Antibody-drug conjugates

ADC per il trattamento del paziente con MMRR

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LE NUOVE FRONTIERE DELL'IMMUNOTERAPIA PER LA CURA DEL
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Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Amgen					X		
BMS					X	X	
GSK						X	
Janssen					X	X	
Takeda			X			X	
Sanofi			X		X	X	
Pfizer						X	

Outcomes of a majority of patients with RRMM remain suboptimal potentially due to retreatment with prior therapies

STUDY POPULATION

RRMM Patients

- **Longitudinal, retrospective** cohort study using COTA de-identified database (11/16/2015 to 9/12/2022; N=1662)
- Final 2L+ population was **1118 patients** (544 patients excluded d/t stem cell therapy during index LOT or in the prior 100 days)
- Patients must have had active RRMM and received ≥1 prior line of treatment
- Time-to-event outcomes, including PFS, DOT, and TTNT, were evaluated with Kaplan-Meier survival analysis
- The following overlapping sub-cohorts were created based on patients' prior exposure and refractory status:

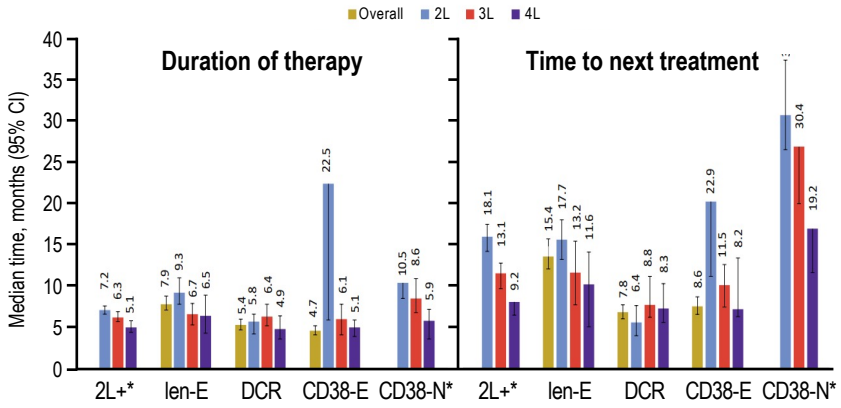
CD38-N (n=757)	len-E (n=1123)	CD38-E (n=764)	DCR (n=713)
(no prior exposure to an anti-CD38 agent)	(prior exposure to lenalidomide)	(prior exposure to an anti-CD38 agent)	(refractory to a PI and an immunomodulatory therapy)

After 2L+ index LOT, 57.3% of the overall population progressed to a subsequent LOT

Despite prior exposure, **many were retreated with an anti-CD38 agent** both during and after index LOT (49.0% and 33.7%, respectively)

Median PFS and TTNT in the overall 2L+ cohort were **21.8** and 18.1 months; shortest in DCR (**6.7** and 7.8 months) and CD38-E cohorts (**5.6** and 8.6 months)

Median DOT was short across overall 2L+ patients (7.2 months at 2L) and sub-cohorts, and generally remained consistent across LOTs



The figure was first presented in Richter J. ASH. December 2022. Poster presentation 1891.

*Overall category is not included for the 2L+ population and CD38-N since LOTs are not mutually exclusive; individual patients could have multiple index dates and appear in multiple LOTs. This does not apply to the len E, DCR, and CD38 E sub cohorts in which patients had a single index date following the exposure or refractory status of interest. DOT was measured from the initiation of index line of therapy to the stop of index line of therapy; TTNT was measured from the initiation of index line of therapy to initiation of the following line of therapy. These figures were first presented in Richter J at ASH. December 2022. Poster presentation 1891.

These findings support the need for increased uptake of new treatments with novel mechanisms of action earlier in the patient journey

- Richter J, et al. Presented at the 64th American Society of Hematology Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Poster 1891.

Single-Agent Belantamab Mafodotin in Patients with Relapsed or Refractory Multiple Myeloma (RRMM): Final Analysis of the DREAMM-2 trial

The efficacy and safety profile of belantamab mafodotin was consistent throughout the duration of DREAMM-2

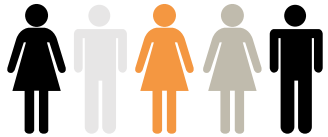
In the primary[1] and 13-month follow-up of DREAMM-2,[2] belantamab mafodotin monotherapy demonstrated rapid, deep, and durable responses with a manageable safety profile for patients with RRMM

This study **analysed the efficacy and safety profile of belantamab mafodotin using the final data from the DREAMM-2 trial,** corresponding to an approximate 3-year follow-up[3]

RRMM, relapsed/refractory multiple myeloma.

1. Lonial S, et al. *Lancet Oncol*. 2020;21:207-221. 2. Lonial S, et al. *Cancer*. 2021;127:4198-4212. 3. Nooka A, et al. Presented at the 64th American Society of Hematology Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3246.

Here we report the end-of-study efficacy and safety analysis of DREAMM-2 for the recommended dose of 2.5 mg/kg



STUDY OVERVIEW

DREAMM-2

- Key Inclusion Criteria:
  - ≥3 prior lines of therapy
  - ECOG performance status of 0-2
  - Refractory to PI and an immunomodulatory agent, and refractory/intolerant to an anti-CD38 mAb
- Primary endpoint: ORR
- Key secondary endpoints: PFS, OS, DOR, safety, ocular symptoms, HRQoL
- Eye exams, including a corneal exam and assessment of change in BCVA, were conducted at baseline and prior to each dose
- The GSK KVA scale was used for grading ocular events; ocular symptoms were graded per CTCAE

Final cutoff date: March 31, 2022

Belantamab mafodotin 2.5 mg/kg Q3W cohort (N=97)	**Belantamab mafodotin 3.4 mg/kg Q3W cohort (N=99)**
Median follow-up: 12.5 months	Median follow-up: 13.8 months

BCVA, best corrected visual acuity; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HRQoL, health-related quality of life; KVA, Keratopathy and Visual Acuity; mAb, monoclonal antibody; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; Q3W, every three weeks; RRMM, relapsed/refractory multiple myeloma.

1. Nooka A, et al. Presented at the 64th ASH Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3246.

DREAMM-2 study patients were heavily pretreated with a median of 7 prior lines of therapy

Characteristic	2.5 mg/kg Cohort (N=97)
Age, median (range), years	**65 (60-70)**
18 to <65 years	45 (46)
65 to <75 years	39 (40)
≥75 years	13 (13)
Sex	
Male	51 (53)
Female	46 (47)
Race	
White	72 (74)
Black or African American	16 (16)
Renal impairment per eGFR (mL/min/1.73 m^2)	
Normal (≥90)	19 (20)
Mild (≥60 to <90)	48 (49)
Moderate (≥30 to <60)	**24 (25)**
Severe (≥15 to <30)	2 (2)
Time from initial diagnosis, median (range), years	5.49 (4.01-7.02)
ISS disease stage at screening	
Stage I	21 (22)
Stage II	33 (34)
Stage III	**42 (43)**
Unknown	1 (1)
Cytogenetic abnormalities	
t(11;14)	16 (16)
t(14;20)	3 (3)
Del 13	18 (19)
Hyperdiploidy	7 (7)
Other	28 (29)
High-risk cytogenetics	**41 (42)**
17p13del	16 (16)
t(4;14)	11 (11)
t(14;16)	7 (7)
1q21+	25 (26)

Characteristic	2.5 mg/kg Cohort (N=97)
Type of myeloma	
IgG	65 (67)
Non-IgG	33 (33)
Extramedullary disease	**22 (23)**
Prior lines of therapy*	
Median (range)	**7 (3-21)**
≤4 lines	16 (16)
>4 lines	81 (84)
Prior therapies received	
Proteasome inhibitor	
Bortezomib	5 (98)
Carfilzomib	74 (76)
Immunomodulatory drug	
Lenalidomide	97 (100)
Pomalidomide	89 (92)
Anti-CD38 monoclonal antibody	
Daratumumab	97 (100)
Isatuximab	3 (3)
Refractory to prior therapies†	
Proteasome inhibitor	
Bortezomib	74 (76)
Carfilzomib	63 (65)
Immunomodulatory drug	
Lenalidomide	87 (90)
Pomalidomide	84 (87)
Anti-CD38 monoclonal antibody	
Daratumumab	97 (100)
Isatuximab	3 (3)

The chart has been independently created by GSK from original data first presented in Lonial S et al. *Lancet Oncol.* 2020.

All patients were refractory to a proteasome inhibitor, immunomodulatory drug, and an anti-CD38 monoclonal antibody as per eligibility criteria

Responses observed with belantamab mafodotin in DREAMM-2 were rapid, deep, and durable[1]

Efficacy	Belantamab mafodotin 2.5 mg/kg Q3W (N=97)[a]	Belantamab mafodotin 3.4 mg/kg Q3W (N=99)
ORR, % (97.5% CI)	32 (21.7-43.6)	35 (24.8-47)
Median time to response, months (95% CI)	1.5 (1-2.1)	1.4 (0.9-2.1)
MRD[b] negativity rate in patients who achieved ≥VGPR, % (95% CI)	36 (12.8-64.9)	23 (5-53.8)
Median DOR, months (95% CI)	12.5 (4.2-19.3)	6.2 (4.8-18.7)
Median PFS, months (95% CI) Median PFS in patients who achieved ≥VGPR, months (95% CI)	2.8 (1.6-3.6) 14 (9.7-NR)	3.9 (2-5.8) 16.8 (7.7-NR)
Median OS, months (95% CI) Median OS in patients who achieved ≥VGPR, months (95% CI)[c]	15.3 (9.9-18.9) 30.7 (19.7-37.9)	14 (10-18.1) 35.5 (14.1-NR)

This chart has been independently created by GSK from original data first presented in Nooka A et al at ASH. December 2022. Poster presentation 3246.

The median DOR and OS reported here are longer than those reported at the 13-month update[2]

[a]Currently the only recommended dose as the 3.4 mg/kg dose was not further pursued. [b]Minimal residual disease was measured by next generation sequencing with a threshold of 10^{-5}. [c]Median OS in ≥VGPR was a post hoc analysis.

