FDA is committed to ensuring digital accessibility for people with disabilities. We are continually improving the user experience for everyone and applying the relevant accessibility standards. At the time of initial posting on **July 17, 2025**, the attached **Event Materials** may not be fully accessible to users using assistive technology. A fully accessible version of the **Event Materials** is in preparation and will be posted as soon as it is ready. We regret any inconvenience that this may cause our readers.

Please let us know if you encounter accessibility barriers by contacting **Division of Advisory Committee and Consultant Management (DACCM)** at:

- **ODAC@fda.hhs.gov**

Belantamab Mafodotin
BLA 761440

Oncologic Drugs Advisory Committee Meeting

FDA Introductory Comments

July 17, 2025

Deepti Telaraja, MD
Division of Hematologic Malignancies II
Office of Oncologic Diseases

Outline

- Background
  - History
  - Proposed indications
  - DREAMM-7 and DREAMM-8 Trials
  - Current RRMM treatment landscape
- Key Issues
  - High rates of ocular toxicity
  - Uncertainty regarding the proposed dosages
- Dose Optimization Considerations
- Benefit-Risk Considerations

Abbreviations: RRMM, relapsed or refractory multiple myeloma

Belantamab Mafodotin

- BCMA-directed antibody-drug conjugate
- Previous approval was as monotherapy for the treatment of RRMM, after 4 or more prior therapies, including PI, IMID, anti-CD38 mAb (August 2020)
- Voluntarily withdrawn from U.S. market due to a failed confirmatory trial (February 2023)

Abbreviations: BCMA, B-cell maturation antigen; RRMM, relapsed or refractory multiple myeloma; PI, proteasome inhibitor; IMID, immunomodulatory agent

Toxicity and Dosing Concerns

- ODAC held to discuss impact of ocular toxicity on benefit-risk (July 2020)
- Approved with a Risk Evaluation and Mitigation Strategy (REMS)
- Postmarketing requirement (PMR) was issued to evaluate alternative dosing regimens and lower doses

Abbreviations: ODAC, Oncologic Drug Advisory Committee

Indications and Dosing Regimens

DREAMM-7

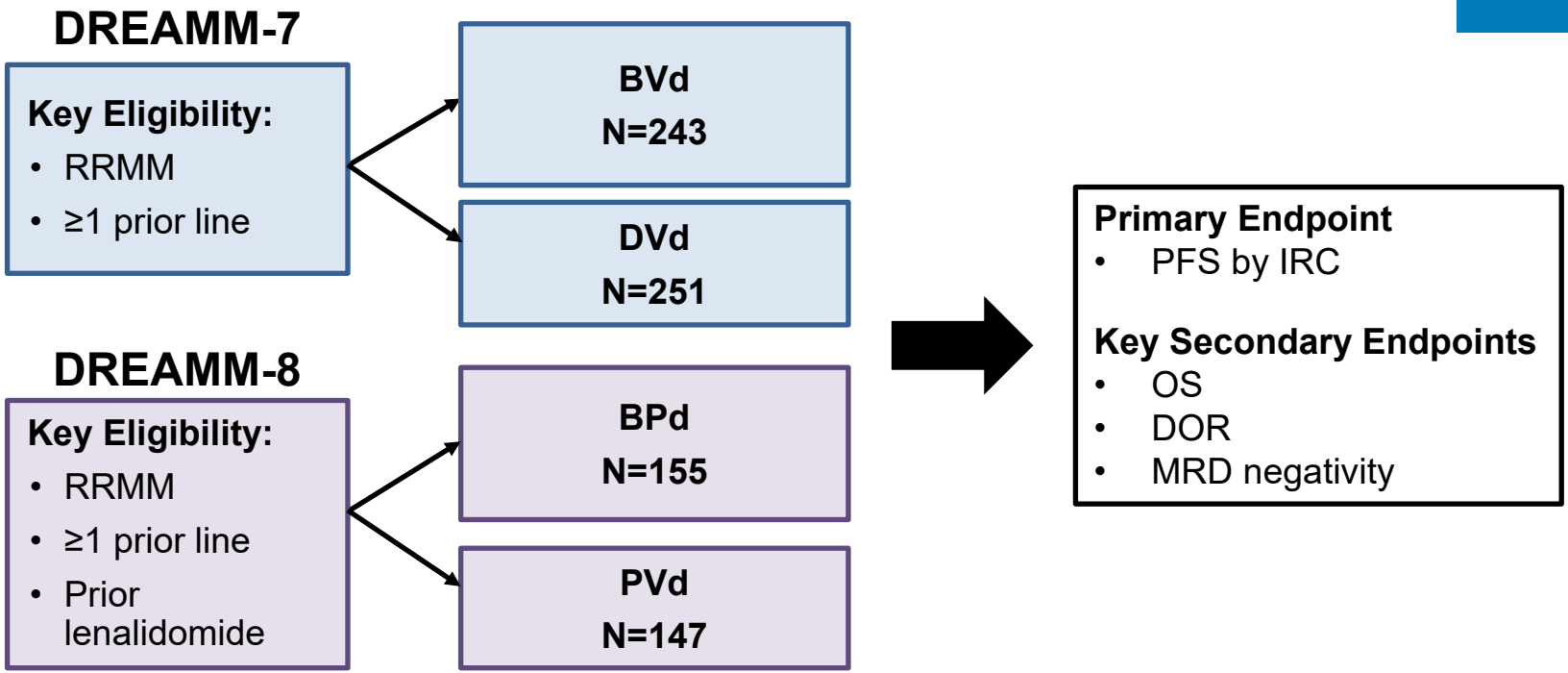
- Belantamab mafodotin in combination with bortezomib and dexamethasone (BVd)
- RRMM; at least one prior line of therapy
- Dosage: 2.5 mg/kg Q3W

