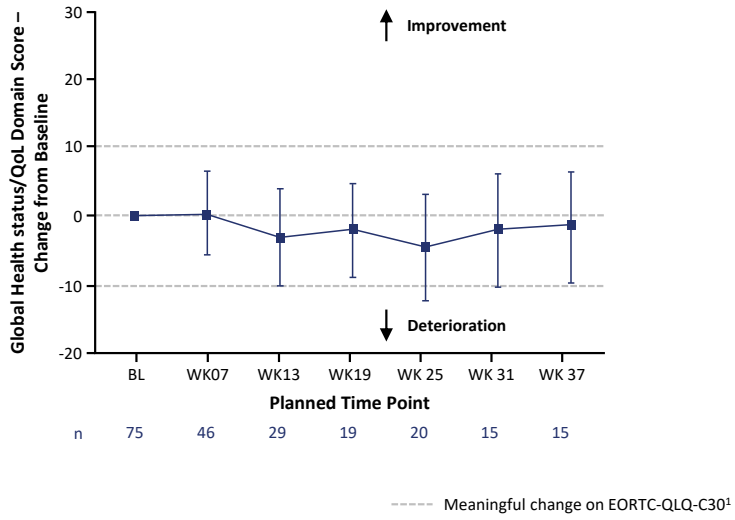
Global and MM-related HRQoL: EORTC-QLQ-C30 and EORTC-QLQ-MY20

Global health status/QoL remained relatively stable over time

>25% of patients had meaningful within-patient improvements in physical functioning and disease symptoms by Week 7†

>30% of patients had meaningful within-patient improvements in fatigue at Weeks 19 and 25†

EORTC-QLQ-C30 Global Health Status/QoL[1]*



Patients with ≥10-point improvement[2] from baseline in EORTC-QLQ-C30 and EORTC-QLQ-MY20[1†]

	Week	Patients n/N (%)
EORTC-QLQ-C30 Domain		
Fatigue	7	21/46 (46)
	13	12/29 (41)
	19	6/19 (32)
	25	6/19 (32)
Physical Functioning	7	13/46 (28)
	13	8/29 (28)
	19	3/19 (16)
	25	4/19 (21)
Pain	7	14/46 (30)
	13	9/29 (31)
	19	4/19 (21)
	25	3/19 (16)
EORTC-QLQ-MY20 Domain		
Disease Symptoms (pain in different locations)	7	17/45 (38)
	13	8/28 (29)
	19	5/18 (28)
	25	6/18 (33)

*13-month follow-up; cut-off date January 31, 2020, †6-month follow-up; cut-off date June 21, 2019.

Note that numbers of patients decline over time as fewer patients completed PRO questionnaires at later visits, and these numbers represent the number are calculated among patients still enrolled at the respective time point.

B, baseline; CI, confidence interval; EORTC-QLQ, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (C30, core 30; MY20, Myeloma 20)

1. Popat R, et al. EHA 2020; Poster EP1746. **2**. Osoba, D, et al. *J Clin Oncol*. 1998;16:139–44.

Results

Vision-Related Function: OSDI

49.5% and 44.2% of patients reported a change on the OSDI vision-related function (VRF) sub-scale of 12.5 and 16.67 points, respectively, which is generally in line with eye care professional examination findings

Patient-reported VRF reduction occurred at around the same time as symptom onset and shortly after eye examination findings

A high proportion of patients recovered* from their VRF reduction, similar to outcomes with eye examination findings and symptoms

Median time to improvement from a worst-case score on the OSDI VRF domain was 24 and 45 days with the 12.5 and 16.67 thresholds, respectively

Scale	OSDI		KVA[1]		
Measure	**Patient-reported Visual Function Sub-scale**		**Eye Care Professional Examination Finding**		
	≥12.5-point worsening from baseline (n=95)	**≥16.67-point worsening from baseline (n=95)**	**Keratopathy (MECs) (n=95)**	**BCVA change (n=95)**	**Keratopathy (MECs) + BCVA change (n=95)**
Patients with event, n (%)	47 (49.5)	42 (44.2)	Any Grade: 68 (72) *Grade 1: 8 (8)* *Grade 2: 16 (17)* *Grade 3: 43 (45)* *Grade 4: 1 (1)*	Any Grade: 51 (54) *Grade 1: 7 (7)* *Grade 2: 15 (16)* *Grade 3: 28 (29)* *Grade 4: 1 (1)*	Any Grade: 68 (72) *Grade 1: 7 (7)* *Grade 2: 14 (15)* *Grade 3: 45 (47)* *Grade 4: 2 (2)*
Time to onset of first occurrence, days median (range)	44 (21–231)	60.7 (21–231)	37.0 (19–143)	64.0 (20–213)	36.0 (19–143)
Duration of first event, days median (range)	24[1] (7–350)	45.1 (9–350)	86.5 (8–358)	33.0 (8–127)	96.0 (8–358)
Event outcomes, n/N (%) **Recovered** **Not recovered**	 34/47 (72)[†] 13/47 (28)	 32/42(76)[†] 10/42 (24)	 46/60 (77)[‡] 14/60 (23)	 34/44 (77)[‡] 10/44 (23)	 45/61 (74)[‡] 16/61 (26)

