haematologica
Journal of the Ferrata Storti Foundation

Belantamab mafodotin monotherapy for relapsed or refractory multiple myeloma: a real-world observational study in the United States

by Malin Hultcrantz, David Kleinman, Ravi Vij, Fernando Escalante, Michel Delforge, Nirali Kotowsky, Jacopo Bitetti, Natalie Boytsov, Leena Camadoo-O'Byrne, Lindsey Powers Happ, Guillaume Germain, Ana Urosevic, Malena Mahendran, Mei Sheng Duh, François Laliberté, Michele Cavo, and Hans C. Lee

Received: May 20, 2024.
Accepted: October 8, 2024.

Citation: Malin Hultcrantz, David Kleinman, Ravi Vij, Fernando Escalante, Michel Delforge, Nirali Kotowsky, Jacopo Bitetti, Natalie Boytsov, Leena Camadoo-O'Byrne, Lindsey Powers Happ, Guillaume Germain, Ana Urosevic, Malena Mahendran, Mei Sheng Duh, François Laliberté, Michele Cavo, and Hans C. Lee. Belantamab mafodotin monotherapy for relapsed or refractory multiple myeloma: a real-world observational study in the United States. Haematologica. 2024 Oct 17. doi: 10.3324/haematol.2024.285893 [Epub ahead of print]

Belantamab mafodotin monotherapy for relapsed or refractory multiple myeloma: a real-world observational study in the United States

Authors: Malin Hultcrantz[1], David Kleinman[2], Ravi Vij[3], Fernando Escalante[4], Michel Delforge[5], Nirali Kotowsky[6], Jacopo Bitetti[7], Natalie Boytsov[6], Leena Camadoo-O'Byrne[8], Lindsey Powers Happ[9], Guillaume Germain[10], Ana Urosevic[10], Malena Mahendran[10], Mei Sheng Duh[11], François Laliberté[10], Michele Cavo[12], Hans C. Lee[13]

[1]Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, NY, USA

[2]Flaum Eye Institute, University of Rochester Medical Center, Rochester, NY, USA

[3]Division of Medical Oncology, Washington University School of Medicine, St. Louis, MO, USA

[4]Hematology Department, University Hospital of Leon, Leon, Spain

[5]Department of Hematology, Catholic University of Leuven, Leuven, Belgium

[6]Value, Evidence and Outcomes, GSK, Upper Providence, PA, USA

[7]Global Medical Affairs, GSK, Zug, Switzerland

[8]Real World Study Delivery, GSK, Stevenage, UK

[9]Real World Data Strategy and Partnerships, Value, Evidence and Outcomes, GSK, Collegeville, PA, USA

[10]Groupe d'Analyse, Ltée., Montreal, Quebec, Canada

[11]Analysis Group, Inc., Boston, MA, USA

[12]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Università degli Studi di Bologna, Bologna, Italy

[13]Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Running title (38/50 characters): Belantamab mafodotin in the real world

Corresponding author: Malin Hultcrantz

Email: hultcram@mskcc.org

Data-sharing statement: The datasets generated and/or analyzed during the current study are not publicly available due to the proprietary nature of the electronic health records. The protocol and study report may be available from the corresponding author on reasonable request.

Main text word count: 1533 words (limit: 1500 words)

Figures/Tables: 3 (limit: 3 total)

Supplementary files: 1 document (containing 1 figure, 2 tables; limit 3 total)

Acknowledgements: Medical writing support (in the form of writing assistance, including preparation of the draft manuscript under the direction and guidance of the authors, collating and incorporating authors' comments for each draft, assembling tables and figures, grammatical editing and referencing) was provided by Priyanka Vaz, PhD, and Elisabeth Walsby, PhD, CMPP, from Avalere Health and was funded by GSK.

Contributions: **MH, DK, RV, FE, MD, NK, JB, NB, LCO, GG, AU, MM, MSD, FL, MC** and **HCL** contributed to the conception or design of the study, data analysis, and data interpretation. **LPH** contributed to data analysis and interpretation.

Disclosures: **MH** reports research funding from GSK, Beigene, Abbvie, SpringWorks Therapeutics, Daiichi Sankyo; and consultancy/advisory boards for BMS, Janssen, and GSK; **DK** has leadership roles in Calm Water Therapeutics LLC, has ownership interests in Calm Water Therapeutics LLC, reports consultancy for GSK and Triphase Accelerator Corp, advisory roles in Calm Water Therapeutics LLC, speakers' bureau membership in Calm Water Therapeutics LLC; **RV** received honoraria from Adaptive, Beigene, BMS, GSK, Janssen, Oncopetides legend, Sanofi, and Takeda; **FE** serves on the advisory board for Amgen, BMS, GSK, Janssen, Sanofi, and Takeda; **MD** received honoraria from Amgen, BMS, Janssen, GSK, Sanofi, Stemline; **NK, JB, NB, LCO**, and **LPH** are employees of GSK and hold stocks in GSK; **GG, AU, MM, MSD**, and **FL** are employees of Analysis Group, Inc., which received research funding from GSK; **MC** has received honoraria from Janssen, Celgene, BMS, Sanofi, GSK, Pfizer, and Amgen; **HCL** reports consulting for BMS, Genentech, Karyopharm, GSK, Sanofi, Pfizer, Janssen, AbbVie, Oncopetides, Takeda Pharmaceuticals, and Allogene Therapeutics.

