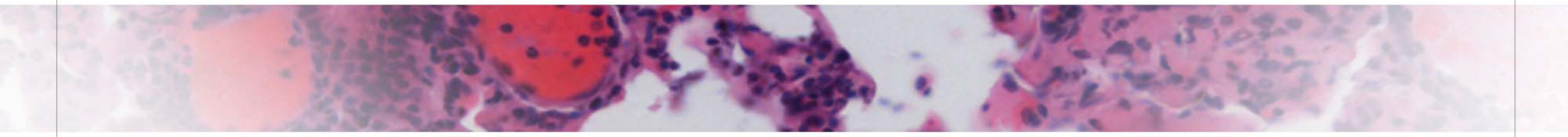


DREAMM-2: Single-Agent Belantamab Mafodotin (Belamaf) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM) – 1-Year Outcomes by Prior Therapies

Sagar Lonial[1], Hans C. Lee[2], Ashraf Badros[3], Suzanne Trudel[4], Ajay K. Nooka[1], Ajai Chari[5], Al-Ola Abdallah[6], Natalie Callander[7], Douglas Sborov[8], Attaya Suvannasankha[9], Katja Weisel[10], Peter M. Voorhees[11], Joanna Opalinska[12], Eric Zhi[12], January Baron[12], Trisha Piontek[12], Ira Gupta[12], Adam D. Cohen[13]

[1]Emory University, Winship Cancer Institute, Atlanta, GA, USA; [2]MD Anderson Cancer Center, Houston, TX, USA; [3]University of Maryland at Baltimore, Baltimore, MD, USA; [4]Princess Margaret Cancer Centre, Toronto, ON, Canada; [5]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [6]University of Kansas Cancer Center, Fairway, KS, USA; [7]University of Wisconsin, Carbone Cancer Center, Madison, WI, USA; [8]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [9]Indiana University Simon Cancer Center and Roudebush VAMC, Indianapolis, IN, USA; [10]University Medical Center of Hamburg-Eppendorf, Hamburg, Germany; [11]Levine Cancer Institute, Atrium Health, Charlotte, NC, USA; [12]GlaxoSmithKline, Philadelphia, PA, USA; [13]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA

Poster No. 1417 | Presented at the 62nd American Society of Hematology Annual Meeting and Exposition | December 5–8, 2020

Background

Aim:
Assess the efficacy and safety of belamaf 2.5 mg/kg in DREAMM-2 at 13 months by number of prior therapies

Belantamab mafodotin (belamaf; GSK2857916; BLENREP) is a first-in-class ADC-targeting BCMA approved in August 2020 by the US FDA and EMA for the treatment of patients with RRMM[1–3]

BCMA, a cell membrane receptor, is expressed on malignant plasma cells and is essential for their proliferation and survival.[4] Belamaf binds to BCMA and eliminates MM cells by a multimodal mechanism of action[4]

RRMM patients who have received and become refractory to multiple prior therapies have a poor prognosis with limited treatment options, presenting a significant clinical challenge[5]

In the pivotal Phase II DREAMM-2 study (NCT03525678), single-agent belamaf demonstrated deep and durable clinical responses in heavily pre-treated RRMM patients and had a manageable safety profile.[1] This post-hoc analysis examined patients treated with the 2.5 mg/kg Q3W dose of single-agent belamaf categorized into two sub-populations: 3–6 and ≥7 prior therapies