DREAMM-8

- Belantamab mafodotin in combination with pomalidomide and dexamethasone (BPd)
- RRMM; at least one prior line of therapy including lenalidomide
- Dosage: 2.5 mg/kg on Cycle 1 followed by 1.9 mg/kg Q4W starting on Cycle 2

Abbreviations: RRMM, relapsed or refractory multiple myeloma; Q‘x’W, every ‘x’ weeks

DREAMM-7 and DREAMM-8 Trials



Abbreviations: RRMM, relapsed/refractory multiple myeloma; BVd, belantamab mafodotin, bortezomib, dexamethasone, DVd, daratumumab, bortezomib, dexamethasone; BPd, belantamab mafodotin, pomalidomide, dexamethasone; PVd, pomalidomide, bortezomib, dexamethasone; PFS, progression-free survival; OS, overall survival; DOR, duration of response; MRD, minimal residual disease

DREAMM-7 and DREAMM-8 Results

DREAMM-7

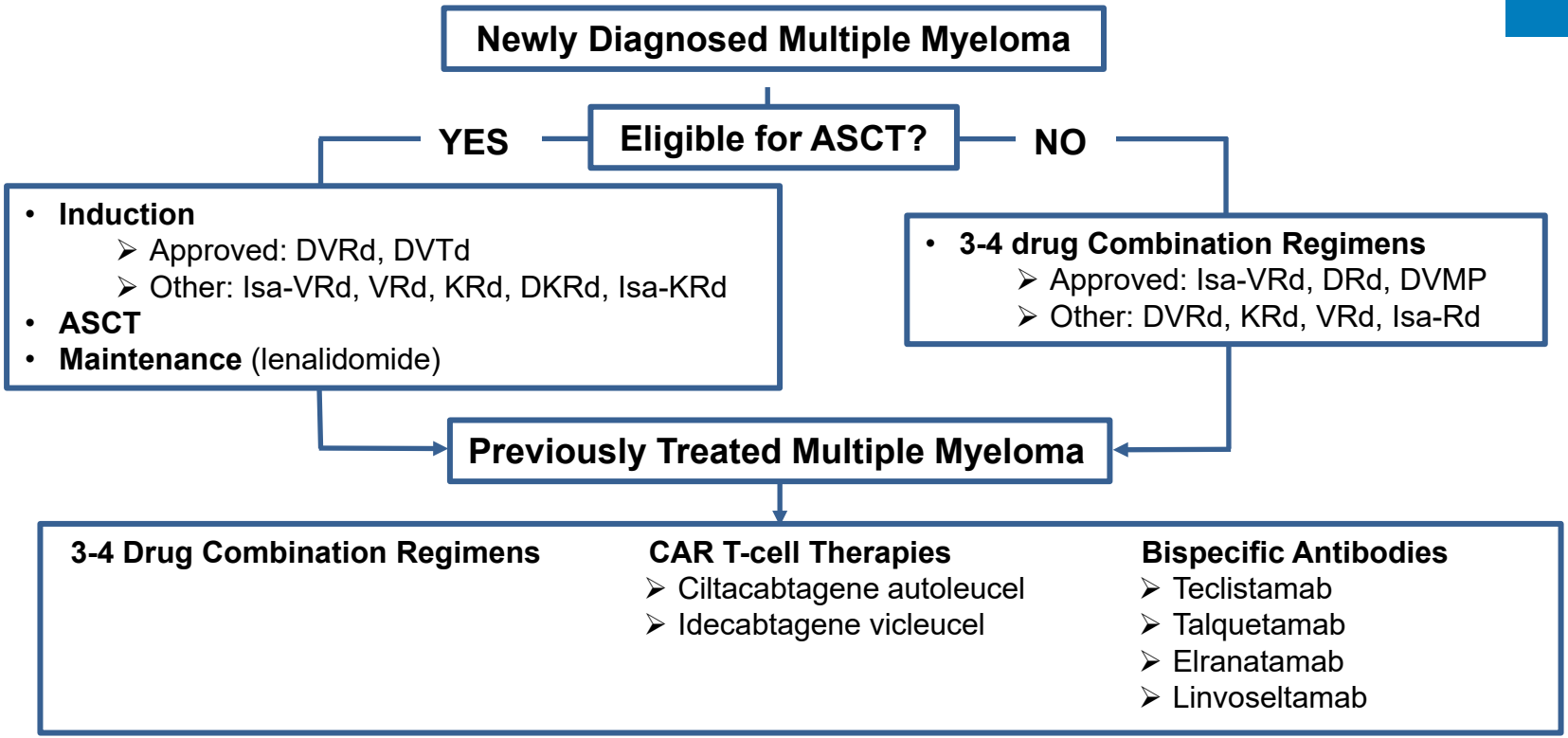
- Met PFS primary endpoint
  - HR=0.41 (95% CI: 0.31, 0.53); p-value <0.0001
- OS statistically significant
  - HR=0.58 (95% CI: 0.43, 0.79); p-value 0.0005