Funding: This study was funded by GSK (218905). The sponsor was involved in study design and implementation, as well as data collection, analysis, interpretation, writing the study report and reviewing this manuscript. All authors had full access to the data upon request and had final responsibility for the decision to submit for publication. Research support was also supplied by the Memorial Sloan Kettering Core Grant (P30 CA008748).

Belantamab mafodotin, a humanized, monoclonal antibody, conjugated to the microtubule inhibitor monomethyl auristatin F, binds to B-cell maturation antigen (BCMA) on plasma cells.[1] Accelerated approval as monotherapy was granted by the United States (US) Food and Drug Administration (FDA) in August 2020 for patients with relapsed/refractory multiple myeloma (RRMM) who received at least four prior lines of therapy,[2,3] and conditional marketing authorization was granted by the European Medicines Agency (EMA).[4] The subsequent DREAMM-3 confirmatory study (NCT04162210) did not meet the primary endpoint of progression-free survival (PFS) superiority versus pomalidomide and dexamethasone, resulting in US marketing authorization withdrawal in February 2023 and conditional marketing authorization non-renewal by the EMA in 2023.[4,5]

Studies assessing belantamab mafodotin in combination with standard-of-care treatments in second line and later for RRMM are ongoing.[6-8] Recent readouts of two Phase 3 studies have demonstrated the potential of belantamab mafodotin combinations as new treatment options.[9,10] In DREAMM-7, belantamab mafodotin in combination with bortezomib and dexamethasone resulted in significantly greater PFS (36.6 months, 95% confidence interval [CI] 28.4, not reached [NR]) compared with daratumumab, bortezomib, and dexamethasone (13.4 months, 95% CI 11.1, 17.5,) in patients with at least one prior line of therapy.[9] In DREAMM-8, belantamab mafodotin in combination with pomalidomide and dexamethasone conferred a significantly greater PFS (NR months, 95% CI NR, NR) compared with pomalidomide, bortezomib, and dexamethasone (12.7 months, 95% CI 9.1, 18.5) in lenalidomide-exposed patients.[10]

During belantamab mafodotin approval for use in the US, patients underwent risk evaluation and mitigation strategy (REMS) ophthalmic monitoring.[11] With the evolving clinical program of belantamab mafodotin combinations, there is a need to understand how ocular events are managed in patients with RRMM who were treated with belantamab mafodotin in the real world. This retrospective, observational study evaluated the real-world treatment effectiveness and management of ocular events in patients with RRMM who received belantamab mafodotin. This study complied with all applicable laws regarding patient privacy and used data from anonymized US electronic health records (EHRs) from the Flatiron Health database between January 1, 2011, and June 30, 2022. Due to the nature of the study, patient identification was not possible. Therefore, informed consent, ethics committee and institutional review board approval were not required. ***Online Supplementary Figure S1A*** depicts the study design, eligibility criteria, and endpoints.

Ocular events were categorized into keratopathy, blurred vision, dry eye, and keratitis. Eye examinations included best corrected visual acuity (BCVA) score assessments and slit lamp examinations. Keratopathy severity was classified as mild, moderate, or severe according to the first slit lamp examination occurring on or after the keratopathy onset date, and the action taken after onset was reported for all patients with an ocular event.

Of 247 patients with MM, 184 were eligible for the study (***Online Supplementary Figure S1B***); the median age was 69.6 years, 46.7% were female, and 63.6% were White (***Online Supplementary Table S1***). Most patients were treated in a community setting (71.2%) and had an Eastern Cooperative Oncology Group performance status of 0–2 (84.8%). High-risk cytogenetics were reported in 39.7%, 87.0% were triple-class exposed, and 82.1% were triple-class refractory. From initial MM diagnosis to treatment start, 67.9% of patients had ≥1 BCVA assessment. Patient treatment history is shown in ***Online Supplementary Table S1***.

The median (interquartile range) treatment period was 2.0 (1.1, 4.5) months, with a follow-up of 4.1 (1.9, 8.5) months. Treatment patterns and effectiveness are summarized in ***Online Supplementary Table S2***. Median real-world overall survival was 7.9 months, and median real-world PFS was 4.5 months.

