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- *Aggregate data will be included; with any direct reference to individual patients excluded*

**Complete removal of patient data listings may mean that page numbers are no longer consecutively numbered*

NON-INTERVENTIONAL STUDY REPORT

TITLE PAGE

Division: Research and Development

Information Type: Non-Interventional PASS Final Study Report

Title:	***B****LENREP* **E**ffectiveness **a**nd Safety in **M**ultiple **M**yeloma (BEaMM) – Real-World Evidence on Patients Taking Belantamab Mafodotin in Europe.
Compound Number:	GSK2857916
Effective Date:	
Subject:	Real-world use, safety, and effectiveness
Author(s):	PPD ; GSK – Global Epidemiology PPD ; Syneos Health
Indication Studied:	Adults with RRMM who have received at least 4 prior therapies including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

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STUDY INFORMATION

Title	**B**LENREP **E**ffectiveness **a**nd Safety in **M**ultiple **M**yeloma (BEaMM) – Real-World Evidence on Patients Taking Belantamab Mafodotin in Europe.
Report version identifier	217240
Date of last version of report	Interim Report – 01 October 2023
EU PAS (ENCEPP) register number	EUPAS44701
Active substance	Belantamab mafodotin - L01XC39
Medicinal product	BLENREP
Product reference	EU/1/20/1474/001
Procedure number	EMEA/H/C/004935
Marketing authorization holder(s)	GSK (Ireland) Limited
Joint PASS	No
Research question and objectives	The purpose of this study was to evaluate the safety and effectiveness of belantamab mafodotin in RRMM patients in Europe in the real-world setting.
Country(-ies) of study	Patients will be included from sites in selected countries across Europe: Austria, Belgium, Germany, Greece, Italy, Norway, Spain
Author	PPD PPD, Global Epidemiology, Organisation of the Chief Medical Office, 79 New Oxford St, London, WC1A 1DG, UK PPD PPD Epidemiology Syneos Health United States

MARKETING AUTHORIZATION HOLDER(S)

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STUDY DETAILS

UNIQUE IDENTIFIER	217240
TITLE	**B**LENREP **E**ffectiveness **a**nd Safety in **M**ultiple **M**yeloma (BEaMM) – Real-World Evidence on Patients Taking Belantamab Mafodotin in Europe.
STUDY ACCOUNTABLE PERSON	PPD
CONTRIBUTING AUTHORS	PPD, Senior Scientist VEO Europe PPD European Hematology Lead Medical Affairs PPD Data Quality Lead PPD PPD, Global Medical Affairs Lead
ASSET ID	GSK2857916
GSK ASSET	Belantamab mafodotin
EFFECTIVE DATE	
INDICATION	Multiple Myeloma

REPORT REVISION HISTORY

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SPONSOR SIGNATORY

Title:	**B**LENREP **E**ffectiveness **a**nd Safety in **M**ultiple **M**yeloma (BEaMM) – Real-World Evidence on Patients Taking Belantamab Mafodotin in Europe
Compound Number:	GSK2857916

Vicky Tribble
Primary Author/NI Scientific Lead

Date (DD Month YYYY)

Linda Kalilani, Senior Director and Head, Oncology Epidemiology

Date (DD Month YYYY)

Note: Not applicable if an eSignature process is used to get the sponsor approval.

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LIST OF ABBREVIATIONS

AE	Adverse event
AESI	Adverse event of special interest
ATC	Anatomical Therapeutic Chemical
ATU	Authorization for use
BCVA	Best Corrected Visual Acuity
BLENREP	Belantamab mafodotin
BMI	Body mass index
BOR	Best overall response
CAR-T	Chimeric antigen receptor-T cell therapy
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence interval
CR	Complete response
DoR	Duration of response
DoT	Duration of treatment
EAP	Early access program
EC	European Commission
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
EDC	Electronic data capture
EHA	European Hematology Association
EMA	European Medicines Agency
EP	Enrolled population
ESMO	European Society for Medical Oncology
EU	European Union

GVP	Good Pharmaco Vigilance Practice
ICF	Informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent ethics committee
Ig	Immunoglobulin
IMWG	International Myeloma Working Group
ISS	International Staging System
KM	Kaplan-Meier
KVA	Keratopathy and Visual Acuity
LDH	Lactate dehydrogenase
LoT	Line of treatment
mAB	Monoclonal antibody
max	Maximum
MedDRA	Medical Dictionary for Regulatory Activities
min	Minimum
MM	Multiple myeloma
n	Frequency count
NCCN	National Comprehensive Cancer Network
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NPP	Named Patient Program
ORR	Overall response rate
OS	Overall survival
PASS	Post-authorization safety study
PD	Progressive disease

PFS	Progression-free survival
PI	Proteasome inhibitor
PR	Partial response
PT	Preferred term
Q1	First quartile
Q3	Third quartile
RMP	Risk management plan
RRMM	Relapsed or refractory MM
rwPFS	Real-world progression-free survival
SAE	Serious adverse event
SAP	Statistical analysis plan
sCR	Stringent complete response
SD	Standard deviation
SE	Standard error
SMA	Site management associate
SmPC	Summary of product characteristics
SOC	System organ class
SOP	Standard operating procedures
SP	Safety population
SPK	Superficial Punctuate Keratopathy
TFL	tables, figures and listings
US	United States
VGPR	Very good partial response
WHO	World Health Organization

TRADEMARK INFORMATION

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BLENREP	SAS

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2. SYNOPSIS

Title

B*LENREP* **E**ffectiveness **a**nd Safety in **M**ultiple **M**yeloma (BEaMM) – Real-World Evidence on Patients Taking Belantamab Mafodotin in Europe

Keywords

BLENREP, Belantamab Mafodotin, Multiple Myeloma, Safety, Effectiveness

Rationale and background

MM is a rare and incurable hematological malignancy which typically affects adults 60 years of age and older. Current MM therapies include glucocorticoids, chemotherapy, PIs, immunomodulatory agents and mAbs, including daratumumab. Since the approval of daratumumab, MM patients have emerged who are refractory to at least one PI, one immunomodulatory agent and one anti-CD38 mAb. There is a clear unmet medical need for new therapies among patients with RRMM as current treatment options are very limited with a median OS of 22.3 and 11.6 months for double-class refractory and triple-class refractory patients, respectively.

Belantamab mafodotin (*BLENREP*) is a first in-class anti-B-cell maturation antigen therapy that was approved for use as a monotherapy in the US and the EU based on data from the pivotal Phase 2 DREAMM-2 study (Study 205678).

In the EU, belantamab mafodotin monotherapy was granted a Conditional Marketing Authorization on 25 August 2020 for the treatment of MM in adult patients who have received at least 4 prior therapies and whose disease is refractory to at least one PI, one immunomodulatory agent, and an anti-CD38 mAb, and who have demonstrated disease progression on the last therapy. Because of the risk of ocular toxicity, the EMA required additional monitoring and additional risk minimization measures in the form of educational materials for prescribers and patients as detailed in the EU RMP. The goal of the EU RMP was to mitigate the risk of ocular toxicity of belantamab mafodotin by educating prescribers and patients. The EU SmPC stated that ophthalmic examinations should be performed at the baseline, and before initiation of each of the subsequent 3 treatment cycles, and during treatment as clinically indicated. On 14 December 2023, CHMP adopted a final negative opinion recommending the non-renewal of the Conditional Marketing Authorization of *BLENREP* (belantamab mafodotin) in the EU. On 23 February 2024, the EC issued a decision to endorse the final negative CHMP opinion of the non-renewal of the *BLENREP* Conditional Marketing Authorization. Due to this, the sponsor decided to close the study early. In addition, on 14 November 2022, GSK requested voluntary revocation in the US also based on the outcome of the confirmatory DREAMM-3 trial thus failed to meet the regulatory requirements for conversion from accelerated approval to full approval. The revocation was effective on 06 February 2023.

To better understand the real-world management of RRMM patients exposed to belantamab mafodotin and the occurrence of ocular toxicity in routine clinical practice, this study aimed to evaluate the real-world use, safety, and effectiveness of belantamab mafodotin monotherapy in RRMM patients in Europe.

Research questions and objectives

The purpose of this study was to collect real-world data on the use, safety, and effectiveness of belantamab mafodotin monotherapy in RRMM patients in Europe.

Objectives	Description
Primary Objective	• Characterize RRMM patients treated with belantamab mafodotin monotherapy per routine clinical care in terms of demographics, disease status, clinical characteristics, and treatment history overall and by LoT
Key Secondary Objectives	• Characterize patients who experience ocular AEs that have been associated with belantamab mafodotin treatment (ocular AESIs) (overall and by LoT) in terms of: o Belantamab mafodotin treatment received (i.e., dose and duration) o Ophthalmic disease history o Ocular AESI type, duration, and severity o The frequency and timing of ophthalmic monitoring visits relative to belantamab mafodotin administration (for each cycle; overall and by LoT, the occurrence of ocular AESIs as well as treatment dose and frequency)
Other Secondary Objectives	• Assess the incidence of ocular AESIs (overall and by LoT) and their impact on treatment discontinuation, interruption/delay, or dose modifications (overall and by LoT, comorbidity, ocular AESI type and severity as well as treatment dose and frequency) • Evaluate persistence and adherence with belantamab mafodotin • Describe reasons for treatment discontinuation • Describe the duration and reasons of treatment interruptions/delays, or dose modifications • Evaluate effectiveness in terms of disease response to treatment, DoR, DoT, rwPFS and OS

Study design

This was a multinational, multisite, non-interventional study aimed to collect real-world data on the use, safety, and effectiveness of belantamab mafodotin monotherapy in RRMM patients in Europe. RRMM patients from participating European sites due to receive their first dose of belantamab mafodotin (or who had initiated belantamab mafodotin treatment within 3 months of enrolment) were prospectively invited to enroll in the study. The study enrolment goal was 150 patients.

The final analysis includes data collected from the start of enrolment (05 September 2022) to the data cut date of 07 June 2024. Data for 84 enrolled patients were collected from the time of their first dose of belantamab mafodotin to patient discontinuation from the study for any reason, withdrawal of informed consent or death or study closure; whichever came first. All 84 enrolled patients received at least 1 dose of belantamab mafodotin.

As the study was non-interventional, the decision to treat patients with belantamab mafodotin was made prior to and independent from the decision to enroll patients into the study. The sponsor decided to close the study early based on the decision made by the EC on 23 February 2024 to enact the loss of the Conditional Marketing Authorization for belantamab mafodotin in the EU.

The total study duration was estimated to be a maximum of 2 years and 3 months per site based on an estimated study enrolment period of 12 months and a follow-up period of 15 months. Due to the early closure of the study, total study duration across patients ranged from 0.9 to 16.2 months.

Setting

A total of 84 patients who received belantamab mafodotin monotherapy as part of routine clinical care were enrolled into this study from 27 sites across 7 European countries (Austria, Belgium, Germany, Greece, Italy, Norway, and Spain).

Participants and study size

A sample size of 150 evaluable RRMM patients was planned for the total study. Countries and sites in Europe were included based on the expected belantamab mafodotin market uptake and site availability. At the time of the final database lock, which was earlier than expected as the study closed early, 84 patients were enrolled in the study.

Inclusion Criteria:

A patient who met all of the following criteria was eligible for inclusion:

- Written informed consent
- Male or female, ≥18 years of age at the start of belantamab mafodotin treatment
- Confirmed diagnosis of RRMM

- Received or due to receive belantamab mafodotin treatment per routine clinical care by an oncologist or hematologist consistent with the approved labelling.

Exclusion Criteria:

A patient who met any of the following criteria was not eligible for inclusion:

- Concurrent enrollment in an interventional clinical trial involving either an investigational medicinal product (including belantamab mafodotin) or medical device
- Concurrent enrollment in a belantamab mafodotin EAP, NPP ATU program.

Variables and data sources

Data sources

After obtaining informed consent, data were planned to be collected retrospectively from medical records and prospectively, where applicable, from the time of the first dose of belantamab mafodotin to the end of follow-up at 15 months, study discontinuation for any reason, informed consent withdrawal or death, whichever came first. Data were collected by Investigators or their designees (i.e., hematologists, oncologists, and ophthalmologists) and included into the eCRF. The Investigator followed ocular AESIs until they were resolved or until the last study visit of the patient.

Variables

- Demographics, disease status, clinical characteristics, and treatment history data
- Belantamab mafodotin treatment details including dose, duration, discontinuations, interruptions/delays, and dose changes
- Ophthalmic examination details (e.g., type, frequency, date) and results
- Information on all ocular AESIs, including severity, seriousness, duration, relationship to and impact on daily living, belantamab mafodotin treatment and actions taken
- Treatment effectiveness data including survival status, progression, and tumor response according to the International Myeloma Working Group criteria if feasible or to local standard practice

Statistical Methods:

Analysis populations:

Two analysis populations were defined per the SAP:

- EP – All patients for whom written informed consent was obtained.
- SP – All patients in the EP who received at least 1 dose of belantamab mafodotin. The SP was used for descriptive, safety and effectiveness analyses.

All patients in the EP received at least 1 dose of belantamab mafodotin and were therefore also in the SP.

Statistical Methods:

For the primary objective, characteristics of RRMM patients treated with belantamab mafodotin per routine clinical care were described for the SP (overall and by LoT). Characteristics included demographics, disease status, clinical characteristics and treatment history collected before or at the time of the first dose.

For the secondary objectives, the following were described for the SP (overall and by LoT):

- Treatment dose, duration, and persistence
- Ocular AESIs during the study period:
    - Number, proportions, co-occurrence, time to (specific) ocular AESIs and incidence rate (at the patient and event level); overall and by SOC and PT terms under MedDRA classification and according to severity, grade, seriousness, action taken, duration, impact on daily living and relationship to treatment as well as treatment dose and frequency
    - Number, proportion, severity, grade, seriousness, and duration of ocular AESIs by ophthalmic monitoring frequency, type(s), and timing relative to administration
- Treatment response (e.g., CR, VGPR; PR; according to IMWG criteria if feasible or to local standard practice) and time to events (i.e., death, progression, discontinuation).

Continuous variables were described (distribution) by their mean, SD, median, Q1 and Q3, extreme values (min, max) and the number of non-missing and missing data. Categorical variables were described using frequency counts and percentages.

Data analysis:

The following measures were reported:

- Median, 95% CIs, Q1 and Q3 using the KM method for time to event outcomes (i.e., OS, rwPFS, DoR, time to discontinuation, time to first [specific] ocular AESI)
- OS rates with 95% CIs at specified time points, including 12- and 15-months of follow-up
- ORR with 95% CIs calculated based on the exact binomial distribution (Clopper-Pearson method).

Additional subgroup analyses were conducted for primary and secondary outcomes by key patient characteristics (e.g., ECOG performance status, age groups at the index date, MM subtype, retrospective vs prospective data, and presence or absence of ocular AESIs) when deemed applicable and feasible, as described in the SAP). Duration of treatment,

treatment adherence and reasons of treatment interruptions/delays, or dose modifications due to an ocular AESI are also reported.

Results and Discussion

The study closed early with a data cut-off date for final analysis of 07 June 2024. There were 84 patients enrolled (Austria=14 patients; Belgium=5 patients; Germany=4 patients; Greece=3 patient; Italy=32 patients; Norway=15 patients; Spain=11 patients).

Forty patients (47.6%) completed the study, including 27 patients (32.1%) who died during follow-up. In total, 44 patients (52.4%) did not complete the study, mostly due to study termination (n=39, 46.4%). The mean number of days post-index was 259.0 days (SD 138.78; min, max: 27, 492; median 236.5; Q1, Q3: 139.0, 399.0). The cumulative proportion of patients still in the study was 86.9% at 3 months (95% CI: 77.6, 92.5), 63.1% at 6 months (95% CI: 51.8, 72.4), 44.0% at 9 months (95% CI: 33.3, 54.3), 26.2% at 12 months (95% CI: 17.4, 35.9), and 10.7% at 15 months (95% CI: 5.3, 18.4).

All 84 patients received at least 1 dose of belantamab mafodotin either as early line (LoT<4; n=7, 8.3%), fourth-line (n=8, 9.5%), fifth-line (n=36, 42.9%) or at sixth-line or beyond (n=33, 39.3%). Four patients (4.8%) were ongoing on treatment at the time of study completion by patient and 21 patients (25.0%) were ongoing on treatment at the time of study termination by the Sponsor. Fifty-nine patients (70.2%) discontinued treatment during the study, mostly due to disease progression (n=28; 33.3%) or death (n=13; 15.5%). The mean duration of exposure was 161.5 days (SD 122.90; median 125.5 days; Q1, Q3: 70.5, 230.5). The proportion of patients with at least 4 LoT in the prior treatment period in this study (92%) is comparable to proportions reported in a retrospective study with 82.9% receiving ≥4 LoT.

The mean age at initial MM diagnosis was 63.7 years (SD 10.06; min, max: 34, 88; median 63.5; Q1, Q3: 58.0, 71.5 years). The mean age for the SP at the index date was 70.7 years (SD 9.59; min, max 40, 93 years) with a lower mean age among patients treated with LoT<4 years (mean 62.4; SD 12.11). The mean time since initial MM diagnosis to the index date was 84.9 months (SD 48.11; min, max: 7.0, 243.8 months; median 79.0; Q1, Q3: 53.2, 119.3 months). Many of the patients were elderly, 35.7% were between 65 years and 74 years of age, while 39.3% were 75 years or older. Patients were slightly more likely to be female (n=46; 54.8%).

Patients in the current study were on average slightly older at index and more often female than patients in the Phase 2 DREAMM-2 study and recently published real-world data in the US evaluating belantamab mafodotin. The median age at initial MM diagnosis of 63.7 years (Q1, Q3: 58.0, 71.5 years) in this study was similar to that reported from real-world chart data by (Vaxman, 2021). (61 years; min, max 37, 83).

In contrast, the median age at index in the current study of 71 years (Q1, Q3: 40, 93 years) was higher than the median age of patients randomized to 2.5 mg/kg and 3.4 mg/kg belantamab mafodotin in the DREAMM-2 trial (65 years; Q1, Q3: 60, 70; and 67 years; Q1, Q3: 61, 72 years respectively). The median age at index was also slightly higher than the median age of 67 years reported from real-world chart data but comparable to the median age of 70 years from claims data.

The median time from initial MM diagnosis to first belantamab mafodotin dose for the DREAMM-2 clinical study was reported at 5.08 and 5.49 years, dependent on the dosage administered (2.5 mg/kg or 3.4 mg/kg). Results from the US real-world data studies showed a slightly higher median time from initial diagnosis to first belantamab mafodotin dose; ranging from approximately 6 years using the claims data to 7 years using retrospective medical record data. This final report showed a similar trend to other US real-world data with a median of 6.6 years from initial MM diagnosis to first belantamab mafodotin dose.

This study included 45.2% males compared to a higher proportion of males in retrospective studies (64%, 53%, 50%,) and in the DREAMM-2 clinical study across both dosage groups (53% and 57%).

ECOG performance status data was available for 59 patients (70.2%) across the SP; the ECOG score was 0 for 40.7% (n=24/59), 1 for 33.9% (n=20/59), 2 for 23.7% (n=14/59) and 3 for 1.7% (n=1/59) of patients. None of the patients had an ECOG score of 4.

Regarding ISS staging, amongst those with a value, 35.6% (n=21/59) were in stage I, 23.7% (n=14/59) in stage II, 40.7% (n=24/59) in stage III; data was missing for 29.8% (n=25/84). Most common MM subtypes were the IgG subtype (51.2%), followed by light chain (21.4%), IgA subtype (15.5%), other subtype (10.7%) and IgD (1.2%). Most patients did not have a high cytogenetic risk (72.6%), with remaining patients having a high cytogenetic risk (27.4%) or high-IMWG cytogenetic risk (20.2%).

Comorbid renal disease, pulmonary diseases, cardiac diseases, diabetes, and eye diseases were present at the index date, in 20.2%, 17.9%, 39.3% 23.8%, and 31.0% of the SP, respectively. Twenty-six patients (31.0%) reported eye diseases at the index date, which included a history of dry eyes/eye injuries affecting the BCVA.

Among the SP with available refractory data, 37.2% (n=29/78) were triple-refractory, 35.9% (n=28/78) were quad-refractory, 26.9% (n=21/78) were penta-refractory: 7.7% (6/84) had missing refractory data. Most patients (n=82, 97.6%) had at least 1 prior corticosteroid treatment and at least 1 prior monoclonal antibody treatment. A large proportion of the SP also had at least 1 prior chemotherapy treatment (n=66, 78.6%) and almost 50% at least 1 prior stem cell transplant (n=41, 48.8%).

For patients with an ocular AESI, the percentage of patients receiving at least 1 ophthalmic exam prior to each of the first 4 dose administrations individually was higher than for those without an ocular AESI (87.9% vs 53.8% during the baseline period, 74.5% vs 57.1% between first and second dose, 63.6 % vs 26.7% between second and third dose and 65.7% vs 40.0% between the third and fourth doses), however without the ophthalmic examinations, some of the AESI may have not have been identified.

Overall, 58 patients (69.0%) from the SP reported 85 ocular AESI episodes, of which 83 were assessed as related to belantamab mafodotin. The median number of doses of belantamab mafodotin taken before the first ocular AESI was 2.0. Similar to the DREAMM-2 trial where a majority of the patients with keratopathy (97.1%) experienced their first event by their fourth dose, this study shows that all patients who experienced keratopathy (n=42, 50.0%) did so by their fourth dose, most between their first and

second dose (n=17/42, 40.5%) or between their second and third dose (n=15/42, 35.7%), however, only 5 patients received 4 or more doses during the study period.

Among the SP, ocular AESIs led to dose reductions in 13 patients (15.5%), treatment interruption/delay in 37 patients (44.0%), and treatment discontinuation in 7 patients (8.3%), which is lower than reported treatment interruption/delays in 27.7% and treatment discontinuation in 60.3% of patients from real-world study. There were no AESIs leading to study withdrawal or death. The mean duration of exposure was 193.0 days (SD 127.19; median 142.5 days; Q1, Q3: 106.0, 279.0) in the presence of an ocular AESI and 91.4 days (SD 76.48; median 67.0 days; Q1, Q3: 44.0, 102.0) in the absence of an ocular AESI.

The most frequently reported AESI was keratopathy, which occurred in 42 (50.0%) patients, followed by 'other' AESIs (19.0% including corneal epithelial microcysts, punctate keratitis, reduced visual acuity, cataract, conjunctivitis, dry eye, eye disorder, keratitis, meibomian gland dysfunction, ocular discomfort, optic neuropathy, sudden vision loss), corneal erosions or defects (8.3%), blurred vision (7.1%), a change in BCVA (4.8%), a dry eye event (1.2%) and photophobia (1.2%). The incidence of keratopathy (50%) in this study is lower than the 72% keratopathy reported for patients in the DREAMM-2 trial over a 13-month follow-up period (current study duration of 1.2 to16.2 months), but within the range of proportions between 44% and 83% reported in real-world studies over a median of 4.1 months follow-up.

The majority of ocular AESIs were mild or moderate in severity. The mean duration of keratopathy was available for 16 of the 42 patients (maximum grade of episode was used) and was 232.6 days (SD 115.17; min; max 112.0; 411.0) for mild episodes (n=5), 129.0 days (SD 76.21; min; max 23.0; 260.0) for moderate severe episodes (n=9) and 153.0 days (SD 125.87; min; max 64.0; 242.0) for severe episodes (n=2). Of the 42 patients with keratopathy, 29 (69.0%) patients had ongoing keratopathy at the end of the study. Limited data were available on the duration of other ocular AESIs. The highest impact on daily living was reported by patients with keratopathy with 31.0% reporting eye irritation/pain, 23.8% reporting reading impairment, 4.8% reporting driving impairments, 2.4% reporting a need for caregiver support and 19.0% reporting other impacts (with data missing for 21.4% of patients with keratopathy). The percentage of specific AESI episodes was higher among responders than among non-responders. However, since preservative-free artificial tear eye drops are also used for symptomatic relief, this factor may have skewed reporting such that patients with ocular events were documented to utilize this supportive-care therapy more so than those without ocular adverse events.

Two patients reported a total of 3 serious AESIs (1 patient with keratopathy and a change in BCVA and 1 patient with a blurred vision event) none of which resulted in death.

There were 27 deaths reported during the study; 17 were due to the disease, 2 due to adverse events other than ocular AESIs, 1 due to disease progression, and 7 with an unknown cause of death.

The best overall response among the 84 patients in the SP was CR in 1.6% (n=1/62), VGPR in 16.1% (n=10/62), PR in 21.0% (n=13/62), and stable disease in 38.7% (n=24/62). Progressive disease occurred in 22.6% (n=14/62). BOR data was missing in

26.2% (n=22). Comparatively, real-world studies reported 6% of patients achieving CR, 8% of patients achieving VGPR, 19% of patients achieving PR, 28% of patients achieving stable disease, and 36% of patients progressed while on belantamab therapy.

The median DoR was 10.7 months (95% CI: 3.9, not reached) and the median DoT 4.1 months (95% CI: 2.9, 4.8). For patients with a partial response or better (n=24), the mean duration of exposure was 238.5 days (SD 127.26; median 236.5 days; Q1, Q3: 115.5, 332.0). For non-responders, the mean duration of exposure was 123.5 days (SD 100.78; median 112.5 days; Q1, Q3: 50.0, 145.0).

The median OS for the SP was not estimable. OS was 89.2% (95% CI: 80.3, 94.2) at 3 months, 78.5% (95% CI: 67.6, 86.1) at 6 months, 68.6% (95% CI: 56.3, 78.1) at 9 months and 59.9% (95% CI: 46.3, 71.1) at 12 and 15 months.

The median rwPFS was 4.5 months (95% CI: 3.48, 5.16 months), in line with reports from a real-world US electronic health record study with a median rwPFS of 4.5 months. The rwPFS was 69.8% (95% CI: 56.7, 79.6) at 3 months, 36.6% (95% CI: 23.9, 49.4) at 6 months, 26.3% (95% CI: 15.2, 38.8) at 9 months and 21.9% (95% CI: 10.8, 35.5) at 12 months. The median rwPFS was higher than the median PFS for the 2.5 mg/kg group in the DREAMM-2 trial (2.8 months; 95% CI: 1.6, 3.6 months).

Conclusions

Clinical characteristics of patients included in this real-world European prospective study (i.e., regarding prior LoT, presence of ocular AESIs) as well as the frequency of ocular AESIs, specifically keratopathy, were similar to those reported in other clinical and real-world studies assessing belantamab mafodotin monotherapy in RRMM patients. The frequency of ocular exams prior to the each (subsequent) dose of belantamab mafodotin suggests that most patients were monitored in accordance with label recommendations. The final data also show that dose reduction, treatment interruption/delay treatment discontinuation and common management were used to manage presence of ocular AESIs.

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3. AMENDMENTS AND UPDATES

Data collection began after the implementation of Protocol Amendment 1 (01 April 2022). The study closed early based on the decision made by the EC on 23 February 2024 to not renew the Conditional Marketing Authorization for belantamab mafodotin in the EU.

4. MILESTONES

Milestone	Planned date	Actual Date	Comments
Start of data collection	April 2022	05 September 2022	NA
End of data collection	June 2024	07 June 2024	NA
Registration in the EU PASS register	Q4 2021 to Q1 2022	10 May 2022	NA
Interim report 1	September 2023	19 September 2023	NA
Interim report 2	February 2024	Cancelled	The study closed early based on the decision made by the European Commission on 23 February 2024 to not renew the Conditional Marketing Authorization for belantamab mafodotin in the EU.
Final report of study results	Q2 2025		NA

5. RATIONALE AND BACKGROUND

MM is a rare and incurable hematological malignancy which typically affects adults 60 years of age and older. It is the second most common hematological malignancy (after non-Hodgkin's lymphoma), representing 1% of all cancers and 2% of all cancer deaths. In 2022, the estimated annual, age-standardized, worldwide MM incidence rate was 1.8 per 100,000 (Ferlay, 2024).

Current MM therapies include glucocorticoids (e.g., dexamethasone), chemotherapy, PIs, (e.g., bortezomib), immunomodulatory agents (e.g., thalidomide, lenalidomide and pomalidomide), monoclonal antibodies (mAbs, e.g., daratumumab, isatuximab and elotuzumab) and the histone deacetylase inhibitor panobinostat. Since the approval of daratumumab, MM patients have emerged who are refractory to at least 1 PI, 1 immunomodulatory agent and 1 anti-CD38 mAb. There is a clear unmet medical need for new therapies among patients with relapsed or RRMM as current treatment options are very limited with a median OS of 22.3 and 11.6 months for double-class refractory and triple-class refractory patients, respectively (Wang, 2022).