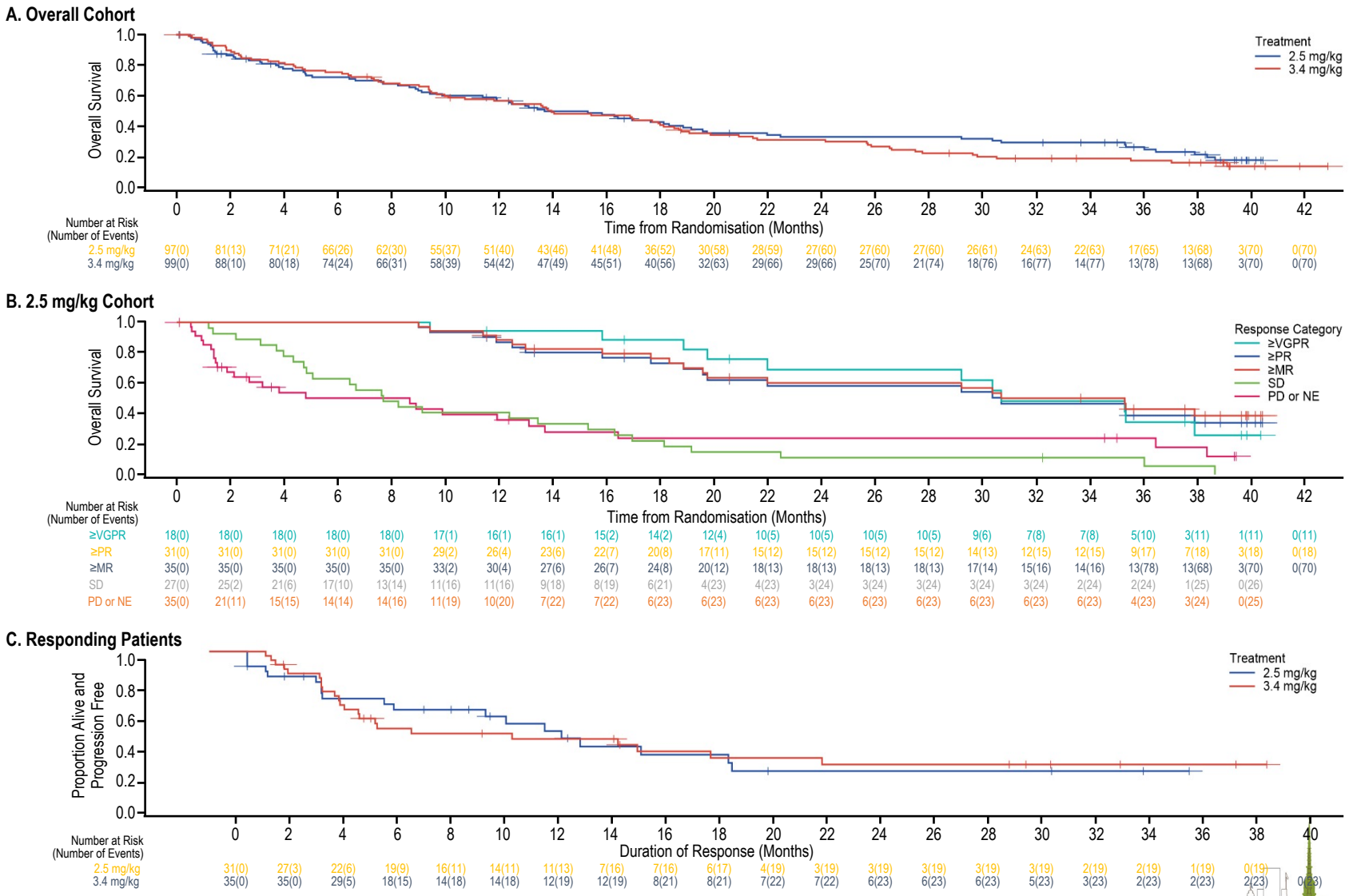
1. Nooka A, et al. Presented at the 64th ASH Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3246.

When examining those achieving VGPR or better, responses were even deeper and more durable

Median OS (95% CI) for the 2.5 mg/kg cohort was 15.3 (9.9-18.9) months[a]

For patients in the 2.5 mg/kg cohort[a] who achieved ≥VGPR:

- Estimated median OS was 30.7 months (n=19, 20%)
- Estimated median PFS was 14.0 months
- Median DoR (95% CI) was 12.5 months (4.2-19.3)



[a]Currently the only recommended dose as the 3.4 mg/kg dose was not further pursued.

CI, confidence interval; DoR, duration of response; OS, overall survival; PFS, progression-free survival; VGPR, very good partial response.

DREAMM-2 Results in Special Populations

- Prognosis remains especially poor for hard-to-treat special populations with RRMM, including patients with **high-risk cytogenetic markers, renal impairment**, and **extramedullary disease**

High-risk Cytogenetic Markers

Patients can develop cytogenetic abnormalities. Standard therapies may be less effective in this population

Renal Impairment

Common in RRMM patients and can develop as a result of some treatments

Necessitates avoiding certain therapies or having doses adjusted

Extramedullary Disease

Some patients at baseline or may have malignant plasma cells outside the bone marrow

There are no treatment guidelines and patients have a poor prognosis

The 13-month follow-up included subanalyses to explore the safety and efficacy of belantamab mafodotin these special hard-to-treat patient populations

DREAMM 2: Efficacy of belantamab mafodotin in special populations

Independent Review Committee-Assessed Best Response*	Overall (N=97)	HR-IMWG (N=26)†	HR-cyto (N=41)‡	SR-cyto (N=56)§	Normal renal function (N=19)¶	Mild renal impairment (N=48)#	Moderate renal impairment (N=24)**	Extramedullary disease (N=22)
ORR, n (%)††	31 (32)	9 (35)	12 (29)	19 (34)	7 (37)	16 (33)	8 (33)	1 (5)
(97.5%/95% CI)‡‡	(21.7–43.6)	(17.2–55.7)	(16.1–45.5)	(21.8–47.8)	(16.3–61.6)	(20.4–48.4)	(15.6–55.3)	(-)
sCR	2 (2)	0 (0)	1 (2)	1 (2)	1 (5)	0 (0)	1 (4)	0 (0)
CR	5 (5)	2 (8)	3 (7)	2 (4)	0 (0)	2 (4)	3 (13)	0 (0)
VGPR	11 (11)	5 (19)	5 (12)	6 (11)	1 (5)	6 (13)	4 (17)	0 (0)
PR	13 (13)	2 (8)	3 (7)	10 (18)	5 (26)	8 (17)	0 (0)	0 (0)
MR, n (%)	4 (4)	3 (12)	3 (7)	1 (2)	2 (11)	2 (4)	0	2 (9)
SD, n (%)	27 (28)	5 (19)	9 (22)	18 (32)	6 (32)	13 (27)	8 (33)	8 (36)
CBR, n (%)§§	35 (36)	12 (46)	15 (37)	20 (36)	9 (47)	18 (38)	8 (33)	3 (14)
(95% CI)	(26.6–46.5)	(26.6–66.6)	(22.1–53.1)	(23.4–49.6)	(24.4–71.1)	(24.0–52.6)	(15.6–55.3)	(2.9–34.9)
Median DoR (95% CI)	11.0 (4.2-NR)	10.3 (1.4-13.1)	10.3 (1.4-13.1)	NR (4.2-NR)	4.2 (1.4-NR)	12.5 (2.2-NR)	13.1 (4.2-NR)	1.4¶¶
Median PFS (95% CI)	2.8 (1.6-3.6)	3.3 (0.9-7.1)	2.1 (0.8-3.7)	2.9 (1.6-4.8)	3.0 (1.3-6.2)	2.2 (2.0-3.6)	3.7 (1.0-12.5)	1.1 (0-8.3)
Median estimated OS (95% CI)	13.7 (9.9-NR)	9.9 (4.3-NR)	13.1 (8.2-NR)	17.0 (12.4-NR)	14.9 (7.7-NR)	13.7 (11.4-NR)	NR (5.1-NR)	13.4 (2.7-NR)

This chart has been independently created by GSK from original data first presented in Lonial S et al. *Cancer*. 2021.

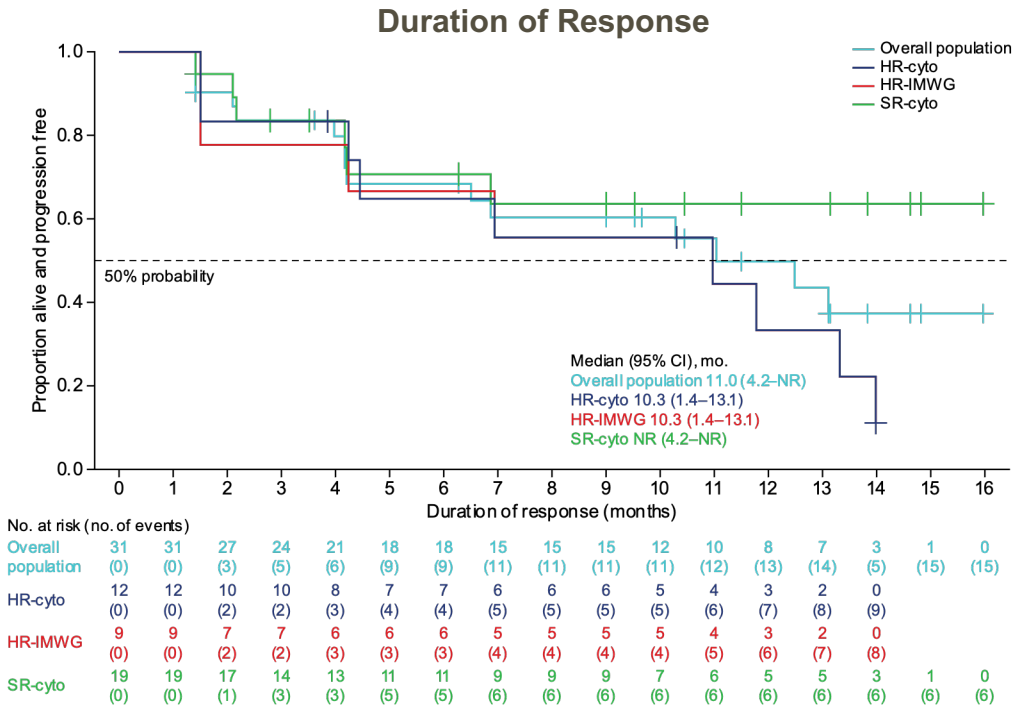
The efficacy of belantamab mafodotin in patients with high-risk cytogenetic markers or renal impairment was similar to the overall population. Patients with EMD had comparably poorer outcomes, and additional studies are necessary to understand if responses vary by EMD subtype.