During follow-up, 92 patients (50.0%) had ≥1 ocular event, with a median time from treatment initiation to first ocular event of 31.5 days and 2.0 administrations of belantamab mafodotin (**Table 1**). Multiple ocular events were reported in 48 patients (26.1%). The most common ocular events were keratopathy (41.3%), blurred vision (28.3%), dry eye (17.4%), and keratitis (9.8%).

A total of 76 (41.3%) patients had keratopathy events; six (3.3%) had multiple events, and 72 had ≥1 ocular examinations on or after the first keratopathy onset date (**Table 1**). Keratopathy severity was determined for 62 patients, with mild, moderate, and severe keratopathy reported for 38 (20.7%), 19 (10.3%), and five (2.7%) patients, respectively (**Table 2**). Following a keratopathy finding, 50 (27.2%) patients had an action taken following the keratopathy onset date.

When stratified by severity, action following keratopathy onset was taken in 27 of 38 patients with mild keratopathy, all 19 patients with moderate keratopathy, and four of five patients with severe keratopathy (**Table 2**). Therapy holds occurred in 19 patients (10.3%) with mild keratopathy, 15 patients (8.2%) with moderate keratopathy, and four patients (2.2%) with severe keratopathy (**Table 2**). After therapy holds, belantamab mafodotin was subsequently administered in 17 of 38 patients with mild keratopathy, 12 of 19 with moderate keratopathy, and two of five with severe keratopathy; median time

to subsequent administration was shorter for cases of mild (21.0 days) than for moderate (59.5 days) and severe (46.0 days) keratopathy (**Table 2**).

Dose or schedule changes were also used to manage keratopathy (**Table 2**). Belantamab mafodotin was discontinued in three of 38, four of 19, and one of five patients with mild, moderate, and severe keratopathy, respectively (**Table 2**), equating to keratopathy-related discontinuation in eight patients (4.3%).

Overall, frequency of eye examinations in the real world was generally high prior to the first 2 visits, with 169 patients (91.8%) having ≥1 recorded ophthalmic examination before the start of treatment, of which 164 (89.1%) were within 28 days before the first administration. For 142 patients with ≥2 belantamab mafodotin administrations (77.2%), 131 had ≥1 ophthalmic examination between the first and second administration (71.2% overall; **Table 3**), all within 28 days of first administration. The median ratio of ophthalmic visits to belantamab mafodotin administrations was 1.0. Median BCVA score (logMAR, Snellen equivalent [feet]) was similar between patients with ≥1 ophthalmic examination (0.0, 20/20; n=135) or with ≥2 ophthalmic examinations (0.0, 20/20; n=98) during the follow-up period (**Table 3**).

An ophthalmic examination was taken within 14 days of worsening symptoms in 59 of 76 patients with keratopathy (77.6%). Subsequent ophthalmic examinations were performed in 56 patients (73.7%), with keratopathy reported as mild, moderate, and severe in 33 (17.9% overall), 20 (10.9% overall), and five (2.7% overall) patients, respectively (**Table 3**).

Over the treatment period, ocular treatments were received by 85.3% of patients. Preservative-free artificial tears (70.7% of patients) followed by eye drops (18.5%) were the most frequent ocular treatments observed in the overall population (**Table 3**).

Ocular events were observed in half of patients in this study, which is lower than the ocular adverse event rates reported in the DREAMM-2 and DREAMM-3 trials (66–74%).[12,13] Ocular events that were not systematically captured in the EHR data, as well the shorter follow-up period for this study (median 4.1 months compared with ~3 years and 11.5 months in DREAMM-2 and DREAMM-3, respectively) [12,13] may have contributed to the lower event rate observed. Keratopathy was the most common ocular event reported in patients receiving belantamab mafodotin, with more cases of mild keratopathy reported than moderate or severe cases combined.

Ocular events were effectively managed through dose modifications with minimal treatment discontinuation. Our findings highlight that belantamab mafodotin-related ocular events are manageable in the real world. Temporary therapy hold was the most frequent action taken for ocular events. When stratified by keratopathy severity, 40–63% of patients had a subsequent belantamab mafodotin dose following a dose hold due to keratopathy, highlighting the transient nature of the holds for a sizeable proportion of patients. These findings highlight that ocular events associated with belantamab mafodotin can be effectively managed in real-world academic and community settings as well as clinical trials.[9,10]

This study should be interpreted within the context of some of the limitations common to real-world studies. First, in contrast to the stringent evaluation criteria applied to clinical trials, outcomes assessed retrospectively in real-world studies may vary across physicians and between patients due to subjective assessment and reporting. Furthermore, less rigorous real-world monitoring may have led to delayed or under-identification of toxicity or disease progression. Second, as patients may have been treated at multiple practices, events and eye examinations may not have been systematically captured in the EHRs available. Data from EHRs may have been subject to coding error and misclassification, which may have led to misrepresentation of events. Third, ocular events reported in the data may not be all events experienced by patients receiving belantamab mafodotin, as data were only abstracted for prespecified events. Fourth, patients were excluded from this study if they had participated in a clinical trial; including a wider range of patients may have improved the generalizability of the data. Fifth, the Flatiron Health database does not include all US oncology centers and may not be representative of the broader US RRMM population. Lastly, the withdrawal of belantamab mafodotin from the US market attenuated new patients initiating treatment after February 2023.