DREAMM-8

- Met PFS primary endpoint
  - HR=0.52 (95% CI: 0.37, 0.73); p-value =0.0001
- OS did not reach statistical significance
  - OS IA1: HR 0.77 (95% CI: 0.53, 1.14)

Abbreviations: PFS, progression-free survival; HR, hazard ratio; CI, confidence interval; OS, overall survival; IA, interim analysis

Multiple Myeloma Treatment



Abbreviations: ASCT, autologous stem cell transplant; D, daratumumab; V, bortezomib; R, lenalidomide; d, dexamethasone; Isa, isatuximab; K, carfilzomib; M, melphalan

Uncertain Relevance to Current Patients

- Clinical meaningfulness of DREAMM-7 and DREAMM-8 trial results to current U.S. patients may be limited
  - Limited enrollment within the U.S. (<5% in each trial)
  - Limited relevance of comparator arms to current practice
    - Current U.S. patients receive 4 drug regimens (e.g., DVRd) upfront
    - DREAMM-7 comparator (DVd) may not be an appropriate regimen for the 2nd line and beyond setting
    - DREAMM-8 comparator (PVd) is not approved in the U.S. and has limited usage

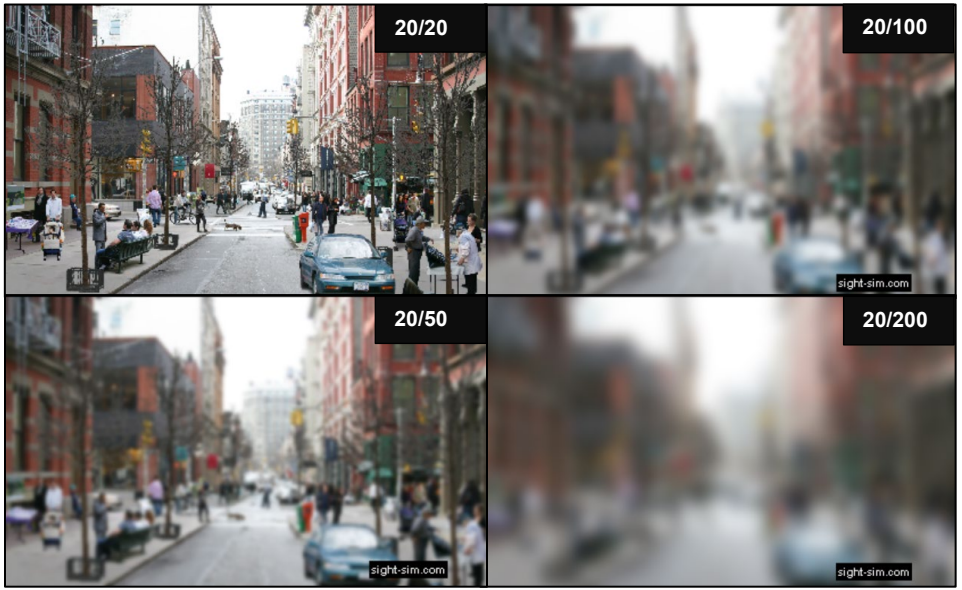
Abbreviations: D, daratumumab; V, bortezomib; R, lenalidomide; d, dexamethasone; P, pomalidomide