Figure 1. Belamaf mode of action*

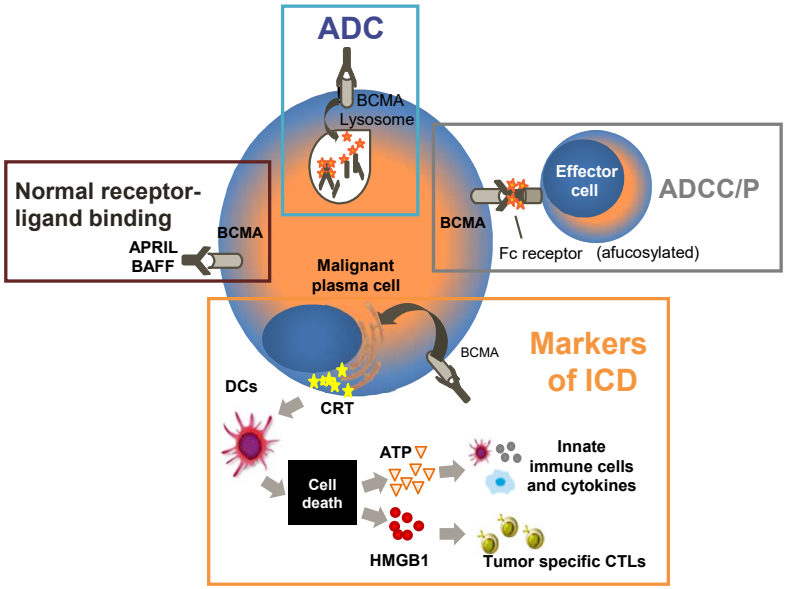


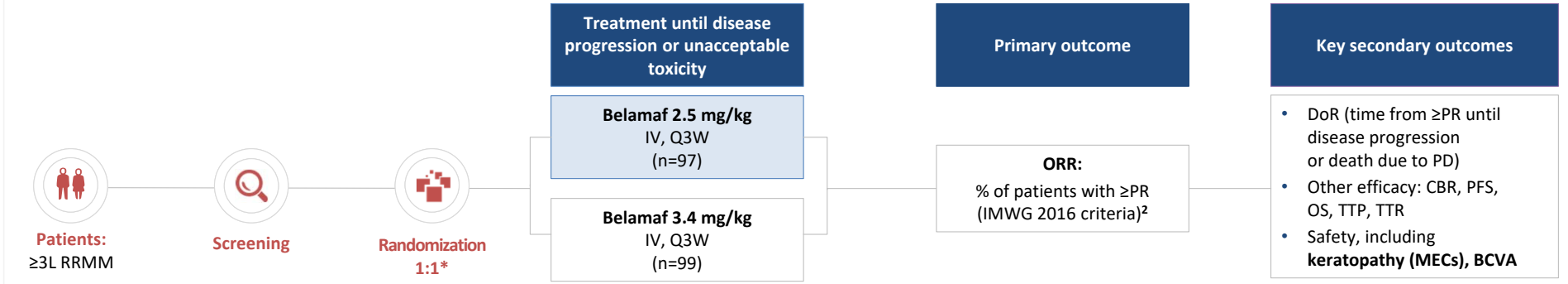
*Figure adapted from Richardson P, et al. Presented at the 61st Annual Meeting of the American Society of Hematology, December 7–10, 2019, Orlando, FL. Poster 1857. ADC, antibody-drug conjugate; ADCC/P, antibody-directed cell cytotoxicity/phagocytosis; APRIL, a proliferation-inducing ligand; ATP, adenosine triphosphate; BAFF, B-cell activating factor; BCMA, B-cell maturation antigen; CRT, calreticulin; CTLs, cytotoxic T-lymphocytes; DCs, dendritic cells; EMA, European Medicines Agency; Fc, fragment crystallizable; FDA, Food and Drug Administration; HMGB1, high mobility group box 1; ICD, immune cell death; MM, multiple myeloma; RRMM, relapsed or refractory multiple myeloma; Q3W, every 3 weeks.

1. Lonial S, et al. *Lancet Oncol.* 2020;21:207–21**; 2**. BLENREP Prescribing Information: GSK plc. 2020; **3**. BLENREP SmPC. GSK plc. 2020; **4**. Tai YT, et al. *Immunotherapy.* 2015;7:1187–99; **5**. Robak P, et al. *Cancer Treat Rev.* 2018 Nov;70:199.

Methods

DREAMM-2 was an open label, randomized study to investigate the efficacy and safety of belamaf in patients with RRMM who had received ≥3 prior lines of treatment

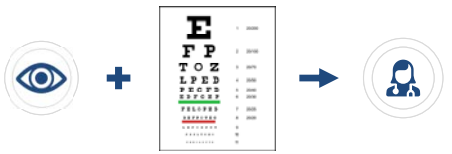
Figure 2. DREAMM-2 study design[1]