This study provides insight into ocular event management following belantamab mafodotin treatment in real-world settings and highlights effectiveness in patients with RRMM. These findings support ongoing studies of belantamab mafodotin in combination therapies and provide important insights into ocular event management, as well as the benefits and risks associated with the use of belantamab mafodotin in the real world.

References

1. Tai YT, Mayes PA, Acharya C, et al. Novel anti-B-cell maturation antigen antibody-drug conjugate (GSK2857916) selectively induces killing of multiple myeloma. Blood. 2014;123(20):3128-3138.
2. US Food and Drug Administration. FDA granted accelerated approval to belantamab mafodotin-blmf for multiple myeloma. 2020; https://www.fda.gov/drugs/resources-information-approved-drugs/fda-granted-accelerated-approval-belantamab-mafodotin-blmf-multiple-myeloma. Accessed November 16, 2023.
3. Lonial S, Lee HC, Badros A, et al. Belantamab mafodotin for relapsed or refractory multiple myeloma (DREAMM-2): a two-arm, randomised, open-label, phase 2 study. Lancet Oncol. 2020;21(2):207-221.
4. European Medicines Agency. EMA recommends non-renewal of authorisation of multiple myeloma medicine Blenrep. 2023; https://www.ema.europa.eu/en/news/ema-recommends-non-renewal-authorisation-multiple-myeloma-medicine-blenrep. Accessed January 11, 2024.
5. US Food and Drug Administration. Announcement of the Revocation of the Biologics License for BLENREP. 2023; https://www.govinfo.gov/content/pkg/FR-2023-03-30/pdf/2023-06576.pdf. Accessed December 11, 2023.
6. Rifkin RM, Boyd K, Grosicki S, et al. DREAMM-7: A Phase III Study of the Efficacy and Safety of Belantamab Mafodotin (Belamaf) with Bortezomib, and Dexamethasone (B-Vd) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM). Blood. 2020;136(Supplement 1):53-54.
7. Trudel S, Davis R, Lewis NM, et al. DREAMM-8: A Phase III Study of the Efficacy and Safety of Belantamab Mafodotin with Pomalidomide and Dexamethasone (B-Pd) Vs Pomalidomide Plus Bortezomib and Dexamethasone (PVd) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM). Blood. 2020;136(Supplement 1):4.
8. Trudel S, McCurdy A, Louzada ML, et al. Belantamab mafodotin, pomalidomide and dexamethasone in refractory multiple myeloma: a phase 1/2 trial. Nat Med. 2024;30(2):543-551.
9. Hungria V, Robak P, Hus M, et al. Belantamab Mafodotin, Bortezomib, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2024; 391(5):393-407.
10. Dimopoulos MA, Beksac M, Pour L, et al. Belantamab Mafodotin, Pomalidomide, and Dexamethasone in Multiple Myeloma. N Engl J Med. 2024;391(5):408-421.
11. US Food and Drug Administration. BLENREP. Highlights of Prescribing Information. 2020; https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761158s000lbl.pdf. Accessed November 16, 2023.
12. Dimopoulos MA, Hungria VTM, Radinoff A, et al. Efficacy and safety of single-agent belantamab mafodotin versus pomalidomide plus low-dose dexamethasone in patients with relapsed or refractory multiple myeloma (DREAMM-3): a phase 3, open-label, randomised study. Lancet Haematol. 2023;10(10):e801-e812.
13. Nooka AK, Cohen AD, Lee HC, et al. Single-agent belantamab mafodotin in patients with relapsed/refractory multiple myeloma: Final analysis of the DREAMM-2 trial. Cancer. 2023;129(23):3746-3760.

Table 1: Assessment of ocular events during follow-up

Ocular events	**Patients N=184**
Post-index period, months, mean ± SD [median]	5.6 **±** 4.8 [4.1]
Number of events, median [mean ± SD]	0.5 [0.9 ± 1.1]
Patients with ≥1 event, n (%)	92 (50.0)
Time from start of treatment to first event, days, median [mean ± SD]	31.5 [39.4 ± 31.6]
Number of belantamab mafodotin administrations prior to first event, median [mean ± SD]	2.0 [2.1 ± 1.1]
By number of prior administrations, n (%)	
1	30 (16.3)
2	40 (21.7)
≥3	22 (12.0)
Number of events, median [mean ± SD]	2.0 [1.7 ± 0.9]
By number of events, n (%)	
1	44 (23.9)
>1	48 (26.1)
2	34 (18.5)
≥3	14 (7.6)
Type of event, n (%)	
Keratopathy	76 (41.3)
Patients with multiple keratopathy events, n (%)	6 (7.9)
Keratopathy severity of first event	
Patients with ≥1 ocular exam on or after the keratopathy onset date, n (%)	72 (94.7)
BCVA score assessment	63 (82.9)
Slit lamp examination	71 (93.4)
Blurred vision	52 (28.3)
Dry eye	32 (17.4)
Keratitis	18 (9.8)
Action taken, n (%)	
Therapy hold*	57 (31.0)
Patients with subsequent belantamab mafodotin administration	41 (22.3)
Time from last administration before the onset date to subsequent administration,[†] days, median [mean ± SD]	42.0 [48.4 ± 27.2]
Hold >28 days	26 (14.1)
Treatment for adverse event	55 (29.9)
Therapy dose or schedule change	18 (9.8)
None	14 (7.6)
Therapy discontinuation	13 (7.1)