Key Issues

- High rates of ocular toxicity
- Uncertainty regarding the proposed dosages

Ocular Toxicity

- Key manifestations include corneal changes and visual acuity changes
  - Corneal changes range from mild superficial changes to severe epithelial defects with ulceration
  - Visual acuity changes are based on best corrected visual acuity
  - Graded using the Keratopathy and Visual Acuity (KVA) scale
    - Dose modifications were recommended for Grade ≥2 KVA events



Source: Sight-Sim™ Software Tool

High Rates of Grade ≥3 KVA Events

AE Category, %	DREAMM-7		DREAMM-8	
	BVd (N=242)	DVd (N=246)	BPd (N=150)	PVd (N=145)
Any Grade KVA events	92	50	93	39
Grade 1	5	24	6	19
Grade 2	9	15	1	13
Grade 3	56	7	69	6
Grade 4	21	4	9	<1

Source: FDA Analysis

Grade 3-4 KVA events occurred in >75% of patients

Abbreviations: KVA, keratopathy and visual acuity; B: belantamab mafodotin; V: bortezomib; d: dexamethasone; D, daratumumab; P, pomalidomide

Key Ocular Toxicity Considerations

- A substantial percentage of patients experienced clinically significant visual acuity changes
  - Over 60% had unilateral worsening of BCVA to 20/50 or worse
  - Over 25% had unilateral worsening of BCVA to 20/100 or worse
  - Over 10% had unilateral worsening of BCVA to 20/200 or worse
- High rates of recurrent KVA events
- Over 70% of patients had ongoing KVA events at the data cut-off

Abbreviations: BCVA, best corrected visual acuity; KVA, Keratopathy and Visual Acuity

Limited Data Supporting Dosage Selection

- Dosage selection for DREAMM-7 (BVd) and DREAMM-8 (BPd) based on limited data:
  - DREAMM-6 (BVd): Evaluated doses ranging from 1.9 mg/kg to 3.4 mg/kg at Q3W and Q6W intervals
  - ALGONQUIN (BPd): Evaluated doses ranging from 1.92 mg/kg to 2.5 mg/kg at Q4W, Q8W, and Q12W intervals
  - **Lower doses and longer intervals** were associated with similar response rates and lower rates of dose modifications

- Dosage selected for DREAMM-7: 2.5 mg/kg Q3W
- Dosage selected for DREAMM-8: 2.5 mg/kg once; 1.9 mg/kg Q4W thereafter

Abbreviations: B: belantamab mafodotin; V: bortezomib; d: dexamethasone; D: daratumumab; P: pomalidomide; Q‘x’W, every ‘x’ weeks

Ongoing Development

Lower Doses and Longer Dosing Intervals

- DREAMM-10: Ongoing trial of belantamab mafodotin in combination with lenalidomide and dexamethasone (BRd)
  - Belantamab mafodotin dose of 1.9 mg/kg Q8W for 24 weeks, then Q12W thereafter
- Supported by DREAMM-14 (PMR study) suggesting improved safety and tolerability, and comparable efficacy, with lower doses/longer dosing intervals

Abbreviations: Q‘x’W, every ‘x’ weeks PMR, postmarketing requirement

High Rates of Dose Modifications

	DREAMM-7		DREAMM-8	
	BVd (N=242)	DVd (n= 246)	BPd (N=150)	PVd (n=145)
Dose Modification, %				
Dose interruption	94	75	91	75
Dose reduction	75	59	61	61
Discontinuation	31	19	15	12
Dose Modification Due to KVA Event, %				
Dose interruption	74	-	75	-
Dose reduction	30	-	57	-
Discontinuation	6	-	7	-

Source: FDA Analysis

Abbreviations: B: belantamab mafodotin; V: bortezomib; d: dexamethasone; D: daratumumab; KVA, keratopathy and visual acuity; P: pomalidomide