Belantamab mafodotin (*BLENREP*) is a first in-class anti-B-cell maturation antigen therapy that was previously approved for use as a monotherapy in the US and the EU based on data from the pivotal Phase 2 DREAMM-2 study (Study 205678) (Lonial, 2020; Lonial, 2021). DREAMM-2 was a phase 2, open label, randomized, two-arm study investigating the efficacy and safety of 2 doses of belantamab mafodotin (3.4 mg/kg vs. 2.5 mg/kg) in patients with MM who had ≥3 prior lines of treatment, were refractory to a PI and an immunomodulatory agent and had failed an anti-CD38 antibody (Lonial, 2020; Lonial, 2021). DREAMM-2 results after 13-month follow-up showed an ORR for the 97 patients who received the registration dose (i.e., 2.5 mg/kg) of 32% (97.5% CI, 21.7 to 43.6) with 58% of responders achieving a VGPR or better, including 2 sCRs and 5 CRs (Lonial, 2021). The median estimated DoR, OS, and PFS were 11.0 months (95% CI, 4.2 months to not reached), 13.7 months (95% CI, 9.9 months to not reached), and 2.8 months (95% CI, 1.6, 3.6 months), respectively (Lonial, 2021). The most frequent adverse reactions (≥30%) reported from 95 patients in DREAMM-2 who received belantamab mafodotin 2.5 mg/kg were keratopathy (71%) and thrombocytopenia (38%). The most commonly reported serious adverse reactions were pneumonia (7%), pyrexia (7%) and infusion-related reactions (3%). Permanent discontinuation due to an adverse reaction occurred in 9% of patients who received belantamab mafodotin with 3% related to ocular adverse reactions.

In the EU, belantamab mafodotin was granted a Conditional Marketing Authorization on 25 August 2020 for the treatment of MM in adult patients who have received at least 4 prior therapies and whose disease is refractory to at least 1 PI, 1 immunomodulatory agent, and an anti-CD38 mAb, and who have demonstrated disease progression on the last therapy (*BLENREP US Prescribing Information, 2022*). Because of the risk of ocular toxicity, the EMA required additional monitoring and additional risk minimization measures in the form of educational materials for prescribers and patients as detailed in the EU RMP (Summary RMP, 2021). The goal of the EU RMP was to mitigate the risk of ocular toxicity of belantamab mafodotin by educating prescribers and patients. The EU SmPC stated ophthalmic examinations should be performed at the baseline, and before initiation of each of the subsequent 3 treatment cycles and during treatment as clinically indicated (*BLENREP* SmPC, 2023).

To better understand the real-world management of RRMM patients exposed to belantamab mafodotin and the occurrence of ocular toxicity in routine clinical practice, this study aimed to evaluate the real-world use, safety, and effectiveness of belantamab mafodotin in RRMM patients in Europe.

On 14 December 2023, CHMP adopted a final negative opinion recommending the non-renewal of the Conditional Marketing Authorization of *BLENREP* (belantamab mafodotin) in the EU. On 23 February 2024, the EC issued a decision to endorse the final negative CHMP opinion of the non-renewal of the *BLENREP* Conditional Marketing Authorization. Due to this, the sponsor decided to close the study early. In addition, on 14 November 2022, GSK requested voluntary revocation in the US also based on the outcome of the confirmatory DREAMM-3 trial thus failed to meet the regulatory requirements for conversion from accelerated approval to full approval. The revocation was effective on 06 February 2023.

6. RESEARCH QUESTION AND OBJECTIVE(S)

The primary purpose of this multinational, multisite, non-interventional study was to understand the real-world use of belantamab mafodotin monotherapy by characterizing RRMM patients treated with belantamab mafodotin in routine clinical practice in Europe. In addition, this study provided further evidence on belantamab mafodotin's risk-benefit profile by collecting safety and effectiveness data. No formal hypotheses were being tested in this study.

6.1. Primary Objective

The **primary objective** of this study was to characterize RRMM patients treated with belantamab mafodotin monotherapy per routine clinical care in terms of demographics, disease status, clinical characteristics, and treatment history (overall and by LoT).

6.2. Secondary Objectives

The **key secondary objective** of this study was to characterize patients who experience ocular AEs that have been associated with belantamab mafodotin treatment (ocular AESIs) (overall and by LoT) in terms of:

- Belantamab mafodotin treatment received (i.e., dose and duration)
- Ophthalmic disease history
- Ocular AESI type, duration, and severity
- The frequency and timing of ophthalmic monitoring visits relative to belantamab mafodotin administration (for each cycle; overall and by LoT, the occurrence of ocular AESIs as well as treatment dose and frequency).

Other secondary objectives were the following (overall and by LoT):

- Assess the incidence of ocular AESIs and their impact on treatment discontinuation, interruption/delay, or dose modifications (additionally stratified by comorbidity, ocular AESI type and severity as well as treatment dose and frequency)
- Evaluate persistence and adherence with belantamab mafodotin
- Describe reasons for treatment discontinuation
- Describe the duration and reasons of treatment interruptions/delays, or dose modifications
- Evaluate effectiveness in terms of disease response to treatment, DoR, DoT, rwPFS and OS.

The previous interim report included results per the SAP only for the primary objective and the key secondary objectives. Secondary objectives related to treatment duration, treatment adherence and reasons of treatment interruptions/delays, or dose modifications due to an ocular AESI were estimated for the final data-cut and results are provided in this final report as well as results for the primary objective and key secondary objectives.

7. RESEARCH METHODS

7.1. Study Design

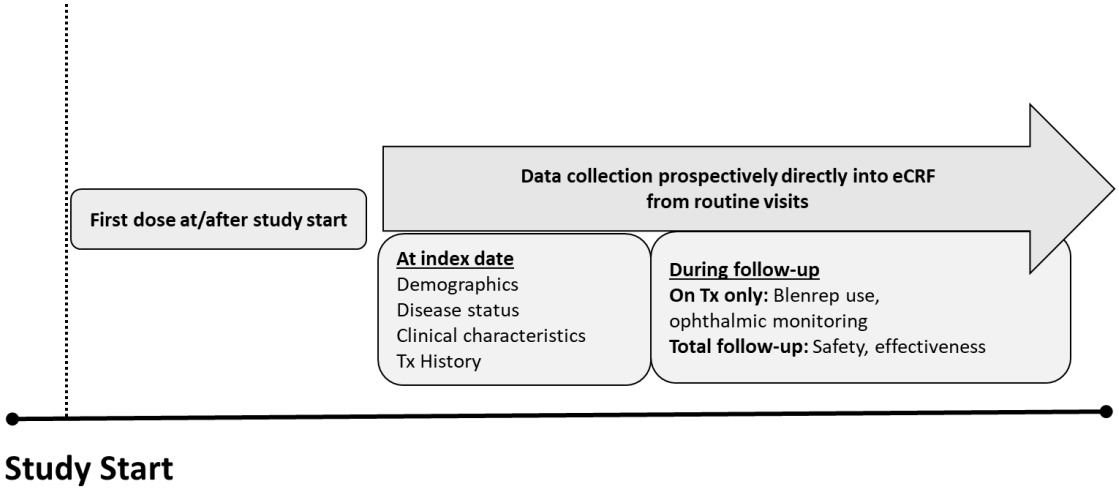
This multinational, multisite, non-interventional study collected real-world data on the use, safety, and effectiveness of belantamab mafodotin. Data for this final study report were analyzed from 84 RRMM patients from sites in selected countries across Europe in the entire study.

Eligible RRMM patients from the European sites who were due to receive belantamab mafodotin were invited for study enrollment by hematologists and/or oncologists affiliated with investigator sites participating in this study. As the study was non-interventional, the decision to treat patients with belantamab mafodotin was made prior to and independent from the decision to enroll patients into the study. The baseline and follow-up assessments were in accordance with local standard medical care.

Written informed consent was obtained from all patients before enrollment into the study. After obtaining informed consent, data were collected retrospectively from medical records and prospectively, where applicable, from the time of the first dose of belantamab mafodotin to the end of study for the final analysis, study discontinuation for any reason, informed consent withdrawal or death, whichever came first.

Figure 7-1 shows the patient and data flow in this study. For patients who received a first dose of belantamab mafodotin at or after study enrollment, baseline and outcome data were entered into the eCRF.

Figure 7-1 Patient and data flow



Abbreviations: eCRF=electronic case report form; Tx=treatment

Belantamab mafodotin use and ophthalmic monitoring data were collected prior to and while patients were on treatment. Safety and effectiveness data were collected regardless of whether patients were on treatment or have discontinued treatment during follow-up.

7.2. Study Population/Participants and Setting

It was planned to include approximately 150 evaluable RRMM patients from sites in selected countries across Europe who are due to receive belantamab mafodotin as part of routine clinical care after study enrolment. The final report provides data on 84 enrolled patients, from enrolment on 05 September 2022 to the final data cut-off date of 07 June 2024. Data from all patients in Austria, Belgium, Germany, Greece, Italy, Norway, and Spain across 27 sites were included in this final report.

The decision to receive treatment was made independent from the decision to enroll patients into the study. Eligible RRMM patients, due to receive belantamab mafodotin as part of routine clinical care, were invited for enrolment by health care providers affiliated with investigator sites participating in this study.

The total study duration was planned to be a maximum of 2 years and 3 months per site based on an estimated study enrolment period of 12 months and a follow-up period of 15 months. The sponsor decided to close the study early based on the decision made by the EC on 23 February 2024 to enact the loss of the Conditional Marketing Authorization for belantamab mafodotin in the EU. Total study duration across patients ranged from 0.9 to 16.2 months (Data Source Listing 16.2.1.2).

There were 2 interim analyses performed with the aim to provide data to regulatory submissions or future conference abstracts and manuscripts, with enrolment-based cut-offs as follows:

1. Approximately 6 months after first patient enrollment (Interim Report V1.0 01 October 2023)
2. 15 months after first patient in (no interim report was developed due to study closure soon after; results were disseminated through a conference abstract)

7.2.1. Eligibility Criteria

Inclusion Criteria

A patient who met all of the following criteria was eligible for inclusion:

- Written informed consent
- Male or female, ≥18 years of age at the start of belantamab mafodotin treatment
- Confirmed diagnosis of RRMM
- Received or due to receive belantamab mafodotin treatment per routine clinical care by an oncologist or hematologist consistent with the approved labelling.

Exclusion Criteria

A patient who met any of the following criteria was not eligible for inclusion:

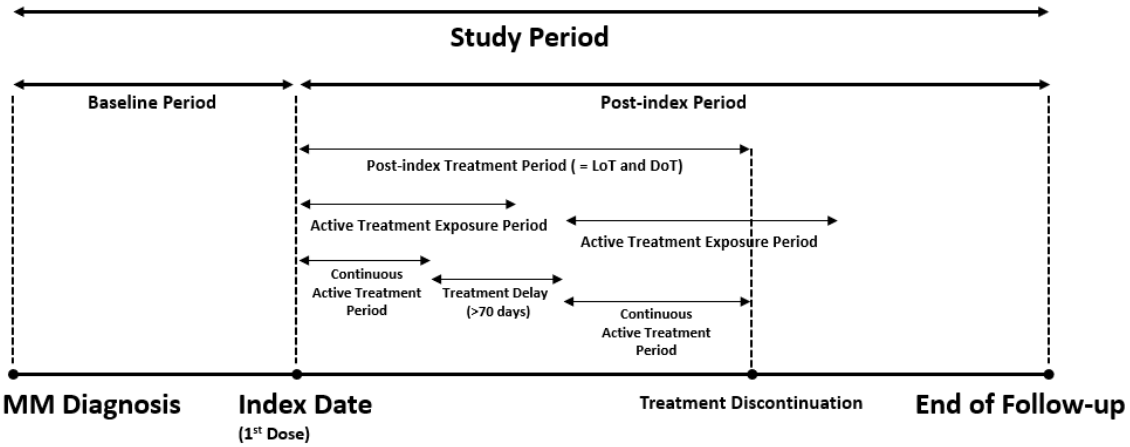
- Concurrent enrollment in an interventional clinical trial involving either an investigational medicinal product (including belantamab mafodotin) or medical device
- Concurrent enrollment in a belantamab mafodotin EAP, NPP or ATU program.

7.3. Variables

The following definitions were applied to the different timings of data collection (see Figure 7-2):

- ***Index date*** was defined as the time of the first (non-missing) dose of belantamab mafodotin.
- The ***baseline period*** for data collection was defined as the time from the initial MM diagnosis until the index date (the first dose of belantamab mafodotin).
- The ***post-index period*** spanned from the index date until the date of the earliest of the following events: end of study period (planned end of follow-up at 15 months), informed consent withdrawal, study withdrawal due to any reasons (except lost to follow-up), last contact for lost to follow-up patients or death; whichever came first.
- The ***post-index treatment period*** was defined as the duration of the belantamab mafodotin LoT (DoT). This ranged from the index date until the confirmed decision date of permanent discontinuation of belantamab mafodotin treatment, the confirmed date of a new LoT or the date of the planned end of follow-up at 15 months, study discontinuation for any reason, informed consent withdrawal or death; whichever came first.
- The ***study period*** spanned from the time from the initial MM diagnosis until the planned end of follow-up at 15 months, study discontinuation for any reason, informed consent withdrawal or death; whichever came first.
- ***Active treatment exposure periods*** were defined as the time that belantamab mafodotin was considered to have a treatment effect during the post-index treatment period. This period included all doses occurring within 70 days of the previous dose (belantamab mafodotin's half-life) from the date of the first belantamab mafodotin dose of that sequence to the date of the last dose +70 days or the date of the end of the post-index treatment period; whichever came first.
- ***Continuous active treatment period*** (as defined in the SAP) included all doses occurring from the date of the first belantamab mafodotin dose of a sequence (either the index date, or the date of the first dose of belantamab mafodotin following a treatment) to the start of a treatment delay, or the date of the end of the post-index treatment period, whichever came first.

Figure 7-2 Timings of Data Collection



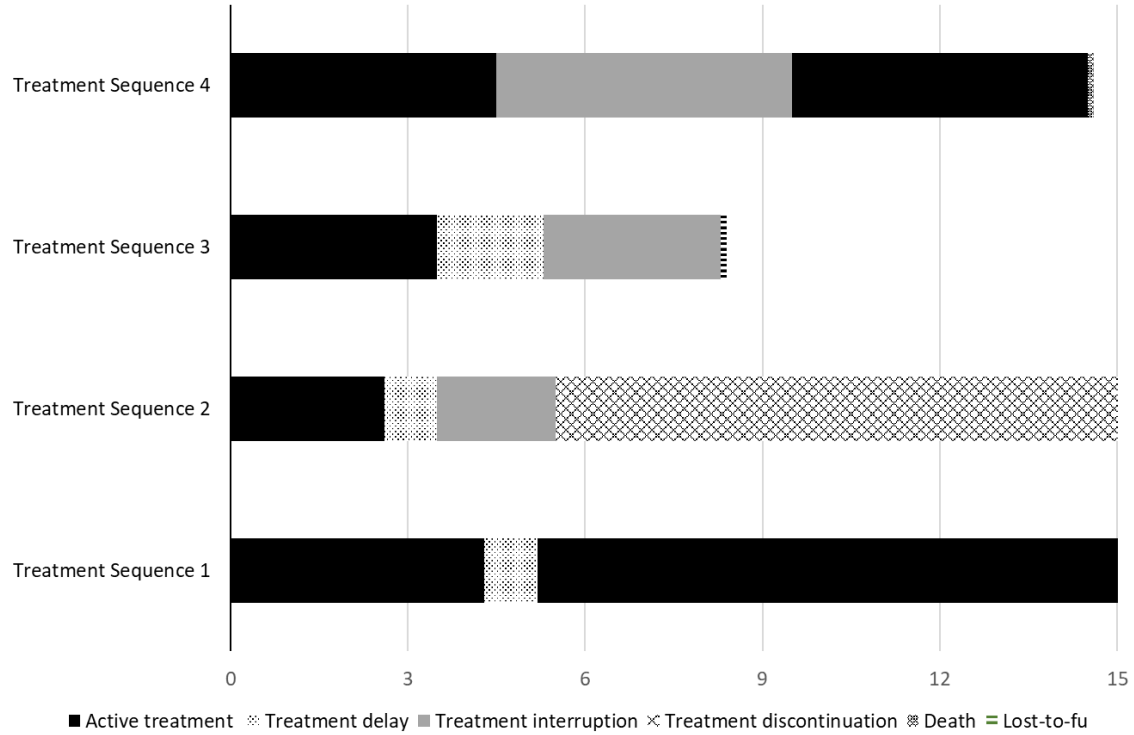
Abbreviations: DoT=duration of treatment; LoT=line of treatment; MM=multiple myeloma

The following definitions were applied to collection of treatment data:

- LoT was defined as 1 or more completed cycles of a single agent, a regimen consisting of a combination of several drugs, or a planned sequential therapy of various regimens (McCambridge, 2014 ; Rajkumar, 2015).
- A treatment cycle was defined as the belantamab mafodotin label-approved dosing interval, which was 21 days (with a real-world scheduling grace period of +7 days).
- Treatment discontinuation was defined as a recorded clinician decision (with an associated decision date) to permanently discontinue belantamab mafodotin treatment.
- Treatment interruption/delay was defined as at the end of the study, patients whose treatment dose interval was ≥ to the assumed cycle length and did not have a confirmed permanent discontinuation or delay of belantamab mafodotin was recorded as being within a treatment delay (see further detail in the SAP).

Figure 7-3 shows examples of treatment sequences that patients might have undergone during the follow-up period.

Figure 7-3 Examples of treatment sequences during the post-index period



Note: Example treatment sequences are displayed in months.

The following definitions were applied to derived outcomes for statistical analyses:

- ORR was defined as the proportion of patients with a best response (sCR, CR, VGPR or PR) during the follow-up period evaluated by the responsible physician based on IMWG criteria if feasible or to local standard practice (IMWG, 2021).
- OS was defined as the time in months from the start of belantamab mafodotin treatment (i.e. index date) to the date of death due to any cause.
- rwPFS was defined as the time in months from the start of belantamab mafodotin treatment (i.e. index date) to the date of the first documented disease progression or death, whichever occurs first.
- DoR was defined as the time from the first documented evidence of response (sCR, CR, VGPR or PR) to the earliest date of PD or death due to any cause.

7.3.1. Baseline Characteristics

For the primary objective of characterizing RRMM patients treated with belantamab mafodotin per routine clinical care, data at the time of the first belantamab mafodotin dose (i.e., the index date) or from the initial MM diagnosis until the index date (i.e., the baseline period) were collected retrospectively or at study enrollment, where applicable. Data collected are shown in Table 7-1.

Table 7-1 Demographics, disease, and treatment history

Item	Variable	Definition	Timing
Demographics	Date of birth	Year of birth	Index date
	Sex	Categorical variable: • Male • Female	Index date
	Height (cm)	Continuous variable	Index date
	Weight (kg)	Continuous variable	Index date
	ECOG Performance Status	Categorical variable: • 0 • 1 • 2 • 3 • 4	Index date
MM History	Date initial diagnosis	Date of first MM diagnosis	Baseline period
	Extramedullary disease	Categorical variable	Baseline period
	ISS stage	Categorical variable: stage at initial MM diagnosis • I • II • III	Baseline period
	MM subtype	Categorical variable: subtype at initial diagnosis • IgG • IgA • IgM • IgD • Biclonal (G,A) • Light chain MM • Other	Baseline period
	Cytogenetic risk	Categorical variable: • High [e.g., t(4;14), t(14;16), del17p] • Standard	Baseline period
	Progression status	Categorical variable: disease progression (per IMWG criteria or to local standard practice) on last line of therapy: • Yes • No	Baseline period
	Refractory status	Categorical variable: • Triple refractory • Quad refractory • Penta refractory	Index date
MM Treatment History	Prior MM therapies	Categorical variable: therapy type* by line per EHA-ESMO and NCCN guidelines	Baseline period
	Dates of prior MM therapies	Date of first and last dose of each prior therapy	Baseline period
Medical History	Pre-existing comorbidities	Categorical variable: type of comorbidity** per category such as: • Renal diseases • Pulmonary diseases • Cardiac diseases • Diabetes	Baseline period

Item	Variable	Definition	Timing
		• Eye diseases including history of dry eye/eye injuries affecting the BCVA • Other	
Ophthalmic Health	BCVA	Continuous variable per type of measurement	Baseline period
	Slit lamp exam	Categorical variable: most recent corneal examination finding: • Keratopathy • Microcyst-like epithelial changes • Other corneal findings/ conditions	Baseline period
Laboratory measurements	Lactate dehydrogenase, creatinine	Continuous variables: based on most recent assessments: • Lactate dehydrogenase • Serum creatinine • Creatinine clearance using the Cockcroft-Gault formula	Baseline period

Abbreviations: BCVA=Best Corrected Visual Acuity, ECOG=Eastern Cooperative Oncology Group; EHA=European Hematology Association; ESMO= European Society for Medical Oncology; Ig=Immunoglobulin; IMWG=International Myeloma Working Group; ISS=International Staging System; MM=multiple myeloma; NCCN=National Comprehensive Cancer Network.

*The World Health Organization (WHO) Drug Dictionary for medications were used for coding drugs. **The Medical Dictionary for Regulatory Activities (MedDRA) was used for coding concomitant diseases.

7.3.2. Belantamab Mafodotin Treatment

Belantamab mafodotin treatment data collected during follow-up from standard of care visits are shown in Table 7-2. Data were collected from the time of the first belantamab mafodotin dose until permanent discontinuation of belantamab mafodotin treatment, the end of follow-up, study discontinuation for any reason, informed consent withdrawal or death; whichever came first.

Table 7-2 Belantamab mafodotin treatment

Variable	Definition	Timing
Date(s) of Administration	Date of each administration	Index date and post-index treatment period
Dose	Continuous variable: prescribed and administered doses	Index date and post-index treatment period
Treatment status change	Categorical variable: prospectively captured or derived retrospectively • Dose modification • Treatment interruption / delay • Discontinued	Post-index treatment period
Primary reason dose modification	Categorical variable: • Any AE • Other	Post-index treatment period
Primary reason treatment interruption/delay	Categorical variable: • Any AE • Patient decision unrelated to AEs • Other	Post-index treatment period

Variable	Definition	Timing
Primary reason treatment discontinuation	Categorical variable: • Disease progression • Any AE • Patient decision unrelated to AEs • End of treatment • Death (unrelated to therapy) • Other	Post-index treatment period
Concomitant Medications	Categorical variable: type of concomitant medication* Continuous variable: dose at index date for each concomitant medication	Index date and post-index treatment period

Abbreviations: AE=adverse event.

7.3.3. Ophthalmic Monitoring

As part of the key secondary objectives, ophthalmic monitoring information (Table 7-3) was collected during follow-up from standard of care visits from the time of the first belantamab mafodotin dose until permanent discontinuation of belantamab mafodotin treatment, the end of follow-up, study discontinuation for any reason, informed consent withdrawal or death; whichever came first.

Table 7-3 Ophthalmic Monitoring

Variable	Definition	Timing
Date(s) ophthalmic examination(s)	Date of each examination	Index date and post-index treatment period
Type(s) of ophthalmic examination(s)	Categorical variable: • BCVA score (Snellen test or equivalent test) • Slit lamp examination • Other	Index date and post-index treatment period

Result of Examination	Categorical variable, result for each eye:
	• BCVA score (continuous variable)
	• Corneal examination findings:
	  ○ No change
	  ○ Mild superficial keratopathy
	  ○ Moderate superficial keratopathy
	  ○ Severe superficial keratopathy
	  ○ Corneal epithelial defect /ulcer
	• KVA scale grade for worst eye:
	  ○ Normal
	  ○ Grade 1
	  ○ Grade 2
	  ○ Grade 3
	  ○ Grade 4
		Index date and post-index treatment period

Use of contact lenses while on treatment*	Categorical variable: • Yes – specify use • No	Index date and post-index treatment period
Use of preservative-free lubricant eye drops while on treatment	Categorical variable: • Yes – specify use • No	Index date and post-index treatment period

Variable	Definition	Timing
Use of bandage contact lenses while on treatment	Categorical variable: • Yes – specify use • No	Index date and post-index treatment period
Use of cooling eye masks while on treatment	Categorical variable: • Yes – specify use • No	Index date and post-index treatment period

Abbreviations: BCVA=best Corrected Visual Acuity; KVA=Keratopathy and Visual Acuity.
*Patients should have avoided using contact lenses until the end of treatment unless directed by an ophthalmologist.

7.3.4. Safety

All ocular AESIs that occurred during and/or after administration of belantamab mafodotin were recorded regardless of a causal relationship to belantamab mafodotin. Data shown in Table 7-4 were collected for any ocular AESI (serious or non-serious) until the end of follow-up, study discontinuation for any reason, informed consent withdrawal or death; whichever came first.

Table 7-4 Ocular AESI

Variable	Definition	Timing
Date(s) ocular AESI(s)	Date of onset of each ocular AESIs	Index date and post-index period
Ocular AESI type	Categorical variable: type of ocular AESI* categorized by: • Keratopathy** • Blurred vision events# • Dry eye events## • Photophobia • Eye irritation • Ulcerative keratitis • Infective keratitis • Corneal erosions or defects • Other	Index date and post-index period
Ocular AESI severity at onset	Categorical variable: NCI CTCAE Version 5.0 grading: • Grade 1 • Grade 2 • Grade 3 • Grade 4 • Grade 5 KVA scale grade: • Normal • Grade 1 • Grade 2 • Grade 3 • Grade 4	Index date and post-index period
Ocular AESI severity increase after onset	Categorical variable: • Yes – specify highest grade • No	Index date and post-index period
Ocular AESI seriousness at onset	Categorical variable: • Fatal • Life-threatening • Persistent or significant disability/incapacity	Index date and post-index period

Variable	Definition	Timing
	• Inpatient (or prolongation of existing) hospitalization • Medically important event • None of the above	
Ocular AESI seriousness increase after onset	Categorical variable: • Yes – specify most serious event • No	Index date and post-index period
Ocular AESI impact on daily living	Categorical variable (e.g., need for caregiver support, eye irritation/pain, driving impairment, reading impairment)	Index date and post-index period
Action taken	Categorical variable: • Concomitant medication@ and other mitigation strategies (e.g., bandage contact lenses) • Belantamab mafodotin treatment change – Dose decrease – Treatment interruption/delay – Treatment discontinuation • Change in ophthalmic monitoring • Withdrawn from study • No action taken	Index date and post-index period
Documented relationship to belantamab mafodotin	Categorical variable: • Yes • No • Unknown	Index date and post-index period
Ocular AESI outcome	Categorical variable: • Fatal • Not recovered/not resolved • Recovered/resolved • Resolved with sequelae • Recovering/resolving • Unknown	Index date and post-index period
Ocular AESI stop date, if applicable	Date of ocular AESI resolution	Post-index period

Abbreviations: AESI=adverse event of special interest; KVA=Keratopathy and Visual Acuity; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events.

*MedDRA was used for coding AEs. **Based on eye examination, characterized as corneal epithelium changes with or without symptoms. #Includes diplopia, vision blurred, visual acuity reduced and visual impairment. ##Included dry eye, ocular discomfort, and eye pruritus @The WHO Drug Dictionary for medications was used for coding drugs.

7.3.5. Effectiveness

Table 7-5 shows the effectiveness data collected during the study period from the time of the first belantamab mafodotin dose until the end of follow-up, study discontinuation for any reason, informed consent withdrawal or death; whichever came first.

Table 7-5 Effectiveness

Variable	Definition	Timing
Date of death	Date of death	Post-index period
Tumor response	Assessment dates and categorical variable per IMWG response criteria (IMWG , 2021 criteria) if feasible or to local standard practice: • sCR • CR	Post-index period

Variable	Definition	Timing
	• VGPR • PR • No change/stable disease • PD	

Abbreviations: CR=complete response IMWG=International Myeloma Working Group; PD=Progressive disease; PR=partial response; sCR=stringent complete response; VGPR; very good partial response.

7.3.6. Timings of Assessment

Data were collected from patients' visits per routine clinical care either prospectively, directly into the eCRF or retrospectively from data already available in medical records into the eCRF (Table 7-6).