AE, adverse event; BCVA, best corrected visual acuity; IQR, interquartile range; LOT, line of therapy; SD, standard deviation.

Follow-up was defined as the period between the first belantamab mafodotin administration (start of treatment) and start of participation in a clinical trial, date of last recorded clinical interaction, end of data availability, or death, whichever occurred first. *Defined as any treatment within the given LOT that was held or delayed as a result of the AE, defined as a gap of ≥28 days and <90 days from the previous to the subsequent belantamab mafodotin administration. Therapy holds were dissociated

from the timing of belantamab mafodotin administrations; †reported over all therapy holds to account for patients with multiple therapy holds.

Table 2: Assessment and management of keratopathy events during follow-up, stratified by keratopathy severity by slit lamp examination findings

Keratopathy severity (n=62)	**Mild n=38**	**Moderate n=19**	**Severe n=5**
Patients with an action taken following keratopathy onset date, n (%)	27 (71.1)	19 (100.0)	4 (80.0)
Therapy hold,* n (%)	19 (50.0)	15 (78.9)	4 (80.0)
Patients with subsequent belantamab mafodotin administration	17 (44.7)	12 (63.2)	2 (40.0)
Time from last administration before the onset date to subsequent administration, days, median [mean ± SD]	21.0 [34.7 ± 26.8]	59.5 [64.4 ± 29.8]	46.0 [46.0 ± 5.7]
Hold >28 days	5 (13.2)	10 (52.6)	2 (40.0)
Treatment for event, n (%)	19 (50.0)	11 (57.9)	1 (20.0)
Therapy dose or schedule change, n (%)	7 (18.4)	6 (31.6)	1 (20.0)
Therapy discontinuation, n (%)	3 (7.9)	4 (21.1)	1 (20.0)

AE, adverse event; LOT, line of therapy; SD, standard deviation.

Follow-up was defined as the period between the first belantamab mafodotin administration (start of treatment) and start of participation in a clinical trial, date of last recorded clinical interaction, end of data availability, or death, whichever occurred first. *Defined as any treatment within the given LOT that was held or delayed as a result of the AE, defined as a gap of ≥28 days and <90 days from the previous to the subsequent belantamab mafodotin administration. Therapy holds were dissociated from the timing of belantamab mafodotin administrations.

Table 3: Ophthalmic monitoring during follow-up

Ophthalmic examinations before each belantamab mafodotin administration	**Patients N=184**
Median ratio of ophthalmic visits to administration	1.0
First administration	
Patients with ≥1 ophthalmic examination before first administration, n (%)	169 (91.8)
≤14 days prior to administration, n (%)	142 (77.2)
≤28 days prior to administration, n (%)	164 (89.1)
Second administration	
Patients with ≥2 administrations, n (%)	142 (77.2)
Patients with ≥1 ophthalmic examination between first and second administration, n (%)	131 (71.2)
≤14 days prior to administration, n (%)	126 (68.5)
≤28 days prior to administration, n (%)	131 (71.2)
Median BCVA score	
Patients with ≥1 ophthalmic examination; n=135, logMAR, Snellen equivalent [feet]	0.0, 20/20
Patients with ≥2 ophthalmic examinations; n=98, logMAR, Snellen equivalent [feet]	0.0, 20/20
Ophthalmic examination within 14 days of worsening keratopathy symptoms; n=76, n (%)	59 (77.6)
Subsequent ophthalmic examinations in patients with keratopathy; n=76, n (%)	56 (73.7)
Keratopathy severity, n	
Mild	33
Moderate	20
Severe	5
Ocular treatments, n (%)	
Any	157 (85.3)
Preservative-free artificial tears	130 (70.7)
Eye drops	34 (18.5)
Other	16 (8.7)

Follow-up was defined as the period between the first belantamab mafodotin administration (start of treatment) and start of participation in a clinical trial, date of last recorded clinical interaction, end of data availability, or death, whichever occurred first.