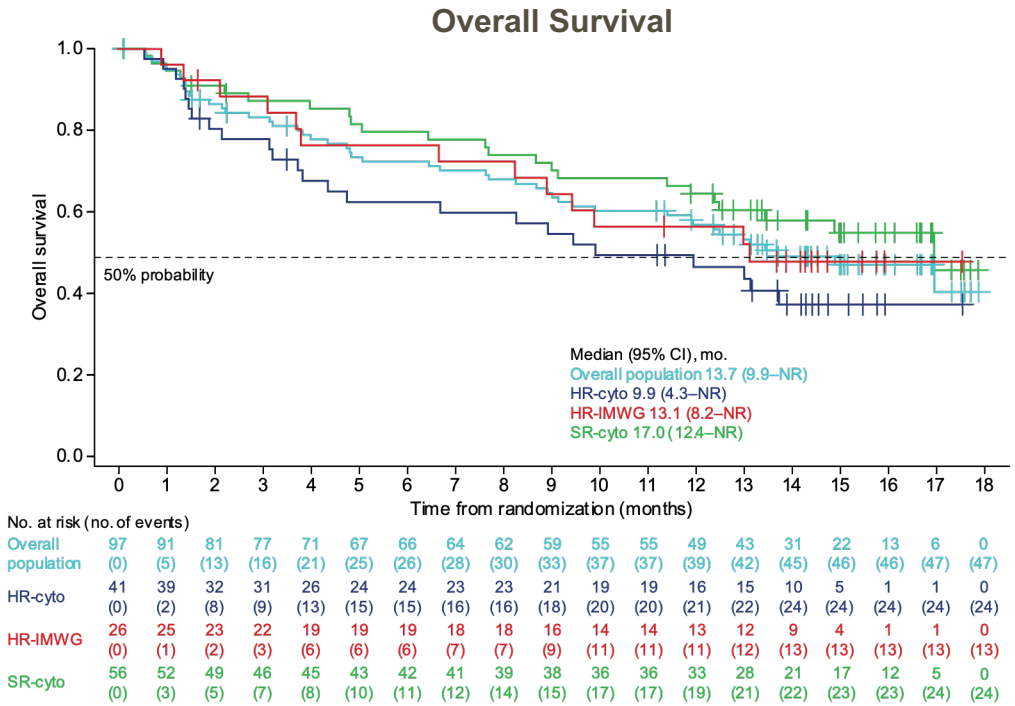
*Responses assessed in the intention-to-treat population by an independent review committee according to the International Myeloma Working Group Uniform Criteria Consensus Recommendations. Six patients (6%) were not evaluable for response and were treated as non-responders; †Defined as patients with any of t(4:14), t(14:16), or 17p13del; ‡Defined as patients with any of t(4:14), t(14:16), 17p13del, or 1q21+; §Defined as patients with none of t(4:14), t(14:16), 17p13del, or 1q21+; ¶Defined as patients with eGFR ≥90 mL/min/1.73 m^2; #Defined as patients with eGFR ≥60–<90 mL/min/1.73 m^2; **Defined as patients with eGFR ≥30–<60 mL/min/1.73 m^2; ††ORR: sCR + CR + VGPR + PR; ‡‡97.5% CI presented for overall population; 95% CI presented for all other groups; §§CBR: sCR + CR + VGPR + PR + MR; ¶¶DoR of the single patient exhibiting a response

CBR = clinical benefit rate; CI = confidence interval; CR = complete response; DoR = duration of response; eGFR = estimated glomerular filtration rate; EMD = extramedullary disease; HR-cyto = high-risk cytogenetics; HR-IMWG = high-risk cytogenetics per International Myeloma Working Group criteria; MR = minimal response; NR = not reached; ORR = overall response rate; PR = partial response; sCR = stringent complete response; SD = stable disease; SR = standard-risk cytogenetics; VGPR = very good partial response.

Lonial S et al. *Cancer*. 2021.

DREAMM 2: Efficacy of belantamab mafodotin in special populations





These figures were first presented in Lonial S et al. *Cancer*. 2021.

Patients with high-risk cytogenetic markers exhibited a duration of response and overall survival comparable with the overall population. Efficacy outcomes were similar in the HR-IMWG (excluding 1q21+) and HR-cyto(including 1q21+) groups (median DoR, 10.3 months for both).

*Responses were assessed in the intention-to-treat population (including all randomly assigned patients) by an independent review committee according to the International Myeloma Working Group Uniform Criteria Consensus Recommendations; †Defined as patients with any of t(4:14), t(14:16), or 17p13del; ‡Defined as patients with any of t(4:14), t(14:16), 17p13del, or 1q21+; §Defined as patients with none of t(4:14), t(14:16), 17p13del, or 1q21+.

HR-cyto = high-risk cytogenetics; HR-IMWG = high-risk cytogenetics per International Myeloma Working Group criteria; SR-cyto =standard-risk cytogenetics.
Lonial S et al. *Cancer*. 2021.

Overall AE profile of belantamab mafodotin was consistent with previous reports[1-3]

Safety and dose modifications	Belantamab mafodotin 2.5 mg/kg Q3W (N=95)[a]	Belantamab mafodotin 3.4 mg/kg Q3W (N=99)
Grade ≥3 AE, n (%)	80 (84)	82 (83)
Keratopathy[b]	29 (31)	25 (25)
Anemia	20 (21)	28 (28)
Thrombocytopenia	21 (22)	32 (32)
AE-related dose modifications, n (%)		
Dose reduction	34 (36)	44 (44)
Dose delay	51 (54)	61 (62)
Permanent discontinuation	11 (12)	12 (12)
Permanent discontinuation due to ocular events	5 (5)	3 (3)

This chart has been independently created by GSK from original data first presented in Nooka A et al in ASH. December 2022. Poster presentation 3246.

Response was maintained in patients with dose delays >63 days

[a]N=95 in the safety analysis in the 2.5 mg/kg cohort. [b]Ocular events (as reported here) and ocular symptoms were assessed using CTCAE scale.
AE, adverse event; BCVA, best corrected visual acuity; Q3W, every three weeks; QoL, quality of life.

Ocular AE[a] profile of belantamab mafodotin was consistent with previous reports and was manageable[1-3]

Most common ocular events,[a] n (%)	Belantamab mafodotin 2.5 mg/kg Q3W (N=95)[b]
Keratopathy	67 (71)
Blurred vision	24 (25)
BCVA reduced to 20/50	46 (48)

Blurred vision includes the preferred terms vision blurred, diplopia, visual acuity reduced, and visual impairment.
This chart has been independently created by GSK from original data first presented in Nooka A et al at ASH. December 2022. Poster presentation 3246.

No new safety signals were noted when comparing the incidence of AEs with earlier reports from this study

The most commonly reported any-grade ocular AEs in both cohorts included keratopathy, blurred vision, and BCVA reduced to 20/50 or worse

[a]Ocular events (as reported here) and ocular symptoms were assessed using CTCAE scale. [b]N=95 in the safety analysis in the 2.5 mg/kg cohort.
AE, adverse event; BCVA, best corrected visual acuity; Q3W, every three weeks; QoL, quality of life.

Ocular adverse events were transient

Resolution of ocular events

Event[a]	Belantamab mafodotin 2.5 mg/kg Q3W (N=95)[b]
Blurred vision	
Incidence, n (%)	24 (25)
Patients with resolved blurred vision, n (% patients with event)	19 (79)
Time to resolution, days (median, range)	43.0 (6-895)
Not resolved, discontinued, end of follow-up, n (%)	5 (21)
BCVA reduced to 20/50 or worse	
Incidence	46 (48)
Time to resolution, days (median, range)*	23.0 (5-103)
Not resolved, discontinued, end of follow-up, n (%)	6 (13)
Keratopathy	
Incidence	67 (71)
Time to resolution, days (median, range)†	120.0 (8-858)
Not resolved, discontinued, end of follow-up, n(%)	18 (27)

*Resolution defined as having a post-baseline score ≥20/50 or no equivalent value in either eye. †Duration defined as the time from onset of any keratopathy event to first time subject is free from event. A gap of at least 1 day was required between resolution of 1st and occurrence of 2nd. This chart has been independently created by GSK from original data first presented in Nooka A et al in ASH. December 2022. Poster presentation 3246

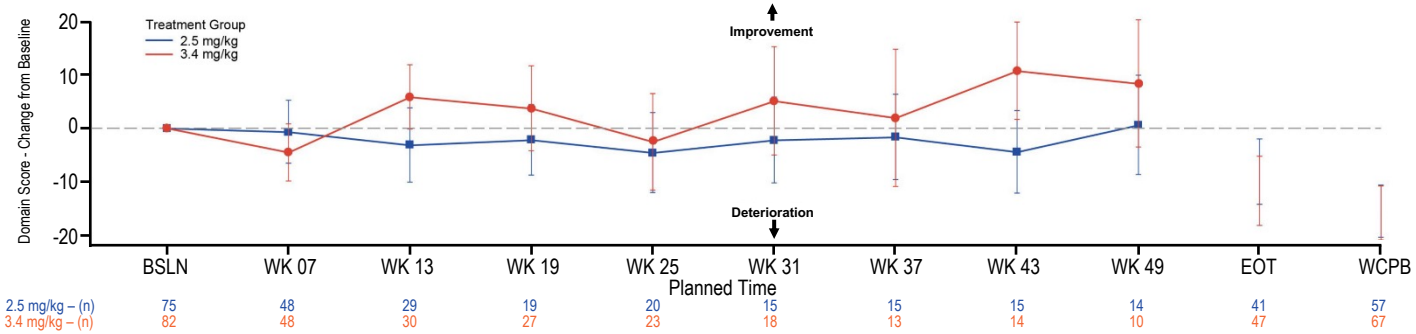
Median time to resolution of the first event of blurred vision, reduced BCVA, and keratopathy was 43, 23, and 120 days, respectively, in the 2.5 mg/kg cohort

[a]Ocular events (as reported here) and ocular symptoms were assessed using CTCAE scale. [b]N=95 in the safety analysis in the 2.5 mg/kg cohort.

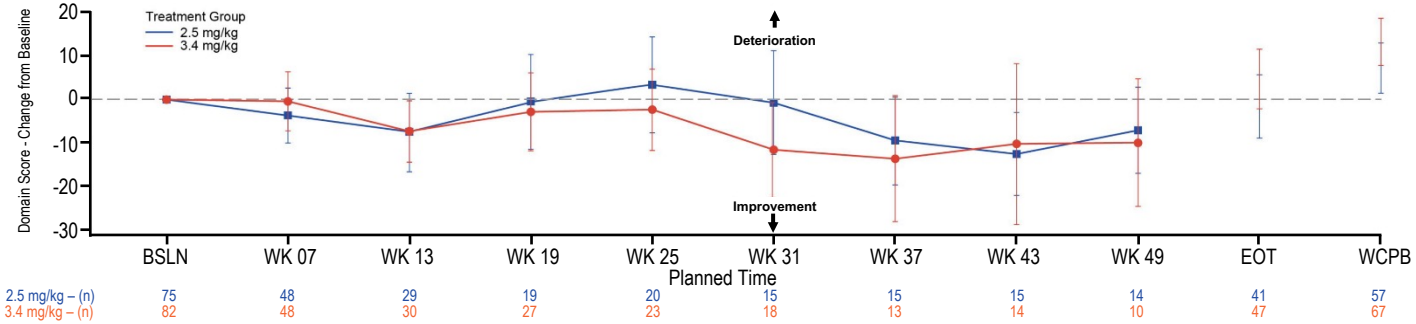
AE, adverse event; BCVA, best corrected visual acuity; Q3W, every three weeks; QoL, quality of life.