Ocular toxicity monitoring in the DREAMM-2 Study†

- Patients had regular ocular examinations (at baseline, prior to each treatment cycle, or every 3 weeks) by an eye care professional
- To fully characterize ocular events, GSK used a protocol-specified KVA scale, which focuses on corneal exam findings (keratopathy [microcyst-like epithelial changes, MECs], changes observed on slit-lamp exam with or without symptoms) as well as changes in visual acuity (measured by the Snellen Test)
- Eye-related adverse events such as blurred vision and dry eye were assessed by CTCAE criteria (v4.03)[3]

Ocular examinations in the DREAMM-2 study



Slit-lamp exam | BCVA (Snellen test) | Graded on KVA scale

This post-hoc analysis, at median (range) follow-up of 12.4 (0.1–17.9) months, examined patients treated with the 2.5 mg/kg Q3W recommended clinical dose of single-agent belamaf in two sub-populations: patients treated with 3–6 and ≥7 prior therapies

*Patients stratified based on number of previous lines of therapy (≤4 vs >4) and presence or absence of high-risk cytogenetic features; †Please check your local belamaf prescribing information for guidance on ocular toxicity monitoring. BCVA, best-corrected visual acuity; CBR, clinical benefit rate; CTCAE, Common Terminology Criteria for Adverse Events; DoR, duration of response; IMWG, International Myeloma Working Group; IV, intravenous; KVA, Keratopathy and Visual Acuity; MECs, microcyst-like epithelial changes; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; Q3W, every 3 weeks; RRMM, relapsed or refractory multiple myeloma; TTBR, time to best response; TTP, time to progression; TTR, time to response.

1. Lonial S, et al. ASCO 2020. Poster 436; **2**. Kumar S, et al. *Lancet Oncol.* 2016;17:e328–e46; **3**. National Cancer Institute. 2010. Available from: https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf [Accessed Oct 13, 2020].

Results: Patient Population Summary

Baseline demographics, disease characteristics, and prior therapies by drug class were well matched between patient groups: belamaf 2.5 mg/kg

Table 1. Patient baseline characteristics

	3–6* prior lines of anti-cancer therapy (n=47)	≥7† prior lines of anti-cancer therapy (n=50)
Age, median (range)	62 (39–85)	67 (45–85)
BMI, median (range)	27.5 (17.2–48.4)	26.3 (19.4–50)
Ethnicity, n (%)		
White/Caucasian/European	34 (72%)	38 (76%)
Black or African American	6 (13%)	10 (20%)
ISS grade at screening I	11 (23%)	11 (22%)
II	19 (40%)	14 (28%)
III	17 (36%)	25 (50%)
High-risk cytogenetics n (%)	12 (26%)	14 (28%)

Table 2. Patients refractory to prior therapies by drug class‡

	3–6 prior lines of anti-cancer therapy (n=47)	≥7 prior lines of anti-cancer therapy (n=50)
Immunomodulator	47 (100%)	50 (100%)
Lenalidomide	47 (100%)	50 (100%)
Pomalidomide	41 (87%)	48 (96%)
Thalidomide	8 (17%)	21 (42%)
Proteasome inhibitor	47 (100%)	50 (100%)
Bortezomib	45 (96%)	50 (100%)
Carfilzomib	33 (70%)	41 (82%)
Ixazomib	9 (19%)	13 (26%)
Monoclonal antibody	47 (100%)	50 (100%)
Daratumumab	47 (100%)	50 (100%)
Elotuzumab	4 (9%)	11 (22%)
Isatuximab	0	3 (6%)
Chemotherapy	42 (89%)	50 (100%)

*3-6 and †≥7 prior lines groups had received a mean of 4.9 and 8.5 prior therapies, respectively; ‡3 most commonly used treatments per category. High-risk cytogenetics defined as t(4;14), f(14;16), and 17p13del.
BMI, body mass index; ISS, International Staging System.

Results: Efficacy I

Efficacy of belamaf 2.5 mg/kg was comparable between groups receiving 3–6 or ≥7 prior therapies

Table 3. Efficacy endpoints, by number of prior lines of anti-cancer therapy: belamaf 2.5 mg/kg