Table 7-6 Data Collection Plan

Variables	Baseline period	Standard of Care Visits*
Informed Consent	X	
Patient Eligibility	X	
Subject Characteristics	X	
Medical/Treatment History	X	
Concomitant Medications	X	X
Belantamab Mafodotin Treatment	X	X
Ophthalmic Monitoring and Results**	X	X
Ocular AESIs#	X	X
Effectiveness Evaluations		X

Abbreviations: AESI=adverse event of special interest.

*Data were collected only if reported as part of standard of care visits, which were assumed to take place about every 3 weeks during treatment in accordance with local treatment guidelines until the end of follow-up.

** In the EU, eye examinations were required before the first 3 treatment cycles. Additional eye examinations were required promptly as clinically indicated (e.g., on worsening of ocular symptoms (*BLENREP* SmPC, 2023).

#Other AEs and serious adverse events (SAEs) were not actively solicited and based on spontaneous reporting.

Note: Baseline and outcome data were extracted retrospectively from medical records or entered prospectively directly into the eCRF, where applicable.

7.4. Data sources

Data for all patients enrolled into this study were collected by Investigators or their designees (i.e., hematologists, oncologists, and ophthalmologists) and included into the eCRF. Countries and sites in Europe were selected based on the expected belantamab mafodotin market uptake and site availability. Data including demographics, disease status, treatment history and clinical characteristics were planned to be collected retrospectively from medical records and entered into eCRFs by participating clinicians. In addition, data including belantamab mafodotin treatment details, ophthalmic examination details, information on ocular AEs and treatment effectiveness data were collected by participating clinicians during prospective follow-up or retrospectively from medical records, where applicable, from the time of the first dose of belantamab

mafodotin to the end of the study, study discontinuation for any reason, informed consent withdrawal or death; whichever came first.

7.5. Bias

7.5.1. Selection Bias

All eligible RRMM patients from sites who were due to receive belantamab mafodotin were consecutively invited for study enrollment to reduce selection bias. In addition, key data, e.g., patient characteristics, ophthalmic monitoring, safety and effectiveness, were descriptively compared with results from clinical trials and global, prospective, real-world MM studies published in the literature.

Reasons for patient non-participation, withdrawal or loss-to-follow-up were recorded in the eCRF, if available, to address any remaining selection bias, if warranted. There was also risk associated with including patients who were due to receive belantamab mafodotin after study enrollment as these patients might not have contributed to the primary analyses if they did not receive treatment. If a patient did not initiate treatment with belantamab mafodotin after being enrolled in the study, baseline data were still collected, if feasible, to understand reasons for not being treated and differences between those who did and did not receive treatment after study enrollment.

7.5.2. Information Bias

Relying on investigators to fill out the assessment forms might have induced the presence of missing data, which could have resulted in bias. Entry of prospectively collected data into eCRFs minimized missing or incorrect data by having automated queries. Clear instructions and engagement with the study staff, with appropriate training, minimized the amount of missing data.

Some data, including MM history and treatment history were collected retrospectively. Retrospectively collected data may have been of lesser quality than prospectively collected data, with more missing data and fewer details. Rules about how to handle dropouts or missing data was included in the SAP.

7.5.3. Site Selection Bias

After the feasibility assessment for sites to be included in this study, site selection bias was reduced by taking a representative sample of sites, when feasible, given the number of sites per country and the requirement for European sites to have hematology/oncology and ophthalmology departments co-located within the same organization. This co-location of departments was seen in the majority of sites.

7.5.4. Effect Modifiers

Effect modification could have occurred when the effects of a treatment vary by presence/level of another factor (effect modifier). Subgroup analyses or analyses restricted to a selection of the study population was conducted when deemed applicable and feasible.

7.5.5. Patients Lost to Follow-up or without Follow-up Data

Because the follow-up duration was planned to be 15 months, the proportion of discontinued patients might have been significant given the severity of disease of the enrolled patient population. As standard of care visits were assumed to take place approximately every 3 weeks during belantamab mafodotin treatment, this was expected to reduce loss to follow-up. Reasons for loss-to-follow-up were recorded in the eCRF, if available.

7.6. Study size

A sample size of 150 evaluable RRMM patients was planned for the entire study. The sample size was not based on statistical power consideration but on a conservative estimate for each country of interest based on country-specific MM incidence and prevalence rates, the percentage of patients expected to be eligible for belantamab mafodotin treatment, the expected belantamab mafodotin market uptake, site availability and the treatment landscape in terms of ongoing clinical trials.

The sample size of 150 RRMM patients from the European sites was considered sufficient to meet the primary objective of describing RRMM patients treated with belantamab mafodotin per routine clinical care in terms of demographics, disease status, clinical characteristics, and treatment history.

7.7. Data management

All information outlined in Section 7.3 of the study protocol were recorded throughout the study either prospectively directly into an eCRF or retrospectively from medical records into the study database.

Data collection was completed in a validated EDC platform (Veeva EDC). All data collected were stored at secure servers ensuring compliance with local or national regulations. The investigator was responsible for ensuring data were entered in a timely manner and verifying that data were accurate and correct.

7.8. Data analysis

The planned analyses are described in the final version of the SAP (V5.0 29April 2024) (see Annex 1).

Two analysis populations were defined for study analyses as outlined below:

- The EP included all patients for whom written informed consent was obtained. This population was used for disposition summaries.
- The SP included all patients in the EP who received at least 1 dose of belantamab mafodotin. The SP was used for descriptive, safety and effectiveness analyses.

In this study, the EP and SP were the same population.

7.8.1. Primary Analysis

7.8.1.1. Main Analytical Approach

The primary objective of this study was to characterize RRMM patients treated with belantamab mafodotin. The primary outcome analysis includes the description of demographics, disease status, clinical characteristics and treatment history collected before or at the time of the first dose of belantamab mafodotin (i.e., during the baseline period) as outlined in the SAP.

7.8.2. Key Secondary Analysis

The following key secondary objectives were analyzed as outlined in the SAP:

- Treatment Exposure
  - Duration of Exposure, Cumulative Dose, Treatment Adherence (i.e., the total duration of treatment in days divided by the total follow-up time in days.)
- Ophthalmic Monitoring
- Ocular AESI
  - Pre-defined ocular AESIs for this study were keratopathy, change in BCVA, blurred vision events, dry eye events, photophobia, eye irritation, ulcerative keratitis, infective keratitis, corneal erosions or defects, other ocular AESI.

7.8.3. Other Secondary Objectives Analysis

In addition, the following were analyzed as outlined in the SAP:

- Dose Modifications, Treatment Delays, or Treatment Discontinuations due to an Ocular AESI
- Label Ophthalmic Monitoring Concordance
- Treatment Persistence (i.e., the proportion of patients still on treatment at specified time points, including 3-, 6-, 12- and 15-months of follow-up)
- Patient Outcomes
- BOR and ORR
- OS
- rwPFS

- DoR
- DoT

7.8.4. Subgroup Analysis

The following key subgroup analyses were evaluated as outlined in the SAP:

- LoT
- Ocular AESI during the active treatment exposure period
- Cumulative dose of treatment during the post-index treatment period before any ocular AESI
- Ophthalmic disease history recorded at baseline
- Comorbidity (diabetes) recorded as ongoing at baseline
- Best treatment response during follow-up
- Stem Cell Transplant at baseline.

The following additional subgroup analyses were conducted as outlined in the SAP:

- ECOG performance status at baseline
- Age group at index date
- MM subtype at baseline
- Type of follow-up data collection (Retrospective or Prospective)
- Treatment delay status during the post-index treatment period
- Extramedullary disease recorded at baseline
- ISS stage at baseline
- Cytogenetic risk at baseline
- BMI categories at baseline
- Duration of follow-up (for interim analyses only)
- Use of concomitant MM treatment in combination with belantamab mafodotin during the post-index period
- Use of concomitant eye medication in combination with belantamab mafodotin during the post-index period
- Prior anti-CD38 exposure (daratumumab and/or isatuximab)
- Refractory status
- Lost to follow-up
- Follow-up data

7.8.5. Data Handling Conventions/Data Transformations

All the analyses performed were presented overall and by LoT, unless specified otherwise. Any analysis with insufficient data available for a meaningful summary may not have been performed (e.g. there may not be sufficient data collected for impact on daily living), however all available data in the database was listed, with patient-level graphical presentations considered, where helpful.

Significance Level:

The overall significance level was 0.05, two-sided. All statistical tests were exploratory due to the nature of the study.

CIs:

CIs were two-sided with a confidence probability of 95%, unless otherwise specified. Whenever applicable, two-sided 95% CIs for proportions were calculated using the exact Binomial (Clopper-Pearson) method (Clopper, 1934).

Descriptive Analysis:

Continuous variables were summarized using descriptive statistics, i.e., number of non-missing values and number of missing values, mean, median, SD, min, max, Q1 and Q3.

Qualitative variables were summarized by frequency counts and percentages. Unless otherwise stated, the calculation of proportions/percentages for a given qualitative variable included patients with missing values in the denominator. When applicable, counts of missing observations for a qualitative variable were presented on summary tables. In case the analysis referred only to certain visits, percentages were based on the number of patients who had some study procedure performed at that visit, unless otherwise specified.

Time to Event Analysis:

Time to event data were summarized using the KM method. KM estimates (product-limit estimates) were presented together with a summary of associated statistics as follows:

- Median time, Q1 and Q3 with their corresponding two-sided 95% CIs calculated according to Brookmeyer and Crowley (Brookmeyer, 1982) and range (min, max).
- Event-free rate at specific time points with corresponding two-sided 95% CIs derived using the log-log transformation according to Kalbfleisch and Prentice (Kalbfleisch, 1980). The estimate of the SE was computed using Greenwood's formula.
- Frequency count (n) and percentage (%) of patients with event and censored.

Censoring rules were defined for Time to an AESI, OS, rwPFS, DoR, and DoT analysis, as outlined in the SAP. While it was likely that there was informative censoring, it was not possible to test for this and no adjustments or sensitivity analyses were planned.

Software Version:

All statistical analyses were conducted using SAS® (SAS Institute, North Carolina), version 9.4 or higher.

7.8.6. Amendments to Statistical Plan

Versions of SAP amendments and dates when they were approved are provided in Table 7-7.

Table 7-7 Revision history for the SAP

Version number	Date	Revision Summary
1.0	01 July 2022	Initial Release Version
2.0	30 January 2023	Minor clarifications and consistency edits in preparation for the first interim analysis
3.0	24 March 2023	Updated methodology for interim analysis data cuts to provide only clean data for analysis
4.0	08 November 2023	• Reduced content down to a more focused set of analyses, more closely reflecting the scope of the protocol. • Added overall study summaries to assist with reporting for regulatory submissions and/or manuscripts. • Added a swimmer plot for overall visual presentation of treatment and adverse events of special interest (AESI). • Removed renal impairment subgroup because recent clinical evidence suggests that renal impairment is a rare consideration in Multiple Myeloma (MM) prescribing. • Added subgroups for use of concomitant MM treatment, use of concomitant eye medication, prior anti-CD38 exposure and refractory status. • Changed subgroups for demographic, disease characteristics and patient outcome summaries. • Clarified that ATC level coding will be performed manually by GSK. • Added summaries of dose intensity and ophthalmic examination frequency. • Changed dose reductions to dose modifications for consistency with eCRFs. • Minor amendments to duration of follow-up subgroup, patient disposition summaries, treatment exposure summaries, AESI summaries, patient outcome summaries. • Made updates in line with updated eCRFs. • Other minor administrative updates.

Version number	Date	Revision Summary
5.0	29 April 2024	• Reduction in analysis presentations following early termination of study. Deleted TFLs are denoted in the separate TFL shells document. • Made updates in line with updated eCRFs. • Added ophthalmic disease history subgroup to many tables. • Added summary of prior MM treatments by prior LoT. • Added treatment response table. • Simplified AESI mitigation action definitions. • Consistency, clarification and administrative updates. • Updated standard operating procedure (SOP) numbers.

7.9. Quality control and Quality Assurance

Throughout this study, Syneos Health and GSK were responsible for following SOPs to ensure data quality and integrity, including archiving of statistical programs, appropriate documentation of data cleaning and validity for created variables, and description of available data. All sites were trained by the SMA on the protocol, study logistics, and the EDC system. Investigators were reminded of the processes and importance of reporting all ocular AESIs and other information.

Veeva EDC, used to manage data collection during this study, is a software tool designed to ensure quality assurance and facilitate data capture during clinical studies. The investigator was responsible for ensuring prospective data were entered in a timely manner and verifying that data were accurate and correct by physically or electronically signing the eCRF.

On-line logic checks were built into the EDC system as much as possible, so that missing or illogical data were not submitted. If inconsistent data persisted, queries were issued electronically to the clinical study center and answered electronically by that study center's personnel.

Data management quality review was performed on an ongoing basis. After data entry and clinical/medical reviews were confirmed as complete, any outstanding queries for the patients were reviewed and resolved during the data management quality review.

7.9.1. Access to Source Data/Documents

The Investigator guaranteed access to Sponsor representatives, contract designees, authorized regulatory authority inspectors, and IEC to all documents pertaining to the study had it been required.

7.9.2. Archiving Study Documents

Essential clinical documents were maintained to demonstrate the validity of the study and the integrity of the data collected. All study materials will be returned to the Sponsor after the study has been completed.

Master files were established at the beginning of the study, maintained for the duration of the study, and retained according to the appropriate regulations. According to the ICH guidelines, essential documents should be retained for a minimum of 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplatedmarketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the study treatment.

7.9.3. Study Monitoring

Participant data were monitored remotely. Monitoring visits were scheduled throughout the study, when needed. Monitoring visits were scheduled in advance, to ensure that the investigator has sufficient time to meet with the SMA and discuss all relevant findings. Participant data were reviewed and/or audited, and all deficiencies corrected on site, if possible. A complete audit trail of all monitoring visits and data changes was maintained. A virtual close-out visit was scheduled when all documents and data were collected, reviewed and necessary data changes were made after the last visit for the last participant. After study termination, a virtual study close-out visit was scheduled with the site if needed to retrieve all remaining study records. As long as COVID-19 restrictions applied, on-site study initiation and monitoring visits were not scheduled until restrictions were alleviated.

7.9.4. Audits and Inspections

Responsible IEC/competent authorities and/or the Sponsor’s clinical quality assurance group, or its designee, may request access to all source documents, case report forms, and other study documentation for on-site audit or inspection. Direct access to these documents is guaranteed by the Investigator, who will provide support at all times for these activities, as applicable.

8. PROTECTION OF HUMAN SUBJECTS

8.1. Ethical Approval and Subject Consent

The study was conducted in accordance with ethical principles founded in the Declaration of Helsinki (version 2008) and applicable legal and regulatory requirements and related guidance, especially Directive 2001/83/EC, Regulation (EC) No 726/2004 (REG) and Commission Implementing Regulation (EU) No 520/2012 (IR) as detailed in GVP Modules V, VI and VIII.

The IEC/Competent Authorities reviewed the study protocol, protocol amendments, and other relevant documents (e.g., ICFs). The study was only conducted at sites where IEC approval had been obtained. Any necessary extensions or renewals of IEC approval were obtained for changes to the study such as amendments to the protocol, the ICF, or other study documentation.

Informed consent was obtained from all patients before enrollment into the study. Each investigator ensured that each patient who needed to provide informed consent was given

full and adequate oral and written information in the local language about the nature and purpose of the study. The patient was given the opportunity to ask questions and allowed time to consider the information provided. All parties ensured protection of patient personal data and did not include names on any sponsor forms, reports, publications, or in any other disclosures, except where required by the local laws and regulations.

The signed and dated informed consent (when applicable) was obtained before any data were entered into the eCRF or available data were transferred to the analysis database. The investigator stored the original, signed ICF. A copy of the signed ICF was given to the patient. If the patient decided not to participate, the reason was collected in the eCRF.

8.2. Participant Withdrawal

Participation in this study was voluntary and patients could withdraw from the study at any time without prejudice. If the patient withdrew or was withdrawn, the reason was collected in the eCRF. In case of withdrawal, all study data collected before withdrawal was kept in the study database.

The Sponsor reserved the right, at any time, to discontinue enrollment of additional patients into the study, at any site; or to discontinue the study, for medical or administrative reasons.

8.3. Subject Confidentiality

The ICF incorporated wording that complied with relevant data protection and privacy legislation in the participating country. Patients authorized the collection, use and disclosure of their personal data by the investigator and by those persons who needed that information for the purposes of the study. The Sponsor and the Investigators followed the EU General Data Protection Regulation that replaces the Data Protection Directive 95/46/EC and that was designed to harmonize data privacy laws across Europe, to protect and empower all the EU citizens' data privacy, and to reshape the way organizations across the region approach data privacy.

The ICF for this study explained that study data was stored in a computer database, maintaining confidentiality in accordance with the local law for data protection. The ICF also explained that for quality check or data verification purposes, a monitor of Syneos Health required direct access to the signed ICF or source documents that were part of the hospital or practice records relevant to the study.

9. RESULTS

9.1. Participants

The study closed early with a data cut-off date for final analysis of 07 June 2024. Up to the data cut-off date, 84 patients were enrolled (Table 9-1).

9.1.1. All Screened Patients

In total, 84 patients were screened and provided informed consent (see Listing 16.2.1.1).

9.1.2. Enrolled Population (EP)

All screened patients met all eligibility criteria and were enrolled in the study. These 84 patients comprised the EP. LoT were grouped into 4 categories, either early line (LoT<4), as fourth-line treatment, as fifth-line treatment or at sixth-line or beyond.

A summary of patient disposition of the EP by LoT is provided in (Table 9-1). In total, 84 patients enrolled in the study (Austria=14 patients; Belgium=5 patients; Germany=4 patients; Greece=3 patients; Italy=32 patients; Norway=15 patients; Spain=11 patients) (Table 9-1). By country patient disposition information can be found in Table 14.1.1.1.

Forty patients (47.6%) completed the study, including 27 patients (32.1%) who died during follow-up (LoT=4 [n=7; 87.5%], LoT=5 [n=9; 25.0%]; LoT≥6 [n=11; 33.3%]).

In total, 44 patients (52.4%) did not complete the study; 39 patients (46.4%) discontinued due to study termination, 2 patients (2.4%) were lost to follow-up, 2 patients (2.4%) discontinued due to "other" reasons, and 1 patient (1.2%) withdrew consent (Table 9-1).

All patients in the EP received at least 1 dose of belantamab mafodotin and were therefore also in the SP.

9.1.3. Safety Population (SP)

All 84 patients received at least 1 dose of belantamab mafodotin either early line (LoT<4; n=7), fourth-line (n=8), fifth-line (n=36) or at sixth-line or beyond (n=33). All primary and secondary analyses below are based on the SP. Fifty-nine patients (70.2%) discontinued treatment mostly due to disease progression (n=28; 33.3%) or death (n=13; 15.5%) (Table 9-1).

Table 9-1 Patient Disposition (All Enrolled Patients)

Patient disposition	LoT<4	LoT=4	LoT=5	LoT≥6	Overall
Enrolled patients, n					84
Eligible patients, n					84
Safety Population, n (%)	7 (100)	8 (100)	36 (100)	33 (100)	84 (100)
Austria, n	4	3	2	5	14
Belgium, n	0	1	2	2	5
Germany, n	0	1	1	2	4
Greece, n	0	1	1	1	3
Italy, n	0	0	25	7	32
Norway, n	1	1	2	11	15
Spain, n	2	1	3	5	11
Patients with follow-up data, n (%)	7 (100)	8 (100)	36 (100)	33 (100)	84 (100)

Patient disposition	LoT<4	LoT=4	LoT=5	LoT≥6	Overall
Completed the study or died, n (%)	2 (28.6)	8 (100)	15 (41.7)	15 (45.5)	40 (47.6)
Died, n (%)	0	7 (87.5)	9 (25.0)	11 (33.3)	27 (32.1)
Withdrew from the study (reasons other than death), n (%)	5 (71.4)	0	21 (58.3)	18 (54.5)	44 (52.4)
Study terminated by sponsor	3 (42.9)	0	18 (50.0)	18 (54.5)	39 (46.4)
Withdrawal of consent	0	0	1 (2.8)	0	1 (1.2)
Ocular AESI	0	0	0	0	0
Other adverse event	0	0	0	0	0
Withdrawal by investigator	0	0	0	0	0
Lost to follow-up	0	0	2 (5.6)	0	2 (2.4)
Other	2 (28.6)	0	0	0	2 (2.4)
Discontinued treatment, n (%)	4 (57.1)	8 (100)	24 (66.7)	23 (69.7)	59 (70.2)
Disease progression	3 (42.9)	1 (12.5)	15 (41.7)	9 (27.3)	28 (33.3)
Ocular AESI	1 (14.3)	3 (37.5)	2 (5.6)	1 (3.0)	7 (8.3)
Other adverse event	0	0	2 (5.6)	0	2 (2.4)
Patient decision unrelated to adverse events	0	0	0	2 (6.1)	2 (2.4)
End of treatment	0	0	0	0	0
Death (unrelated to therapy)	0	3 (37.5)	4 (11.1)	6 (18.2)	13 (15.5)
Other	0	1 (12.5)	1 (2.8)	5 (15.2)	7 (8.3)

Table Source: 14.1.1.1

AESI: Adverse Event of Special Interest; LoT: Line of Treatment.

Note: Percentages are calculated using the number of patients included in the Safety Population and subgroup as denominator

Four patients (4.8%) were ongoing on treatment at the time of study completion by patient (LoT<4 [n=1; 14.3%], LoT=5 [n=2; 5.6%]; LoT≥6 [n=1; 3.0%]). Twenty-one patients (25.0%) were ongoing on treatment at the time of study termination by Sponsor (LoT<4 [n=2; 28.6%], LoT=5 [n=10; 27.8%]; LoT≥6 [n=9; 27.3%]). Of those 21 patients ongoing on treatment at the time of study termination, 18 patients (85.7%) were continuing on treatment via an NPP (Table 14.1.1.1).

Listings of individual patients on all LoT and by country are provided in Listing 16.2.1.1, Listing 16.2.1.2, Listing 16.2.3.1, and Listing 16.2.3.2.

9.1.4. Protocol Deviations

There were 12 major protocol deviations during the course of the study. Twelve patients did not meet eligibility criteria as they were included in the study with <4 lines of previous therapy. Per protocol inclusion criterion “Received (first dose up to 3 months before study enrollment; if deemed required based on enrollment rate) or due to receive belantamab mafodotin treatment per routine clinical care by an oncologist or hematologist consistent with the approved labelling” According to the approved labelling, patients should have received at least 4 prior therapies (except within Spain, where there is not a requirement for receiving at least 4 prior therapies) (Listing 16.2.2.1). These 12 patients were included in the SP.

In addition, there were 104 minor deviations, the majority being deviations from study procedures (Listing 16.2.2.1).

9.2. Outcome Data

All 84 patients included in the SP had follow-up data. The mean number of days post-index was 259.0 days (SD 138.78; min, max: 27, 492; median 236.5; Q1, Q3: 139.0, 399.0). The mean number of days post-index was 276.4 (SD 135.96) among those with an ongoing ophthalmic disease at baseline, 272.3 (SD 127.10) among those with a prior ophthalmic disease history only and 251.0 (SD 142.19) among those without an ophthalmic disease history (Table 14.1.2.1).

The cumulative proportion of patients still in the study was 86.9% at 3 months (95% CI: 77.6, 92.5), 63.1 % at 6 months (95% CI: 51.8, 72.4), 44.0% at 9 months (95% CI: 33.3, 54.3), 26.2% at 12 months (95% CI: 17.4, 35.9), and 10.7% at 15 months (95% CI: 5.3, 18.4) (Table 14.1.2.1).

9.3. Results of Primary Analyses

9.3.1. Demographic Characteristics by Line of Treatment (LoT) and Subgroups

A summary of patient demographics and baseline characteristics for the SP is provided in Table 9-2. Demographics and baseline characteristics including age, sex, height (cm), weight (kg), BMI and ECOG performance status are listed at the patient level in Listing 16.2.4.1.

The mean age for the SP was 70.7 years (SD 9.59; min, max 40, 93 years) with a lower mean age among patients treated with LoT<4 years (mean 62.4; SD 12.11). The median age of the SP was 72 years (Q1, Q3: 40, 93). Patients were slightly more likely to be female (n=46, 54.8%). The mean BMI of the SP was 25.3 kg/m2 (SD 4.51), with approximately 41% categorized as overweight or obese.

Across age categories, 33 patients (39.3%) were 75 years or older, 30 patients (35.7%) were between 65 years and 74 years of age, and 21 patients (25.0%) were between 18 and 64 years of age.

ECOG performance status data was available for 59 patients (70.2%) across the SP. Most patients had an ECOG score of 0 (n=24/59; 40.7%) and score of 1 (n=20/59; 33.9%) with fewer patients having a score of 2 (n=14/59; 23.7%) or 3 (n=1/59; 1.7%). None of the patients had an ECOG score of 4. Note: ECOG performance status worsens as the ECOG score increases.

Demographic characteristics (including subgroups of lost to follow up and completed follow-up) are provided in Table 14.1.3.1.1.

Table 9-2 Demographics and Baseline Characteristics (Safety Population)

Characteristic	LoT<4 (N=7)	LoT=4 (N=8)	LoT=5 (N=36)	LoT>=6 (N=33)	Total (N=84)
Age at index (years) [a]					
N	7	8	36	33	84
Mean (SD)	62.4 (12.11)	71.4 (8.63)	69.8 (8.02)	73.3 (10.08)	70.7 (9.59)
Median	62.0	71.5	70.5	74.0	72.0
Q1; Q3	52.0; 76.0	65.0; 78.0	64.5; 76.0	69.0; 79.0	64.5; 78.0
Min; Max	44; 78	58; 84	51; 83	40; 93	40; 93
Age at index categories, n (%)					
>=18 years to <65 years	5 (71.4)	2 (25.0)	9 (25.0)	5 (15.2)	21 (25.0)
>=65 years to <75 years	0	3 (37.5)	15 (41.7)	12 (36.4)	30 (35.7)
>=75 years	2 (28.6)	3 (37.5)	12 (33.3)	16 (48.5)	33 (39.3)
Sex, n (%)					
Female	4 (57.1)	3 (37.5)	21 (58.3)	18 (54.5)	46 (54.8)
Male	3 (42.9)	5 (62.5)	15 (41.7)	15 (45.5)	38 (45.2)
Height (cm)					
N	6	8	33	31	78
Mean (SD)	172.2 (6.94)	165.6 (8.37)	165.6 (9.89)	167.0 (11.76)	166.6 (10.35)
Median	172.0	167.0	165.0	165.0	165.5
Q1; Q3	170.0; 176.0	159.5; 171.0	160.0; 173.0	160.0; 174.0	160.0; 173.0
Min; Max	161; 182	153; 177	150; 180	142; 193	142; 193
Missing	1	0	3	2	6
Weight (kg)					
N	7	8	36	30	81
Mean (SD)	79.01 (14.689)	64.38 (12.223)	73.71 (13.787)	67.55 (15.119)	70.96 (14.596)
Median	74.60	66.00	73.00	65.50	70.00
Q1; Q3	69.00; 95.00	55.50; 73.50	65.20; 80.00	55.00; 79.00	60.00; 80.00
Min; Max	56.5; 95.0	45.0; 80.0	49.0; 115.0	47.0; 100	45.0; 115.0
Missing	0	0	0	3	3
BMI (kg/m2) [b]					
N	6	8	33	29	76
Mean (SD)	25.688 (4.1550)	23.446 (3.9057)	26.879 (4.7199)	23.924 (4.0358)	25.296 (4.5131)
Median	24.000	24.140	25.390	23.850	24.610
Q1; Q3	22.520; 30.670	21.745; 25.945	23.770; 29.380	20.830; 27.470	22.465; 28.310

Min; Max	21.80; 31.14	15.57; 28.34	19.88; 39.79	17.58; 33.12	15.57; 39.79
Missing	1	0	3	4	8
BMI categories, n (%)					
Underweight (<18.5 kg/m2)	0	1 (12.5)	0	2 (6.1)	3 (3.6)
Normal (>=18.5 kg/m2 to <25.0 kg/m2)	4 (57.1)	4 (50.0)	15 (41.7)	16 (48.5)	39 (46.4)
Overweight (>=25.0 kg/m2 to <30.0 kg/m2)	0	3 (37.5)	11 (30.6)	9 (27.3)	23 (27.4)
Obese (>=30.0 kg/m2)	2 (28.6)	0	7 (19.4)	2 (6.1)	11 (13.1)
Missing	1 (14.3)	0	3 (8.3)	4 (12.1)	8 (9.5)
ECOG performance status, n (%)					
0	0	1 (12.5)	12 (33.3)	11 (33.3)	24 (28.6)
1	3 (42.9)	1 (12.5)	8 (22.2)	8 (24.2)	20 (23.8)
2	0	2 (25.0)	7 (19.4)	5 (15.2)	14 (16.7)
3	0	1 (12.5)	0	0	1 (1.2)
4	0	0	0	0	0
Missing	4 (57.1)	3 (37.5)	9 (25.0)	9 (27.3)	25 (29.8)

Table Source: 14.1.3.1.1

AESI: Adverse Event of Special Interest; BMI: Body Mass Index; ECOG: Eastern Cooperative Oncology Group; LoT: Line of Treatment; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation.