Evidentiary Criteria for Approval

- **Safe and Effective**
  - FDA must determine that the drug is safe and effective for use under the conditions prescribed, recommended, or suggested in the proposed labeling

- **Benefits must outweigh the risks**
  - Demonstration of effectiveness requires substantial evidence that the drug will have the effect it purports or is represented to have
  - Demonstration of safety requires showing that benefits of the drug outweigh its risks

Sources: Guidance for Industry: Benefit-Risk Assessment for New Drug and Biological Products; Guidance for Industry: Demonstrating Substantial Evidence of Effectiveness for Human Drugs and Biological Products

Risk Evaluation and Mitigation Strategy

- REMS: a drug safety program that FDA can require for certain medications with serious safety concerns
  - Post-approval tool implemented when a drug has a positive benefit-risk profile but requires additional risk management beyond routine prescribing and dispensing
  - Designed to achieve specific goals to mitigate risks
  - Can not compensate for an unfavorable benefit-risk

Abbreviation: REMS, Risk Evaluation and Mitigation Strategy

Dosage Optimization Principles

A dose that may be unnecessarily high and is poorly or not adequately tolerated may adversely impact functioning, quality of life, and a patient's ability to remain on the drug and derive maximal clinical benefit.

Source: Guidance for Industry: Optimizing the Dosage of Human Prescription Drugs and Biological Products for the Treatment of Oncologic Diseases

Dose Optimization: Prior to Approval

- A safe and effective dose should be established **prior to approval**
- Multiple challenges exist with post-approval dose optimization
  - Exposure of large numbers of patients to poorly tolerated dosages
  - Trial feasibility
  - Extrapolation of benefit-risk assessment based on dose optimization trials conducted after a randomized trial

Post-approval dose optimization studies may not provide necessary information to establish a safe and effective dose

Benefit-Risk Considerations

Benefit	DREAMM-7 and DREAMM-8 both met primary PFS endpoint
	DREAMM-7 showed statistically significant improvement in OS
Risk	Ocular toxicity: High rates of all-grade and Grade ≥3 events, frequent recurrences, and unresolved events
	Dosing concerns: • Poor tolerability of proposed dosages • Limited dose exploration; available data suggest improved tolerability with lower doses and longer dosing intervals

Abbreviations: PFS, progression-free survival; OS, overall survival

Benefit-Risk Considerations

Benefit	DREAMM-7 and DREAMM-8 both met primary PFS endpoint
	DREAMM-7 showed statistically significant improvement in OS
Risk	Ocular toxicity: High rates of all-grade and Grade ≥3 events, frequent recurrences, and unresolved events
	Dosing concerns: • Poor tolerability of proposed dosages • Limited dose exploration; available data suggest improved tolerability with lower doses and longer dosing intervals

In the context of the current treatment landscape:
- **Relevance of the DREAMM-7 and DREAMM-8 results is uncertain**
- **Benefit-risk for patients who have received ≥1 prior line is uncertain**

Abbreviations: PFS, progression-free survival; OS, overall survival

Discussion Topic

Discuss whether appropriate dosages of belantamab mafodotin have been identified for the proposed patient population with relapsed or refractory multiple myeloma

Voting Questions

1. Is the overall benefit-risk of belantamab mafodotin in combination with bortezomib and dexamethasone favorable at the proposed dosage in the proposed patient population?

2. Is the overall benefit-risk of belantamab mafodotin in combination with pomalidomide and dexamethasone favorable at the proposed dosage in the proposed patient population?


FDA
U.S. FOOD & DRUG
ADMINISTRATION

FDA is committed to ensuring digital accessibility for people with disabilities. We are continually improving the user experience for everyone and applying the relevant accessibility standards. At the time of initial posting on **July 17, 2025**, the attached **Event Materials** may not be fully accessible to users using assistive technology. A fully accessible version of the **Event Materials** is in preparation and will be posted as soon as it is ready. We regret any inconvenience that this may cause our readers.