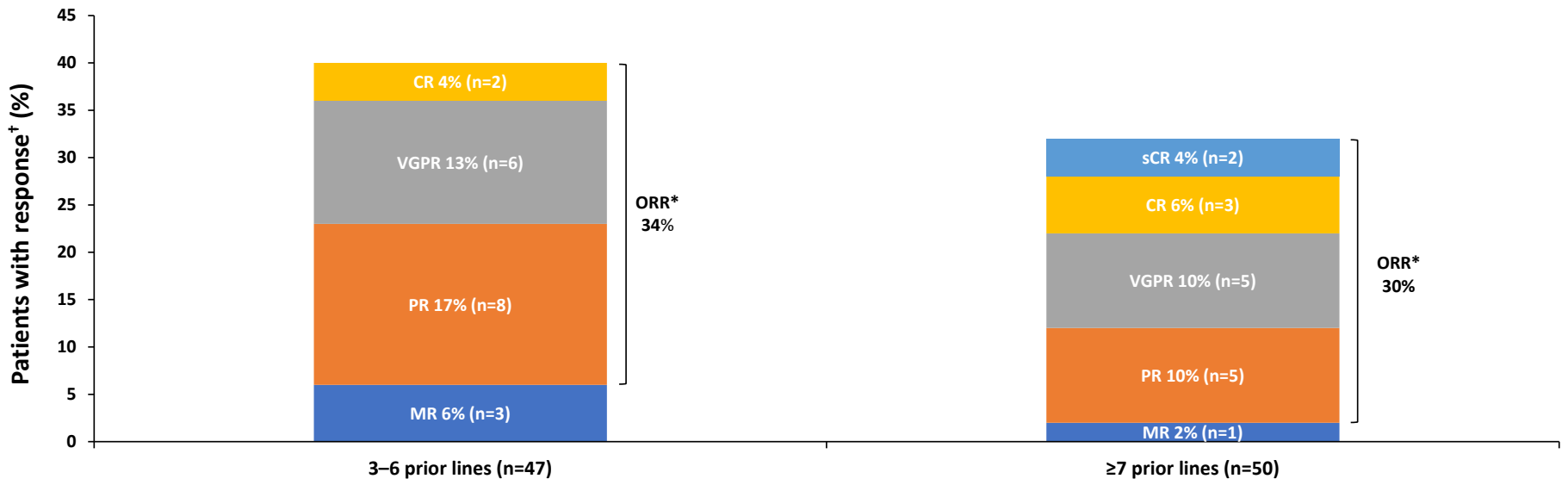
	3–6 prior lines of anti-cancer therapy (n=47)	≥7 prior lines of anti-cancer therapy (n=50)	All Patients (N=97)
ORR, % (97.5% CI)	34 (19.3–51.4)	30 (16.5–46.6)	31 (21.7–43.6)
OS, months (95% CI)*	13.7 (9.1–NR)	13.4 (8.7–NR)	13.7 (9.9–NR)
Median DoR, months (95% CI estimates)	11.0 (4.2–NR)	13.1 (4.0–NR)	11.0 (4.2–NR)
Probability of DoR, ≥6 months, % (95% CI estimates)	63 (31–83)	73 (44–89)	68 (48–82)
Median PFS, months (95% CI estimates)	2.9 (1.5–5.7)	2.2 (1.2–3.6)	2.8 (1.6–3.6)
Probability of PFS at 6 months, % (95% CI estimates)	35 (20–50)	30 (17–43)	32 (22–42)

*38/97 patients in the 2.5 mg/kg combined cohort received ≥1 anti-cancer treatment post-belamaf, recorded as; small molecule targeted therapy, n=30; hormonal therapy, n=29; chemotherapy, n=18; biologic therapy, n=12; immunotherapy, n=9; radioactive therapy, n=2, unknown, n=2. Median (range) time from belamaf discontinuation to next treatment was 43 (11–145) days, based on n=37.
CI, confidence interval; DoR, duration of response; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival

Results: Efficacy II

Overall response rate of belamaf 2.5 mg/kg was comparable between the two sub-populations

Figure 3. Overall response rate for belamaf 2.5 mg/kg



*ORR included PR or better; labels indicate percentages rounded to 0 decimal places; †independent reviewer-assessed best confirmed response per International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma 2016.
CR, confirmed response; MR, minimal response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Results: Safety I

Rates of AEs and SAEs were similar irrespective of the number of prior therapies

Table 4. Overview of AEs and SAEs, by number of prior lines of anti-cancer therapy: belamaf 2.5 mg/kg