[a] Age (years) = year of index date - year of birth.

[b] BMI (kg/m2) = weight at index date (kg) / [height at index date (cm)/100].

Note: Percentages are calculated based on the number of patients (N) in the SP within each treatment group.

9.3.2. Disease Characteristics by Line of Treatment (LoT) and Subgroups

By-patient MM disease characteristics are presented in Listing 16.2.4.3.

The mean age at initial MM diagnosis was 63.7 years (SD 10.06; min, max: 34, 88; median 63.5; Q1, Q3: 58.0, 71.5 years). Across the LoT categories, the mean age of initial MM diagnosis ranged from 59.7 years to 68.1 years (Table 9-3).

The mean time since initial MM diagnosis was 84.9 months (SD 48.11; min, max: 7.0, 243.8 months; median 79.0; Q1, Q3: 53.2, 119.3 months). Across the LoT categories, the mean time since initial MM diagnosis ranged from 33.6 to 113.5 months.

Fourteen out of 80 patients (17.5%) had extramedullary disease: 2/7 patients with LoT <4 (28.6%), 2/8 patients (25.0%) with LoT=4, 4/34 patients (11.8%) with LoT=5 and 6/31 patients (19.4%) with LoT ≥6.

A total of 59 patients had ISS staging values: 21/59 patients (35.6%) were in stage I, 14/59 patients (23.7%) in stage II, 24/59 (40.7%) in stage III. ISS staging data was missing for 25/84 patients (29.8%). Most common MM subtypes were the IgG subtype (n=43, 51.2%), followed by light chain (n=18; 21.4%), IgA subtype (n=13; 15.5%), other subtype (n=9; 10.7%) and IgD (n=1; 1.2%).

Most patients did not have a high cytogenetic risk (n=61; 72.6%), with remaining patients having a high cytogenetic risk (n=23; 27.4%) or high-IMWG cytogenetic risk (n=17; 20.2%).

Among the SP with refractory data, 29/78 patients (37.2%) were triple-refractory, 28/78 patients (35.9%) were quad-refractory, 21/78 patients (26.9%) were penta-refractory, and 6/78 patients (7.7%) had missing refractory data (Table 9-3).

MM disease characteristics (including subgroups of ocular AESI presence, ocular AESI absence, diabetes presence, responders, non-responders, at least 1 treatment delay, and no treatment delay) are provided in Table 14.1.3.2.1.

Table 9-3 Disease Characteristics (Safety Population)

Characteristic	LoT<4 (N=7)	LoT=4 (N=8)	LoT=5 (N=36)	LoT>=6 (N=33)	Total (N=84)
Age at initial MM diagnosis (years) [a]					
N	7	8	36	33	84
Mean (SD)	59.7 (11.51)	68.1 (10.03)	63.4 (8.72)	63.9 (11.14)	63.7 (10.06)
Median	58.0	69.5	63.5	66.0	63.5
Q1; Q3	49.0; 72.0	59.5; 76.0	59.0; 69.0	55.0; 72.0	58.0; 71.5
Min; Max	43; 75	53; 82	45; 80	34; 88	34; 88
Time since initial MM diagnosis (months) [b]					
N	7	8	36	33	84
Mean (SD)	33.56 (18.755)	37.95 (26.902)	79.15 (37.740)	113.45 (47.067)	84.90 (48.108)
Median	36.40	25.71	70.64	98.00	78.98
Q1; Q3	15.51; 55.85	22.26; 47.92	49.71; 111.21	80.13; 138.09	53.16; 119.31
Min; Max	7.0; 56.3	15.7; 96.1	27.2; 167.8	59.1; 243.8	7.0; 243.8
Extramedullary disease, n (%)					
Yes	2 (28.6)	2 (25.0)	4 (11.1)	6 (18.2)	14 (16.7)
No	5 (71.4)	6 (75.0)	30 (83.3)	25 (75.8)	66 (78.6)
Unknown	0	0	2 (5.6)	2 (6.1)	4 (4.8)
ISS stage, n (%)					
I	0	3 (37.5)	7 (19.4)	11 (33.3)	21 (25.0)
II	0	1 (12.5)	7 (19.4)	6 (18.2)	14 (16.7)
III	4 (57.1)	2 (25.0)	9 (25.0)	9 (27.3)	24 (28.6)
Missing	3 (42.9)	2 (25.0)	13 (36.1)	7 (21.2)	25 (29.8)
MM subtype, n (%)					
IgA	1 (14.3)	3 (37.5)	5 (13.9)	4 (12.1)	13 (15.5)
IgD	0	0	1 (2.8)	0	1 (1.2)
IgG	6 (85.7)	3 (37.5)	20 (55.6)	14 (42.4)	43 (51.2)
IgM	0	0	0	0	0
Biclonal (G, A)	0	0	0	0	0
Light chain	0	0	7 (19.4)	11 (33.3)	18 (21.4)
Other	0	2 (25.0)	3 (8.3)	4 (12.1)	9 (10.7)
Cytogenetic risk, n (%) [c]					

Characteristic	LoT<4 (N=7)	LoT=4 (N=8)	LoT=5 (N=36)	LoT>=6 (N=33)	Total (N=84)
High-cyto	1 (14.3)	5 (62.5)	9 (25.0)	8 (24.2)	23 (27.4)
High-IMWG	1 (14.3)	5 (62.5)	6 (16.7)	5 (15.2)	17 (20.2)
Non-high	6 (85.7)	3 (37.5)	27 (75.0)	25 (75.8)	61 (72.6)
Refractory status, n (%)					
Triple refractory	6 (85.7)	6 (75.0)	12 (33.3)	5 (15.2)	29 (34.5)
Quad refractory	1 (14.3)	1 (12.5)	20 (55.6)	6 (18.2)	28 (33.3)
Penta refractory	0	0	4 (11.1)	17 (51.5)	21 (25.0)
Missing	0	1 (12.5)	0	5 (15.2)	6 (7.1)

Table Source: 14.1.3.2.1

IgA: Immunoglobulin A; IgD: Immunoglobulin D; IgG: Immunoglobulin G; IgM: Immunoglobulin M; IMWG: International Myeloma Working Group; ISS: International Staging System; LoT: Line of Treatment; Max: Maximum; Min: Minimum; MM: Multiple Myeloma; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation.

[a] Age at initial MM diagnosis (years) = year of initial MM diagnosis - year of birth.

[b] Time since initial MM diagnosis (months) = (index date - date of initial MM diagnosis)/30.4375.

[c] High-cyto: t(4;14), t(14;16), del17p, or 1q+; High-IMWG: t(4;14), t(14;16), or del17p. A patient can be included in both high-cyto and high-IMWG.

Note: Percentages are calculated based on the number of patients (N) in the Safety Population and subgroup as the denominator.

9.3.3. Medical History

Medical history at screening is summarized in Table 9-4. More than half of the patients (60.7%) had ongoing comorbid conditions. Renal disease, pulmonary diseases, cardiac diseases and diabetes occurred at baseline, respectively, in 20.2%, 17.9%, 39.3% and 23.8% of the SP.

Twenty-six patients (31.0%) reported a history of eye diseases including a history of dry eyes/eye injuries affecting the BCVA (including keratopathy, glaucoma, cataracts, dry eye events, change in BCVA, corneal erosions or defects, blurred vision events, eye irritation, macular degeneration, ulcerative keratitis, and glaucoma; Data Source Listing 16.2.4.2.1). The percentage of patients with eye diseases across LoT categories ranged widely and was highest (48.5%) in LoT ≥6 patients who were also older (see Table 9-4). Twenty-three patients (27.4%) had an ongoing ophthalmic disease history, 4 patients (4.8%) had prior ophthalmic disease history only, and 57 patients (67.9%) had no ophthalmic disease history (Table 14.1.3.3.3).

Regarding baseline ophthalmic health, a total of 55 patients of the SP reported similar mean BCVA scores for their right and left eyes (mean 0.14, SD 0.26 for the right eye; mean 0.15, SD 0.26 for the left eye) (Table 14.1.3.4.1). Baseline ophthalmic health (including subgroups of ongoing ophthalmic disease history, prior ophthalmic disease history only, and no ophthalmic disease history) is provided in Table 14.1.3.4.1.

Other comorbid conditions were present in 71.4% of the SP (Table 9-4) (see by-patient listing in Listings 16.2.4.2.1 and 16.2.4.2.2, and summary statistics in Table 14.1.3.3.2). Seventy-three patients (86.9%) had at least 1 pre-existing comorbidity (Table 9-4).

Baseline laboratory assessments including creatinine clearance (n=34; mean 58.40 ml/min; SD 26.03), LDH (n=54; mean 267.2 U/L; SD 267.41) and serum creatinine (n=64; mean 132.07 umol/L; SD 124.24) were estimated for the SP and across the LoT categories (Table 14.1.3.5.1). Across the LoTs, the mean values for laboratory assessments varied with high levels of each found in LoT=4 patients (Table 14.1.3.5.1).

Table 9-4 Medical History (Safety Population)

Characteristic	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Pre-existing or ongoing comorbidity of Interest					
Ongoing	2 (28.6)	5 (62.5)	24 (66.7)	20 (60.6)	51 (60.7)
Prior only	1 (14.3)	0	5 (13.9)	3 (9.1)	9 (10.7)
None	4 (57.1)	2 (25.0)	7 (19.4)	10 (30.3)	23 (27.4)
Missing	0	1 (12.5)	0	0	1 (1.2)
Renal disease					
Yes	2 (28.6)	2 (25.0)	5 (13.9)	8 (24.2)	17 (20.2)
Mild with dialysis	0	0	0	0	0
Moderate/Severe with dialysis	1 (14.3)	1 (12.5)	2 (5.6)	0	4 (4.8)
Mild with no dialysis	0	1 (12.5)	1 (2.8)	4 (12.1)	6 (7.1)
Moderate/Severe with no dialysis	0	0	1 (2.8)	4 (12.1)	5 (6.0)

Characteristic	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
No	5 (71.4)	6 (75.0)	31 (86.1)	25 (75.8)	67 (79.8)
Unknown	0	0	0	0	0
Pulmonary diseases					
Yes	1 (14.3)	1 (12.5)	7 (19.4)	6 (18.2)	15 (17.9)
No	6 (85.7)	7 (87.5)	29 (80.6)	27 (81.8)	69 (82.1)
Unknown	0	0	0	0	0
Cardiac diseases					
Yes	1 (14.3)	2 (25.0)	14 (38.9)	16 (48.5)	33 (39.3)
No	6 (85.7)	6 (75.0)	22 (61.1)	17 (51.5)	51 (60.7)
Unknown	0	0	0	0	0
Diabetes					
Yes	2 (28.6)	1 (12.5)	12 (33.3)	5 (15.2)	20 (23.8)
No	5 (71.4)	7 (87.5)	24 (66.7)	28 (84.8)	64 (76.2)
Unknown	0	0	0	0	0
Eye diseases including the history of dry eye/eye injuries affecting the BCVA					
Yes	1 (14.3)	2 (25.0)	7 (19.4)	16 (48.5)	26 (31.0)
No	6 (85.7)	5 (62.5)	29 (80.6)	17 (51.5)	57 (67.9)
Unknown	0	1 (12.5)	0	0	1 (1.2)
Other					
Yes	6 (85.7)	8 (100)	22 (61.1)	24 (72.7)	60 (71.4)
No	1 (14.3)	0	14 (38.9)	9 (27.3)	24 (28.6)
Patients with at least 1 pre-existing comorbidity	6 (85.7)	8 (100)	31 (86.1)	28 (84.8)	73 (86.9)

Table Source: 14.1.3.3.1 and 14.1.3.3.2
BCVA: Best Corrected Visual Acuity; LoT: Line of Treatment.

9.3.4. Treatment History

All patients had at least 1 prior MM therapy, at least 1 prior immunomodulatory treatment, and at least 1 prior proteasome inhibitor treatment. Most patients (97.6%) had at least 1 prior corticosteroid treatment and at least 1 prior monoclonal antibody treatment. A large proportion of the SP also had at least 1 prior chemotherapy treatment (78.6%) and almost 50% at least 1 prior stem cell transplant (48.8%) (Table 9-4). The percentage of patients per prior treatment category ranged widely across LoT categories (see Table 9-4). Prior MM treatment (including subgroups of prior LoT) is provided in Table 14.1.4.1. Concomitant MM treatment (including subgroups of ongoing ophthalmic disease history, prior ophthalmic disease history only, and no ophthalmic disease history) is provided in Table 14.1.4.2. Concomitant eye medications (including subgroups of ongoing ophthalmic disease history, prior ophthalmic disease history only, and no ophthalmic disease history) is provided in Table 14.1.4.3. A by-patient listing of prior MM medications assessed during the baseline visit for the SP is provided in Listing 16.2.4.5.1. A by-patient listing of concomitant medications for the SP is provided in Lising 16.2.4.4.

At least 1 concomitant MM treatment was reported in 38.1% of patients (reasons for medication use included MM treatment, AESI; cataract surgery [right eye], phacoemulsification + intraocular lens of left eye, lower jaw paresthesia, pre-medication, anti-inflammatory, intracranial hemorrhage, allergic reaction, prophylaxis to nausea,

basic disease, new therapy line step up phase, maintenance therapy, new multiple myeloma therapy after discontinuation of belantamab mafodotin, palliative myeloma treatment, In combination with belantamab mafodotin treatment, prophylactic for tumor therapy; Data Source Listing 16.2.4.5.2); 32.1% had corticosteroids, 11.9% had chemotherapy, 10.7% had a bispecific antibody, 7.1% had a proteasome inhibitor, 4.8% had an immunodulator, and 2.4% had monoclonal antibody (Table 9-6). A by-patient listing of concomitant MM medications assessed during the baseline visit for the SP is provided in Listing 16.2.4.5.2.

A large proportion of patients (n=69/84, 82.1%) had at least 1 concomitant eye medication; Among the SP, 72.6% had 'other' ophthalmologicals, 19.0% had corticosteroids (plain), 7.1% had viscoelastic substances, 3.6% had beta blocking agents, 3.6% had fluoroquinolones, 2.4% had anti-inflammatory agents (non-steroids), 2.4% had corticosteroids, 2.4% had combination corticosteroids and anti-infectives and 2.4% had uncoded medications (insulin NOS). In addition, the following concomitant eye medications were reported in 1 (1.2%) patient each: anti-infectives, antivirals, carbonic anhydrase inhibitors, herbal ophthalmologicals, other, other anti-infectives, and prostaglandin analogues (Table 9-7). A by-patient listing of concomitant eye medications assessed during the baseline visit for the SP is provided in Listing 16.2.4.5.3.

Table 9-5 Prior MM treatment history (Safety Population)

Characteristic	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Patients with at least 1 prior MM Therapy	7 (100)	8 (100)	36 (100)	33 (100)	84 (100)
Patients with at least 1 prior corticosteroid treatment	7 (100)	8 (100)	35 (97.2)	32 (97.0)	82 (97.6)
Dexamethasone	7 (100)	8 (100)	35 (97.2)	32 (97.0)	82 (97.6)
Refractory	5 (71.4)	5 (62.5)	31 (86.1)	28 (84.8)	69 (82.1)
Prednisone	0	1 (12.5)	5 (13.9)	9 (27.3)	15 (17.9)
Refractory	0	1 (12.5)	4 (11.1)	4 (12.1)	9 (10.7)
Prednisolone	0	0	1 (2.8)	7 (21.2)	8 (9.5)
Refractory	0	0	1 (2.8)	5 (15.2)	6 (7.1)
Other	0	0	0	1 (3.0)	1 (1.2)
Refractory	0	0	0	1 (3.0)	1 (1.2)
Patients with at least 1 prior immunomodulator treatment	7 (100)	8 (100)	36 (100)	33 (100)	84 (100)
Lenalidomide	7 (100)	7 (87.5)	33 (91.7)	31 (93.9)	78 (92.9)
Refractory	5 (71.4)	4 (50.0)	25 (69.4)	17 (51.5)	51 (60.7)
Pomalidomide	1 (14.3)	7 (87.5)	32 (88.9)	28 (84.8)	68 (81.0)
Refractory	1 (14.3)	5 (62.5)	28 (77.8)	24 (72.7)	58 (69.0)
Thalidomide	1 (14.3)	2 (25.0)	12 (33.3)	13 (39.4)	28 (33.3)
Refractory	1 (14.3)	1 (12.5)	2 (5.6)	5 (15.2)	9 (10.7)
Other	0	1 (12.5)	1 (2.8)	1 (3.0)	3 (3.6)
Refractory	0	0	1 (2.8)	1 (3.0)	2 (2.4)
Patients with at least 1 prior monoclonal antibody treatment	7 (100)	8 (100)	34 (94.4)	33 (100)	82 (97.6)
Daratumumab	5 (71.4)	7 (87.5)	27 (75.0)	33 (100)	72 (85.7)
Refractory	5 (71.4)	6 (75.0)	25 (69.4)	30 (90.9)	66 (78.6)
Elotuzumab	0	1 (12.5)	11 (30.6)	6 (18.2)	18 (21.4)
Refractory	0	1 (12.5)	10 (27.8)	5 (15.2)	16 (19.0)

Characteristic	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Isatuximab	2 (28.6)	2 (25.0)	10 (27.8)	1 (3.0)	15 (17.9)
Refractory	1 (14.3)	1 (12.5)	8 (22.2)	1 (3.0)	11 (13.1)
Other	0	0	0	1 (3.0)	1 (1.2)
Refractory	0	0	0	1 (3.0)	1 (1.2)
Patients with at least 1 prior proteasome inhibitor treatment	7 (100)	8 (100)	36 (100)	33 (100)	84 (100)
Bortezomib	6 (85.7)	4 (50.0)	31 (86.1)	30 (90.9)	71 (84.5)
Refractory	0	2 (25.0)	17 (47.2)	17 (51.5)	36 (42.9)
Carfilzomib	4 (57.1)	7 (87.5)	26 (72.2)	26 (78.8)	63 (75.0)
Refractory	3 (42.9)	4 (50.0)	19 (52.8)	18 (54.5)	44 (52.4)
Xiaomi	1 (14.3)	1 (12.5)	5 (13.9)	7 (21.2)	14 (16.7)
Refractory	1 (14.3)	1 (12.5)	4 (11.1)	5 (15.2)	11 (13.1)
Patients with at least 1 prior chemotherapy treatment	3 (42.9)	4 (50.0)	28 (77.8)	31 (93.9)	66 (78.6)
Cyclophosphamide	3 (42.9)	1 (12.5)	22 (61.1)	26 (78.8)	52 (61.9)
Refractory	0	0	14 (38.9)	14 (42.4)	28 (33.3)
Melphalan	3 (42.9)	1 (12.5)	10 (27.8)	15 (45.5)	29 (34.5)
Refractory	0	1 (12.5)	5 (13.9)	7 (21.2)	13 (15.5)
Other	0	1 (12.5)	2 (5.6)	8 (24.2)	11 (13.1)
Refractory	0	0	0	6 (18.2)	6 (7.1)
Doxorubicin	0	0	3 (8.3)	5 (15.2)	8 (9.5)
Refractory	0	0	2 (5.6)	1 (3.0)	3 (3.6)
Etoposide	0	0	3 (8.3)	3 (9.1)	6 (7.1)
Refractory	0	0	2 (5.6)	0	2 (2.4)
Bendamustine	0	1 (12.5)	1 (2.8)	3 (9.1)	5 (6.0)
Refractory	0	1 (12.5)	1 (2.8)	2 (6.1)	4 (4.8)
Cisplatin	0	0	2 (5.6)	1 (3.0)	3 (3.6)
Refractory	0	0	2 (5.6)	0	2 (2.4)
Patients with at least 1 prior stem cell transplant	0	3 (37.5)	18 (50.0)	20 (60.6)	41 (48.8)
Autologous	0	3 (37.5)	18 (50.0)	20 (60.6)	41 (48.8)
Refractory	0	0	3 (8.3)	3 (9.1)	6 (7.1)
Allogeneic	0	0	1 (2.8)	1 (3.0)	2 (2.4)
Refractory	0	0	1 (2.8)	0	1 (1.2)
Patients with at least 1 prior stem cell transplant induction	0	0	6 (16.7)	9 (27.3)	15 (17.9)
Patients with at least 1 prior stem cell transplant maintenance	0	0	7 (19.4)	3 (9.1)	10 (11.9)
Patients with at least 1 prior maintenance therapy	0	2 (25.0)	6 (16.7)	3 (9.1)	11 (13.1)
Lenalidomide	0	1 (12.5)	3 (8.3)	2 (6.1)	6 (7.1)
Refractory	0	1 (12.5)	2 (5.6)	2 (6.1)	5 (6.0)
Thalidomide	0	0	3 (8.3)	1 (3.0)	4 (4.8)
Refractory	0	0	0	1 (3.0)	1 (1.2)
Bortezomib	0	0	2 (5.6)	0	2 (2.4)
Refractory	0	0	1 (2.8)	0	1 (1.2)
Other	0	1 (12.5)	1 (2.8)	0	2 (2.4)
Refractory	0	0	1 (2.8)	0	1 (1.2)
Daratumumab	0	0	1 (2.8)	0	1 (1.2)
Refractory	0	0	1 (2.8)	0	1 (1.2)
Pomalidomide	0	0	0	1 (3.0)	1 (1.2)
Refractory	0	0	0	1 (3.0)	1 (1.2)
Patients with at least 1 prior bispecific antibody	0	0	0	1 (3.0)	1 (1.2)

Characteristic	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Other	0	0	0	1 (3.0)	1 (1.2)
Refractory	0	0	0	1 (3.0)	1 (1.2)
Patients with at least 1 prior CAR T-cell therapy	0	0	1 (2.8)	1 (3.0)	2 (2.4)
Ide-cell	0	0	1 (2.8)	1 (3.0)	2 (2.4)
Refractory	0	0	1 (2.8)	1 (3.0)	2 (2.4)
Patients with at least 1 prior histone deacetylase treatment	0	0	0	1 (3.0)	1 (1.2)
Panobinostat	0	0	0	1 (3.0)	1 (1.2)
Refractory	0	0	0	1 (3.0)	1 (1.2)
Patients with prior anti-CD38 exposure, n (%)	7 (100)	8 (100)	34 (94.4)	33 (100)	82 (97.6)
Number of prior LOTs, n (%)					
2	7 (100)	0	0	0	7 (8.3)
3	0	8 (100)	0	0	8 (9.5)
4	0	0	36 (100)	0	36 (42.9)
5	0	0	0	15 (45.5)	15 (17.9)
6	0	0	0	7 (21.2)	7 (8.3)
>6	0	0	0	11 (33.3)	11 (13.1)

Table Source: 14.1.4.1

CAR-T: Chimeric antigen receptor-T cell therapy; Ide-cell: Idecabtagene vicleucel; MM: Multiple Myeloma; Lot: Line of Treatment

Note: Percentages are calculated using the number of patients included in the SP as the denominator.

Note: Prior MM treatments are displayed in terms of frequency tables, sorted by descending order of incidence of prior MM therapy type. In case of equal incidence, alphabetical order was applied.

Table 9-6 Concomitant MM treatment (Safety Population)

Drug Class Preferred Term	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Patients with at least 1 concomitant MM treatment	4(57.1)	1(12.5)	12(33.3)	15(45.5)	32(38.1)
Corticosteroids	3(42.9)	1(12.5)	10(27.8)	13(39.4)	27(32.1)
Dexamethasone	3(42.9)	1(12.5)	9(25.0)	13(39.4)	26(31.0)
Prednisolone	0	0	1(2.8)	0	1(1.2)
Prednisone	0	0	1(2.8)	0	1(1.2)
Chemotherapy	1(14.3)	1(12.5)	5(13.9)	3(9.1)	10(11.9)
Cyclophosphamide	1(14.3)	1(12.5)	2(5.6)	1(3.0)	5(6.0)
Bendamustine	0	0	2(5.6)	1(3.0)	3(3.6)
Etoposide	0	0	0	1(3.0)	1(1.2)
Melphalan	0	0	1(2.8)	0	1(1.2)
Bispecific Antibody	1(14.3)	0	5(13.9)	3(9.1)	9(10.7)
Talquetamab	1(14.3)	0	4(11.1)	3(9.1)	8(9.5)
Teclistamab	0	0	2(5.6)	0	2(2.4)
Proteasome Inhibitors	1(14.3)	1(12.5)	3(8.3)	1(3.0)	6(7.1)
Carfilzomib	1(14.3)	1(12.5)	1(2.8)	1(3.0)	4(4.8)
Bortezomib	1(14.3)	0	2(5.6)	0	3(3.6)
Immunomodulators	2(28.6)	1(12.5)	1(2.8)	0	4(4.8)
Pomalidomide	2(28.6)	1(12.5)	1(2.8)	0	4(4.8)
Monoclonal Antibodies	0	0	1(2.8)	1(3.0)	2(2.4)
Elotuzumab	0	0	1(2.8)	0	1(1.2)
Isatuximab	0	0	0	1(3.0)	1(1.2)

Table Source: 14.1.4.2

MM: Multiple Myeloma; Lot: Line of Treatment
Note: Percentages are calculated using the number of patients included in the SP as the denominator.
Note: Each patient is counted only once within a given drug class and preferred term.