Please let us know if you encounter accessibility barriers by contacting **Division of Advisory Committee and Consultant Management (DACCM)** at:

- **ODAC@fda.hhs.gov**

U.S. FOOD & DRUG ADMINISTRATION

BLA 761440
Belantamab Mafodotin (BLENREP)

Oncologic Drugs Advisory Committee Meeting
July 17, 2025

Andrea Baines, MD, PhD
Division of Hematologic Malignancies II
Office of Oncologic Diseases

William Boyd, MD
Division of Ophthalmology
Office of Specialty Medicine

Ankit Shah, PhD
Division of Cancer Pharmacology I
Office of Clinical Pharmacology

FDA Review Team

Division of Hematologic Malignancies II
Nicole Gormley, MD
Nicholas Richardson, DO, MPH
Bindu Kanapuru, MD
Deepti Telaraja, MD
Andrea Baines, MD, PhD
Theresa Carioti, MPH
Ashlee Bow, PharmD

Division of Cancer Pharmacology-I
Brian Booth, PhD
Olanrewaju Okusanya, PharmD, MS
Ankit Shah, PhD
Wentao Fu, PhD

Division of Pharmacometrics
Jiang Liu, PhD
Yangbing Li, PhD

Division of Biometrics IX
Yuan-Li Shen, DrPH
Jonathon Vallejo, PhD
Jing Zhang, PhD
Saahithi Rao, MS

Division of Hematology-Oncology Toxicology
Haleh Saber, MS, PhD
Michael Manning, PhD
Brenda Gehrke, PhD
Moran Choe, PhD

Office of Oncologic Diseases-Safety
Abhilasha Nair, MD
Shan Pradhan, MD
Jessica Kim, PharmD

Oncology Center of Excellence
Richard Pazdur, MD
R. Angelo de Claro, MD
Vishal Bhatnagar, MD

Division of Ophthalmology
William Boyd, MD
Rhea Lloyd, MD
Jennifer Hammer, MD

Division of Risk Management
Laura Zendel, PharmD, BCPS
Naomi Boston, PharmD
Celeste Will, PharmD, MPH
Ingrid Chapman, PharmD, BCPS

Outline

- Background/Regulatory History
  - Initial approval and withdrawal
  - Concerns with ocular toxicity and dosing
  - Proposed patient population and treatment landscape
- DREAMM-7 and DREAMM-8 Trial Designs and Results
- Issues for Discussion
  - High Rates of Ocular Toxicity
  - Uncertainty Regarding the Proposed Dosages
- Benefit-Risk Considerations

Belantamab Mafodotin

Proposed Indication: BLENREP, a B-cell maturation antigen (BCMA)-directed antibody and microtubule inhibitor conjugate, is indicated for the treatment of adults with multiple myeloma:

- in combination with bortezomib and dexamethasone in patients who have received **at least one prior line of therapy**; and
- in combination with pomalidomide and dexamethasone in patients who have received **at least one prior line of therapy** including lenalidomide.

Proposed Dosage:

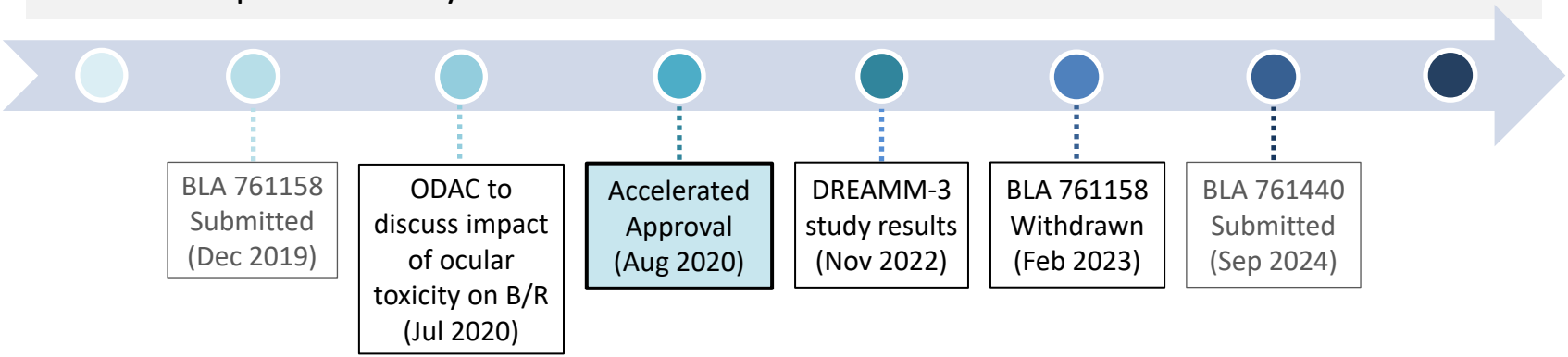
Combination Regimen	Recommended Starting Dose Schedule for BLENREP
With bortezomib and dexamethasone **(BVd)**	**2.5 mg/kg** intravenously (IV) **once every 3 weeks (Q3W)**
With pomalidomide and dexamethasone **(BPd)**	**2.5 mg/kg** IV once on Cycle 1 followed by **1.9 mg/kg** IV **once every 4 weeks (Q4W)** starting on Cycle 2