Data suggests that patients' quality of life was maintained or improved with long-term belantamab mafodotin treatment

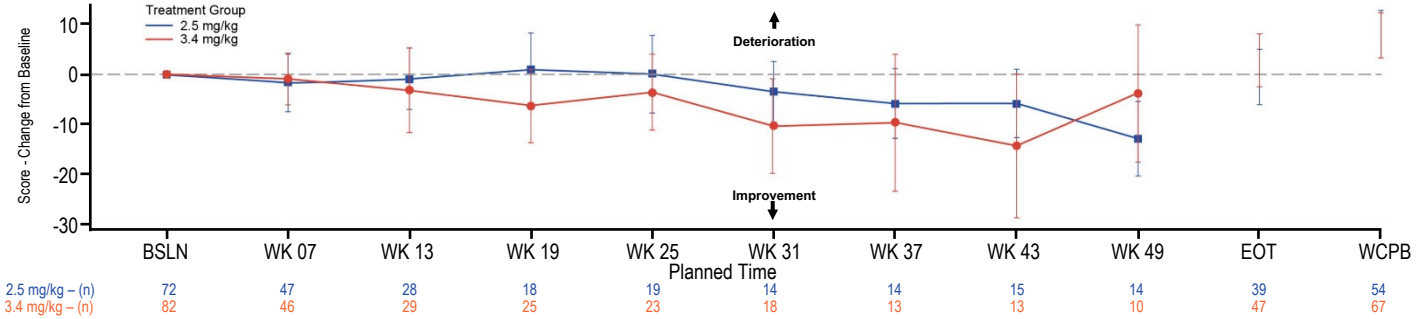
Global Health Status/QoL



Fatigue



Disease Symptoms

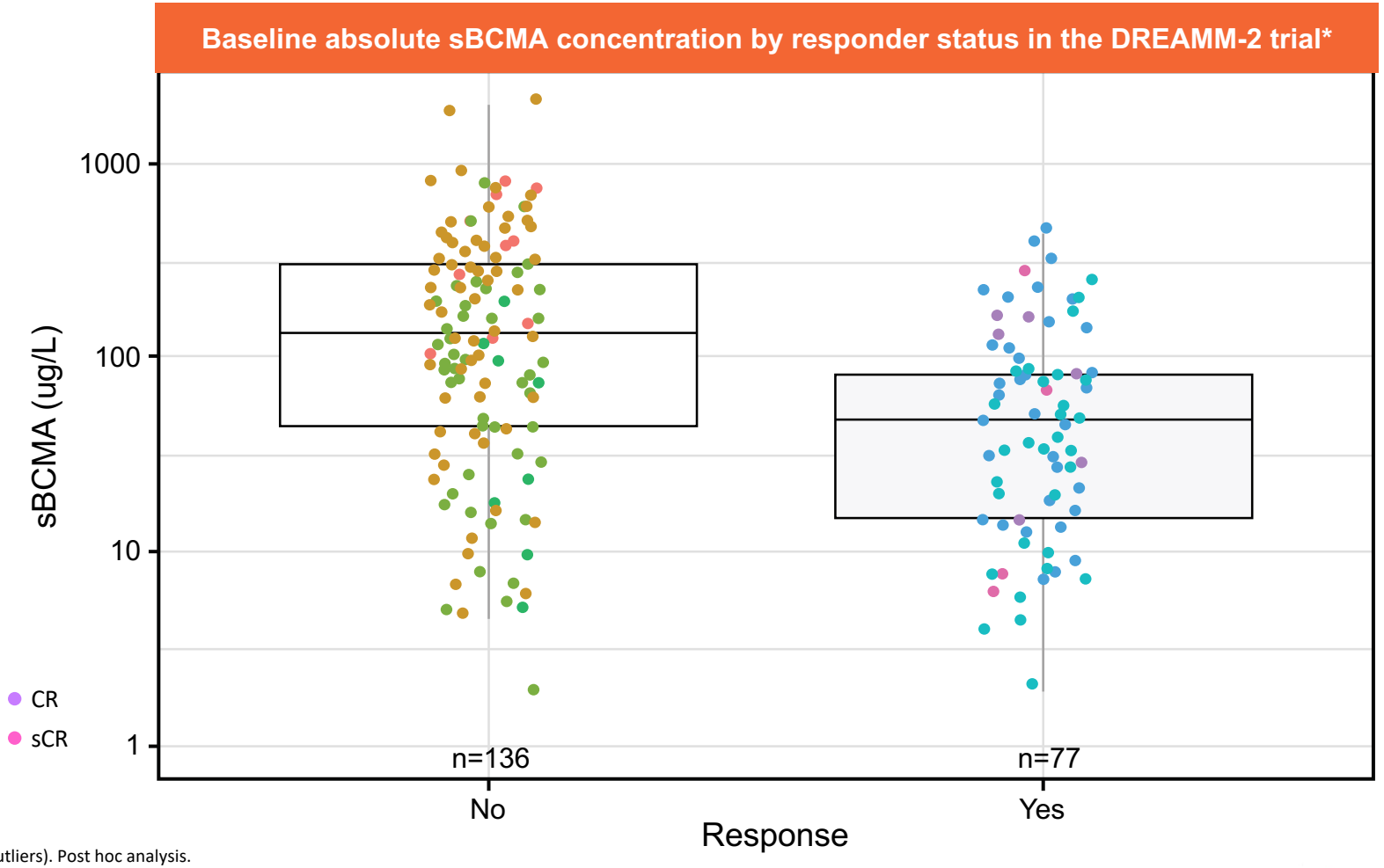


Data indicates that **overall global health status/QoL, physical and role functioning, and overall disease symptoms were maintained or improved** during belantamab mafodotin treatment

Nooka A, et al. Presented at the 64th American Society of Hematology Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3246.

There was no sBCMA threshold identified to delineate responders vs non-responders, suggesting that baseline sBCMA did not dictate a response

A substantial overlap in baseline sBCMA levels was observed between responders (≥PR) and non-responders



*Box and whisker plot: box denotes median and IQR; whiskers indicate the range (excluding outliers). Post hoc analysis.

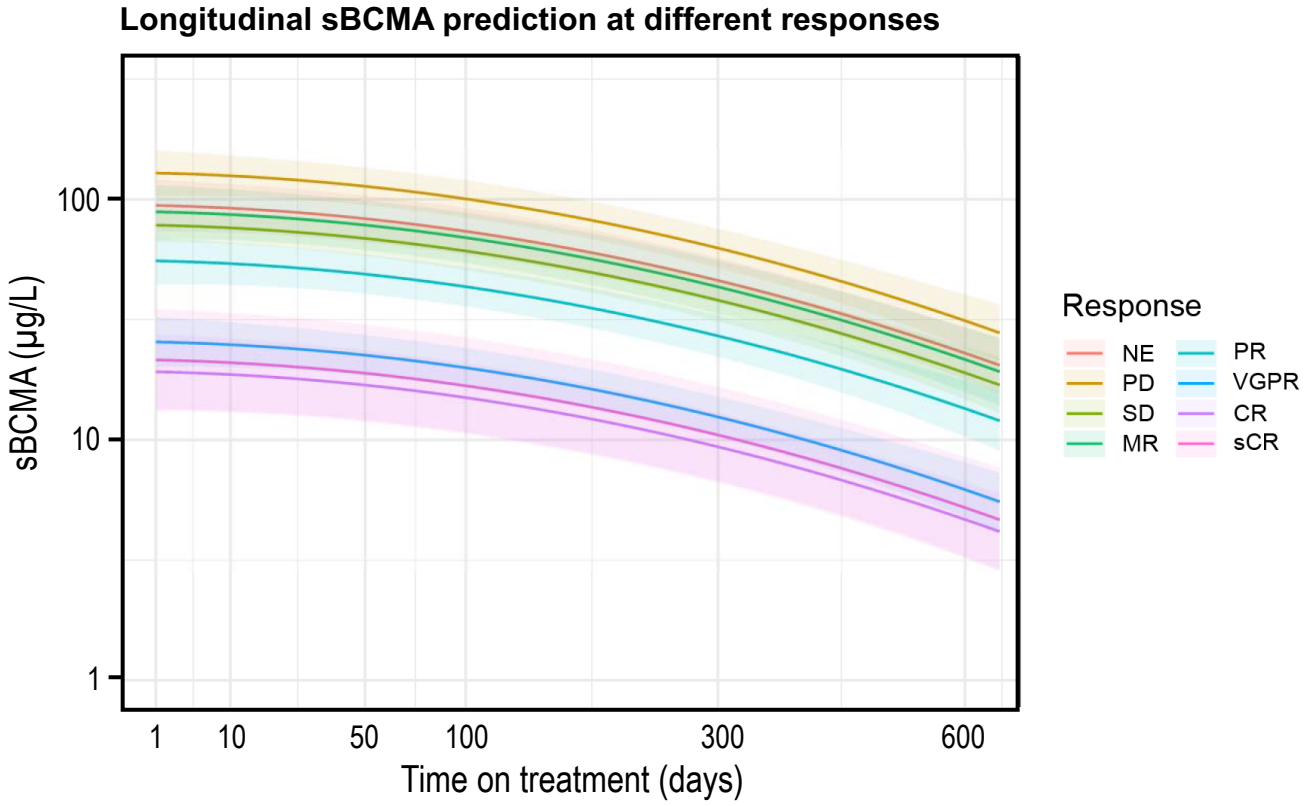
CR, complete response; MR, minimal response; NE, not estimable; PD, progressive disease; PR, partial response; sBCMA, soluble B-cell maturation antigen; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

sBCMA levels decreased with time on belantamab mafodotin treatment, but complete loss was not observed

sBCMA levels over time

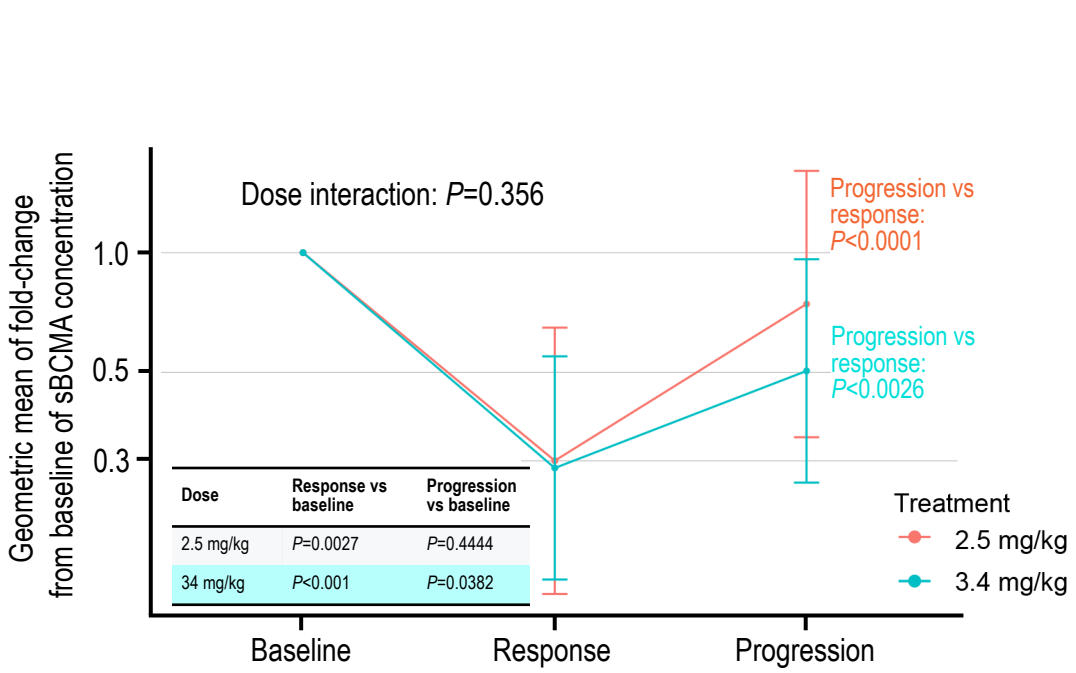
sBCMA levels, adjusted for disease burden, appear to **decrease with time on treatment at all response levels**