Table 9-7 Concomitant Eye Medications (Safety Population)

ATC Class 4th Level Preferred Term	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Patients with at least 1 concomitant eye medication	5(71.4)	7(87.5)	27(75.0)	30(90.9)	69(82.1)
Other Ophthalmologicals	5(71.4)	7(87.5)	25(69.4)	24(72.7)	61(72.6)
Hyaluronate Sodium	3(42.9)	1(12.5)	6(16.7)	4(12.1)	14(16.7)
Hyaluronate Sodium;trehalose	0	1(12.5)	5(13.9)	6(18.2)	12(14.3)
Carbomer	1(14.3)	1(12.5)	3(8.3)	5(15.2)	10(11.9)
Hyaluronic Acid	1(14.3)	0	6(16.7)	3(9.1)	10(11.9)
Acetylcysteine	3(42.9)	0	2(5.6)	1(3.0)	6(7.1)
Other Ophthalmologicals	2(28.6)	1(12.5)	0	3(9.1)	6(7.1)
Retinol Palmitate	1(14.3)	1(12.5)	1(2.8)	3(9.1)	6(7.1)
Dexpanthenol	0	0	2(5.6)	3(9.1)	5(6.0)
Trehalose	1(14.3)	1(12.5)	1(2.8)	2(6.1)	5(6.0)
Dextran 70;hypromellose	0	1(12.5)	1(2.8)	2(6.1)	4(4.8)
Ectoine;hyaluronate Sodium	2(28.6)	0	0	2(6.1)	4(4.8)
Dextran;hypromellose	0	0	2(5.6)	1(3.0)	3(3.6)
Carmellose Sodium	0	1(12.5)	1(2.8)	0	2(2.4)
Dexpanthenol;hyaluronate Sodium	0	2(25.0)	0	0	2(2.4)
Dexpanthenol;retinol	0	0	1(2.8)	1(3.0)	2(2.4)
Dexpanthenol;retinol;vitamin E Nos	1(14.3)	0	0	1(3.0)	2(2.4)
Albumin Human	0	0	0	1(3.0)	1(1.2)
Carmellose	0	0	1(2.8)	0	1(1.2)
Centella Asiatica;foeniculum Vulgare;ginkgo Biloba;hyaluronate Sodium;vaccinium Macrocarpon	0	0	1(2.8)	0	1(1.2)
Dexpanthenol;hypromellose	0	0	1(2.8)	0	1(1.2)
Eye Lubricants	0	0	1(2.8)	0	1(1.2)
Gentamicin Sulfate	1(14.3)	0	0	0	1(1.2)
Hypromellose;ozonised Sunflower Oil;phospholipids Soybean	1(14.3)	0	0	0	1(1.2)
Macrogol 400;propylene Glycol	1(14.3)	0	0	0	1(1.2)
Paraffin, Liquid;petrolatum	0	0	0	1(3.0)	1(1.2)
Povidone	0	0	0	1(3.0)	1(1.2)
Corticosteroids, Plain	4(57.1)	1(12.5)	5(13.9)	6(18.2)	16(19.0)
Hydrocortisone Sodium Phosphate	3(42.9)	1(12.5)	2(5.6)	2(6.1)	8(9.5)
Fluorometholone	0	0	2(5.6)	3(9.1)	5(6.0)
Prednisolone Acetate	0	0	1(2.8)	2(6.1)	3(3.6)
Dexamethasone Sodium Phosphate	1(14.3)	0	0	1(3.0)	2(2.4)
Dexamethasone	0	0	1(2.8)	0	1(1.2)
Viscoelastic Substances	0	1(12.5)	1(2.8)	4(12.1)	6(7.1)
Hypromellose	0	1(12.5)	1(2.8)	4(12.1)	6(7.1)

ATC Class 4th Level Preferred Term	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Beta Blocking Agents	1(14.3)	1(12.5)	0	1(3.0)	3(3.6)
Latanoprost;timolol Maleate	0	1(12.5)	0	1(3.0)	2(2.4)
Dorzolamide Hydrochloride;timolol Maleate	0	1(12.5)	0	0	1(1.2)
Timolol	1(14.3)	0	0	0	1(1.2)
Fluoroquinolones	1(14.3)	0	0	2(6.1)	3(3.6)
Ofloxacin	1(14.3)	0	0	2(6.1)	3(3.6)
Antiinflammatory Agents, Non-Steroids	0	0	0	2(6.1)	2(2.4)
Diclofenac Sodium	0	0	0	2(6.1)	2(2.4)
Corticosteroids	0	0	0	2(6.1)	2(2.4)
Dexamethasone	0	0	0	2(6.1)	2(2.4)
Corticosteroids And Antiinfectives In Combination	0	0	1(2.8)	1(3.0)	2(2.4)
Dexamethasone;tobramycin	0	0	1(2.8)	1(3.0)	2(2.4)
Antiinfectives	0	1(12.5)	0	0	1(1.2)
Doxycycline	0	1(12.5)	0	0	1(1.2)
Antivirals	0	0	0	1(3.0)	1(1.2)
Aciclovir	0	0	0	1(3.0)	1(1.2)
Carbonic Anhydrase Inhibitors	0	1(12.5)	0	0	1(1.2)
Dorzolamide Hydrochloride	0	1(12.5)	0	0	1(1.2)
Herbal Ophthalmologicals, Other	0	0	1(2.8)	0	1(1.2)
Herbal Ophthalmologicals, Other	0	0	1(2.8)	0	1(1.2)
Other Antiinfectives	0	1(12.5)	0	0	1(1.2)
Cethexonium Bromide	0	1(12.5)	0	0	1(1.2)
Prostaglandin Analogues	0	0	1(2.8)	0	1(1.2)
Latanoprost	0	0	1(2.8)	0	1(1.2)
Uncoded	1(14.3)	0	0	1(3.0)	2(2.4)
Insulin Nos	1(14.3)	0	0	1(3.0)	2(2.4)

Table Source: 14.1.4.3

MM: Multiple Myeloma; Lot: Line of Treatment

Note: Percentages are calculated using the number of patients included in the SP as the denominator.

Note: Each patient is counted only once within a given ATC level and PT.

Note: Concomitant medications are displayed in terms of frequency tables, sorted by descending order of incidence of ATC and PT within each ATC. In case of equal incidence regarding ATC/PT, alphabetical order was applied.

9.4. Key Secondary Analyses

9.4.1. Treatment Exposure

9.4.1.1. Duration of Treatment

The mean duration of belantamab mafodotin exposure was 161.5 days (SD 122.90; median 125.5 days; Q1, Q3: 70.5, 230.5); 206.1 days (SD 164.14; median 148.0 days; Q1, Q3: 79.0, 400.0) for LoT<4 patients, 56.5 days (SD 32.25; median 45.0 days; Q1, Q3: 39.0, 65.0) for LoT=4 patients, 165.9 days (SD 115.19; median 136.0 days; Q1, Q3: 86.5, 221.0) for LoT=5 patients and 172.8 days (SD 126.66; median 124.0 days; Q1, Q3: 70.0, 254.0) for LoT≥6 patients (Table 9-8).

More AESIs were reported for patients who had a longer duration of treatment. For patients with the presence of an ocular AESI on treatment, the mean duration of belantamab mafodotin exposure prior to the event was 193.0 days (SD 127.19; median 142.5 days; Q1, Q3: 106.0, 279.0). For patients absent of an ocular AESI, the mean duration of exposure was 91.4 days (SD 76.48; median 67.0 days; Q1, Q3: 44.0, 102.0) (Table 9-8).

The mean duration of belantamab mafodotin exposure was 173.5 days (SD 127.64; median 140.0 days; Q1, Q3: 85.0, 169.0) for patients with a cumulative treatment dose of ≤180 mg before an ocular AESI, 206.3 days (SD 139.03; median 152.5 days; Q1, Q3: 107.0, 308.0) for patients with a cumulative treatment dose of >180 mg to ≤270 mg before an ocular AESI, 188.9 days (SD 112.15; median 134.0 days; Q1, Q3: 110.0, 254.0) for patients with a cumulative treatment dose of >270 mg to ≤400 mg before an ocular AESI, and 200.9 days (SD 140.47; median 138.0 days; Q1, Q3: 79.0, 345.0) for patients with a cumulative treatment dose >400 mg before an ocular AESI (Table 9-8).

For patients with ongoing ophthalmic disease history, the mean duration of exposure was 211.4 days (SD 134.75; median 149.0 days; Q1, Q3: 117.0, 338.0). For patients with a prior ophthalmic disease history only, the mean duration of exposure was 200.8 days (SD 104.54; median 185.5 days; Q1, Q3: 113.5, 288.0). For patients with no ophthalmic disease history, the mean duration of exposure was 138.7 days (SD 114.05; median 89.0 days; Q1, Q3: 61.0, 169.0) (Table 9-8).

For patients with diabetes, the mean duration of exposure was 199.2 days (SD 133.19; median 171.0 days; Q1, Q3: 95.5, 308.0) (Table 14.2.1.1).

For patients with a partial response or better (n=24), the mean duration of exposure was 238.5 days (SD 127.26; median 236.5 days; Q1, Q3: 115.5, 332.0). For non-responders, the mean duration of exposure was 123.5 days (SD 100.78; median 112.5 days; Q1, Q3: 50.0, 145.0) (Table 14.2.1.1).

For patients with a stem cell transplant, the mean duration of exposure was 177.7 days (SD 131.94; median 124.0 days; Q1, Q3: 78.0, 258.0). For patients with no stem cell transplant, the mean duration of exposure was 146.2 days (SD 113.04; median 127.0 days; Q1, Q3: 57.0, 169.0) (Table 14.2.1.1).

Table 9-8 Duration of Exposure (Days) by LoT Subgroups (SP)

	LoT<4 (N=7)	**LoT=4 (N=8)**	**LoT=5 (N=36)**	**LoT>=6 (N=33)**	**Total (N=84)**
n	7	8	36	33	84
Mean (SD)	206.1 (164.14)	56.5 (32.25)	165.9 (115.19)	172.8 (126.66)	161.5 (122.90)
Median	148.0	45.0	136.0	124.0	125.5
Q1; Q3	79.0, 400.0	39.0, 65.0	86.5, 221.0	70.0, 254.0	70.5, 230.5
Min; Max	51, 476	27, 127	21, 459	44, 455	21, 476
Subgroup: Ocular AESI Presence	LoT<4 (N=6)	LoT=4 (N=3)	LoT=5 (N=27)	LoT>=6 (N=22)	Total (N=58)
n	6	3	27	22	58
Mean (SD)	215.8 (177.60)	84.7 (39.80)	174.6 (117.96)	224.1 (125.48)	193.0 (127.19)
Median	144.5	79.0	138.0	217.5	142.5
Q1; Q3	79.0, 400.0	48.0, 127.0	106.0, 235.0	117.0, 337.0	106.0, 279.0

Min; Max	51, 476	48, 127	22, 459	48, 455	22, 476
Subgroup: Ocular AESI Absence	**LoT<4 (N=1)**	**LoT=4 (N=5)**	**LoT=5 (N=9)**	**LoT>=6 (N=11)**	**Total (N=26)**
n	1	5	9	11	26
Mean (SD)	148.0 (-)	39.6 (8.71)	140.0 (108.68)	70.0 (29.18)	91.4 (76.48)
Median	148.0	41.0	102.0	64.0	67.0
Q1; Q3	148.0, 148.0	37.0, 42.0	71.0, 207.0	50.0, 78.0	44.0, 102.0
Min; Max	148, 148	27, 51	21, 331	44, 149	21, 331
Subgroup: Cumulative Dose of Treatment Before any AESI = ≤180 mg	**LoT<4 (N=1)**	**LoT=4 (N=0)**	**LoT=5 (N=6)**	**LoT>=6 (N=6)**	**Total (N=13)**
n	1	0	6	6	13
Mean (SD)	140.0 (-)	-	223.5 (151.75)	129.0 (102.32)	173.5 (127.64)
Median	140.0	-	157.0	104.5	140.0
Q1; Q3	140.0, 140.0	-	145.0, 360.0	61.0, 129.0	85.0, 169.0
Min; Max	140, 140	-	63, 459	48, 327	48, 459
Subgroup: Cumulative Dose of Treatment Before any AESI = >180 mg to ≤270 mg	**LoT<4 (N=1)**	**LoT=4 (N=0)**	**LoT=5 (N=8)**	**LoT>=6 (N=7)**	**Total (N=16)**
n	1	0	8	7	16
Mean (SD)	149.0 (-)	-	165.5 (135.67)	261.1 (143.44)	206.3 (139.03)
Median	149.0	-	114.5	238.0	152.5
Q1; Q3	149.0, 149.0	-	95.0, 217.5	117.0, 409.0	107.0, 308.0
Min; Max	149, 149	-	22, 448	83, 455	22, 455
Subgroup: Cumulative Dose of Treatment Before any AESI = >270 mg to ≤400 mg	**LoT<4 (N=1)**	**LoT=4 (N=2)**	**LoT=5 (N=4)**	**LoT>=6 (N=6)**	**Total (N=13)**
n	1	2	4	6	13
Mean (SD)	400.0 (-)	87.5 (55.86)	105.5 (29.83)	243.2 (83.09)	188.9 (112.15)
Median	400.0	87.5	112.0	240.0	134.0
Q1; Q3	400.0, 400.0	48.0, 127.0	85.5, 125.5	209.0, 322.0	110.0, 254.0
Min; Max	400, 400	48, 127	64, 134	110, 338	48, 400
Subgroup: Cumulative Dose of Treatment Before any AESI = >400 mg	LoT<4 (N=3)	LoT=4 (N=1)	LoT=5 (N=8)	LoT>=6 (N=3)	Total (N=15)
n	3	1	8	3	15
Mean (SD)	202.0 (237.70)	79.0 (-)	182.3 (107.26)	290.0 (143.63)	200.9 (140.47)
Median	79.0	79.0	143.5	345.0	138.0
Q1; Q3	51.0, 476.0	79.0, 79.0	111.5, 237.0	127.0, 398.0	79.0, 345.0
Min; Max	51, 476	79, 79	72, 402	127, 398	51, 476
Subgroup: Ophthalmic Disease History = Ongoing Ophthalmic Disease History	**LoT<4 (N=1)**	**LoT=4 (N=2)**	**LoT=5 (N=8)**	**LoT>=6 (N=12)**	**Total (N=23)**
n	1	2	8	12	23
Mean (SD)	400.0 (-)	84.5 (60.10)	137.0 (100.13)	266.4 (126.96)	211.4 (134.75)
Median	400.0	84.5	125.5	282.5	149.0
Q1; Q3	400.0, 400.0	42.0, 127.0	85.0, 147.0	139.0, 368.0	117.0, 338.0
Min; Max	400, 400	42, 127	21, 360	84, 455	21, 455
Subgroup: Ophthalmic Disease History = Prior Ophthalmic Disease History Only	**LoT<4 (N=0)**	**LoT=4 (N=0)**	**LoT=5 (N=0)**	**LoT>=6 (N=4)**	**Total (N=4)**
n	0	0	0	4	4
Mean (SD)	-	-	-	200.8 (104.54)	200.8 (104.54)

Median	-	-	-	185.5	185.5
Q1; Q3	-	-	-	113.5, 288.0	113.5, 288.0
Min; Max	-	-	-	110, 322	110, 322
Subgroup: Ophthalmic Disease History = No Ophthalmic Disease History	**LoT<4 (N=6)**	**LoT=4 (N=6)**	**LoT=5 (N=28)**	**LoT>=6 (N=17)**	**Total (N=57)**
n	6	6	28	17	57
Mean (SD)	173.8 (153.50)	47.2 (17.76)	174.2 (119.50)	100.1 (81.03)	138.7 (114.05)
Median	144.0	44.5	141.5	70.0	89.0
Q1; Q3	79.0, 149.0	37.0, 51.0	86.5, 237.0	53.0, 85.0	61.0, 169.0
Min; Max	51, 476	27, 79	22, 459	44, 345	22, 476

Table Source: 14.2.1.1

AESI: Adverse Event of Special Interest; LoT: Line of Treatment; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Note: Note: Duration of exposure (days) = min(confirmed decision date of permanent discontinuation of belantamab mafodotin treatment, start date of a new LoT, end of study date) - index date + 1.

9.4.1.2. Treatment Adherence

For patients with any ophthalmic disease history, mean treatment adherence was 69.2% (SD 34.76). For patients with ongoing ophthalmic disease history, mean treatment adherence was 78.6% (SD 29.59). For patients with prior ophthalmic disease history only, mean treatment adherence was 78.8% (SD 29.36). For patients with no ophthalmic disease history, mean treatment adherence was 64.8% (SD 36.58) (Table 14.2.1.2).

9.4.1.3. Treatment Dose Modifications

Table 14.2.3.1 reports the number and reasons for dose modifications of belantamab mafodotin during the study. Each patient is counted only once within a given treatment dose and reason, but more than 1 treatment dose and reason could have been reported.

Any dose: Twenty-seven patients (32.1%) had a dose modification for any reason, 20 patients (23.8%) had a dose modification due to an ocular AESI, 7 patients (8.3%) had a dose modification for other reasons, and 2 patients (2.4%) had a dose modification for other adverse events.

1.9 mg/kg: Twenty-two patients (26.2%) had a dose modification to 1.9 mg/kg for any reason, 19 patients (22.6%) had a dose modification to 1.9 mg/kg due to an ocular AESI, 2 patients (2.4%) had a dose modification to 1.9 mg/kg for other reasons, and 2 patients (2.4%) had a dose modification to 1.9 mg/kg due to other adverse events.

2.5 mg/kg: Three patients (3.6%) had a dose modification to 2.5 mg/kg for other reasons.

Other dose: Six patients (7.1%) had a dose modification to another dose for any reason, 4 patients (4.8%) had a dose modification to another dose for other reasons, and 2 patients (2.4%) had a dose modification to another dose due to an ocular AESI. Other doses included 1.3, 1.6, 1.88, 2.35 mg/kg.

Table 14.2.3.1 reports further dose modification details by line of treatment, treatment dose at start of treatment delay and subgroups (including diabetes, ongoing ophthalmic disease history, prior ophthalmic disease history only, and no ophthalmic disease history).

9.4.1.4. Treatment Delays

Table 14.2.4.1 reports on the number and reasons for treatment delays. Each patient is counted only once within a given treatment dose and reason, but more than 1 treatment dose and reason could have been reported.

Any dose: Fifty-two patients (61.9%) had a treatment delay for any reason, 33 patients (39.3%) had a treatment delay due to an ocular AESI, 30 patients (35.7%) had a treatment delay for other reasons, and 12 patients (14.3%) had a treatment delay for other adverse events.

1.9 mg/kg dose at the start of the treatment delay: Seventeen patients (20.2%) with a treatment dose of 1.9 mg/kg had a treatment delay for any reason, 9 patients (10.7%) had a treatment delay for other reasons, 8 patients (9.5%) had a treatment delay due to an ocular AESI, and 5 patients (6.0%) had a treatment delay for other adverse events.

2.5 mg/kg dose at the start of the treatment delay: Forty-three patients (51.2%) with a treatment dose of 2.5 mg/kg had a treatment delay for any reason, 27 patients (32.1%) had a treatment delay due to an ocular AESI, 18 patients (21.4%) had a treatment delay for other reasons, and 6 patients (7.1%) had a treatment delay for other adverse events.

Other dose at the start of the treatment delay: Six patients (7.1%) with another treatment dose had a treatment delay for any reason, 3 patients (3.6%) had a treatment delay for other reasons, 2 patients (2.4%) had a treatment delay due to an ocular AESI, and 1 patient (1.2%) had a treatment delay for other adverse events.

Table 14.2.4.1 reports further details on treatment delays by line of treatment, treatment dose at start of treatment delay and subgroups (including diabetes, ongoing ophthalmic disease history, prior ophthalmic disease history only, and no ophthalmic disease history).

9.4.2. Ophthalmic Monitoring

Of the 84 patients, 65 (77.4%) patients had at least 1 ophthalmic examination and the remaining 19 (22.6%) had no recorded ophthalmic examination during the baseline period. Among the 76 patients who had at least 2 doses, most patients had at least 1 ophthalmic examination (n=57, 75.0%) between the first and second doses. Among the 59 patients who had at least 3 doses, most patients had at least 1 ophthalmic examination (n=41; 69.5%) between the second and third dose. Among the 40 patients who had at least 4 doses, again, most patients had at least1 ophthalmic examination (n=31; 77.5%) between the third and fourth dose (Table 9-9). A small proportion of patients had multiple ocular examinations between doses.

Of the 58 patients with ocular AESIs (4/58 patients [6.9%] had a prior ophthalmic disease history), 51 (87.9%) patients had at least 1ophthalmic examination during the baseline period and the remaining 7 (12.1%) had no recorded ophthalmic examination. Among the 55 patients with ocular AESIs who had at least 2 doses, most patients had at least 1 ophthalmic examination (n=44, 80.0%) between the first and second doses. Among the 44 patients with ocular AESIs who had at least 3 doses, most patients had at least 1 examination (n=37; 84.1%) between the second and third dose. Among the 35 patients

who had at least 4 doses, again, most patients had at least 1 examination (n=29; 82.9%) between the third and fourth dose (Table 9-9).

Of the 26 patients without ocular AESIs 14 (53.8%) patients had at least 1 ophthalmic examination during the baseline period and the remaining 12 (46.2%) had no recorded ophthalmic examination. Among the 21 patients who had at least 2 doses, most patients had at least 1 ophthalmic examination (n=13, 61.9%) between the first and second doses. Among the 15 patients who had at least 3 doses, most patients (n=11, 73.3%) did not have a recorded ophthalmic observation between the second and third dose. Among the 5 patients who had at least 4 doses, most patients (n=3, 60.0%) did not have a recorded ophthalmic observation between the third and fourth dose (Table 9-9).

A similar trend of most patients having received at least 1 examination was found for patients with an ongoing or prior ophthalmic disease history, whereas those without an ocular AESI and no history of ophthalmic disease mostly had no recorded examination.

Table 14.2.6.3.1. also provides information on the average number of examinations after the fourth dose for patients with an ocular AESI compared to patients with no ocular AESI by ophthalmic disease history. It appears that patients were monitored more closely in the presence of an ocular AESI and more patients had an active treatment period exceeding 4 doses.

Table 9-9 Ophthalmic Monitoring Concordance by LoT and ocular AESI subgroup (SP and subgroups)

Characteristic (Safety population)	LoT<4 (N=7)	LoT=4 (N=8)	LoT=5 (N=36)	LoT>=6 (N=33)	Total (N=84)
Number of ophthalmic examinations, n (%)					
During the baseline period [a]					
0	0	1 (12.5)	8 (22.2)	10 (30.3)	19 (22.6)
1	7 (100)	7 (87.5)	28 (77.8)	23 (69.7)	65 (77.4)
>1	0	0	0	0	0
Between the first and second doses [b]					
Number of patients with at least 2 doses	7	7	32	30	76
0	0	2 (28.6)	9 (28.1)	8 (26.7)	19 (25.0)
1	7 (100)	5 (71.4)	21 (65.6)	20 (66.7)	53 (69.7)
>1	0	0	2 (6.3)	2 (6.7)	4 (5.3)
Between the second and third doses [b]					
Number of patients with at least 3 doses	6	1	28	24	59
0	1 (16.7)	1 (100)	10 (35.7)	6 (25.0)	18 (30.5)
1	3 (50.0)	0	17 (60.7)	12 (50.0)	32 (54.2)
>1	2 (33.3)	0	1 (3.6)	6 (25.0)	9 (15.3)
Between the third and fourth doses [b]					
Number of patients with at least 4 doses	2	0	21	17	40
0	0	0	6 (28.6)	3 (17.6)	9 (22.5)
1	1 (50.0)	0	12 (57.1)	12 (70.6)	25 (62.5)
>1	1 (50.0)	0	3 (14.3)	2 (11.8)	6 (15.0)
Characteristic (presence of ocular AESI subgroup)	**Lot<4 (N=6)**	**LoT=4 (N=3)**	**LoT=5 (N=27)**	**LoT>=6 (N=22)**	**Total (N=58)**
Number of ophthalmic examinations, n (%)					
During the baseline period [a]					
0	0	0	5 (18.5)	2 (9.1)	7 (12.1)
1	6 (100)	3 (100)	22 (81.5)	20 (90.9)	51 (87.9)

>1	0	0	0	0	0
Between the first and second doses [b]					
Number of patients with at least 2 doses	6	3	26	20	55
0	0	2 (66.7)	5 (19.2)	4 (20.0)	11 (20.0)
1	6 (100)	1 (33.3)	19 (73.1)	15 (75.0)	41 (74.5)
>1	0	0	2 (7.7)	1 (5.0)	3 (5.5)
Between the second and third doses [b]					
Number of patients with at least 3 doses	5	1	22	16	44
0	0	1 (100)	5 (22.7)	1 (6.3)	7 (15.9)
1	3 (60.0)	0	16 (72.7)	9 (56.3)	28 (63.6)
>1	2 (40.0)	0	1 (4.5)	6 (37.5)	9 (20.5)
Between the third and fourth doses [b]					
Number of patients with at least 4 doses	2	0	17	16	35
0	0	0	4 (23.5)	2 (12.5)	6 (17.1)
1	1 (50.0)	0	10 (58.8)	12 (75.0)	23 (65.7)
>1	1 (50.0)	0	3 (17.6)	2 (12.5)	6 (17.1)
Characteristic (absence of ocular AESI subgroup)	**LoT<4 (N=1)**	**LoT=4 (N=5)**	**LoT=5 (N=9)**	**LoT>=6 (N=11)**	**Total (N=26)**
Number of ophthalmic examinations, n (%)					
During the baseline period [a]					
0	0	1 (20.0)	3 (33.3)	8 (72.7)	12 (46.2)
1	1 (100)	4 (80.0)	6 (66.7)	3 (27.3)	14 (53.8)
>1	0	0	0	0	0
Between the first and second doses [b]					
Number of patients with at least 2 doses	1	4	6	10	21
0	0	0	4 (66.7)	4 (40.0)	8 (38.1)
1	1 (100)	4 (100)	2 (33.3)	5 (50.0)	12 (57.1)
>1	0	0	0	1 (10.0)	1 (4.8)
Between the second and third doses [b]					
Number of patients with at least 3 doses	1	0	6	8	15
0	1 (100)	0	5 (83.3)	5 (62.5)	11 (73.3)
1	0	0	1 (16.7)	3 (37.5)	4 (26.7)
>1	0	0	0	0	0
Between the third and fourth doses [b]					
Number of patients with at least 4 doses	0	0	4	1	5
0	0	0	2 (50.0)	1 (100)	3 (60.0)
1	0	0	2 (50.0)	0	2 (40.0)
>1	0	0	0	0	0

Table Source: 14.2.6.3.1

AESI: Adverse Event of Special Interest; LoT: Line of Treatment.

[a] Percentages are calculated using the number of patients included in the Safety Population and subgroup as denominator.

[b] Percentages are calculated using the number of patients with the relevant number of doses included in the Safety Population and subgroup as denominator.

9.5. Other Secondary Analyses

9.5.1. Best Overall Response (BOR)

The best overall response, among all tumor assessment visits completed after the index date, among the 62 patients with non-missing data in the SP was CR in 1.6% (n=1/62), VGPR in 16.1% (n=10/62), PR in 21.0% (n=13/62), and stable disease in 38.7% (n=24/62). Progressive disease occurred in 22.6% (n=14/62). No patients had a BOR of sCR. BOR data was missing in 22 patients (26.2%) (Table 14.2.7.1.1).

At 3 months: 0 patients had sCR or CR, 9/56 patients (16.1%) had VGPR, 13/56 patients (23.2%) had PR, 21/56 patients (37.5%) had stable disease, 13/56 patients (23.2%) had PD; 28 (33.3%) patients had missing BOR data (Table 14.2.7.1.2).

At 6 months: 0 patients had sCR, 1/39 patient (2.6%) had CR, 7/39 patients (17.9%) had VGPR, 7/39 patients (17.9%) had PR, 8/39 patients (20.5%) had stable disease, 16/39 patients (41.0%) had PD; 45 (53.6%) patients had missing BOR data (Table 14.2.7.1.2).

At 9 months: 0 patients had sCR, 1/27 patient (3.7%) had CR, 8/27 patients (29.6%) had VGPR, 4/27 patients (14.8%) had PR, 6/27 patients (22.2%) had stable disease, 8/27 patients (29.6%) had PD; 57 (67.9%) patients had missing BOR data (Table 14.2.7.1.2).

At 12 months: 0 patients had sCR, 3/16 patients (18.8%) had CR, 2/16 patients (12.5%) had VGPR, 3/16 patients (18.8%) had PR, 5/16 patients (31.3%) had stable disease, 3/16 patients (18.8%) had PD; 68 (81.0%) patients had missing BOR data (Table 14.2.7.1.2).

At 15 months: 0 patients had sCR, 1/9 patient (11.1%) had CR, 1/9 patient (11.1%) had VGPR, 1/9 patient (11.1%) had PR, 5/9 patients (55.6%) had stable disease, 1/9 patient (11.1%) had PD; 75 (89.3%) patients had missing BOR data (Table 14.2.7.1.2).

BOR results were based mostly on small numbers and missing data. More details on BOR by subgroup can be found in Table 14.2.7.1.2.

9.5.2. Overall Survival (OS)

Across the SP, 27 patients (32.1%) died ('LoT=4' n=7, 87.5%; 'LoT=5'n=9, 25.0%; 'LoT ≥6' n=11, 33.3%) and 57 patients (67.9%) were censored at the date of last contact (Table 14.2.7.2.1). Overall, the median OS was not estimable (95% CI: 11.04, not reached; Q1, Q3: not estimable). Minimum and maximum OS time for the SP was 0.9 and 16.2 (censored observation) months, respectively (Table 14.2.7.2.1). OS results were based mostly on small numbers and missing data. More details on OS by subgroup can be found in Table 14.2.7.2.1.

OS was 89.2% (95% CI: 80.3, 94.2) at 3 months, 78.5% (95% CI: 67.6, 86.1) at 6 months, 68.6% (95% CI: 56.3, 78.1) at 9 months and 59.9% (95% CI: 46.3, 71.1) at 12 and 15 months (Table 14.2.7.2.1). Figure 9-1 shows the OS of the cohort.