Source: Modified from Applicant's Proposed US Prescribing Information

Initial Accelerated Approval

Belantamab mafodotin was granted accelerated approval on August 5, 2020

- Indication: Treatment of adults with relapsed or refractory multiple myeloma who have received **at least four prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent**
- Dosing Regimen: **2.5 mg/kg IV once every 3 weeks** until disease progression or unacceptable toxicity



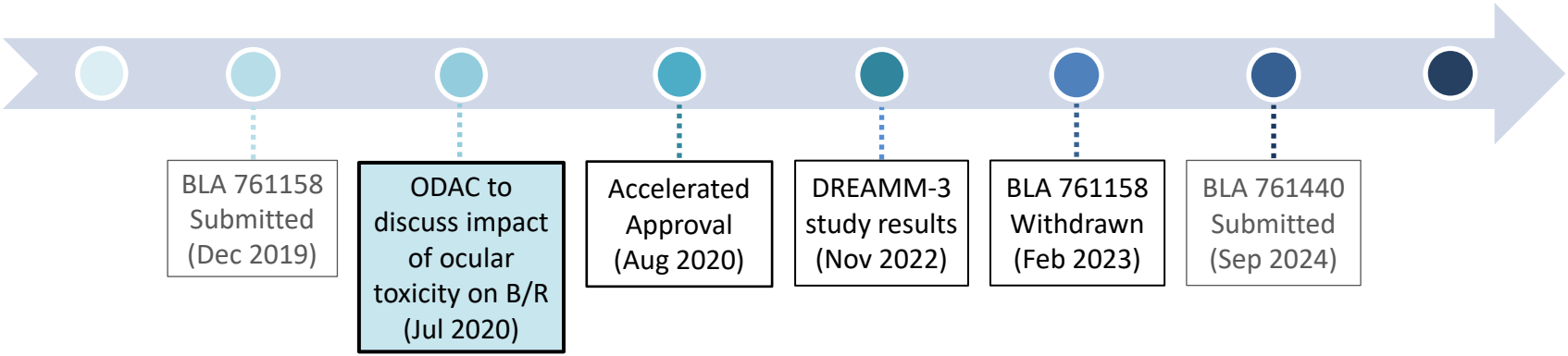
Abbreviations: IV=intravenously; BLA=Biologic Licensing Application; ODAC=Oncologic Drugs Advisory Committee; B/R=benefit-risk

Source: FDA

Ocular Toxicity/Dosing Concerns

Due to ocular toxicity and dosing concerns:

- **ODAC** held on July 14, 2020, to discuss the **impact of ocular toxicity on benefit-risk**
- **Approved with a REMS** (with **ETASU** A, B, D, E) to mitigate the risk of ocular toxicity
- **Post-marketing requirement (PMR)** to evaluate **lower doses or alternative dosing regimens** of belantamab mafodotin monotherapy



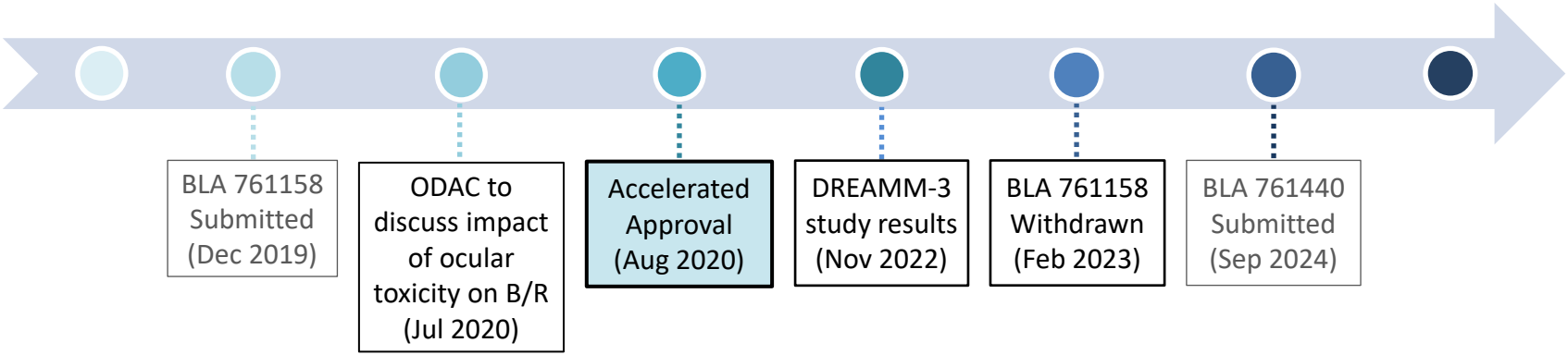
Abbreviations: BLA=Biologic Licensing Application; ODAC=Oncologic Drugs Advisory Committee; B/R=benefit-risk; REMS=Risk Evaluation and Mitigation Strategy; ETASU=Elements to Assure Safe Use; PMR=Post-Marketing Requirement