13-month follow-up; cut-off date January 31, 2020. *it is not possible to assess recovery in all cases as some patients remain on treatment/in follow up, and some were lost to follow up, see Poster 3224 at this congress; [†]Recovery defined as ≥12.5-point improvement. [‡]Recovery of keratopathy (MECs) was defined as an event that was deemed clinically stable by the eye care professional. Clinical stability was defined as any grade 1 exam finding (per KVA scale) or no exam finding, and either a one-line decline in vision or no change in vision when compared with baseline; BSLN, baseline; CI, confidence interval; KVA, keratopathy and visual acuity; OSDI, Ocular Surface Disease Index; PRO, patient-reported outcome; VRF, vision-related function.

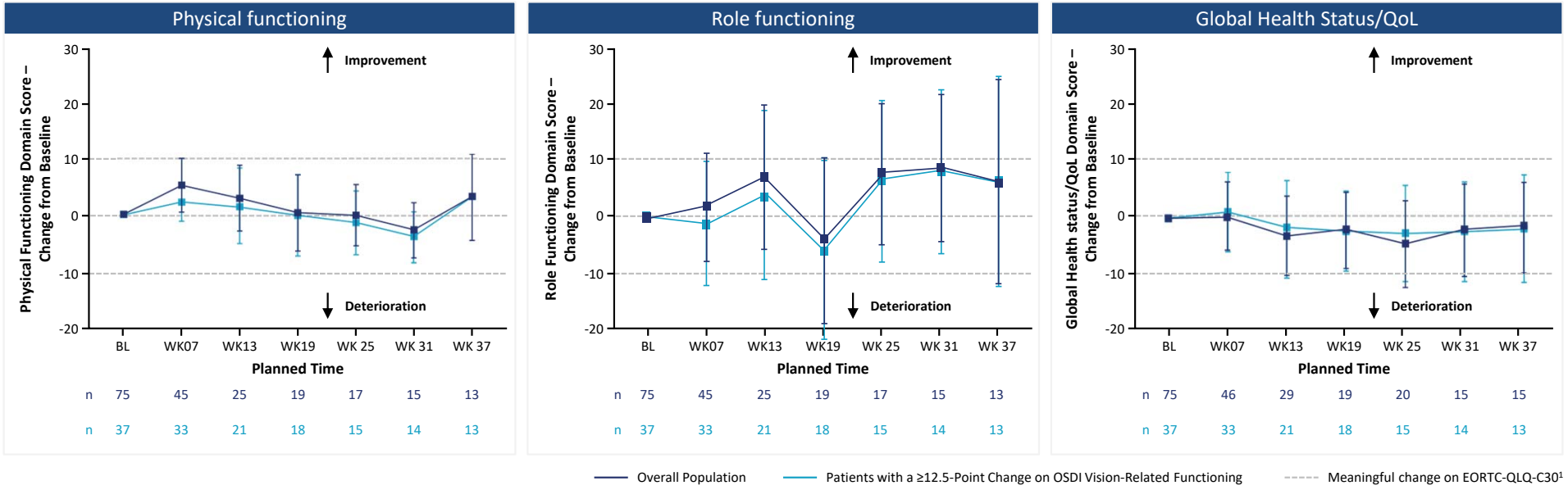
1. Farooq AV, et al. *Ophthalmol Ther* 2020; https://doi.org/10.1007/s40123-020-00280-8.