Figure 9-1 Overall survival (OS) probability for the Safety Population (SP)

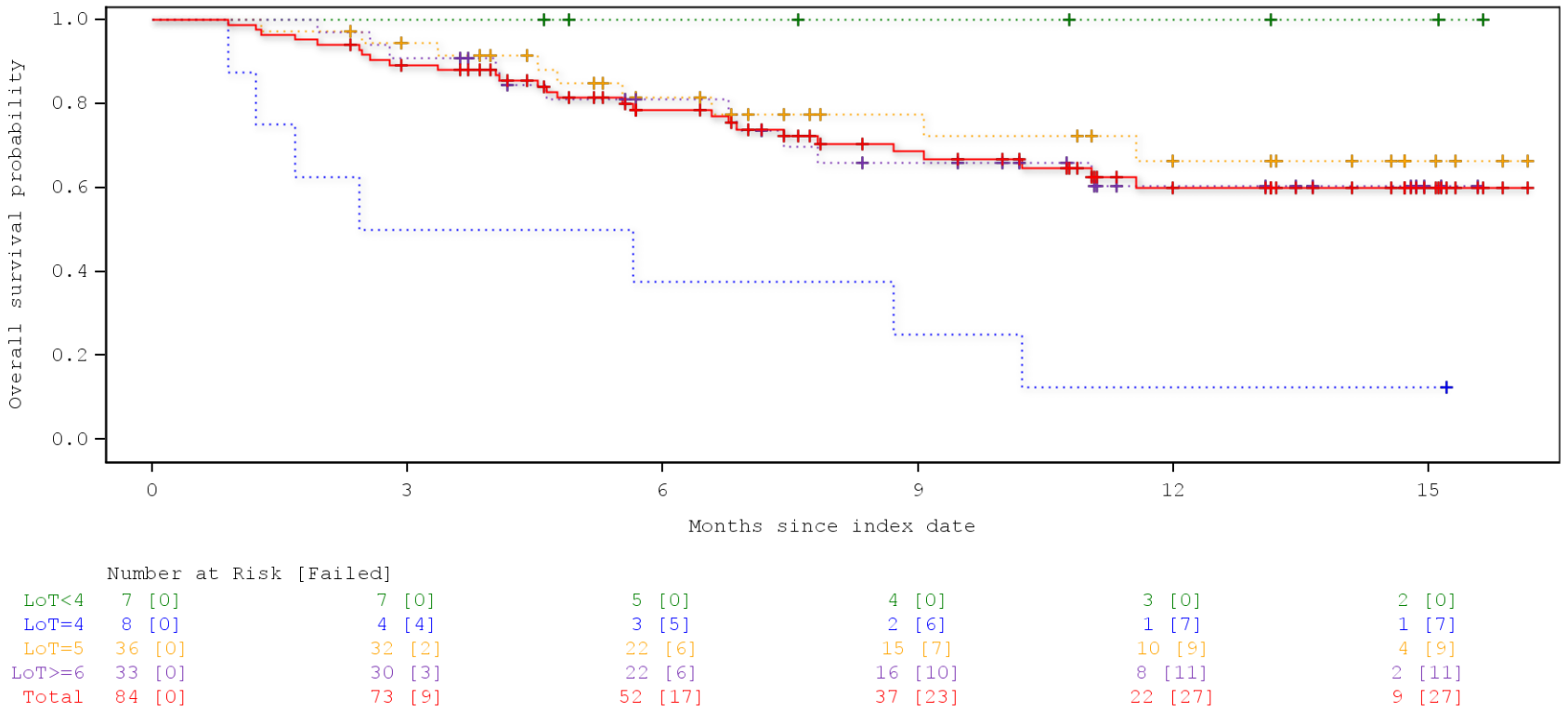


Figure Source: 14.2.7.2.2

9.5.3. Real-world Progression-Free Survival (rwPFS)

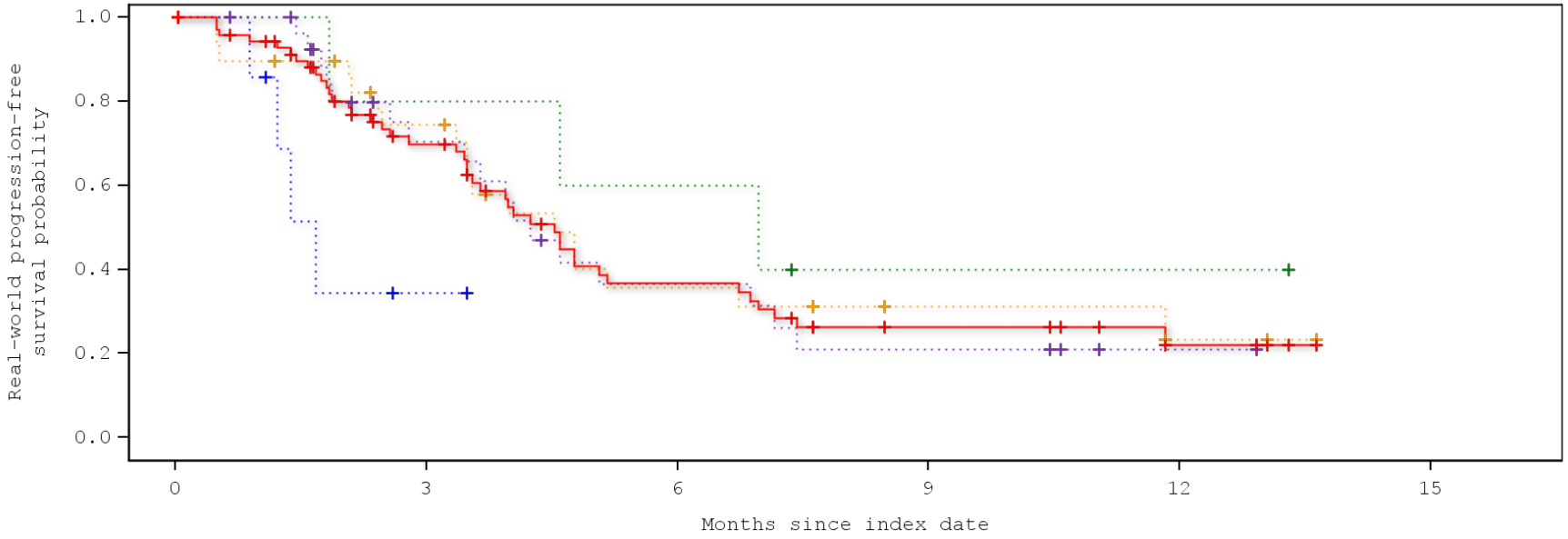
Overall, 42 patients (50%) from the SP showed disease progression or died ('LoT <4' n=3, 42.9%; 'LoT=4' n=4, 50.0%; 'LoT=5' n=18, 50.0%; 'LoT ≥6' n=17; 51.5%). Fifty percent of patients (n=42) were censored either on the last adequate tumor assessment date prior to any new LoT or censored at the index (if there were no adequate tumor assessments). Overall, the median rwPFS was 4.53 months (95% CI: 3.48, 5.16 months; Q1, Q3: 2.464, 11.828). Minimum and maximum rwPFS for the SP were 0.03 and 16.63 months, respectively (14.2.7.3.1).

The rwPFS was 69.8% (95% CI: 56.7, 79.6) at 3 months, 36.6% (95% CI: 23.9, 49.4) at 6 months, 26.3% (95% CI: 15.2, 38.8) at 9 months and 21.9% (95% CI: 10.8, 35.5) at 12 months (Table 14.2.7.3.1).

The rwPFS results were based mostly on small numbers and missing data. More details on rwPFS by subgroup can be found in Table 14.2.7.3.1.

Figure 9-2shows the rwPFS of the cohort. At 12 months and 15 months, rwPFS curves were not estimable (14.2.7.3.1).

Figure 9-2 Real world progression-free survival (rwPFS) probability for the Safety Population (SP)



Number at Risk [Failed]						
LoT<4	7 [0]	4 [1]	3 [2]	1 [3]	1 [3]	0 [3]
LoT=4	8 [0]	1 [4]	0 [4]			
LoT=5	36 [0]	19 [7]	8 [16]	4 [17]	2 [18]	0 [18]
LoT>=6	33 [0]	15 [7]	7 [14]	4 [17]	1 [17]	0 [17]
Total	84 [0]	39 [19]	18 [36]	9 [41]	4 [42]	0 [42]

Figure Source: 14.2.7.3.2

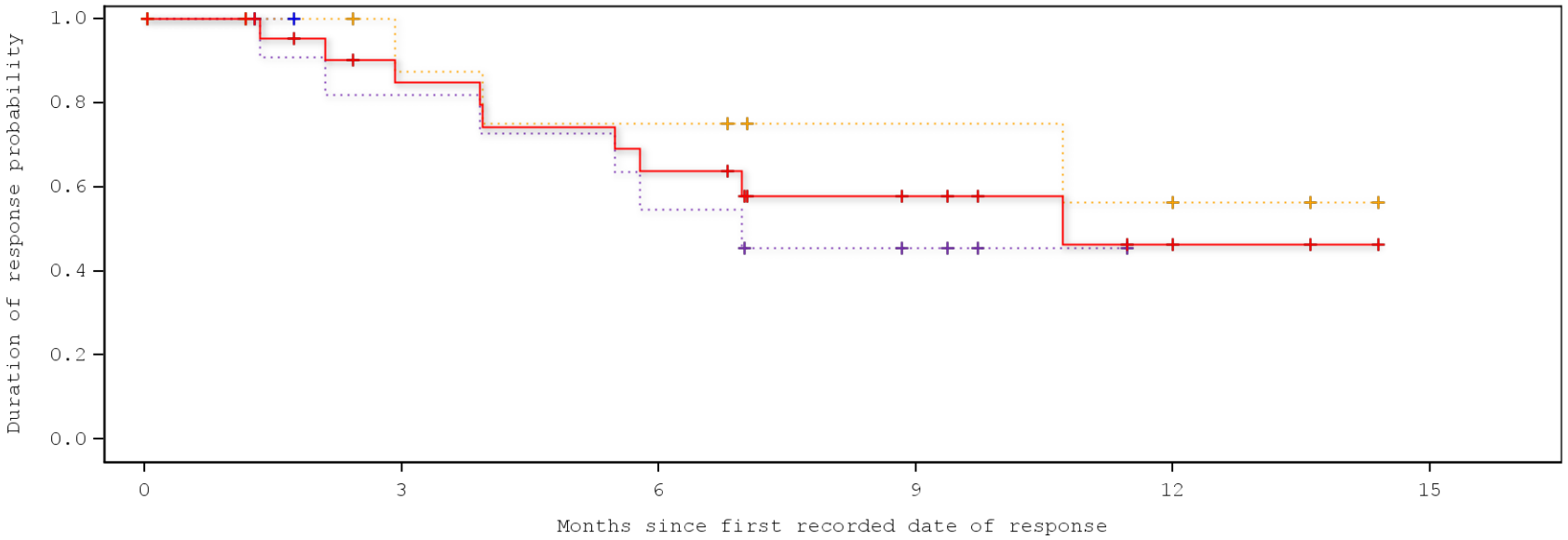
9.5.4. Duration of Response (DoR)

Of the 24 patients in the SP with response (i.e. who had either sCR, CR, VGPR or PR), 9 patients (37.5%) had disease progression or died ('LoT=5' n=3, 27.3%; 'LoT ≥6'n=6, 50.0%) and 15 patients were censored ('LoT=4' n=1, 100%;'LoT=5' n=8, 72.7%; 'LoT ≥6' n=6; 50.0%) . For the SP, the median DoR was 10.71 months (95% CI: 3.94; not reached; Q1, Q3: 3.943, not estimable) (Table 14.2.7.4.1).

DoR was 84.9% (95% CI: 60.1, 94.9) at 3 months, 63.7% (95% CI: 38.5, 80.8) at 6 months, 57.9% (95% CI: 33.0, 76.4) at 9 months and 46.3% (95% CI: 19.3, 69.8) at 12 months (Table 14.2.7.4.1).

Figure 9-3 shows the DoR of the cohort. DoR results were based mostly on small numbers and missing data. More details on DoR by subgroup can be found in Table 14.2.7.4.1.

Figure 9-3 Duration of response (DoR) for the Safety Population (SP)



	Number at Risk [Failed]					
LoT<4						
LoT=4	1 [0]	0 [0]				
LoT=5	11 [0]	7 [1]	6 [2]	4 [2]	2 [3]	0 [3]
LoT>=6	12 [0]	9 [2]	6 [5]	3 [6]	0 [6]	
Total	24 [0]	16 [3]	12 [7]	7 [8]	2 [9]	0 [9]

Figure Source: 14.2.7.4.2

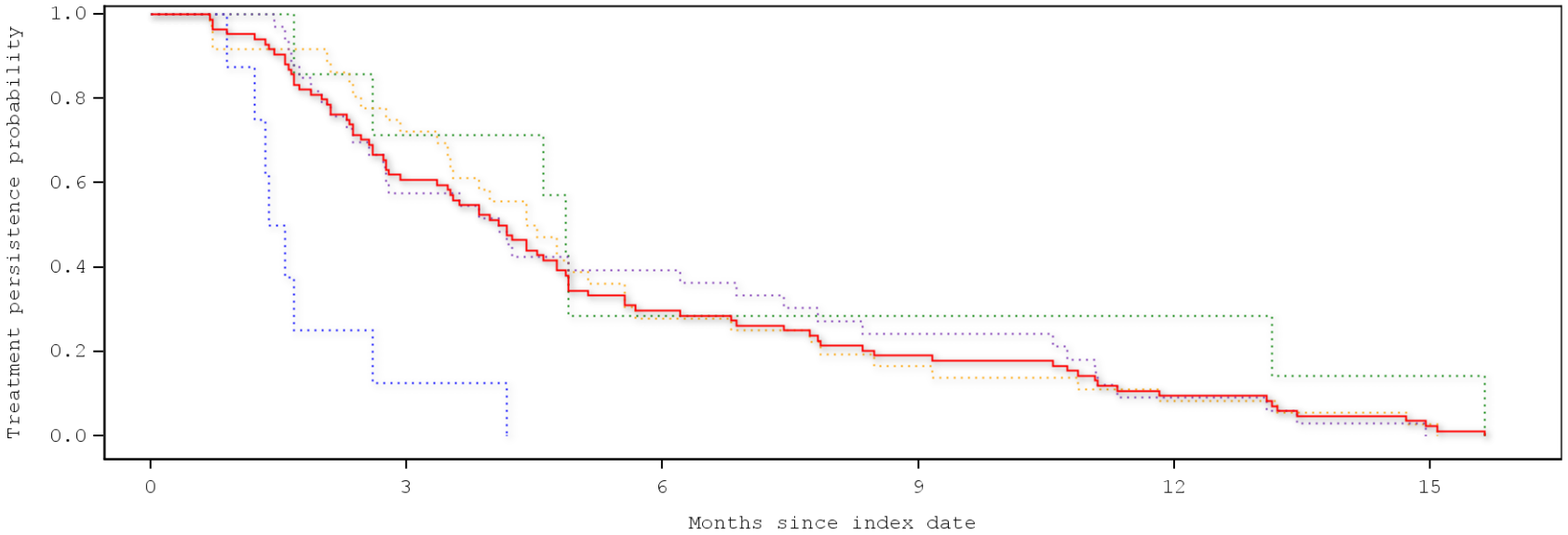
9.5.5. Duration of Treatment (DoT)

Across the SP, all 84 patients discontinued treatment. Overall, median DoT was 4.12 months (95% CI: 2.92, 4.76; Q1, Q3: 2.32, 7.57) (Table 14.2.7.5.1).

Among patients eligible at each time point, treatment persistence rate was 60.7% (95% CI: 49.4, 70.2) at 3 months, 29.8% (95% CI: 20.4, 39.7) at 6 months, 19.0% (95% CI: 11.5, 28.1) at 9 months, 9.5% (95% CI: 4.5,16.9) at 12 months and 2.4% (95% CI:0.5, 7.5) at 12 months (Table 14.2.7.5.1).

Figure 9-4 shows the Dot of the cohort. DoT results were based mostly on small numbers and missing data. More details on DoT by subgroup can be found in Table 14.2.7.5.1.

Figure 9-4 Duration of treatment (DoT) for the Safety Population (SP)



	Number at Risk [Failed]					
LoT<4	7 [0]	5 [2]	2 [5]	2 [5]	2 [5]	1 [6]
LoT=4	8 [0]	1 [7]	0 [8]			
LoT=5	36 [0]	26 [10]	10 [26]	6 [30]	3 [33]	1 [35]
LoT>=6	33 [0]	19 [14]	13 [20]	8 [25]	3 [30]	0 [33]
Total	84 [0]	51 [33]	25 [59]	16 [68]	8 [76]	2 [82]

Figure Source: 14.2.7.5.2

9.6. Ocular AESIs

9.6.1. Incidence of any Ocular AESI/any Serious Ocular AESI

Overall, 58/84 patients (69.0%) from the SP reported 85 ocular AESI episodes of which 83/85; (97.6%) were assessed as related to belantamab mafodotin; 19/84 patients (22.6%) had a National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) ocular AESI of grade ≥ 3 and 19/84 patients (22.6%) had a keratopathy and visual acuity (KVA) grade ≥3. Ocular AESIs led to dose reductions in 13/84 patients (15.5%), treatment interruption/delay in 37/84 patients (44.0%), and treatment discontinuation in 7/84 patients (8.3%). There were no ocular AESIs leading to study withdrawal or death (Table 9-10).

Two patients (2.4%; 1 LoT=4 and 1 LoT≥6) reported 3 serious ocular AESI episodes (1 patient with keratopathy and a change in BCVA and 1 patient with a blurred vision event): 2 patients (2.4%) with a NCI CTCAE grade of ≥ 3 and 1 patient (1.2%) had a KVA grade ≥3. One patient discontinued treatment due to the ocular AESI (LoT=4). All 3 serious ocular AESI episodes were reported to be related to belantamab mafodotin (Table 9-10). Further details on the serious ocular AESI episodes can be found in Table 14.3.1.11.

The most common ocular AESIs reported were keratopathy (42 patients; 50.0%) and other ocular AESIs (16 patients; 19.0%, including corneal epithelial microcysts, punctate keratitis, reduced visual acuity, cataract, conjunctivitis, dry eye, eye disorder, keratitis, meibomian gland dysfunction, ocular discomfort, optic neuropathy, sudden vision loss; Listing 16.2.7.1) 7 patients (8.3%) had corneal erosions or defects, 6 patients (7.1%) had blurred vision, 4 patients (4.8%) had a change in BCVA, 1 patient (1.2%) had dry eye events and 1 patient (1.2%) had photophobia (Table 14.3.1.3). The number of ocular AESI by line of treatment and by subgroups according to ophthalmic disease history (ongoing, prior, or no history) can be found in Table 14.3.1.2.

Table 9-10 Overview of Ocular AESI (SP)

	LoT<4 (N=7) n (%) [E]	LoT=4 (N=8) n (%) [E]	LoT=5 (N=36) n (%) [E]	LoT>=6 (N=33) n (%) [E]	Total (N=84) n (%) [E]
Any AESI	6 (85.7) [8]	3 (37.5) [4]	27 (75.0) [37]	22 (66.7) [36]	58 (69.0) [85]
NCI CTCAE Grade >=3	3 (42.9) [3]	2 (25.0) [2]	6 (16.7) [6]	8 (24.2) [10]	19 (22.6) [21]
KVA Grade >=3	4 (57.1) [4]	2 (25.0) [2]	8 (22.2) [9]	5 (15.2) [6]	19 (22.6) [21]
Leading to dose reduction	3 (42.9) [4]	0	7 (19.4) [7]	3 (9.1) [6]	13 (15.5) [17]
Leading to treatment interruption/delay	4 (57.1) [6]	1 (12.5) [2]	15 (41.7) [23]	17 (51.5) [22]	37 (44.0) [53]
Leading to treatment discontinuation	1 (14.3) [1]	3 (37.5) [4]	2 (5.6) [3]	1 (3.0) [1]	7 (8.3) [9]
Leading to study withdrawal	0	0	0	0	0
Leading to death	0	0	0	0	0
Any treatment-related AESI	6 (85.7) [7]	3 (37.5) [4]	27 (75.0) [37]	22 (66.7) [35]	58 (69.0) [83]
NCI CTCAE Grade >=3	3 (42.9) [3]	2 (25.0) [2]	6 (16.7) [6]	8 (24.2) [10]	19 (22.6) [21]
KVA Grade >=3	4 (57.1) [4]	2 (25.0) [2]	8 (22.2) [9]	5 (15.2) [6]	19 (22.6) [21]
Leading to dose reduction	3 (42.9) [4]	0	7 (19.4) [7]	3 (9.1) [6]	13 (15.5) [17]
Leading to treatment interruption/delay	4 (57.1) [5]	1 (12.5) [2]	15 (41.7) [23]	17 (51.5) [22]	37 (44.0) [52]
Leading to treatment discontinuation	1 (14.3) [1]	3 (37.5) [4]	2 (5.6) [3]	1 (3.0) [1]	7 (8.3) [9]
Leading to study withdrawal	0	0	0	0	0
Leading to death	0	0	0	0	0
Any serious AESI	0	1 (12.5) [2]	0	1 (3.0) [1]	2 (2.4) [3]
NCI CTCAE Grade >=3	0	1 (12.5) [1]	0	1 (3.0) [1]	2 (2.4) [2]
KVA Grade >=3	0	1 (12.5) [1]	0	0	1 (1.2) [1]
Leading to dose reduction	0	0	0	0	0
Leading to treatment interruption/delay	0	1 (12.5) [2]	0	0	1 (1.2) [2]
Leading to treatment discontinuation	0	1 (12.5) [2]	0	0	1 (1.2) [2]
Leading to study withdrawal	0	0	0	0	0
Occurring between end of last active treatment exposure period and end of study	0	0	0	0	0
Any serious treatment-related AESI	0	1 (12.5) [2]	0	1 (3.0) [1]	2 (2.4) [3]

Table Source: 14.3.1.1
AESI: Adverse Event of Special Interest; [E]: Number of AESI Episodes; KVA: Keratopathy and Visual Acuity; LoT: Line of Treatment; NCI CTCAE: National Cancer Institute Common Terminology Criteria for Adverse Events v5.0.
Note 1: Unless otherwise stated, all categories are based on AESI observations reported during the active treatment exposure period.
Note 2: Each patient is counted only once within a given AESI type and category.
Note 3: Percentages are calculated using the number of patients included in the Safety Population and subgroup as denominator.

9.6.2. Ocular AESIs by Maximum Severity

The majority of ocular AESIs were mild or moderate in severity. Of the 42 patients with keratopathy, the maximum grade of severity was severe in 9 patients (21.4%), moderate in 22 patients (52.4%) and mild in 11 patients (26.2%). Of the 16 patients with other ocular AESIs, the maximum grade was severe in 1 patient (6.3%), moderate in 6 patients (37.5%) and mild in 8 patients (50.0%) with data missing for 1 patient (6.3%). Of the 7 patients (8.3%) with corneal erosions or defects, the maximum grade was severe in 1 patient (14.3%), moderate in 4 patients (57.1%) and mild in 2 patients (28.6%). Of the 6 patients with blurred vision events, the maximum grade was severe in 1 patient (16.7%), moderate in 1 patient (16.7%) and mild in 3 patients (50.0%) with data missing for 1 patient (16.7%). Of the 4 patients (4.8%) with a change in BCVA, the maximum grade was severe in 2 patients (50.0%) and moderate in 2 patients (50.0%). One patient (100%) had a moderate dry eye event and 1 patient (100%) had mild photophobia (Table 9-11).

The majority of ocular AESIs were deemed to be treatment-related, except for 2 of the 16 patients with other ocular AESIs (1 of moderate severity and 1 with missing severity data) (Table 9-12).

Table 9-11 Ocular AESI by Maximum Severity (SP)

Measure of Severity	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Keratopathy	5 (71.4)	3 (37.5)	18 (50.0)	16 (48.5)	42 (50.0)
Mild	0	0	5 (27.8)	6 (37.5)	11 (26.2)
Moderate	2 (40.0)	2 (66.7)	9 (50.0)	9 (56.3)	22 (52.4)
Severe	3 (60.0)	1 (33.3)	4 (22.2)	1 (6.3)	9 (21.4)
Other	2 (28.6)	0	9 (25.0)	5 (15.2)	16 (19.0)
Mild	1 (50.0)	0	5 (55.6)	2 (40.0)	8 (50.0)
Moderate	1 (50.0)	0	4 (44.4)	1 (20.0)	6 (37.5)
Severe	0	0	0	1 (20.0)	1 (6.3)
Missing	0	0	0	1 (20.0)	1 (6.3)
Corneal erosions or defects	0	0	3 (8.3)	4 (12.1)	7 (8.3)
Mild	0	0	1 (33.3)	1 (25.0)	2 (28.6)
Moderate	0	0	2 (66.7)	2 (50.0)	4 (57.1)
Severe	0	0	0	1 (25.0)	1 (14.3)
Blurred vision events	1 (14.3)	0	0	5 (15.2)	6 (7.1)
Mild	1 (100)	0	0	2 (40.0)	3 (50.0)
Moderate	0	0	0	1 (20.0)	1 (16.7)
Severe	0	0	0	1 (20.0)	1 (16.7)
Missing	0	0	0	1 (20.0)	1 (16.7)
Change in BCVA	0	1 (12.5)	2 (5.6)	1 (3.0)	4 (4.8)
Mild	0	0	0	0	0
Moderate	0	0	1 (50.0)	1 (100)	2 (50.0)
Severe	0	1 (100)	1 (50.0)	0	2 (50.0)
Dry eye events	0	0	1 (2.8)	0	1 (1.2)
Mild	0	0	0	0	0
Moderate	0	0	1 (100)	0	1 (100)
Severe	0	0	0	0	0
Photophobia	0	0	0	1 (3.0)	1 (1.2)
Mild	0	0	0	1 (100)	1 (100)

Measure of Severity	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Moderate	0	0	0	0	0
Severe	0	0	0	0	0

Table Source: 14.3.1.3
AESI: Adverse Event of Special Interest; BCVA: Best Corrected Visual Acuity
Note 1: Based on AESI observations reported during the active treatment exposure period.
Note 2: Each patient is counted only once within a given AESI type and measure of severity.
Note 3: Percentages are calculated using the number of patients included in the Safety Population and subgroup as denominator.

Table 9-12 Related Ocular AESI by Maximum Severity (SP)

Measure of Severity	LoT<4 (N=7) n (%)	LoT=4 (N=8) n (%)	LoT=5 (N=36) n (%)	LoT>=6 (N=33) n (%)	Total (N=84) n (%)
Keratopathy	5 (71.4)	3 (37.5)	18 (50.0)	16 (48.5)	42 (50.0)
Mild	0	0	5 (27.8)	6 (37.5)	11 (26.2)
Moderate	2 (40.0)	2 (66.7)	9 (50.0)	9 (56.3)	22 (52.4)
Severe	3 (60.0)	1 (33.3)	4 (22.2)	1 (6.3)	9 (21.4)
Other	1 (14.3)	0	9 (25.0)	4 (12.1)	14 (16.7)
Mild	1 (100)	0	5 (55.6)	2 (50.0)	8 (57.1)
Moderate	0	0	4 (44.4)	1 (25.0)	5 (35.7)
Severe	0	0	0	1 (25.0)	1 (7.1)
Corneal erosions or defects	0	0	3 (8.3)	4 (12.1)	7 (8.3)
Mild	0	0	1 (33.3)	1 (25.0)	2 (28.6)
Moderate	0	0	2 (66.7)	2 (50.0)	4 (57.1)
Severe	0	0	0	1 (25.0)	1 (14.3)
Blurred vision events	1 (14.3)	0	0	5 (15.2)	6 (7.1)
Mild	1 (100)	0	0	2 (40.0)	3 (50.0)
Moderate	0	0	0	1 (20.0)	1 (16.7)
Severe	0	0	0	1 (20.0)	1 (16.7)
Missing	0	0	0	1 (20.0)	1 (16.7)
Change in BCVA	0	1 (12.5)	2 (5.6)	1 (3.0)	4 (4.8)
Mild	0	0	0	0	0
Moderate	0	0	1 (50.0)	1 (100)	2 (50.0)
Severe	0	1 (100)	1 (50.0)	0	2 (50.0)
Dry eye events	0	0	1 (2.8)	0	1 (1.2)
Mild	0	0	0	0	0
Moderate	0	0	1 (100)	0	1 (100)
Severe	0	0	0	0	0
Photophobia	0	0	0	1 (3.0)	1 (1.2)
Mild	0	0	0	1 (100)	1 (100)
Moderate	0	0	0	0	0
Severe	0	0	0	0	0

Table Source: 14.3.1.10
AESI: Adverse Event of Special Interest; BCVA: Best Corrected Visual Acuity
Note 1: Related AESI are AESI recorded as “Relationship to belantamab mafodotin” = “Yes” and those of unknown relationship.
Note 2: Based on AESI observations reported during the active treatment exposure period.
Note 3: Each patient is counted only once within a given AESI type and measure of severity.
Note 4: Percentages are calculated using the number of patients included in the Safety Population and subgroup as denominator.