Belantamab mafodotin monotherapy for relapsed or refractory multiple myeloma: a real-world observational study in the United States

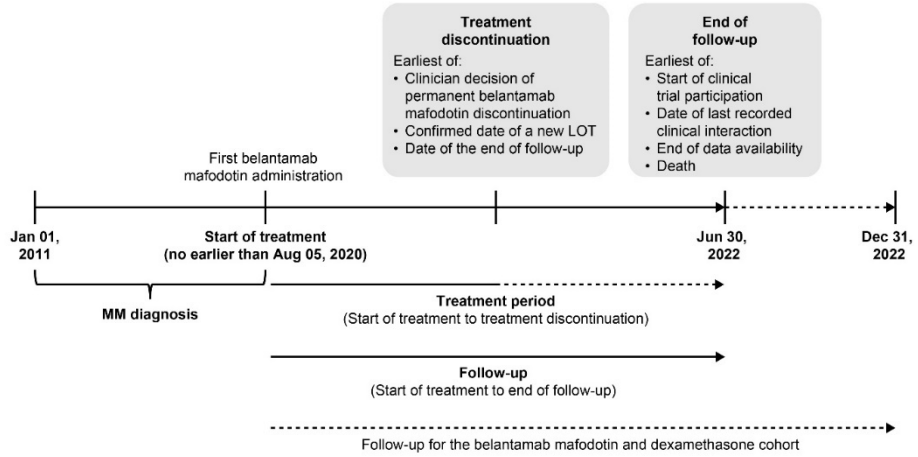
Authors: Malin Hultcrantz, David Kleinman, Ravi Vij, Fernando Escalante, Michel Delforge, Nirali Kotowsky, Jacopo Bitetti, Natalie Boytsov, Leena Camadoo-O'Byrne, Lindsey Powers Happ, Guillaume Germain, Ana Urosevic, Malena Mahendran, Mei Sheng Duh, François Laliberté, Michele Cavo, Hans C. Lee

Supplement

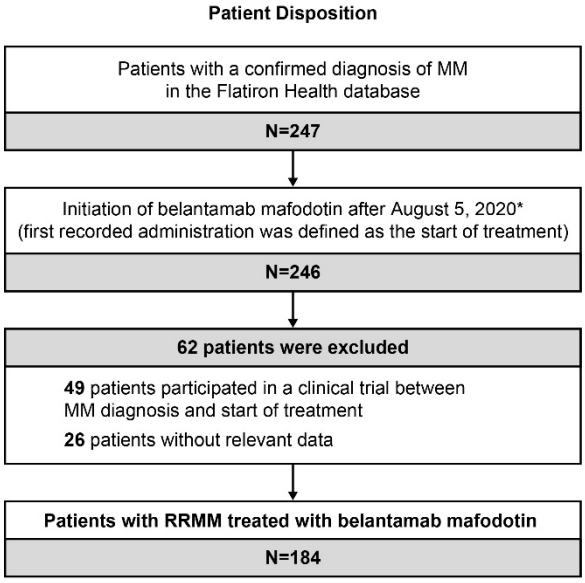
Supplemental figures

Figure S1: Study design (A) and patient disposition (B)

A



B



FDA, US Food and Drug Administration; LOT, line of therapy; MM, multiple myeloma; RRMM, relapsed and refractory multiple myeloma.

*Belantamab mafodotin administrations were assessed post belantamab mafodotin FDA approval date of August 5, 2020. One patient with a belantamab mafodotin initiation date of July 19, 2019, was omitted from the analysis.

Table S1: Patient demographics and clinical characteristics

Characteristics	Patients N=184
Time from MM diagnosis to belantamab mafodotin initiation, years, median (IQR) [mean ± SD]	5.1 (3.0, 7.0) [5.2 ± 2.5]
Demographics at start of treatment	
Age years, median [mean ± SD]	69.6 [68.7 ± 10.0]
Female, n (%)	86 (46.7)
Race/ethnicity, n (%)	
White	117 (63.6)
Black or African American	23 (12.5)
Hispanic or Latino	12 (6.5)
Asian/other	32 (17.4)
Practice type, n (%)	
Community	131 (71.2)
Academic	53 (28.8)
MM characteristics at start of treatment, n (%)	
ECOG performance status	
0–2	156 (84.8)
3–4	9 (4.9)
Unknown	19 (10.3)
Cytogenetic risk	154 (83.7)
High risk*	73 (39.7)
Standard risk†	81 (44.0)
Unknown	30 (16.3)
Class status,‡ n (%)	
Triple (immunomodulatory drug, anti-CD38 mAb, PI)	
Exposed	160 (87.0)
Refractory	151 (82.1)
Penta (bortezomib, carfilzomib, lenalidomide, pomalidomide, anti-CD38 mAb)	
Exposed	122 (66.3)
Refractory	58 (31.5)
MM treatment history	
Lines of therapy	
Median (IQR) [mean ± SD]	5.0 (4.0, 7.0) [5.4 ± 2.4]
Drugs and drug classes at MM diagnosis,‡ n (%)	184 (100)
Corticosteroid§	184 (100)
Immunomodulatory drugs	179 (97.3)
Lenalidomide	169 (91.8)
Pomalidomide	166 (90.2)
Thalidomide	22 (12.0)
Proteasome inhibitor	172 (93.5)
Bortezomib	158 (85.9)
Carfilzomib	145 (78.8)
Ixazomib	51 (27.7)
Monoclonal antibody	168 (91.3)