Results

EORTC-QLQ-C30 changes in patients with reduction in OSDI vision-related function

There was no change in overall patient-reported Global Health Status/QoL, Physical Functioning, or Role Functioning domain scores of the EORTC-QLQ-C30, even among patients with a minimal meaningful within-patient reduction in vision-related function by OSDI

Change from baseline in EORTC-QLQ-C30 scores overall and in patients with ≥12.5-point change in OSDI vision-related function



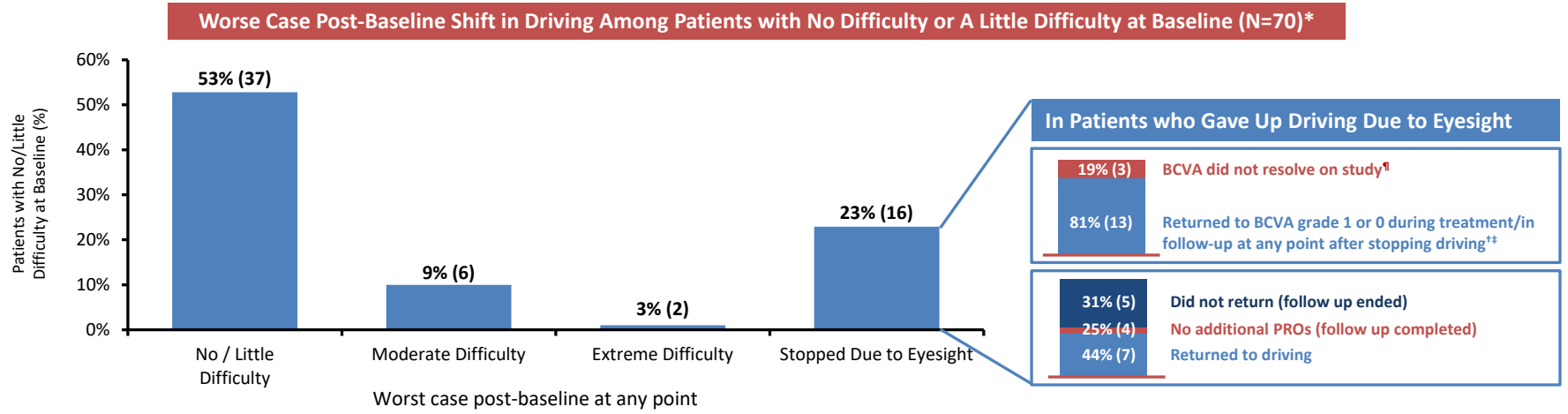
13-month follow-up; cut-off date January 31, 2020.
BL, baseline; EORTC-QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire core 30; GHS, global health status; OSDI, Ocular Surface Disease Index

1. Osoba, D, et al. *J Clin Oncol*. 1998;16:139–44.

Results

NEI-VFQ-25 Item Scores: Impact on driving and recovery as assessed by NEI-VFQ-25

- At the beginning of the study 74% (70) patients reported having No Difficulty or A Little Difficulty with driving
- Of these patients, 53% (37) stated that they were able to drive with No Difficulty or A Little Difficulty while on treatment
- At worst case post-baseline, 9% (6) had Moderate Difficulty with driving during the daytime, 3% (2) had Extreme Difficulty, and 23% (16) Stopped Driving Due to Eyesight
- In the 23% (16) patients who Stopped Driving Due to Eyesight, time to onset of first occurrence was a median of 63.5 days. Of these patients that stopped driving, 81% (13) returned to a BCVA of grade 0 or 1 later during treatment/follow up,[†‡] with 44% (7) returning to driving on-study. Of the 56% (9) patients who did not return to driving, 44% (4) did not have a follow-up PRO assessment