9.6.3. Ocular AESI Duration

The mean duration of keratopathy was available for 16 of the 42 patients (maximum grade of episode was considered) and was 232.6 days (SD 115.17) for mild episodes, 129.0 days (SD 76.21) for moderate severe episodes and 153.0 days (SD 125.87) for severe episodes (Table 9-13). The mean duration of other ocular AESI types can be found in Table 14.3.1.4.

Table 9-13 Ocular AESI Duration (Days) for Keratopathy (SP)

Maximum Grade of Episode	LoT<4 (N=7)	LoT=4 (N=8)	LoT=5 (N=36)	LoT>=6 (N=33)	Total (N=84)
Mild					
n	0	0	2	3	5
Mean (SD)	-	-	309.00(144.250)	181.67(79.977)	232.60(115.171)
Median	-	-	309.00	164.00	207.00
Q1; Q3	-	-	207.00;411.00	112.00;269.00	164.00;269.00
Min; Max	-	-	207.0;411.0	112.0;269.0	112.0;411.0
Missing	0	0	3	3	6
Moderate					
n	0	2	2	5	9
Mean (SD)	-	130.00(12.728)	88.50(92.631)	144.80(91.086)	129.00(76.207)
Median	-	130.00	88.50	106.00	121.00
Q1; Q3	-	121.00;139.00	23.00;154.00	71.00;224.00	71.00;154.00
Min; Max	-	121.0;139.0	23.0;154.0	63.0;260.0	23.0;260.0
Missing	2	0	7	4	13
Severe					
n	0	1	1	0	2
Mean (SD)	-	64.00(-)	242.00(-)	-	153.00(125.865)
Median	-	64.00	242.00	-	153.00
Q1; Q3	-	64.00;64.00	242.00;242.00	-	64.00;242.00
Min; Max	-	64.0;64.0	242.0;242.0	-	64.0;242.0
Missing	3	0	3	1	7
Missing					
n	0	0	0	1	1
Mean (SD)	-	-	-	99.00(-)	99.00(-)
Median	-	-	-	99.00	99.00
Q1; Q3	-	-	-	99.00;99.00	99.00;99.00
Min; Max	-	-	-	99.0;99.0	99.0;99.0
Missing	0	0	0	0	0

Table Source: 14.3.1.4
LoT: Line of Treatment; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation.
Note: Based on AESI reported during the active treatment exposure period.

9.6.4. Ocular AESI Type and Impact on Daily Living

The impact of ocular AESIs on daily living was assessed in terms of the need for caregiver support, eye irritation/pain, driving or reading impairment, or any other impact and can be found in Table 14.3.1.5. Each patient was counted only once within a given ocular AESI type, but more than 1 impact on daily living could be reported per patient. Asymptomatic patients are not included within the counts of patients missing impact on daily living. (Table 14.3.1.5).

Keratopathy*:* Of the 42 patients with keratopathy, 13 patients (31.0%) reported eye irritation/pain, 10 (23.8%) reported reading impairment, 8 patients (19.0%) reported other impacts, 2 patients (4.8%) reported driving impairment, and 1 patient (2.4%) reported a need for caregiver support. Fifteen patients (35.7%) reported no significant impact on daily living. Data on the ocular AESI impact on daily living was missing for 9 patients (21.4%).

Other ocular AESIs: Of the 17 patients with other ocular AESIs, 3 patients (17.6%) reported reading impairment, 3 patients (17.6%) reported other impacts, and 2 patients (11.8%) reported eye irritation/pain. Four patients (23.5%) reported no significant impact on daily living. Data on the ocular AESI impact on daily living was missing for 7 patients (41.2%).

Corneal erosions or defects: Of the 7 patients with corneal erosions or defects, 3 patients (42.9%) reported reading impairment and 1 patient (14.3%) reported other impacts. Two patients (28.6%) reported no significant impact on daily living. Data on the ocular AESI impact on daily living was missing for 3 patients (42.9%).

Blurred vision: Of the 6 patients with blurred vision, 1 patient (16.7%) reported eye irritation/pain and 1 patient (16.7%) reported reading impairment. One patient (16.7%) reported no significant impact on daily living. Data on the ocular AESI impact on daily living was missing for 2 patients (33.3%).

Change in BCVA*:* Of the 4 patients with a change in BCVA, 3 patients (75.0%) reported reading impairment, 2 patients (50.0%) reported eye irritation/pain, 2 patients (50.0%) reported driving impairment, and 1 patient (25.0%) reported the need for caregiver support. One patient (25.0%) reported no significant impact on daily living.

The impact on daily living from dry eye and photophobia was missing (1 patient each, 100%) (Table 14.3.1.5).

9.6.5. Number of Doses of Belantamab Mafodotin Taken Before an Ocular AESI

The median number of doses of belantamab mafodotin taken before the first ocular AESI was 2.0 (Q1, Q3: 1.0, 2.0). Twenty-three patients (27.4%) had 1 dose of belantamab mafodotin before the first ocular AESI, 21 patients (25.0%) had 2 doses of belantamab mafodotin before the first ocular AESI, 9 patients (10.7%) had 3 doses of belantamab mafodotin before the first ocular AESI, 3 patients (3.6%) had 4 doses of belantamab mafodotin before the first ocular AESI and 2 patients (2.4%) had 5 or more doses of belantamab mafodotin before the first ocular AESI (Table 14.1.0.2)

Table 14.3.1.6 reports the number of doses of belantamab mafodotin taken before the first ocular AESI for a specific type of ocular AESI.

Keratopathy: Of the 42 patients with keratopathy, 17 patients (40.5%) had keratopathy after 1 dose, 14 patients (33.3%) after 2 doses, 7 patients (16.7%) after 3 doses, 3 patients (7.1%) after 4 doses, and 1 patient (2.4%) after 5 or more doses.

Other ocular AESI: Of the 16 patients with other ocular AESIs, 1 patient (6.3%) had an ocular AESI after 1 dose, 8 patients (50.0%) after 2 doses, 2 patients (12.5%) after 3 doses, 2 patients (12.5%) after 4 doses, and 3 patients (18.8%) after 5 or more doses.

Corneal erosions or defects: Of the 7 patients with corneal erosions or defects, 3 patients (42.9%) had corneal erosion/defect after 1 dose, 3 patients (42.9%) after 2 doses, and 1 patient (14.3%) after 4 doses.

Blurred vision: Of the 6 patients with blurred vision, 2 patients (33.3%) had blurred vision after 1 dose, 3 patients (50.0%) after 2 doses, and 1 patient (16.7%) after 4 doses.

Change in BCVA: Of the 4 patients with a change in BCVA, 1 patient (25.0%) had a change in BCVA after 1 dose, 2 patients (50.0%) after 2 doses, and 1 patient (25.0%) after 5 or more doses.

Dry eye events: 1 patient reported dry eye event after 1 dose ('LoT=5' n=1; 1.2%).

Photophobia: 1 patient reported photophobia after 2 doses ('LoT≥6' n=1; 1.2%).

Further details on the number of doses of belantamab mafodotin taken before the first ocular AESI of a specific type of ocular AESI by line of treatment and ophthalmic disease history can be found in Table 14.3.1.6.

Table 9-14 shows the number of doses of belantamab mafodotin taken before the first ocular AESI of any type.

Table 9-14 Ocular AESI by Number of Doses of Belantamab Mafodotin Taken Before the first Ocular AESI (SP)

Maximum Grade	1 Dose (N=23) n (%) [E]	2 Doses (N=21) n (%) [E]	3 Doses (N=9) n (%) [E]	4 Doses (N=3) n (%) [E]	5 or More Doses (N=2) n (%) [E]
Keratopathy	17 (73.9) [18]	15 (71.4) [15]	8 (88.9) [8]	2 (66.7) [3]	0
Mild	5 (29.4) [5]	4 (26.7) [4]	1 (12.5) [1]	1 (50.0) [1]	0
Moderate	11 (64.7) [11]	6 (40.0) [6]	4 (50.0) [4]	1 (50.0) [2]	0
Severe	1 (5.9) [1]	5 (33.3) [5]	3 (37.5) [3]	0	0
Missing	0 [1]	0	0	0	0
Other AESI	3 (13.0) [3]	7 (33.3) [9]	3 (33.3) [3]	1 (33.3) [1]	2 (100) [4]
Mild	0	4 (57.1) [6]	2 (66.7) [2]	1 (100) [1]	1 (50.0) [2]
Moderate	2 (66.7) [2]	2 (28.6) [2]	1 (33.3) [1]	0	1 (50.0) [1]
Severe	1 (33.3) [1]	0	0	0	0
Missing	0	1 (14.3) [1]	0	0	0 [1]
Corneal erosions or defects	3 (13.0) [3]	4 (19.0) [5]	0	0	0
Mild	1 (33.3) [1]	1 (25.0) [1]	0	0	0
Moderate	2 (66.7) [2]	2 (50.0) [3]	0	0	0
Severe	0	1 (25.0) [1]	0	0	0
Blurred vision event	3 (13.0) [3]	2 (9.5) [2]	0	1 (33.3) [1]	0
Mild	1 (33.3) [1]	1 (50.0) [1]	0	1 (100) [1]	0
Moderate	1 (33.3) [1]	0	0	0	0
Severe	1 (33.3) [1]	0	0	0	0
Missing	0	1 (50.0) [1]	0	0	0
Change in BCVA	1 (4.3) [1]	2 (9.5) [2]	0	1 (33.3) [2]	0

Maximum Grade	1 Dose (N=23) n (%) [E]	2 Doses (N=21) n (%) [E]	3 Doses (N=9) n (%) [E]	4 Doses (N=3) n (%) [E]	5 or More Doses (N=2) n (%) [E]
Mild	0	0	0	0	0
Moderate	1 (100) [1]	1 (50.0) [1]	0	0 [1]	0
Severe	0	1 (50.0) [1]	0	1 (100) [1]	0
Dry eye events	1 (4.3) [1]	0	0	0	0
Mild	0	0	0	0	0
Moderate	1 (100) [1]	0	0	0	0
Severe	0	0	0	0	0
Photophobia	0	1 (4.8) [1]	0	0	0
Mild	0	1 (100) [1]	0	0	0
Moderate	0	0	0	0	0
Severe	0	0	0	0	0

Table Source: 14.3.1.13.1
AESI: Adverse Event of Special Interest; BCVA: Best Corrected Visual Acuity; [E]: Number of AESI Episodes
Note 1: Based on AESI observations reported during the active treatment exposure period.
Note 2: Each patient is counted only once within a given AESI type and measure of severity.
Note 3: Percentages are calculated using the number of patients included in the Safety Population and subgroup as denominator.

Table 9-15 shows the average ocular AESI duration (for events with appropriate data to calculate duration as outlined in the SAP by the number of doses of belantamab mafodotin taken before the first ocular AESI of any type.

Keratopathy*:* The mean duration of keratopathy occurring between the first and second dose was 180.6 days (n=8, SD 111.68), between the second and third dose was 149.8 days (n=5, SD 92.35), between the third and fourth dose was 190.5 days (n=2, SD 72.83), and after 4 doses was 23.0 days (n=1, SD not estimated).

Other ocular AESI: The mean duration of other ocular AESIs occurring between the first and second dose was 157.0 days (n=2, SD 35.36), between the second and third dose was 80.3 days (n=3, SD 29.14), between the third and fourth dose was 62.0 days (n=1, SD not estimated), between the fourth and fifth dose was 29.0 days (n=1, SD not estimated), and after 5 or more doses was 59.5 days (n=1, SD not estimated).

Corneal erosions or defects: The mean duration of a corneal erosions or defects occurring between the first and second dose was 126.0 days (n=1, SD not estimated) and between the second and third dose was 164.5 days (n=1, SD not estimated).

Blurred vision: The mean duration of blurred vision occurring between the first and second dose was 20.0 days (n=1, SD not estimated), between the second and third dose was 7.0 days (n=1, SD not estimated), and after 4 doses was 22.0 days (n=1, SD not estimated).

Change in BCVA: The mean duration of a change in BCVA occurring between the first and second dose was 55.0 days (n=1, SD not estimated), between the second and third dose was 62.0 days (n=1, SD not estimated), and after 4 doses was 22.0 days (n=1, SD not estimated).

Dry eye events: The mean duration of dry eye events occurring between the first dose and second dose was 127.0 days (n=1, SD not estimated).

Photophobia: The mean duration of photophobia could not be calculated as the event was ongoing.

Table 9-15 Average Ocular AESI Duration (Days) by Number of Doses of Belantamab Mafodotin Taken Before the first Ocular AESI (SP)

	1 Dose (N=23)	2 Doses (N=21)	3 Doses (N=9)	4 Doses (N=3)	5 or More Doses (N=2)
Keratopathy					
n	8	5	2	1	0
Mean (SD)	180.56 (111.679)	149.80 (92.351)	190.50 (72.832)	23.00 (-)	
Median	142.75	121.00	190.50	23.00	
Q1; Q3	109.00;233.50	71.00;224.00	139.00;242.00	23.00;23.00	
Min; Max	63.0;411.0	64.0;269.0	139.0;242.0	23.0;23.0	
Missing	9	10	6	1	0
Other ocular AESI					
n	2	3	1	1	1
Mean (SD)	157.00 (35.355)	80.33 (29.143)	62.00 (-)	29.00 (-)	59.50 (-)
Median	157.00	71.00	62.00	29.00	59.50
Q1; Q3	132.00;182.00	57.00;113.00	62.00;62.00	29.00;29.00	59.50;59.50
Min; Max	132.0;182.0	57.0;113.0	62.0;62.0	29.0;29.0	59.5;59.5
Missing	1	4	2	0	1
Corneal erosions or defects					
n	1	1	0	0	0
Mean (SD)	126.00 (-)	164.50 (-)			
Median	126.00	164.50			
Q1; Q3	126.00;126.00	164.50;164.50			
Min; Max	126.0;126.0	164.5;164.5			
Missing	2	3	0	0	0
Blurred vision event					
n	1	1	0	1	0
Mean (SD)	20.00 (-)	7.00 (-)		45.00 (-)	
Median	20.00	7.00		45.00	
Q1; Q3	20.00;20.00	7.00;7.00		45.00;45.00	
Min; Max	20.0;20.0	7.0;7.0		45.0;45.0	
Missing	2	1	0	0	0
Change in BCVA					
n	1	1	0	1	0
Mean (SD)	55.00 (-)	62.00 (-)		22.00 (-)	
Median	55.00	62.00		22.00	
Q1; Q3	55.00;55.00	62.00;62.00		22.00;22.00	
Min; Max	55.0;55.0	62.0;62.0		22.0;22.0	
Missing	0	1	0	0	0
Dry eye events					
n	1	0	0	0	0
Mean (SD)	127.00 (-)				
Median	127.00				
Q1; Q3	127.00;127.00				
Min; Max	127.0;127.0				
Missing	0	0	0	0	0

Table Source: 14.3.1.13.2

AESI: Adverse Event of Special Interest; BCVA: Best Corrected Visual Acuity; LoT: Line of Treatment; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation.

Note: Based on AESI reported during the active treatment exposure period.

9.6.6. Ocular AESI Leading to Dose Reduction, Treatment Interruption/delay, Treatment Discontinuation and Study Withdrawal

As shown in Table 9-10, among the SP (n=84), ocular AESIs led to dose reductions in 13 patients (15.5%), treatment interruption/delay in 37 patients (44.0%), and treatment discontinuation in 7 patients (8.3%). Tables 14.3.1.7-14.3.1.9 show details by type of ocular AESI on ocular adverse reaction management.

9.6.6.1. Dose Reduction

Amongst the SP (n=84), ten patients (11.9%) had keratopathy, 3 patients (3.6%) had blurred vision events, 2 patients (2.4%) had another ocular AESI, 1 patient (1.2%) had corneal erosion, and 1 patient (1.2%) photophobia as an ocular AESI, leading to dose reduction (Table 14.3.1.7).

9.6.6.2. Dose Modifications Due to Ocular AESI

Table 14.2.3.2 reports the types of ocular AESI for patients with dose modifications of belantamab mafodotin during the study due to an ocular AESI.

Any dose: Of the 20 patients with any dose modification due to an ocular AESI; 10 patients (50.0%) had keratopathy, 3 patients (15.0%) blurred vision events, 2 patients (10.0%) other ocular AESIs, 1 patient (5.0%) a corneal erosion or defect, and 1 patient (5.0%) photophobia.

1.9 mg/kg: Of the 19 patients with a dose modification to 1.9 mg/kg due to an ocular AESI; 10 patients (52.6%) had keratopathy, 3 patients (15.8%) blurred vision events, 2 patients (10.5%) other ocular AESIs, 1 patient (5.3%) a corneal erosion or defect, and 1 patient (5.3%) photophobia.

Other dose: Two patients had a dose modification to another dose due to an ocular AESI; 1 patient (50.0%) had keratopathy and 1 patient (50.0%) blurred vision events.

9.6.6.3. Treatment Interruption/Delay

Among the SP (n=84), 29 patients (34.5%) had keratopathy, 9 patients (10.7%) had another ocular AESI, 4 patients (4.8%) had a change in BCVA, 4 patients (4.8%) had corneal erosion, 2 patients (2.4%) had blurred vision events, and 1 patient (1.2%) had dry eye as an ocular AESI leading to treatment interruption/delay (Table 14.3.1.8).

9.6.6.4. Treatment Dose at Start of Treatment Delay

Table 14.2.4.1 reports on the reasons for treatment delays by treatment dose at the start of the delay.

Any dose: Among the SP, fifty-two patients (61.9%) had a treatment delay for any reason, 33 patients (39.3%) had a treatment delay due to an ocular AESI, 30 patients

(35.7%) had a treatment delay for other reasons, and 12 patients (14.3%) had a treatment delay for other adverse events.

1.9 mg/kg: Seventeen patients (20.2%) with a treatment dose of 1.9 mg/kg had a treatment delay for any reason, 9 patients (10.7%) had a treatment delay for other reasons, 8 patients (9.5%) had a treatment delay due to an ocular AESI, and 5 patients (6.0%) had a treatment delay for other adverse events.

2.5 mg/kg: Forty-three patients (51.2%) with a treatment dose of 2.5 mg/kg had a treatment delay for any reason, 27 patients (32.1%) had a treatment delay due to an ocular AESI, 18 patients (21.4%) had a treatment delay for other reasons, and 6 patients (7.1%) had a treatment delay for other adverse events.

Other dose: Six patients (7.1%) with another treatment dose had a treatment delay for any reason, 3 patients (3.6%) had a treatment delay for other reasons, 2 patients (2.4%) had a treatment delay due to an ocular AESI, and 1 patient (1.2%) had a treatment delay for other adverse events.

Further details on treatment delays by line of treatment, treatment dose at start of treatment delay and subgroups can be found in Table 14.2.4.1.

9.6.6.5. Treatment Delay Duration

Table 14.2.4.2 reports the average treatment delay duration (days) by line of treatment, ocular AESI type, severity at start of treatment delay and ophthalmic disease history.

Keratopathy: The mean treatment delay duration for all severity measures was 31.4 days (n=29, SD 22.00). For mild severity it was 22.0 days (n=5, SD 12.88), for moderate severity it was 35.2 days (n=19, SD 24.54), for severe severity it was 40.9 days (n=4, SD 48.38), and for missing severity it was 24.8 days (n=11, SD 19.89).

Other ocular AESIs: The mean treatment delay duration for all severity measures was 52.4 days (n=8, SD 56.56). For mild severity was 8.7 days (n=2, SD 4.71), for moderate severity was 58.0 days (n=3, SD 35.37), for severe severity was 175.0 days (n=1, SD not estimable), and for missing severity was 42.8 days (n=3, SD 42.70).

Corneal erosions or defects: The mean treatment delay duration for all severity measures was 40.5 days (n=5, SD 37.10), for mild severity was 46.8 days (n=4, SD 66.92), for moderate severity was 47.0 days (n=2, SD 21.21), and for severe severity was 62.0 days (n=1, SD not estimable).

Blurred vision events: The mean treatment delay duration for all severity measures was 23.3 days (n=3, SD 11.50), for mild severity was 30.7 days (n=3, SD 23.46) and for missing severity was 13.0 days (n=1, SD not estimable).

Change in BCVA: The mean treatment delay duration for all severity measures was 46.0 days (n=3, SD 33.45), for moderate severity was 46.0 days (n=3, SD 33.45), and for severe severity was 21.0 days (n=1, SD not estimable).

Dry eye events: The mean treatment delay duration for the mild severity event was 195.0 days (n=1, SD not estimable).

Photophobia: The mean treatment delay duration for the mild severity event was 12.0 days (n=1, SD not estimable).

No ocular AESI: The mean treatment delay duration for patients with no ocular AESI was 29.3 days (n=16, SD 29.65).

Further details on the average treatment delay duration (days) by line of treatment, ocular AESI type, severity at start of treatment delay and ophthalmic disease history can be found in Table 14.2.4.2.

9.6.6.6. Treatment Discontinuation

Treatment discontinuation was reported in 7 patients (8.3%) due to keratopathy ('LoT<4' [n=1; 14.3%]; 'LoT=4' [n=3; 37.5%]; 'LoT=5 [n=2; 5.6%] 'LoT≥6' [n=1; 3.0%]), 1 patient due to change in BCVA ('LoT=4' [n=1; 12.5%]), and 1 patient due to another ocular AESI ('LoT=5' [n=1; 2.8%]) (Table 14.3.1.9).

9.6.6.7. Study Withdrawal

Study withdrawal was not reported in any patient (Table 14.3.1.1).

9.6.6.8. Time to First Ocular AESI

The median time to first keratopathy for the SP was estimated at 91 days (95% CI: 43.0, not reached; min, max; 15 and 402 days [censored observation]). The median time to the first ocular AESI was not estimable for a change in BCVA due to the large amount of censoring data (min, max; 15 and 476 days [censored observation]), other ocular AESIs (min, max; 17 and 476 days [censored observation]), blurred vision events (min, max; 23 and 476 days [censored observation]), corneal erosions or defects (min, max; 19 and 476 days [censored observation]), dry eye events (min, max; 20 and 476 days [censored observation]), photophobia (min, max; 27 and 476 days [censored observation]), eye irritation (min, max; 27 and 476 days [censored observation]), infective keratitis (min, max; 27 and 476 days [censored observation]), or ulcerative keratitis (min, max; 27 and 476 days [censored observation]) (Table 14.3.1.23).

9.6.6.9. Time to Treatment Discontinuation Due to an Ocular AESI

Overall, 7 patients from the SP ('LoT <4' n=1; 'LoT=4' n=3; 'LoT=5' n=2; 'LoT ≥6' n=1) had data regarding treatment discontinuation due to an ocular AESI. The median time to treatment discontinuation was 72.0 days (Q1, Q3: 51.0; 127.0; mean 86.7 days; SD 44.92). The median time to treatment discontinuation for mild ocular AESIs was 169.0 days (Q1, Q3: 169; 169; mean 169.0 days; SD not estimated). The median time to treatment discontinuation for moderate ocular AESIs was 66.5 days (Q1, Q3: 54.5; 75.5; mean 65.0 days; SD 13.54). The median time to treatment discontinuation for severe

ocular AESIs was 51.0 days (Q1, Q3: 51.0; 51.0; mean 51.0 days; SD not estimated) (Table 14.2.5.3).

9.6.7. Ocular AESI and Ophthalmic Scores Measured at Baseline and Last Examination

Ocular AESIs at the baseline and at the last ophthalmic examination were assessed for the SP. Baseline was defined as the last non-missing assessment prior to or on the index date. Last examination was defined as the last non-missing assessment prior to or on the treatment discontinuation date.

Ophthalmic scores at baseline and at last examination

BCVA score:

- For the 7 patients who discontinued treatment due to an ocular AESI, the following BCVA scores were available at baseline and the last examination (Table 14.3.4.1):
  - At baseline
    Right eye: n=5; mean 0.06; SD 0.13; median 0.00; Q1, Q3: 0.00; 0.00
    Left eye: n=5; mean 0.20; SD 0.19; median 0.20; Q1, Q3: 0.10; 0.20
  - At last examination
    Right eye: n=5; mean 0.20; SD 0.31; median 0.00; Q1, Q3: 0.00; 0.30
    Left eye: n=4; mean 0.15; SD 0.24; median 0.05; Q1, Q3: 0.00; 0.30
- For the remaining 77 patients in the SP who did not discontinue treatment due to an ocular AESI, the following BCVA scores were found in the right and left eye at baseline and the last examination (Table 14.3.4.1):
  - At baseline
    Right eye: n=50; mean 0.14; SD 0.27; median 0.10; Q1, Q3: 0.00; 0.20
    Left eye: n=50; mean 0.14; SD 0.27; median 0.00; Q1, Q3: 0.00; 0.20
  - At last examination
    Right eye: n=58; mean 0.20; SD 0.28; median 0.10; Q1, Q3: 0.00; 0.30
    Left eye: n=59; mean 0.19; SD 0.31; median 0.10; Q1, Q3: 0.00; 0.30

BCVA score results by ophthalmic disease history are detailed in Table 14.3.4.1.

Corneal examination findings*:*

- Of the 7 patients who discontinued treatment due to an ocular AESI, corneal examination findings were available for 6 patients at baseline and the last examination (Table 14.3.4.2).
  - At baseline

    Five patients (83.3%) had a normal finding, and 1 patient (16.7%) had a mild superficial punctate keratopathy in the right eye and moderate superficial punctate keratopathy in the left eye (Table 14.3.4.2).

- At last examination

  Two patients (33.3%) had a normal finding, and 4 patients (66.7%) had 4 findings of superficial punctate keratopathy in the right and left eye (1 mild, 1 moderate, 2 severe) and 2 findings (33.3%) of microcyst-like deposits (right and left eye diffuse microcyst-like deposits). In addition, there was 1 missing confirmation of microcyst-like deposits, subepithelial haze, stromal opacity, and corneal epithelial defects (Table 14.3.4.2).

- Of the remaining 77 patients in the SP who did not discontinue treatment due to an ocular AESI, corneal examination findings were available for 54 patients (right eye) and 55 patients (left eye) at baseline and for 72 patients at the last examination (Table 14.3.4.2):
  - At baseline
    - Right Eye: Forty-seven patients (87.0%) had a normal finding, and 7 patients (13.0%) had abnormal findings; 3 findings of mild superficial punctate keratopathy (5.6%), 2 findings of microcyst-like deposits (3.7%; 1 patchy and 1 unknown), 1 finding of central subepithelial haze (1.9%) and 2 findings of corneal epithelial defects (3.7%; 1 corneal erosion) (Table 14.3.4.2).
    - Left Eye: Forty-seven patients (85.5%) had a normal finding, and 8 patients (14.5%) had abnormal findings; 3 findings of mild superficial punctate keratopathy (5.5%), 3 findings of microcyst-like deposits (5.5%; 1 patchy and 2 unknown), 1 finding of central subepithelial haze (1.8%) and 3 findings of corneal epithelial defects (3.7%; 2 corneal erosion) (Table 14.3.4.2).
  - At last examination
    - Right Eye: Twenty-five patients (34.7%) had a normal finding and 47 patients (65.3%) had an abnormal findings; 19 findings of mild superficial punctate keratopathy (26.4%), 16 findings of moderate superficial punctate keratopathy (22.2%), 1 findings of unknown severity of superficial punctate keratopathy (1.4%), 20 findings of microcyst-like deposits (27.8%; 4 patchy, 7 diffuse microcyst-like deposits, 9 unknown microcyst-like deposits, and 4 missing), 4 missing confirmations for subepithelial haze (5.6%), 4 findings of corneal epithelial defects (5.6%; 2 corneal erosion), and 4 missing findings (5.6%) (Table 14.3.4.2).
    - Left Eye: Twenty-four patients (33.3%) had a normal finding and 48 patients (66.7%) had an abnormal findings; 19 findings of mild superficial punctate keratopathy (26.4%), 14 findings of moderate superficial punctate keratopathy (19.4%), 1 finding of severe superficial punctate keratopathy (2.8%), 1 finding of unknown severity of superficial punctate keratopathy (1.4%), 21 findings of microcyst-like deposits in the right eye (29.2%; 5 patchy, 7 diffuse microcyst-like deposits, 9 unknown microcyst-like deposits, and 4 missing confirmations), 4 missing confirmations for subepithelial haze (5.6%), 4 confirmations findings for stromal opacity

(5.6%), 4 findings of corneal epithelial defects (5.6%; 1 corneal erosion), and 4 missing findings (5.6%) (Table 14.3.4.2).