Daratumumab	166 (90.2)
Elotuzumab	55 (29.9)
Isatuximab	19 (10.3)
Chemotherapy	134 (72.8)
Cyclophosphamide	127 (69.0)
Doxorubicin	22 (12.0)
Etoposide	14 (7.6)
Cisplatin	11 (6.0)
Bendamustine	8 (4.3)
Melphalan	4 (2.2)
Targeted inhibitor	51 (27.7)
HDAC inhibitor[¶]	4 (2.2)
Other therapies	
Autologous stem cell transplant	89 (48.4)
Anti-BCMA	0 (0.0)
Pre-existing comorbidities,[#] n (%)	138 (75.0)
Cardiovascular disease	97 (52.7)
Renal disease	71 (38.6)
Cardiac disease	42 (22.8)
Peripheral neuropathy	36 (19.6)
Pulmonary disease	34 (18.5)
Belantamab mafodotin-related eye disease**	26 (14.1)
Diabetes	26 (14.1)
Ophthalmic health	
Patients in dataset with ≥1 BCVA score assessment at the start of treatment, n (%)	22 (12.0)
Patients in dataset with ≥1 BCVA score result between initial MM diagnosis and start of treatment, n (%)	125 (67.9)
BCVA, logMAR, median [mean ± SD]	0.1 [0.1 ± 0.2]
*Corneal diagnosis,** n (%)*	
Other corneal conditions	1 (0.5)
ISS stage, n (%)	
I	42 (22.8)
II	40 (21.7)
III	50 (27.2)
Unknown	52 (28.3)
Extramedullary disease, n (%)	39 (21.2)
Laboratory measurements	
Patients with >1 serum creatinine or creatinine clearance result, n (%)	183 (99.5)
Serum creatinine, mg/dL, median [mean ± SD]	1.0 [1.3 ± 0.9]
Creatinine clearance, mL/min, median [mean ± SD]	67.0 [72.5 ± 37.7]
Year of initial MM diagnosis, n (%)	
2011–2015	75 (40.8)
2016–2021	109 (59.2)
Progression on the last LOT before start of treatment, n (%)	66 (35.9)

anti-CD38 mAb, anti–CD–38 monoclonal antibody; BCMA, B-cell maturation antigen; BCVA, best corrected visual acuity; ECOG, Eastern Cooperative Oncology Group; HDAC, histone deacetylase; ICD-CM, International Classification of Diseases Clinical Modification; IQR, interquartile range; LogMAR, logarithm of the minimal angle of resolution; LOT, line of therapy; MM, multiple myeloma; PI, proteasome inhibitor; SD, standard deviation.

Parameters were assessed between initial MM diagnosis and the first belantamab mafodotin administration (start of treatment), unless otherwise stated. *Defined as presence of del[17p] (16.3%; n=30), t[4;14] (9.2%; n=17), t[14;16] (2.7%; n=5), t[14;20] (n=0), or 1q21 (26.1%; n=48) gains/amplifications identified by FISH or karyotyping; †defined as evidence of genetic testing but no documented presence of high-risk identifiers; ‡patients may have been included in more than one drug class; §corticosteroids included dexamethasone and prednisone; ¶HDAC inhibitors included panobinostat; #comorbidities, evaluated by ICD-10-CM and ICD-9-CM diagnosis codes, in >10% of patients are shown; **evaluated by ICD-10-CM codes H16 (keratitis), H17 (corneal scares and opacities), and H18 (other disorders of the cornea), and ICD-9-CM code 370 (keratitis), 371 (other disorders of the cornea); no keratitis or corneal scars/opacities were reported.