	3–6 prior lines of anti-cancer therapy (n=46)	≥7 prior lines of anti-cancer therapy (n=49)	Total (N=95)*
Any AE, n (%)	44 (96)	49 (100)	93 (98)
AE leading to dose reduction	17 (37)	16 (33)	33 (35)
AE leading to dose interruption/delay	27 (59)	24 (49)	51 (54)
AE leading to permanent discontinuation	4 (9)	5 (10)	9 (9)
Drug-related AE	40 (87)	44 (90)	84 (88)
Drug-related AE leading to permanent discontinuation	3 (7)	4 (8)	7 (7)
Any SAE, n (%)	19 (41)	21 (43)	40 (42)
Fatal SAE	2 (4)	1 (2)	3 (3)
Drug-related SAE	5 (11)	6 (12)	11 (12)
Fatal drug-related SAE†	0 (0)	1 (2)	1 (1)

AEs were mainly managed with dose delays/reductions with few discontinuations, regardless of prior therapies

*Two patients out of 97 did not receive a dose. †Fatal event of Sepsis.
AE, adverse event; SAE, serious adverse event.

Results: Safety II

Rates of AEs and SAEs were mostly similar irrespective of the number of prior therapies

Table 5. Common* AEs by CTCAE grade, by number of prior lines of anti-cancer therapy: belamaf 2.5 mg/kg

	3–6 prior lines of anti-cancer therapy (n=46)		≥7 prior lines of anti-cancer therapy (n=49)		Total (N=95)†	
n (%)	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Any AE	44 (96)	36 (78)	49 (100)	43 (88)	93 (98)	79 (83)
Ocular AE						
Keratopathy (MECs)	32 (70)	15 (33)	35 (71)	13 (27)	67 (71)	28 (29)
Blurred vision	12 (26)	3 (7)	9 (18)	1 (2)	21 (22)	4 (4)
Hematologic AE						
Thrombocytopenia	11 (24)	8 (17)	12 (24)	10 (20)	23 (24)	18 (19)
Anemia‡	8 (17)	5 (11)	18 (37)	15 (31)	26 (27)	20 (21)
Lymphocyte count decreased	6 (13)	5 (11)	7 (14)	7 (14)	13 (14)	12 (13)
AST increased	11 (24)	0 (0)	9 (18)	2 (4)	20 (21)	2 (2)
Non-hematologic AE						
Nausea	14 (30)	0 (0)	10 (20)	0 (0)	24 (25)	0 (0)
Pyrexia	11 (24)	1 (2)	11 (22)	3 (6)	22 (23)	4 (4)

*Grade 3/4 (Common Terminology Criteria for Adverse Events [CTCAE] grading) and occurring in >10% of patients in both groups of patients; †Two patients out of 97 did not receive a dose; ‡evidence of increased incidence of anemia in ≥7 prior lines group.
AE, adverse event; AST, aspartate aminotransferase; MECs, microcyst-like epithelial changes; SAE, serious adverse event.

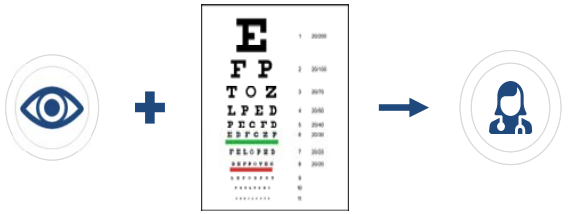
Results: Corneal events

Rates of corneal events graded by investigator per the protocol-defined KVA scale were very similar between the two sub-populations

Table 6. Patients with corneal exam findings by KVA scale

	3–6 prior lines of anti-cancer therapy (n=46)	≥7 prior lines of anti-cancer therapy (n=49)
Patients with corneal exam findings n (%)	30 (65%)	30 (61%)
Time to first occurrence Median (range) days	38 (20–143)	37 (19–84)
Outcome of last event		
Resolved	16 (53%)	13 (43%)
Not resolved, not discontinued	5 (17%)	4 (13%)
Not resolved, follow-up ongoing	3 (10%)	2 (7%)
Not resolved, follow-up ended*	6 (20%)	11 (37%)

Ocular examinations in the DREAMM-2 study



To fully characterize ocular events, GSK used a protocol-specified KVA scale, which focuses on corneal exam findings (keratopathy MECs [+/-symptoms], observed on slit-lamp exam) as well as changes in visual acuity (measured by the Snellen Test)

No difference in the number of corneal events, time to first occurrence, or resolution of last event was observed between sub-populations

*Complete data are not available as some patient's follow-up ended prior to resolution.
BCVA, best-corrected visual acuity; KVA, Keratopathy and Visual Acuity.