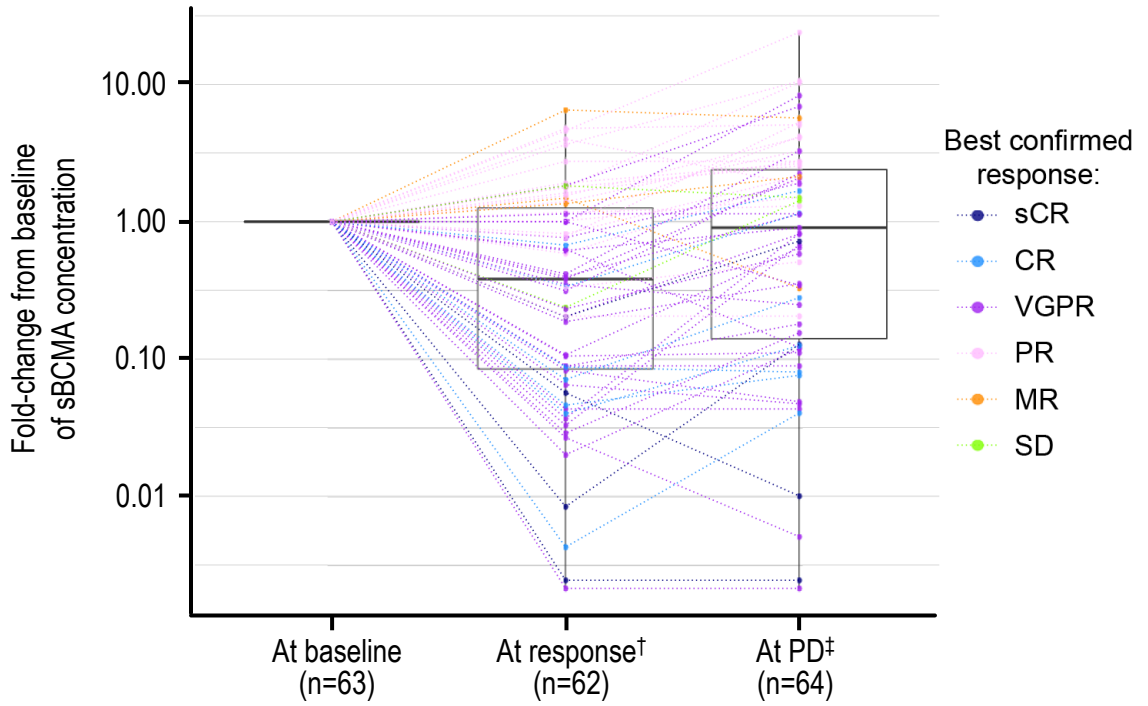
Following correction for survivorship effect, reduction in sBCMA over time remained, but there was not complete loss



This figure was first presented in Lowther DE et al at ASH. December 2022. Oral presentation 248.

In addition to being measurable at progression, sBCMA levels returned to near baseline





This figure was first presented in Lowther DE et al at ASH. December 2022. Oral presentation 248.

sBCMA levels showed a pronounced drop during response but returned to near baseline upon progression

The Patient Experience With Belantamab Mafodotin: Perspectives of Patients Receiving Treatment in Clinical Trials and in the Real-World

Outcomes of patients evaluated in the real-world observational BeAMM study are consistent with the DREAMM-2 study

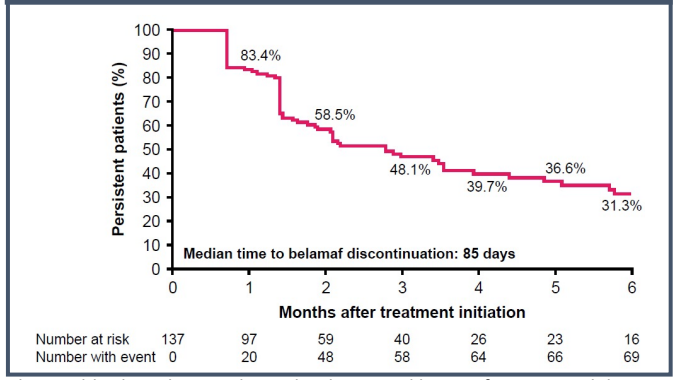
Retrospective, longitudinal, observational study using de-identified data from the US EHR–derived Flatiron Health Database from 01/01/2011 to 12/31/2021

Patient and disease characteristics between MM diagnosis and belantamab mafodotin initiation (n=137)	
Age, years, mean (± SD)	67.9 (± 10.0)
Female, n (%)	69 (50.4)
Race, n (%) White Black or African American	 87 (63.5) 17 (12.4)
Cytogenetic risk, n (%) High	 62 (45.3)
Prior LOTs, n (%) 3 4 5 6 7 >8	 11 (8.0) 28 (20.4) 34 (24.8) 17 (12.4) 15 (10.9) 22 (16.1)
Triple-refractory, n (%)	105 (76.6)

Safety	Post-index period[c] (N=137)	Post-index period of ≥4 mos (N=57)
Patients with ≥1 ocular AESI, n (%)	71 (51.8)	41 (71.9)
Time to first ocular AESI, days, mean (± SD)	39.1 (± 33.6)	44.7 (± 40.2)
Number of ocular AESIs, mean (± SD)	1.8 (± 0.8)	1.4 (± 1.2)
1 ocular AESI, n (%)	30 (21.9)	13 (22.8)
2 ocular AESIs, n (%)	32 (23.4)	21 (36.8)
Type of ocular AESI in >30% of patients, n (%)		
Keratopathy	56 (40.9)	30 (52.6)
Blurred vision	44 (32.1)	30 (52.6)
Severity of first keratopathy event (among patients with keratopathy severity information), n (%)[d]	(N=44)	(N=25)
Mild	27 (61.4)	12 (48.0)
Moderate/severe[e]	17 (38.6)	13 (52.0)
Persistence of belantamab mafodotin treatment, %		
3 months	48.1	-
6 months	31.3	-

Effectiveness	Post-index period[c] (N=137)
ORR 6 months post index date, %	30.2
Median PFS, months	5.4
OS 6 months post index date, %	57.3

Patients continuing on belantamab mafodotin



These tables have been independently created by GSK from original data presented in Hultcrantz M. ASH. December 2022.

Overall, patients with RRMM treated with belantamab mafodotin in the real-world setting experienced similar outcomes to patients in the DREAMM-2 study, including therapy holds to address ocular AESIs

Hultcrantz M, et al. ASH nnual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P4549.

Efficacy and safety of belantamab mafodotin in the real-life setting as reported in the ALFA study were consistent with the DREAMM-2 study

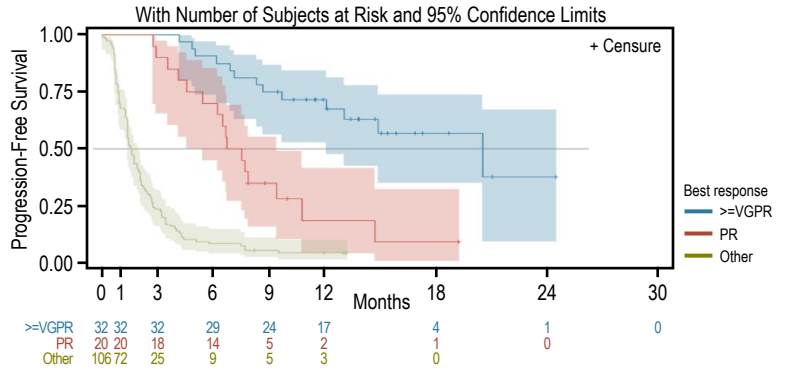
STUDY POPULATION
RRMM Patients

- **Noninterventional, retrospective study of 184 patients** initiating belantamab mafodotin in 46 centres in France during early access programs from April 27, 2020 to June 30, 2021
- **Aim of the study** was to describe the effectiveness and safety of belantamab mafodotin in patients with RRMM in a real-life setting

- In the overall population (N=184), 58% of patients received ≥5 prior LOT, 48% had renal failure, and 79% were penta-exposed
- 33% (27 of 87) had high risk[a] cytogenetics
- 48% had baseline ocular conditions (53% cataract)

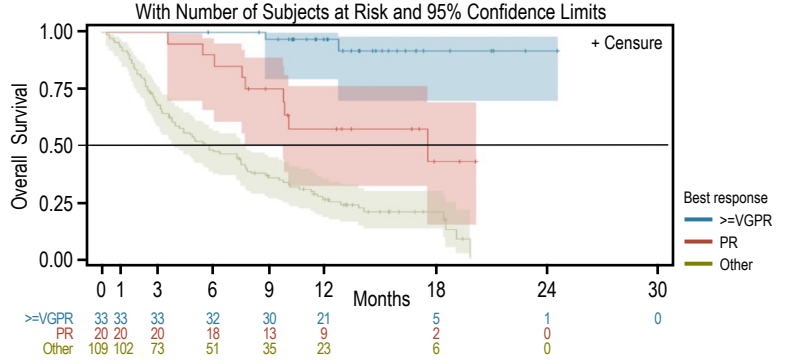
- AEs were reported in 86.4% of patients with ocular AEs being the most common (reported in 56% of patients)
- Permanent discontinuation due to ocular AEs occurred in 12.5% of patients

PFS according to best response to belantamab mafodotin



- The median PFS (mPFS) for the whole population was 2.4 months (95% Confidence Interval 1.9– 3.2)
- According to the best response, mPFS was 20.6 months (95% CI 12.1–not reached) in patients with ≥VGPR, 7.1 months (95% CI 4.6– 9.4) in patients with PR, and 1.6 months (95% CI 1.4–2.0) in the other patients; P<0.01
- No differences were found in subgroups of interest

OS according to best response to belantamab mafodotin



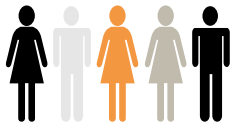
- The median OS (mOS) was 8.8 months (95% CI 6.3–11.6)
- mOS was not reached in patients with ≥VGPR
- mOS was 17.5 months (95% CI 7.7–not reached) in patients with PR and 5.6 months (95% CI 3.9–7.7) in the other patients; including mOS at 14.1 months in MR, 9.5 months in stable disease, and 3.3 months in progressive disease
- No differences were found in subgroup of interest

These figures were first presented in Roussel M. ASH. December 2022. Poster presentation 1856.