Table S2: Belantamab mafodotin treatment patterns and effectiveness

Belantamab mafodotin treatment patterns	Patients N=184
Treatment period, months, median (IQR) [mean ± SD]	2.0 (1.1, 4.5) [3.4 ± 3.5]
Administration	
First dose, mg/kg, n (%)	
1.9	12 (6.5)
2.5	167 (90.8)
Unknown	5 (2.7)
Administered dose,* mg, median [mean ± SD]	180.4 [189.5 ± 54.2]
Patients with 1 administration, n (%)	43 (23.4)
Patients with 2 administrations, n (%)	48 (26.1)
Cycle length, days, median [mean ± SD]	21.0 [23.1 ± 5.9]
Patients with 3 administrations, n (%)	30 (16.3)
Cycle length, days, median [mean ± SD]	21.0 [26.2 ± 10.7]
Patients with ≥4 administrations, n (%)	63 (34.2)
Cycle length, days, median [mean ± SD]	27.3 [32.6 ± 13.4]
Dose change,* n (%)	42 (22.8)
Time from start of treatment to first dose change, days, median [mean ± SD]	63.0 [77.1 ± 63.3]
Number of administrations prior to first dose change, median [mean ± SD]	2.0 [1.8 ± 1.0]
Patients with a dose increase from 1.9 to 2.5 mg/kg, n (%)	13 (7.1)
Patients with a dose decrease from 2.5 to 1.9 mg/kg, n (%)	41 (22.3)
Patients with a documented reason for dose change, n (%)	11 (6.0)
Reason for dose change, n (%)	
Toxic effect of therapy	6 (3.3)
Unknown	3 (1.6)
Cancer-related symptoms not due to therapy	1 (0.5)
Insufficient response[†]	1 (0.5)
Patient request	1 (0.5)
Treatment interruption/delay,[‡] n (%)	51 (27.7)
Time from start of treatment to first treatment interruption/delay, days, median [mean ± SD]	71.0 [95.4 ± 63.2]
Patients with a documented reason for dose interruption/delay, n (%)	39 (21.2)
Reason for dose interruption/delay, n (%)	
Toxic effect of therapy	33 (17.9)
Unknown	9 (4.9)
Non-cancer related medical issue	8 (4.3)
Cancer-related symptoms not due to therapy	2 (1.1)
Patient request	2 (1.1)
Concomitant medication use, n (%)	
Eye disease medication	118 (64.1)
Pulmonary disease medication	111 (60.3)
Non-belantamab mafodotin MM medication[§]	84 (45.7)
Bone disease medication	49 (26.6)
Cardiovascular medication	38 (20.7)

Diabetes medication	3 (1.6)
Treatment discontinuation, ¶ n (%)	111 (60.3)
Number of administrations prior to discontinuation, median [mean ± SD]	2.0 [3.2 ± 2.4]
Patients with 1 administration, n (%)	26 (14.1)
Patients with 2 administrations, n (%)	32 (17.4)
Patients with 3 administrations, n (%)	22 (12.0)
Patients with 4 administrations, n (%)	6 (3.3)
Patients with ≥5 administrations, n (%)	25 (13.6)
Time from start of treatment to discontinuation, days, median [mean ± SD]	49.0 [83.3 ± 81.4]
Patients with a documented reason for discontinuation, n (%)	104 (56.5)
Reasons for discontinuation, # n (%)	
Progression†	57 (31.0)
Toxic effect of therapy	38 (20.7)
Ocular	28 (15.2)
Other	14 (7.6)
Insufficient response§§	9 (4.9)
Cancer-related symptoms not due to therapy	4 (2.2)
Non-cancer related medical issue	4 (2.2)
Patient request	4 (2.2)
Financial	2 (1.1)
Unknown	13 (7.1)
Effectiveness	
Median rwOS, months	7.9
Median rwPFS, months	4.5
Cumulative OR, %	
1 month	6.7
6 months	25.5
12 months	27.4
Median TTNT from final administration, months	2.2

IQR, interquartile range; LOT, line of therapy; MM, multiple myeloma; OR, overall response; PR, partial response; rwOS, real-world overall survival; rwPFS, real-world progression-free survival; SD, standard deviation; TTNT, time to next treatment.

The treatment period was defined as between the first belantamab mafodotin administration (start of treatment) and the earliest of permanent discontinuation of belantamab mafodotin, the confirmed date of a new LOT, start of participation in a clinical trial, date of last recorded clinical interaction, end of data availability, or death. *Dose information was not available for 11 belantamab mafodotin administrations; †documented evidence of treatment status changes due to new sites of disease, increased diseases, and/or worsening disease burden; ‡defined as a ≥28–<90 day gap between belantamab mafodotin administrations; §included corticosteroids (n=73, 40%), proteasome inhibitors (n=13, 7%), immunomodulatory agents (n=12, 7%), chemotherapy (n=12, 7%), monoclonal antibodies (n=7, 4%), and targeted inhibitors (n=4, 2%); ¶defined as the first documented date of discontinuation (21 days after last belantamab mafodotin administration) or a switch to a new LOT; #reasons were not mutually exclusive and may add up to >100%; §§documented evidence that the treatment status changes due to the patient not having sufficient improvement in disease burden despite treatment.

RwOS was defined as the time from the first belantamab mafodotin administration (start of treatment) to the date of death due

to any cause. RwPFS was defined as the time from the start of treatment to the earliest of first documented disease progression or death. Cumulative OR was defined as percentage of patients with PR or better at a given time-point. Patients who did not experience the event were censored at the end of follow-up. Median time to event was defined as the time point when 50% of patients had the event.