Conclusions

ORR and AEs for belamaf 2.5 mg/kg Q3W were comparable between patients in the 3–6 and ≥7 prior therapy sub-populations

Single-agent belamaf 2.5 mg/kg Q3W showed deep and durable responses with a manageable safety profile with comparable ORR, DoR, and PFS between prior therapy sub-populations

There was no apparent difference in occurrences of AEs (including keratopathy [MECs]), SAEs, or events leading to discontinuation, dose delay, or dose reduction between groups of patients with 3–6 or ≥7 prior lines of therapy

Single-agent belamaf at 2.5 mg/kg represents a new treatment option for patients with RRMM, particularly those who have become refractory to multiple prior therapies and have a poor prognosis

Further analyses of the pivotal DREAMM-2 study of single-agent belamaf are presented at this meeting (posters 1420, 1419, 2278, 3221, 3224, 3248)

AE, adverse event; DoR, duration of response; MECs, microcyst-like epithelial changes; ORR, overall response rate; PFS, progression-free survival; Q3W, every 3 weeks; RRMM, relapsed or refractory multiple myeloma; SAE, serious adverse event.

Disclosures and Acknowledgements

SL has received grant funding and personal fees from Celgene and Takeda, and personal fees from Amgen, Bristol-Myers Squibb, GSK, Janssen, Merck, and Novartis. **HCL** has received grant funding and personal fees from Amgen, Celgene, Janssen, and Takeda; personal fees from GSK and Sanofi; and grant funding from Daiichi Sankyo. **AB** received consulting fees from Amgen. **ST** received consulting fees from Amgen, Celgene, and GSK; honoraria from Amgen Canada, Celgene, Janssen, Karyopharm, Sanofi, and Takeda; and research funding from Amgen, Celgene, Genentech, GSK, and Janssen. **AKN** received consulting fees from Amgen, Bristol-Myers Squibb, Celgene, GSK, Janssen Oncology, Karyopharm Therapeutics, Oncopeptides, Spectrum Pharmaceuticals, and Takeda; personal fees from GSK; and research funding from Amgen, Janssen Oncology, and Takeda. **AC** received consulting fees from Amgen, Antengene, Bristol-MyersSquibb, Celgene, Genzyme, GSK, Janssen Oncology, Karyopharm Therapeutics, Novartis, Oncopeptides, Seattle Genetics, Secura Bio, and Takeda; and research funding from Amgen, Celgene, Janssen, Novartis, Pharmacyclics, Seattle Genetics, and Takeda. **A-OA** declares no competing interests. NC received research funding from Cellectar. DS received consulting fees, honoraria, and personal fees from Janssen. **AS** received consulting fees from GSK, Janssen, and Karyopharm Therapeutics; research funding from Bristol-Myers Squibb, Celgene, GSK, and Janssen; and personal fees from GSK and Janssen. **KW** received consulting fees/honoraria from Amgen, Adaptive, BMS, Celgene, GSK, Janssen, Karyopharm, Sanofi, and Takeda; and research funding from Amgen, Celgene, Janssen, and Sanofi. **PV** has received personal fees from Adaptive Biotechnologies, BMS/Celgene, Janssen, Novartis, Oncopeptides, and TeneoBio. **JO**, **EZ**, **JB**, and **TP** are employees of and hold stocks and shares in GSK. **IG** is an employee of and holds stocks/shares in GSK and hold stocks/shares in Novartis. **AC** has received grant funding from BMS, GSK, and Novartis; personal fees from Janssen, Kite Pharma, Oncopeptides, Seattle Genetics, and Takeda; and personal fees and other association with Celgene and GSK.

This study was funded by GSK (205678). Drug linker technology licensed from Seagen Inc.; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa.

Editorial assistance was provided by Mark Powell, Fishawack Indicia Ltd, part of Fishawack Health and funded by GlaxoSmithKline.

A **plain language summary** of this Poster is available via this QR code or at http://tago.ca/ash15

Presenting author contact: sloni01@emory.edu