With a median follow-up of 7.8 mo, belantamab mafodotin showed similar efficacy to that reported in the DREAMM-2 trial, and no new safety concerns were identified in the overall population

Roussel M, et alASH Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P1856.

Safety and activity of belantamab mafodotin in this Spanish real-world study were consistent with that reported in DREAMM-2



STUDY POPULATION

RRMM Patients

- **Observational, retrospective, multicentre study** (N=156)
- **Patients must have received ≥1 dose of belantamab mafodotin** within compassionate use or EA programs in Spain between Nov 2019–Jun 2021
  - Primary endpoint: ORR
  - Secondary endpoints: OS, DOR, PFS, and select TEAEs[a]

- At study entry, 88% of patients were triple-class refractory
- 65% had received ASCT
- The median number of prior therapy was 5

- The ORR was 46.4% (10% CR; 5% sCR)
- Median PFS and OS were 3.6, and 11 months, respectively

- 10/127 evaluable patients (8%) discontinued belantamab mafodotin due to AEs (2 due to keratopathy, 2 thrombocytopenia)

Treatment-emergent adverse events

	All Grades, n (%)	≥ Grade 3, n (%)
Hematologic		
Thrombocytopenia	24 (15.4)	17 (10.9)
Neutropenia	7 (3.8)	5 (3.1)
Anemia	6 (3.9)	2 (1.3)
Nonhematologic		
Infections	25 (15)	10 (5.6)
Increase in transaminase	6	2
Ocular TEAE*	**N=83 (53.2%)**	
Keratopathy	73 (46.8)	28 (17.9)
Reduced visual acuity	50 (32.1)	7 (4.5)
Blurry vision	30 (19.2)	
Dry eye	27 (17.3)	
Foreign body sensation	16 (10.3)	
Ocular discomfort	15 (9.6)	
Photophobia	10 (6.4)	

TEAE, treatment-emergent adverse event. *Data available from 154 patients.
This table was first presented in De La Rubia J. ASH. December 2022. Poster presentation 1881.

At a median follow-up of 13 months, belantamab mafodotin induced deep and durable responses with a manageable safety profile in the heavily pretreated patients evaluated in this real-world study

Efficacy and safety for belantamab mafodotin in the real-world data from MSKCC were consistent with those reported in the DREAMM-2 trial

STUDY POPULATION

RRMM Patients

- 90 heavily pretreated patients with RRMM treated with at least one dose of commercial belantamab mafodotin at MSKCC between October 1, 2020, and October 31, 2022, were included in the study
- **Aim:** To assess response rates, dose modifications, and frequency of ocular AEs in patients treated with belantamab mafodotin in a real-world setting and in relation to prior treatment with BCMA-targeted therapies

Responses and AEs with belantamab mafodotin in the real-world setting were consistent with those reported in clinical trials

61% of patients had **high-risk cytogenetics**

Patients received **6 prior LoT**[a]

19% of patients received **≥1 BCMA-targeted agent** [bispecific antibody (n=6), **CAR T-cell therapy** (n=12), and **prior belantamab mafodotin** (n=2)]

ORR was 42% (VGPR: 16% and CR: 14%) with a median DoR of 13.1 months

21% of patients had SD and **36% had PD**

Median **PFS was 4 months**

Median **OS was 20.5 months**

Response was similar in **BCMA-exposed and BCMA-naïve patients**

Ocular AEs comparable to previous studies, with 64% having an ocular AE

63% of patients had **any Grade keratopathy**[b] (Grade 3-4 in 16% of patients)

46% of patients had any Grade reduced BCVA (Grade 3-4 in 4% of patients)

26 patients had **dose reductions**[c]

31 patients had **dose delays**[d]

Most patients who had dose modifications due to ocular events continued therapy on a lower dose with maintained response

9 patients discontinued treatment due to ocular AE

Hulcrantz M, et al. ASH Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3225.

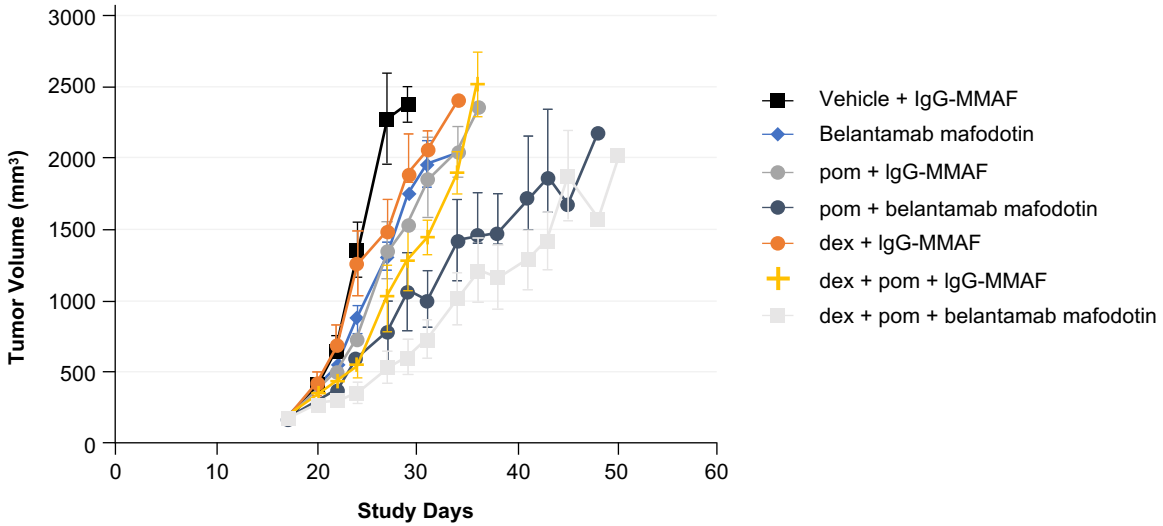
Algonquin Study: Belantamab Mafodotin in Combination with Pomalidomide and Dexamethasone for RRMM

Preclinical studies have demonstrated that belantamab mafodotin may work synergistically in combination therapy with immunomodulatory agents

Preclinical studies of belantamab mafodotin + immunomodulatory agents or bortezomib

- In vitro, combination with a standard-of-care agent (bor, dex, len, or pom) led to synergistic activity in both OPM-2 and MOLP-8 cells
- In vivo, combination with len, pom, or bor enhanced anti-tumor activity and provided additional survival benefit compared to each single agent in immune-compromised mice bearing OPM-2 and MOLP-8 xenografts

Combination of belantamab mafodotin + pom and/or dex in vivo OPM-2 xenograft model

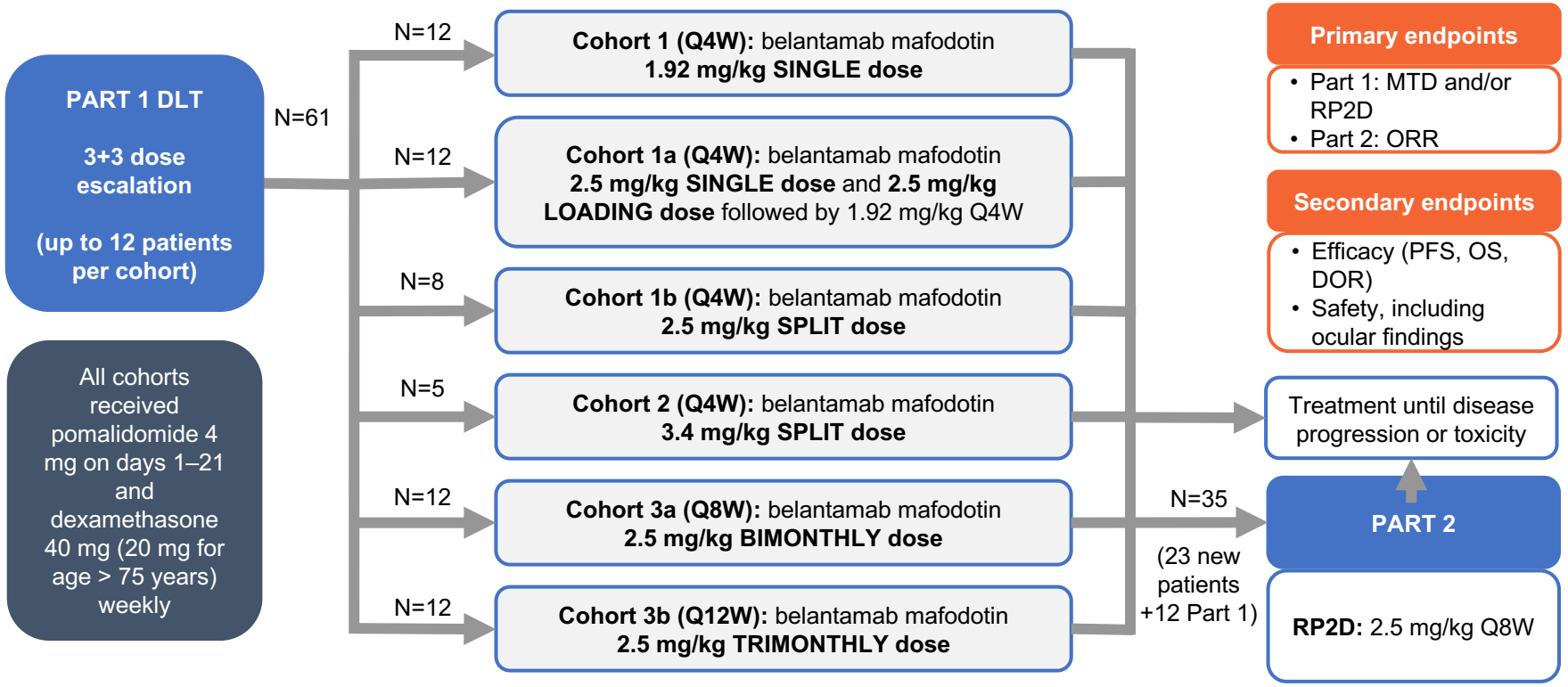


This figure was originally presented in Montes de Oca et al. AACR. 2020.

This synergy observed in *in vivo* xenograft models and *in vitro* cell cultures supports the combination of belantamab mafodotin + immunomodulatory agents

Trudel S, et al. Presented at the 64th ASG Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3248.

The Algonquin study is a two-part phase 1/2 trial evaluating the safety and efficacy of different doses and schedules of belantamab mafodotin + pom/dex in patients with RRMM

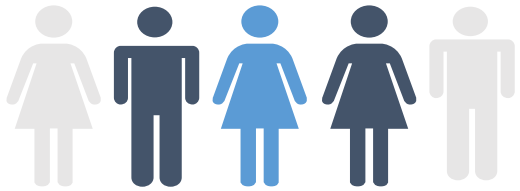


This figure was independently created by GSK from original data first presented in Trudel S et al. ASH. 2022.

Part 1 of the Algonquin study established an RP2D of 2.5mg/kg Q8W

Trudel S, et al. Presented at the 64th ASG Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3248.