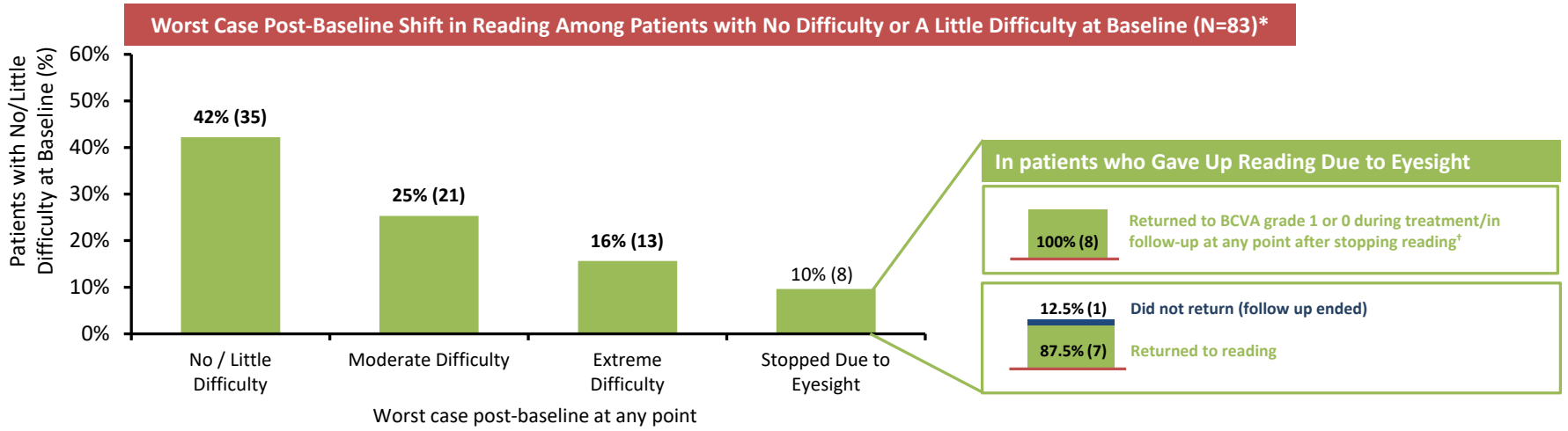


13-month follow-up; cut-off date January 31, 2020. BCVA recovery based on routine study-mandated ophthalmic exam.
*Three patients (4%) with no/little difficulty in visual functioning at baseline stopped driving due to reasons not related to visual functioning change. Post-baseline assessments were missing for 6 patients (9%) †Patients may have experienced grade ≥2 BCVA events after recovery of the first event.‡One patient did not have Grade ≥2 BCVA events before or after stopping driving ¶For 2 patients who did not return to grade 0/1 BCVA post stopping driving, follow-up ended due to death or end of treatment
BCVA, best corrected visual acuity; NEI-VFQ-25, National Eye Institute Visual Function Questionnaire-25 item; PRO, patient-reported outcomes

Results

NEI-VFQ-25 Item Scores: Impact on reading and recovery as assessed by NEI-VFQ-25

- At the beginning of the study 87% (83) patients reported having No Difficulty or A Little Difficulty reading
- Of these patients, 42% (35) stated that they were able to read ordinary print with No Difficulty or A Little Difficulty throughout the study
- At worst case post-baseline, 25% (21) had Moderate Difficulty reading ordinary print, 16% (13) had Extreme Difficulty, and 10% (8) Stopped Reading Due To Eyesight
- Time to first occurrence of Stopped Reading Due to Eyesight was a median of 85 days. Of the 8 patients who stopped reading, 100% (8) returned to a BCVA of grade 0 or 1 later during treatment/follow up,† with 87.5% (7) able to start reading again while on study



13-month follow-up; cut-off date January 31, 2020. BCVA recovery based on routine study-mandated ophthalmic exam.
*Post-baseline assessments were missing for 8 patients (10%). †Patients may have experienced grade ≥2 BCVA events after recovery of the first event.
BCVA, best corrected visual acuity; NEI-VFQ-25, National Eye Institute Visual Function Questionnaire-25 item.

Conclusions

These PRO results from the DREAMM-2 study demonstrate general maintenance or improvement of HRQoL, despite transient reductions in vision-related function. Together with clinical efficacy, these data support the use of belamaf in patients with RRMM

Overall disease symptoms (pain), functioning, and QoL remained stable during treatment. At Week 7, 46% of patients reported a **meaningful improvement in fatigue**, often a difficult-to-manage symptom for patients with RRMM[1]

Changes in OSDI vision-related functioning were transient; almost three-quarters of the patients with a decline in OSDI vision-related functioning to or beyond the minimum change threshold used here improved after a median of 24 days

Over **40% of patients continued everyday activities** such as reading and driving with No Difficulty/A Little Difficulty while on treatment. Some patients had to temporarily stop these activities due to changes in their eyesight, though many reported resuming. We were not able to assess resolution in all patients due to missing PRO data, death, study withdrawal, or being lost to follow-up

Despite ocular symptoms, even in patients with minimal meaningful within-patient reductions in vision-related function, EORTC-QLQ-C30 data suggest that **overall Global Health Status/QoL, Physical and Role functioning was maintained or improved** during treatment

DREAMM-2 included heavily pre-treated RRMM patients with few treatment options. The results reported here need to be weighed for each patient and **close collaboration among hematologist/oncologists and eye care professionals is needed to provide optimal care** in relation to the belamaf benefit:risk profile

HRQoL, health-related qualtiy of life; OSDI, Ocular Surface Disease Index; PRO, patient-reported outcome; QoL, quality of life; RRMM, relapsed/refractory multiple myeloma.

1. Dvorak C. *J Am Acad Nurse Pract*. 2006;18:190–4.

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QR, Quick Response