9.6.8. Ocular AESI by Ophthalmic Disease

Table 14.2.3.1 and Table 14.3.1.14.1 include results of the number of ocular AESI episodes by ophthalmic disease history. In total, 23 patients had an ongoing ophthalmic disease history, 4 patients a prior ophthalmic disease history only and 57 patients no ophthalmic disease history.

Keratopathy: Keratopathy was reported in 14 patients (60.9%) who had an ongoing ophthalmic disease history, 2 patients (50.0%) who had a prior ophthalmic disease history only, and 26 patients (45.6%) who had no ophthalmic disease history.

Other ocular AESI: Other ocular AESIs were reported in 5 patients (21.7%) who had an ongoing ophthalmic disease history, 1 patient (25.0%) who had a prior ophthalmic disease history only, and 10 patients (17.5%) who had no ophthalmic disease history.

Corneal erosions or defects: Corneal erosions or defects were reported in 4 patients (17.4%) who had an ongoing ophthalmic disease history, 2 patients (50.0%) who had a prior ophthalmic disease history only, and 1 patient (1.8%) who had no ophthalmic disease history.

Blurred vision event: Blurred vision events were reported in 2 patients (8.7%) who had an ongoing ophthalmic disease history, 1 patient (25.0%) who had a prior ophthalmic disease history only, and 3 patients (5.3%) who had no ophthalmic disease history.

Change in BCVA: Change in BCVA was reported in 2 patients (8.7%) who had an ongoing ophthalmic disease history and 2 patients (3.5%) who had no ophthalmic disease history.

Dry eye events: Dry eye events was reported in 1 patient (1.8%) who had no ophthalmic disease history.

Photophobia: Photophobia was reported in 1 patient (4.3%) who had an ongoing ophthalmic disease history.

Further information by line of treatment, ocular AESI type and maximum severity can be found in Table 14.2.3.1 and Table 14.3.1.14.1. The average ocular AESI duration by ophthalmic disease history, ocular AESI type, line of treatment and maximum severity can be found in Table 14.3.1.14.2.

9.6.9. Ocular AESI by Best Treatment Response

Table 14.3.1.15.1 includes the below results of the number of ocular AESI episodes by best treatment response (24 responders and 38 non-responders).

Keratopathy: Keratopathy was reported in 16 (66.7%) of the responders (PR or better) and 15 (39.5%) of the non-responders.

Other ocular AESI: Other ocular AESIs were reported in 8 (33.3%) responders (PR or better) and 6 (15.8%) non-responders.

Corneal erosions or defects: Corneal erosions or defects were reported in 4 (16.7%) responders (PR or better) and 3 (7.9%) non-responders.

Blurred vision event: Blurred vision events were reported in 1 (4.2%) responder (PR or better) and 4 (10.5%) non-responders.

Change in BCVA: Change in BCVA was reported in 1 (4.2%) responder **(**PR or better) and 2 (5.3%) non-responders.

Dry eye events: Dry eye events were reported in 1 (2.6%) non-responder.

Photophobia: Photophobia was reported in 1 (2.6%) non-responder.

Further information by line of treatment, ocular AESI type and maximum severity can be found in Table 14.3.1.15.1 and the average ocular AESI duration by best treatment response, line of treatment, ocular AESI type and maximum severity can be found in Table 14.3.1.15.2.

9.6.10. Ocular AESI by Use of Ocular Medical Devices During the Active Treatment Exposure Period

Table 14.3.1.16.1 includes the below results of the number of ocular AESI episodes by use of ocular medical devices during the active treatment exposure period. Overall, 65 patients used preservative-free lubricant eye drops, 19 patients did not use preservative-free lubricant eye drops, 83 patients did not use (bandage) contact lenses, 11 patients used cooling eye masks, and 73 patients did not use cooling eye masks during the active treatment exposure period. Note that in the EU, artificial tears are typically classified as a medical device.

Keratopathy: Keratopathy was reported in 42 patients; specifically, among 36 patients (55.4%) who used preservative-free lubricant eye drops, in 6 patients (31.6%) who did not use preservative-free lubricant eye drops, in 41 patients (49.4%) who did not use (bandage) contact lenses, in 7 patients (63.6%) who used cooling eye masks, and in 35 patients (47.9%) who did not use cooling eye masks.

Other ocular AESI: Other ocular AESIs were reported in 16 patients; specifically among 15 patients (23.1%) who used preservative-free lubricant eye drops, in 1 patient (5.3%) who did not use preservative-free lubricant eye drops, in 16 patients (19.3%) who did not use contact lenses, in 15 patients (18.1%) who did not use bandage contact lenses, in none of the patients who used cooling eye masks, and in 16 patients (21.9%) who did not use cooling eye masks.

Corneal erosions or defects: Corneal erosions and/or defects were reported in 7 patients; specifically among 4 patients (6.2%) who used preservative-free lubricant eye drops, in 3 patients (15.8%) who did not use preservative-free lubricant eye drops, in 7 patients (8.4%) who did not use contact lenses, in 6 patients (7.2%) who did not use bandage

contact lenses, in 0 patients who used cooling eye masks, and in 7 patients (9.6%) who did not use cooling eye masks.

Blurred vision event: Blurred vision events reported in 6 patients; specifically among 4 patients (6.2%) who used preservative-free lubricant eye drops, 2 patients (10.5%) who did not use preservative-free lubricant eye drops, 5 patients (6.0%) that did not use contact lenses, 6 patients (7.2%) that did not use bandage contact lenses, 1 patient (9.1%) who used cooling eye masks, and 5 patients (6.8%) that did not use cooling eye masks.

Change in BCVA: Change in BCVA was reported in 4 patients; specifically among 3 patients (4.6%) who used preservative-free lubricant eye drops, in 1 patients (5.3%) who did not use preservative-free lubricant eye drops, in 4 patients (4.8%) who did not use contact lenses, in 4 patients (4.8%) who did not use bandage contact lenses, in 0 patients who used cooling eye masks, and in 4 patients (5.5%) who did not use cooling eye masks.

Dry eye events: Dry eye events were reported in 1 patient (1.5%) who used preservative-free lubricant eye drops, in 0 patients who did not use preservative-free lubricant eye drops, in 1 patient (1.2%) who did not use contact lenses, in 1 patient (1.2%) who did not use bandage contact lenses, in 0 patients who used cooling eye masks, and in 1 patient (1.4%) who did not use cooling eye masks.

Photophobia: Photophobia was reported in 1 patient (1.5%) who used preservative-free lubricant eye drops, 0 patients who did not use preservative-free lubricant eye drops, in 1 patient (1.2%) who did not use contact lenses, in 1 patient (1.2%) who did not use bandage contact lenses, in 0 patients who used cooling eye masks, and in 1 patient (1.4%) who did not use cooling eye masks. (Table 14.3.1.16.1).

Further information by line of treatment, ocular AESI type and maximum severity can be found in Table 14.3.1.16.1. The average ocular AESI duration by use of ocular medical devices during the active treatment exposure period, line of treatment, ocular AESI type and maximum severity can be found in Table 14.3.1.16.2.

9.6.11. Ocular AESI by Use of Concomitant Medication Taken

Table 14.3.1.17.1 includes the below results of the number of ocular AESI episodes by use of concomitant medication taken for ocular AESI mitigation during the active treatment exposure period.

Among the 19 patients using concomitant medication for ocular AESI mitigation, 15 patients (78.9%) had keratopathy, 6 patients (31.6%) had another ocular AESI, 3 patients (15.8%) had corneal erosions or defects, 2 patients (10.5%) had blurred vision events, 1 patient (5.3%) had a change in BCVA, 0 patients had dry eye events or photophobia.

Of the 65 patients, who did not use concomitant medication for ocular AESI mitigation, 27 patients (41.5%) had keratopathy, 10 patients (15.4%) had another ocular AESI, 4 patients (6.2%) had corneal erosions or defects, 4 patients (6.2%) had blurred vision

events, 3 patients (4.6%) had a change in BCVA, 1 patient (1.5%) had a dry eye event, and 1 patient (1.5%) had photophobia (Table 14.3.1.17.1).

Further information by line of treatment, ocular AESI type and maximum severity can be found in Table 14.3.1.17.1. The average ocular AESI duration by use of concomitant medication taken for ocular AESI mitigation during the active treatment exposure period, line of treatment, ocular AESI type and maximum severity can be found in Table 14.3.1.17.2.

9.6.12. Serious Ocular AESI

Two patients reported a total of 3 serious ocular AESIs (Table 14.3.2.2).

One male patient (Patient PPD ; LoT=4) developed a serious, belantamab mafodotin-related keratopathy (occurring between Study Days 41 to 64 [PPD 2022 to PPD 2023]) and a serious, belantamab mafodotin-related change in BCVA (occurring between Study Days 43 to 62 [PPD 2022 to PPD 2023]). The patient's BCVA values and corneal/slit lamp examination results are provided in Table 9-16. The patient received 2 doses (PPD 2022 and PPD 2022) of belantamab mafodotin before both serious ocular AESIs and then permanently discontinued belantamab mafodotin due to the ocular AESIs (Data Source Listings 16.2.5.1.1 and 16.2.5.1.2). As can be seen in the table, this patient developed a three-line loss in visual acuity in the right eye and severe SPK in both eyes on PPD 2023. Improvement was documented at follow-up visits. The serious ocular AESIs recovered/resolved. At baseline, the patient reported ongoing Type 2 diabetes mellitus, esophagitis, constipation, diarrhea, hypertension, and ongoing eye diseases of keratopathy and glaucoma (Data Source Listing 16.2.4.2.1 and 16.2.4.2.2).

One male patient (Patient PPD , LoT≥6) reported a serious, belantamab mafodotin-related blurred vision event which began on Study Day 63 (PPD 2023) and was ongoing at the time of study closure (outcome unknown). The patient's BCVA values and corneal/slit lamp examination results are provided in Table 9-16. The eye exam closest to the SAE is PPD 2023, and visual acuity was unchanged from Baseline at this visit and also unchanged from Baseline at the last available eye exam on PPD 2023. The patient received 1 dose (PPD 2022) of belantamab mafodotin before the serious ocular AESI and then permanently discontinued belantamab mafodotin due to disease progression (Data Source Listings 16.2.5.1.1 and 16.2.5.1.2). The patient reported historical medical history of prolapse and calculus urinary (Data Source Listing 16.2.4.2.2).

Table 9-16 Ocular AESI Duration (Days) for Keratopathy (SP)

		BCVA			Corneal/Slit Lamp Examination					
Date of Opthalmic Examination	Eye	Reported as	Recorded Value	LogMAR Value	Corneal Exam	SPK	Microcyst-like Deposits	Subepithelial Haze	Stromal Opacity	Corneal Epithelial Defect Present?
Patient PPD										
PPD 2022	Left	Decimal	0.7	+0.2*	ABNORMAL*	MODERATE	N	N	N	N
	Right	Decimal	1	0.0*	ABNORMAL*	MILD	N	N	N	N
2022	Left	Decimal	0.9	0.0	ABNORMAL	MILD	N	N	N	N
	Right	Decimal	1	0.0	ABNORMAL	MILD	N	N	N	N
2022	Left	Decimal	0.4	+0.4	ABNORMAL	MODERATE	N	N	N	N
	Right	Decimal	1	0.0	ABNORMAL	MODERATE	N	N	N	N
023	Left	Decimal	0.4	+0.4	ABNORMAL	SEVERE	N	N	N	N
	Right	Decimal	0.5	+0.3	ABNORMAL	SEVERE	N	N	N	N
023	Left	Decimal	0.4	+0.4	ABNORMAL	MILD	N	N	N	N
	Right	Decimal	0.7	+0.2	ABNORMAL	MILD	N	N	N	N
2023	Left	Decimal	0.8	+0.1	ABNORMAL	NONE	N	N	N	N
	Right	Decimal	0.8	+0.1	ABNORMAL	NONE	N	N	N	N
2023	Left	Decimal	0.9	0.0	ABNORMAL	MILD	N	N	N	N
	Right	Decimal	1	0.0	ABNORMAL	MILD	N	N	N	N
Patient PPD										
PPD 2022	Left	Decimal	0.7	+0.2*	NORMAL*					
	Right	Decimal	0.75	+0.1*	NORMAL*					
023	Left	Decimal	0.7	+0.2	NORMAL					
	Right	Decimal	0.7	+0.2	NORMAL					
2023	Left	Decimal	0.7	+0.2	NORMAL					
	Right	Decimal	0.7	+0.2	NORMAL					

Table Source: Listing 16.2.8.2.2

*Baseline assessment.

BCVA: Best Corrected Visual Acuity; LogMAR: Logarithm of the Minimum Angle of Resolution; SPK: Superficial Punctate Keratopathy.

Note 1: Baseline is defined as the last non-missing assessment prior to or on the index date.

Note 2: A blank value indicates that an assessment is unknown, not reported or not applicable.

9.6.13. Deaths

There were 27 deaths reported during the study; 17 were due to the disease, 2 due to adverse events other than ocular AESIs, 1 due to progression, 5 with an unknown cause of death and 2 causes were not listed (Table 14.3.2.1).

10. DISCUSSION

10.1. Key Results

The study closed early with a data cut-off date for final analysis of 07 June 2024. There were 84 patients enrolled (Austria=14 patients; Belgium=5 patients; Germany=4 patients; Greece=3 patient; Italy=32 patients; Norway=15 patients; Spain=11 patients).

Forty patients (47.6%) completed the study, including 27 patients (32.1%) who died during follow-up. In total, 44 patients (52.4%) did not complete the study, mostly due to study termination (n=39 46.4%). The mean number of days post-index was 259.0 days (SD 138.78; min, max: 27, 492; median 236.5; Q1, Q3: 139.0, 399.0). The cumulative proportion of patients still in the study was 86.9% at 3 months (95% CI: 77.6, 92.5), 63.1% at 6 months (95% CI: 51.8, 72.4), 44.0% at 9 months (95% CI: 33.3, 54.3), 26.2% at 12 months (95% CI: 17.4, 35.9), and 10.7% at 15 months (95% CI: 5.3, 18.4).

All 84 patients received at least 1 dose of belantamab mafodotin either as early line (LoT<4; n=7, 8.3%), fourth-line (n=8, 9.5%), fifth-line (n=36, 42.9%) or at sixth-line or beyond (n=33, 39.3%). Four patients (4.8%) were ongoing on treatment at the time of study completion by patient and 21 patients (25.0%) were ongoing on treatment at the time of study termination by the Sponsor. Fifty-nine patients (70.2%) discontinued treatment during the study, mostly due to disease progression (n=28; 33.3%) or death (n=13; 15.5%). The mean duration of exposure was 161.5 days (SD 122.90; median 125.5 days; Q1, Q3: 70.5, 230.5). The proportion of patients with at least 4 LoT in the prior treatment period in this study (92%) is comparable to proportions reported in a US retrospective study with 82.9% receiving ≥4 LoT (Boytsov, 2021).

The mean age at initial MM diagnosis was 63.7 years (SD 10.06; min, max: 34, 88, median 63.5; Q1, Q3: 58.0, 71.5 years). The mean age for the SP at the index date was 70.7 years (SD 9.59; min, max 40, 93 years) with a lower mean age among patients treated with LoT<4 years (mean 62.4; SD 12.11). The mean time since initial MM diagnosis to the index date was 84.9 months (SD 48.11; min, max: 7.0, 243.8 months; median 79.0; Q1, Q3: 53.2, 119.3 months). Many of the patients were elderly, 35.7% were between 65 years and 74 years of age, while 39.3% were 75 years or older. Patients were slightly more likely to be female (n=46; 54.8%).Patients in the current study were on average slightly older at index and more often female than patients in the Phase 2 DREAMM-2 study (Lonial, 2020) and recently published real-world data in the US evaluating belantamab mafodotin (Boytsov, 2021; Vaxman, 2021; Hultcrantz , 2024). The median age at initial MM diagnosis of 63.7 years (Q1, Q3: 58.0, 71.5 years) in this study was similar to that reported from real-world chart data by (Vaxman, 2021). (61 years; min, max 37, 83).

In contrast, the median age at index in the current study of 71 years (Q1, Q3: 40, 93 years) was slightly higher than the median age of patients randomized to 2.5 mg/kg and 3.4 mg/kg belantamab mafodotin in the DREAMM-2 trial (65 years; Q1, Q3: 60, 70; and 67 years; Q1, Q3: 61, 72 years respectively) (Lonial, 2020). The median age at index was also slightly higher than the median age of 67 years reported from real-world chart data (Vaxman, 2021) but comparable to the median age of 70 years from claims data (Boytsov, 2021; Hultcrantz , 2024).

The median time from initial MM diagnosis to first belantamab mafodotin dose for the DREAMM-2 clinical study was reported at 5.08 and 5.49 years, dependent on the dosage administered (2.5 mg/kg or 3.4 mg/kg) (Lonial, 2020). Results from the US real-world studies showed a slightly higher median time from initial diagnosis to first belantamab mafodotin dose; ranging from approximately 6 years using the claims data (Boytsov, 2021) to 7 years using retrospective medical record data (Vaxman, 2021). This final report showed a similar trend to other US real-world data with a median of 6.6 years from initial MM diagnosis to first belantamab mafodotin dose.

This study included 45.2% males compared to a higher proportion of males in retrospective studies (64%, Vaxman, 2021; 53%, Hultcrantz , 2024; 50%, Boytsov, 2021) and in the DREAMM-2 clinical study across both dosage groups (53% and 57%) (Lonial, 2020).

ECOG performance status data was available for 59 patients (70.2%) across the SP; the ECOG score was 0 for 40.7% (n=24/59), 1 for 33.9% (n=20/59), 2 for 23.7% (n=14/59) and 3 for 1.7% (n=1/59) of patients. None of the patients had an ECOG score of 4.

Regarding ISS staging, amongst those with a value, 35.6% (n=21/59) were in stage I, 23.7% (n=14/59) in stage II, 40.7% (n=24/59) in stage III; data was missing for 29.8% (n=25/84). Most common MM subtypes were the IgG subtype (51.2%), followed by light chain (21.4%), IgA subtype (15.5%), other subtype (10.7%) and IgD (1.2%). Most patients did not have a high cytogenetic risk (72.6%), with remaining patients having a high cytogenetic risk (27.4%) or high-IMWG cytogenetic risk (20.2%).

Comorbid renal disease, pulmonary diseases, cardiac diseases, diabetes, and eye diseases were present at the index date in 20.2%, 17.9%, 39.3% 23.8%, and 31.0% of the SP, respectively. Twenty-six patients (31.0%) reported eye diseases at the index date which included a history of dry eyes/eye injuries affecting the BCVA.

Among the SP with available refractory data, 37.2% (n=29/78) were triple-refractory, 35.9% (n=28/78) were quad-refractory, 26.9% (n=21/78) were penta-refractory; 7.7% (6/84) had missing refractory data. Most patients (n=82, 97.6%) had at least 1 prior corticosteroid treatment and at least 1 prior monoclonal antibody treatment. A large proportion of the SP also had at least 1 prior chemotherapy treatment (n=66, 78.6%) and almost 50% at least 1 prior stem cell transplant (n=41, 48.8%).

For patients with an ocular AESI, the percentage of patients receiving at least 1 ophthalmic exam prior to each of the first 4 dose administrations individually was higher than for those without an ocular AESI (87.9% vs 53.8% during the baseline period, 74.5% vs 57.1% between first and second dose, 63.6 % vs 26.7% between second

and third dose and 65.7% vs 40.0% between the third and fourth doses), however without the ophthalmic examinations, some of the AESI may have not have been identified.

Overall, 58 patients (69.0%) from the SP reported 85 ocular AESI episodes, of which 83 were assessed as related to belantamab mafodotin. The median number of doses of belantamab mafodotin taken before the first ocular AESI was 2.0. Similar to the DREAMM-2 trial where a majority of the patients with keratopathy (97.1%) experienced their first event by their fourth dose, this report shows that all patients experienced keratopathy (n=42, 50.0%) did so by their fourth dose, most between their first and second dose (n=17/42, 40.5%) or between their second and third dose (n=15/42, 35.7%), however, only 5 patients received 4 or more doses during the study period.

Among the SP, ocular AESIs led to dose reductions in 13 patients (15.5%), treatment interruption/delay in 37 patients (44.0%), and treatment discontinuation in 7 patients (8.3%), which is lower than reported treatment interruption/delays in 27.7% and treatment discontinuation in 60.3% of patients from real-world study (Hultcrantz, 2024). There were no AESIs leading to study withdrawal or death. The mean duration of exposure was 193.0 days (SD 127.19; median 142.5 days; Q1, Q3: 106.0, 279.0) in the presence of an ocular AESI and 91.4 days (SD 76.48; median 67.0 days; Q1, Q3: 44.0, 102.0) in the absence of an ocular AESI.

The most frequently reported AESI was keratopathy, which occurred in 42 (50.0%) patients, followed by other AESIs (19.0%, including corneal epithelial microcysts, punctate keratitis, reduced visual acuity, cataract, conjunctivitis, dry eye, eye disorder, keratitis, meibomian gland dysfunction, ocular discomfort, optic neuropathy, sudden vision loss), corneal erosions or defects (8.3%), blurred vision (7.1%), a change in BCVA (4.8%), a dry eye event (1.2%) and photophobia (1.2%). The incidence of keratopathy of 50% in this study is lower than the 72% keratopathy reported for patients in the DREAMM-2 trial over a 13-month follow-up period (current study duration across patients of 0.9 to16.2 months) (Lonial, 2021), but within the range of proportions between 44% and 83% reported in real-world studies over a median of 4.1 months follow-up (Vaxman, 2021; Hultcrantz, 2024).

The majority of ocular AESIs were mild or moderate in severity. The mean duration of keratopathy was available for 16 of the 42 patients (maximum grade of episode was used) and was 232.6 days (SD 115.17; min; max 112.0; 411.0) for mild episodes (n=5), 129.0 days (SD 76.21; min; max 23.0; 260.0) for moderate episodes (n=9) and 153.0 days (SD 125.87; min; max 64.0; 242.0) for severe episodes (n=2). Of the 42 patients with keratopathy, 29 (69.0%) patients had ongoing keratopathy at the end of the study. Limited data were available on the duration of other ocular AESIs. The highest impact on daily living was reported by patients with keratopathy with 31.0% reporting eye irritation/pain, 23.8% reporting reading impairment, 4.8% reporting driving impairments, 2.4% reporting a need for caregiver support and 19.0% reporting other impacts (with data missing for 21.4% of patients with keratopathy). The percentage of specific AESI episodes was higher among responders than among non-responders. However, since preservative-free artificial tear eye drops are also used for symptomatic relief, this factor may have skewed reporting such that patients with ocular events were documented to utilize this supportive-care therapy more so than those without ocular adverse events.

Preservative free eye drops were used for symptomatic relief therefore patients without ocular events may be less likely to use them.

Two patients reported a total of 3 serious AESIs (1 patient with keratopathy and a change in BCVA and 1 patient with a blurred vision event), none of which resulted in death.

There were 27 deaths reported during the study; 17 were due to the disease, 2 due to adverse events other than ocular AESIs, 1 due to disease progression, and 7 with an unknown cause of death.

The best overall response among the 84 patients in the SP was CR in 1.6% (n=1/62), VGPR in 16.1% (n=10/62), PR in 21.0% (n=13/62), and stable disease in 38.7% (n=24/62). Progressive disease occurred in 22.6% (n=14/62). BOR data was missing in 26.2%. Comparatively, real-world studies reported 6% of patients achieving CR, 8% of patients achieving VGPR, 19% of patients achieving PR, 28% of patients achieving stable disease, and 36% of patients progressed while on belantamab therapy (Vaxman, 2021).

The median DoR was 10.7 months (95% CI: 3.9, not reached) and the median DoT 4.1 months (95% CI: 2.9, 4.8). For patients with a partial response or better (n=24), the mean duration of exposure was 238.5 days (SD 127.26; median 236.5 days; Q1, Q3: 115.5, 332.0). For non-responders, the mean duration of exposure was 123.5 days (SD 100.78; median 112.5 days; Q1, Q3: 50.0, 145.0).

The median OS for the SP was not estimable. OS was 89.2% (95% CI: 80.3, 94.2) at 3 months, 78.5% (95% CI: 67.6, 86.1) at 6 months, 68.6% (95% CI: 56.3, 78.1) at 9 months and 59.9% (95% CI: 46.3, 71.1) at 12 and 15 months.

The median rwPFS was 4.5 months (95% CI: 3.48, 5.16 months), in line with reports from a real-world study with a median rwPFS of 4.5 months (Hultcrantz, 2024). The rwPFS was 69.8% (95% CI: 56.7, 79.6) at 3 months, 36.6% (95% CI: 23.9, 49.4) at 6 months, 26.3% (95% CI: 15.2, 38.8) at 9 months and 21.9% (95% CI: 10.8, 35.5) at 12 months. The median rwPFS was higher than the median PFS for the 2.5 mg/kg group in the DREAMM-2 trial (2.8 months; 95% CI: 1.6, 3.6 months) (Lonial, 2021).

10.2. Limitations

Data being obtained from ophthalmologists might not have been consistent across sites and there is a possibility that centers with both hematology and ophthalmology sites may have better ophthalmology data available than sites without the presence of both specialties. Most of the sites within the study had both hematology and ophthalmology located in the same organization with only a few exceptions (such as within Greece). Also, hematology/oncology sites may not be as familiar with ophthalmology reports and therefore interpretation of the data can be difficult and inconsistent across sites. In addition, patient enrollment in Europe was challenging likely due to competition with clinical trials and the decision made by the FDA (before the EU) to not authorize belantamab mafodotin in the US.

There may also be bias due to the so-called Hawthorne effect (i.e., potential change in clinical staff behavior because of being directly observed) (McCambridge, 2014). This might be particularly the case for the frequency of ophthalmic monitoring, which clinical staff might have performed more frequently as part of this study as mandated per the label. As a result ophthalmic monitoring might be overestimated versus routine practice.

Because follow-up was cut short by the premature closure of the study some analysis of duration may be skewed shorter. Similarly, observation periods are somewhat skewed towards the earlier period of the belantamab mafodotin treatment periods; later occurring AESI, ORR, or other cumulative time observations may be under-reported, however, all keratopathy events occurred prior to the fourth dose.

10.3. Interpretation of Results

The study did not statistically compare patients treated with belantamab mafodotin with a comparator group or between subgroups. As a result, caution must be exercised in interpreting the findings and any differences for example found between cannot be considered causal.

10.4. Generalizability

Missing patients and data and large numbers of censored patients due to early termination or loss to follow-up could have introduced selection bias and information bias and might have reduced generalizability to the overall patient population using belantamab mafodotin. However, clinical characteristics of patients included in this study were similar to those reported in other clinical and real-world studies assessing belantamab mafodotin in RRMM patients.

11. OTHER INFORMATION

Not applicable.

12. CONCLUSIONS

Clinical characteristics of patients included in this real-world European prospective study (i.e., regarding prior LoT, presence of ocular AESIs) as well as the frequency of ocular AESIs, specifically keratopathy, were fairly similar to those reported in real-world studies assessing belantamab mafodotin monotherapy in RRMM patients. The frequency of ocular exams prior to the each (subsequent) dose of belantamab mafodotin suggests that most patients were monitored in accordance with label recommendations. The final data also show that dose reduction, treatment interruption/delay treatment discontinuation and common management were used to manage presence of ocular AESIs.

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14. TABLES AND FIGURES

14.1. List of Tables

14.2. List of Figures

14.3. List of Listings

ANNEX 1 LIST OF STAND-ALONE DOCUMENTS

No.	Document Reference No	Date	Title
1.	TMF-14443087	01 April 2022	Protocol Amendment 1
2.	TMF-20504948	29 April 2024	Statistical Analysis Plan, V5.0

ANNEX 2 ADDITIONAL INFORMATION

[Additional annexes may be included if necessary.]

Signature Page for 217240 TMF-20292688 v0.9

Reason for signing: Approved	Name: PPD Role: Approver Date of signature: 20-Dec-2024 15:42:01 GMT+0000

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