The Algonquin study enrolled patients with RRMM, including those with triple-class exposed/refractory (TCE/R*) MM



KEY

ELIGIBILITY CRITERIA

Adult patients ≥18 years

- Confirmed diagnosis of multiple myeloma and relapsed and/or refractory disease
- Undergone stem cell transplant, or have been considered transplant ineligible
- ECOG performance status 0–2
- ≥1 prior line of treatment that must have included len and a proteasome inhibitor
- Refractory to len and exposed or refractory to a proteasome inhibitor

Patients were required to have measurable disease, defined as having at least one of the following:

Serum M-protein concentrations	Urine M-protein concentrations	Serum FLC assay
5 g/L or higher	200 mg per 24 hours or higher	FLC level 100 mg/L or higher and abnormal serum FLC ratio (<0.26 or >1.65)

This analysis consists of updated safety and efficacy data for the subgroup of TCE/R MM patients treated at doses of 1.92 or 2.5 mg/kg belantamab mafodotin + pom/dex

Trudel S, et al. Presented at the 64th ASG Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3248.

61 TCE patients were enrolled in dose cohorts received either 1.92 or 2.5 mg/kg belantamab mafodotin + pom/dex*

Patient Disposition (N=61)	n (%)
Ongoing	33 (54.1%)
Discontinued	28 (45.9%)
Progressive disease	20 (32.7%)
Adverse event (AE)	2 (3.3%)
Death†	4 (6.6%)
Patient withdrawal	2 (3.3%)

Median age was 67 years and median prior LOT was 3 (2-5)

Characteristics (N=61)	
Age, median (range), years	67 (36–85)
Previous LOT, median (range)	3 (2–5)
Stem cell transplant (%)	37 (60.7%)
len exposed/refractory (%)	61 (100%) / 60 (98.4%)
PI exposed/refractory (%)	61 (100%) / 61 (100%)
dara exposed/refractory (%)	61 (100%) / 60 (98.4%)
len and PI exposed/refractory (%)	61 (100%) / 60 (98.4%)
len, PI, and dara exposed/refractory (%)	61 (100%) / 60 (98.4%)
ISS Stage I/II/III/Unknown (%)	23.0% / 39.3% / 23.0% / 14.8%
High-risk cytogenetics [del17p13, t(4;14), t(14;16)] (%)	14/34 (41.2%)

These tables were independently created by GSK from original data first presented in Trudel S et al. ASH. 2022.

Consistent with inclusion criteria, 100% of patients were len refractory and PI exposed, 100% were TCE, and 98% were dara, len, and PI refractory (TCR)

The combination of belantamab mafodotin + pom/dex resulted in deep and durable responses in high unmet need TCE patients

- 55 patients were evaluable for response with median follow-up of 10.2 (0–30.5) months
- Across all dosing cohorts, the ORR(≥PR)/VGPR rates were 85%/56% for TCE patients
- The ORR/VGPR for patients treated at the RP2D (2.5 mg/kg Q8W) (n=33) was 82%/55%

- The **PFS** and **OS** for patients treated at the RP2D was 21.2 months and NYR, respectively
- **Median follow-up** was 10.2 months (0–30.5)

Efficacy Outcomes	Belantamab mafodotin 1.92 mg/kg Q4W N=6	Belantamab mafodotin 2.5 mg/kg Q4W N=6	Belantamab mafodotin 2.5 mg/kg Q8W N=38	Belantamab mafodotin 2.5 mg/kg Q12W N=11
ORR	4/6 (66.7%)	6/6 (100%)	27/33 (82%)	10/10 (100%)
sCR/CR	1/6 (16.7%)	1/6 (16.7%)	4/33 (12.1%)	3/10 (30%)
VGPR	2/6 (33.3%)	3/6 (50%)	14/33 (42.4%)	3/10 (30%)
PR	1/6 (16.7%)	2/6 (33.3%)	9/33 (27.3%)	4/10 (40%)
mPFS (95% CI), months	16.8 (10.2–NYR)	24.4 (11.9–NYR)	21.2 (13.67–NYR)	22.5 (10.2–NYR)
mOS (95% CI), months	21.4 (15.7–NYR)	NYR (24.4–NYR)	NYR (NYR–NYR)	22.5 (NYR–NYR)
Median follow-up, months	16.8 (9.2–21.4)	18.6 (6.6–30.5)	6.2 (0–21.2)	11.3 (0.9–22.5)

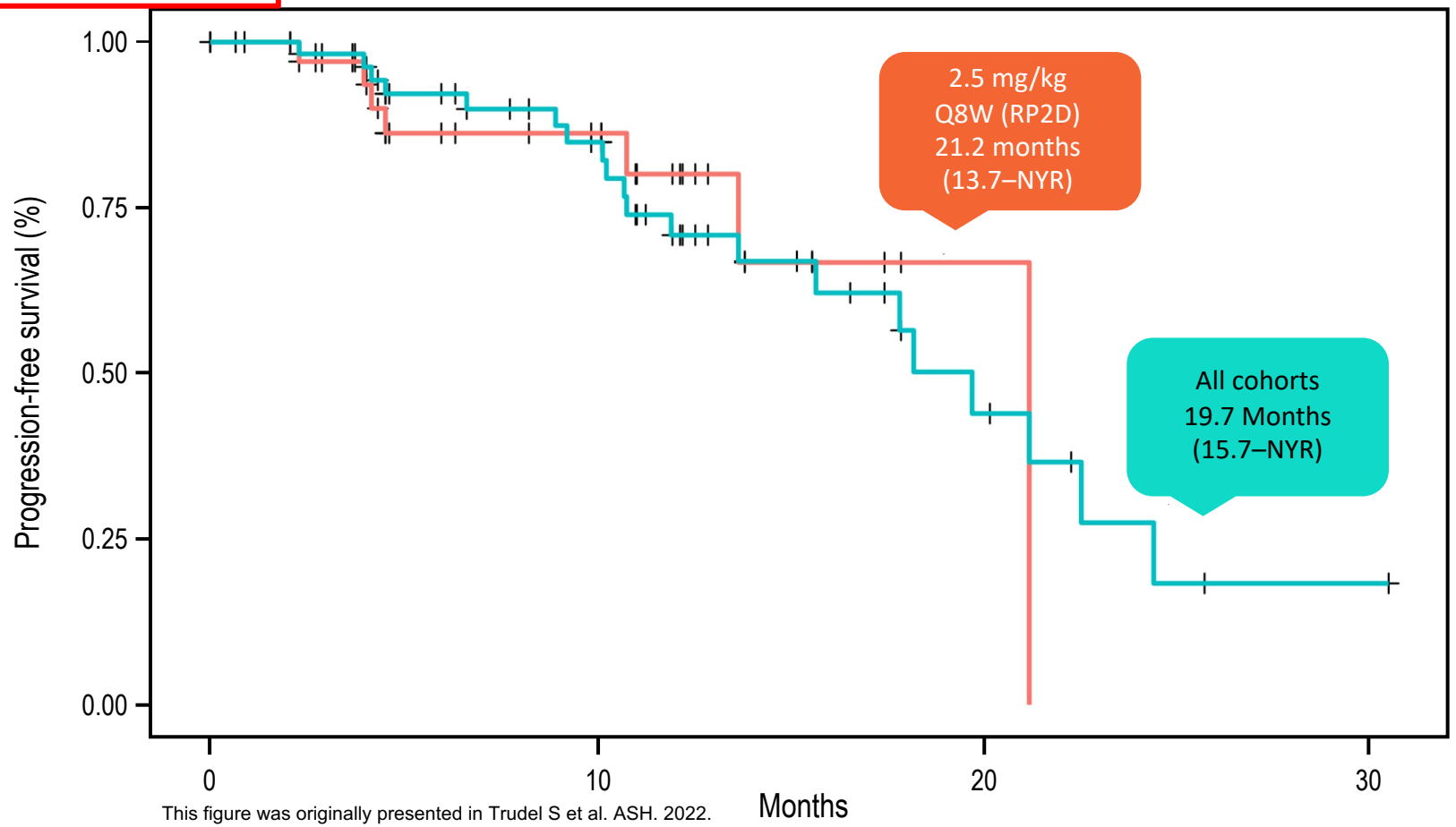
This table was independently created by GSK from original data presented in Trudel S et al. ASH. 2022.

Trudel S, et al. Presented at the 64th ASG Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3248.

PFS for TCE patients compares favorably when compared to historical data from the LocoMMotion study and to anti-CD38 antibody/pom/dex regimens

Cross-trial comparisons are not appropriate

PFS for all cohorts and for 2.5 mg/kg Q8W (RP2D) cohort[1]



This figure was originally presented in Trudel S et al. ASH. 2022.

LocoMMotion is a prospective study of real-life SOC in TCE RRMM[2]

- Patients (N=248) were treated with median 4.0 (range, 1–20) cycles of SOC therapy
- Primary endpoint was ORR
- Secondary clinical assessments included ScR, CR, VGPR, DOR, PFS and OS

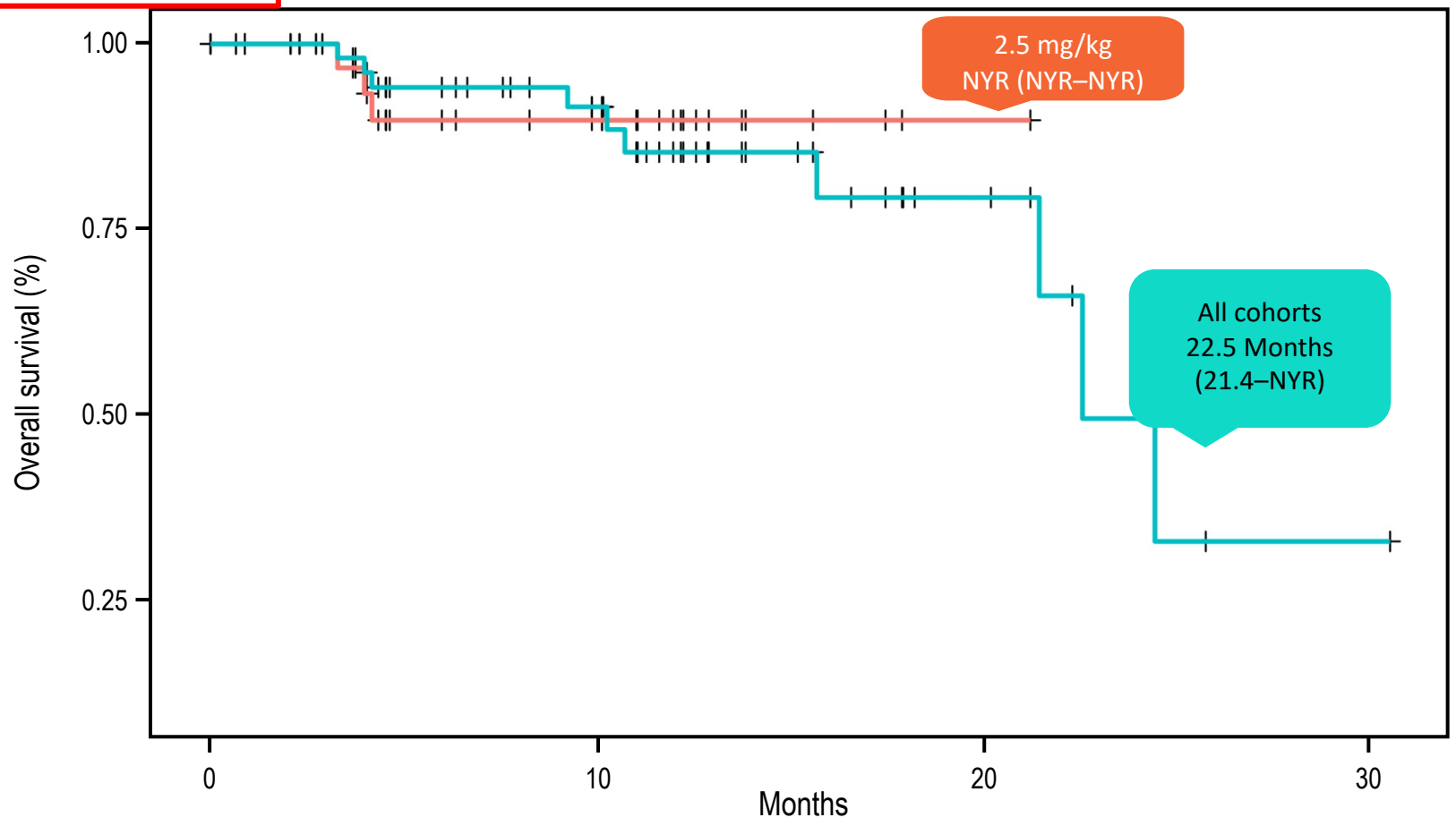
A PFS of 4.6 months was reported in the LocoMMotion study[2*]

Trudel S, et al. Presented at the 64th ASG Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3248.

OS for TCE patients from all cohorts compares favorably to historical data from the LocoMMotion study*

Cross-trial comparisons are not appropriate

OS for all cohorts and for 2.5 mg/kg Q8W (RP2D) cohort[1]



An OS of 12.4 months was reported in the LocoMMotion study[2]

Trudel S, et al. Presented at the 64th ASG Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3248.

Safety profile is consistent with that of the individual agents

- SAEs were observed in 45.9% (28/61) of patients
- 4 fatal events occurred:
  - 2 upper respiratory tract infections (1 COVID-19)
  - 1 MDS
  - 1 not specified

- **Most common TEAEs >25% and dose modifications by cohort**

Cohort	All cohorts N=61		Belantamab mafodotin 2.5 mg/kg Q8W N=38	
TEAE	**All Grades**	**Grade 3/4**	**All Grades**	**Grade 3/4**
Any TEAE, n (%)	60 (98.4%)	55 (90.2%)	37 (97.4%)	34 (89.5%)
Keratopathy	45 (73.8%)	33 (54.1%)	27 (71.1%)	19 (50.0%)
Decreased visual acuity	33 (54.1%)	19 (31.1%)	20 (52.6%)	12 (31.6%)
Fatigue	32 (52.5%)	5 (8.2%)	20 (52.6%)	2 (5.3%)
Thrombocytopenia	25 (41.0%)	17 (27.9%)	14 (36.8%)	10 (26.3%)
Neutropenia	25 (41.0%)	20 (32.8%)	13 (34.2%)	10 (26.3%)
Diarrhea	17 (27.9%)	3 (4.9%)	9 (23.7%)	2 (5.3%)
Peripheral edema	16 (26.2%)	0 (0%)	10 (26.3%)	0 (0%)

This table was independently created by GSK from original data presented in Trudel S et al. ASH. 2022.

Trudel S, et al. Presented at the 64th ASG Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3248.

Safety profile is consistent with that of the individual agents

Incidence of SAEs and AEs leading to dose modifications (belantamab mafodotin)

Cohort	All cohorts N=61	Belantamab mafodotin 2.5 mg/kg Q8W N=38
Any SAE	28 (45.9%)	8 (66.7%)
Fatal SAE	4 (6.6%)	1 (2.6%)
Led to dose hold	32 (52%)	18 (47.4%)
Led to discontinuation	2 (2.9%)	0 (0%)
Median dose holds	4 (0–31)	3 (0–12)

3 patients (4.9%) discontinued due to AEs: one Grade 3 increase in liver function tests and one MDS

Incidence of AEs > Grade 3 of special interest by cohort

AE	Belantamab mafodotin 1.92 mg/kg Q4W N=6	Belantamab mafodotin 2.5 mg/kg Q4W N=6	Belantamab mafodotin 2.5 mg/kg Q8W N=38	Belantamab mafodotin 2.5 mg/kg Q12W N=11
Keratopathy	2 (33.3%)	5 (83.3%)	19 (50.0%)	7 (63.6%)
Decreased visual acuity	1 (16.7%)	3 (50.0%)	12 (31.6%)	3 (27.3%)
Neutropenia	3 (50.0%)	2 (33.3%)	10 (26.3%)	5 (45.5%)
Thrombocytopenia	3 (50%)	1 (16.7%)	10 (26%)	3 (27.3%)

These tables were independently created by GSK from original data presented in Trudel S et al. ASH. 2022.

Trudel S, et al. Presented at the 64th ASG Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3248.

The belantamab mafodotin + pom/dex regimen represents a substantial improvement over SOC treatments for patients with TCE/TCR MM

Summary[1]

- PFS of **19.7 months** (all cohorts) and **21.2 months** (at the RP2D) for TCE patients compares favorably to historical data from the LocoMMotion study where a PFS of 4.6 months[2] was reported
  - → The combination of belantamab mafodotin + pom/dex represents an improvement over widely available SOC treatments for this poor prognosis patient population
  - → This combination of belantamab mafodotin + pom/dex also compares favorably with that of anti-CD38 antibody/pom/dex regimens (ORR: 60% - 69%; mPFS: 11.5 - 12.4 months) in anti-CD38 naïve patients at first or later relapse[3]
- With longer follow-up **no new** AEs have emerged
- The most common AEs are keratopathy, decreased visual acuity, fatigue, thrombocytopenia and neutropenia
  - → The safety profile is **consistent** with that of the individual agents
- **Enrollment continues** at the RP2D and schedule of belantamab mafodotin 2.5 mg/kg Q8W

Trudel S, et al. Presented at the 64th ASG Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3248.

Conclusion

In the DREAMM-2 trial, single-agent belantamab mafodotin (Q2.5 mg/kg 3W) demonstrated rapid, deep, and durable (>12-month DOR, >15-month OS) activity in all-comer patients at third relapse with triple-class exposed/refractory MM

- The median DOR and the median OS were longer than those reported at the 13-month update
- The 3.4 mg/kg dose is not being pursued

AEs were as expected (no new safety signals) and managed with dose modifications

Data suggests that quality of life of patients in DREAMM-2 was maintained or improved

Efficacy of belantamab mafodotin in patients with high-risk cytogenetic abnormalities and in patients with renal impairment was comparable with the overall population

Patients with EMD had poorer outcomes and additional research is needed to understand responses by EMD subtype

Responses and AEs with belantamab mafodotin in the real-world setting were consistent with those reported in clinical trials

No evidence that BCMA expression, as measured by sBCMA level, is completely lost following treatment with belantamab mafodotin

These data suggest that belantamab mafodotin can be followed by other BCMA-targeted therapies

Nooka A, et al. Presented at the 64th American Society of Hematology Annual Meeting & Exposition. December 10-13, 2022. New Orleans, LA. Abstract P3246.

Clinical Trial Program

Alternate Dosing Schedules and Regimens in the Clinical Trial Program

Fourth-line combination studies

DREAMM-4[1]

Combination with pembrolizumab (single arm) in patients with RRMM (6 patients receiving belantamab mafodotin 2.5mg/kg evaluated)

- **ORR: 67%**
- **AEs*: keratopathy† (83%) and anemia (67%)**

DREAMM-5[2]

Monotherapy and combination with GSK3174998, feladilimab, nirogacestat, dostarlimab, and isatuxamib in patients with RRMM (N=464‡)

Study in progress

Second-line combination studies

DREAMM-6[3]

Combination with Rd or Vd in patients with RRMM who received ≥1 prior therapy (18 patients receiving belantamab mafodotin + Vd evaluated)

Arm B

- **ORR: 78%**
- **≥VGPR: 67%**
- **AEs*: keratopathy† (100%) and thrombocytopenia (78%)**

DREAMM-7[4]

Combination with Vd versus DaraVd in patients with RRMM who failed 1 prior therapy (N=478‡)

Study in progress

DREAMM-8[5]

Combination with Pd versus PVd in patients with RRMM who failed 1 prior therapy (N=450‡)

Study in progress

Second-line combination studies (cont'd)

ALGONQUIN[6]

Combination with Pd in patients with RRMM who received ≥1 prior therapy (n=56 patients receiving belantamab mafodotin in different dosing cohorts)

- **All cohorts demonstrated deep and durable responses with combination therapy of belantamab mafodotin and Pd**
- **The 2.5 mg/kg dose showed a longer PFS**

First-line combination

DREAMM-9[7]

Combination with VRd in different dose schedules in patients with NDMM who are transplant ineligible (N=144‡)

- Initial analysis in 36 patients in 5 cohorts with no new safety concerns
- At least half of patients in each cohort achieving a VGPR

Company sponsored

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*Most commonly reported AEs.[1,3,6] †Keratopathy: superficial punctuate keratopathy with or without microcyst-like epithelial changes (MECs). ‡Estimated enrollment.[2,4,5,7]

AE, adverse event; DaraVd, daratumumab/bortezomib/dexamethasone; NDMM, newly diagnosed multiple myeloma; ORR, overall response rate; Pd, pomalidomide/dexamethasone; PVd, pomalidomide/bortezomib/dexamethasone; Rd, lenalidomide/dexamethasone; RRMM, relapsed/refractory multiple myeloma; SOC, standard of care; Vd, bortezomib/dexamethasone; VGPR, very good partial response; VRd, bortezomib/lenalidomide/dexamethasone.

1. Nooka AK et al. Presented at: European Hematology Association Congress; June 11-14, 2020; virtual format. Poster EP955. **2**. Nooka AK et al. Presented at: Internation Myeloma Workshop; September 8-11, 2021. **3**. Popat R et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 5-8, 2020; virtual format, USA. Poster 1419. 4. ClinicalTrials.gov. Updated July 22, 2021. Accessed August 25, 2021. https://www.clinicaltrials.gov/ct2/show/NCT04246047. **5.** ClinicalTrials.gov. Updated July 19, 2021. Accessed August 25, 2021. https://www.clinicaltrials.gov/ct2/show/NCT04484623 **6.** Trudel S et al. Presented at the 63rd American Society of Hematology Annual Meeting 2021. **7.** Usmani SZ, et al. Presented at the 63rd American Society of Hematology Annual Meeting 2021 **8**..GlaxoSmithKline Press Release. June 4, 2020. Accessed August 25, 2021. https://www.gsk.com/en-gb/media/press-releases/gsk-announces-new-data-presentations-from-the-dreamm-programme/

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