Source: FDA

Confirmatory Trial: DREAMM-3

Under the accelerated approval pathway:

- **PMR** issued to conduct a randomized phase 3 clinical trial to **verify clinical benefit** of belantamab mafodotin in patients with relapsed or refractory multiple myeloma
  - DREAMM-3: phase 3, randomized (2:1) trial of **belantamab mafodotin 2.5 mg/kg Q3W** vs. pomalidomide + dexamethasone in patients with ≥2 prior lines of therapy



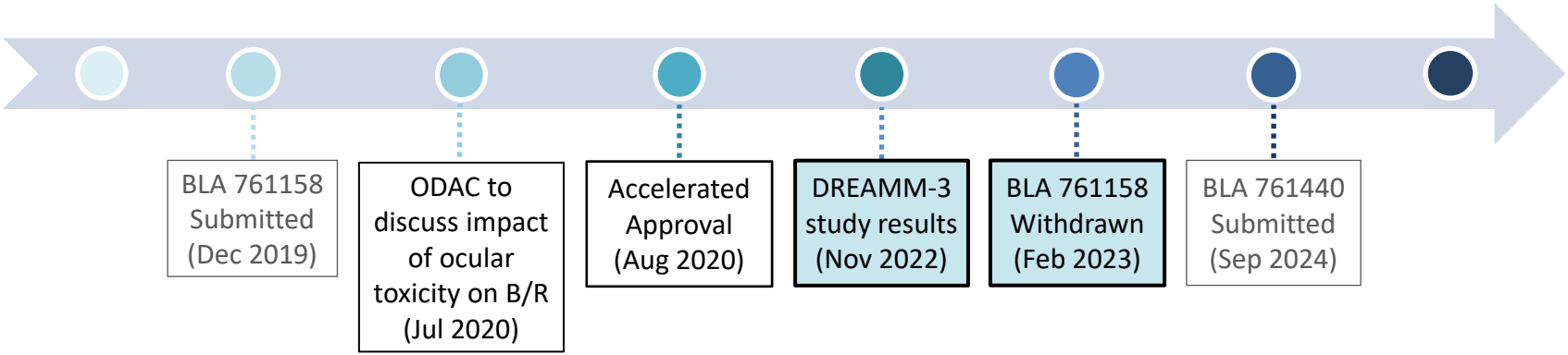
Abbreviations: Q3W=every 3 weeks; BLA=Biologic Licensing Application; ODAC=Oncologic Drugs Advisory Committee; B/R=benefit-risk; PMR=Post-Marketing Requirement

Source: FDA

DREAMM-3 Results and Withdrawal

DREAMM-3 topline results became available in November 2022:

- **PFS HR 1.03** (95% CI: 0.72, 1.47); **OS HR 1.14** (95% CI: 0.77, 1.68)
- Belantamab mafodotin was **voluntarily withdrawn** from U.S. market on February 6, 2023, **due to failure of the confirmatory trial** to verify clinical benefit
  - Possible negative impact of poor tolerability of 2.5 mg/kg Q3W dose on efficacy



Abbreviations: BLA=Biologic Licensing Application; ODAC=Oncologic Drugs Advisory Committee; B/R=benefit-risk; PFS=progression-free survival; HR=hazard ratio; CI=confidence interval; OS=overall survival; Q3W=every 3 weeks

Source: FDA

Previous vs. Current Application

Previously approved indication (2020):

- For the treatment of adults with relapsed or refractory multiple myeloma who have received **at least four prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent**

Currently proposed indication (2025):

- For the treatment of adults with multiple myeloma:
  - in combination with bortezomib and dexamethasone in patients who have received **at least one prior line of therapy**; and
  - in combination with pomalidomide and dexamethasone in patients who have received **at least one prior line of therapy including lenalidomide**

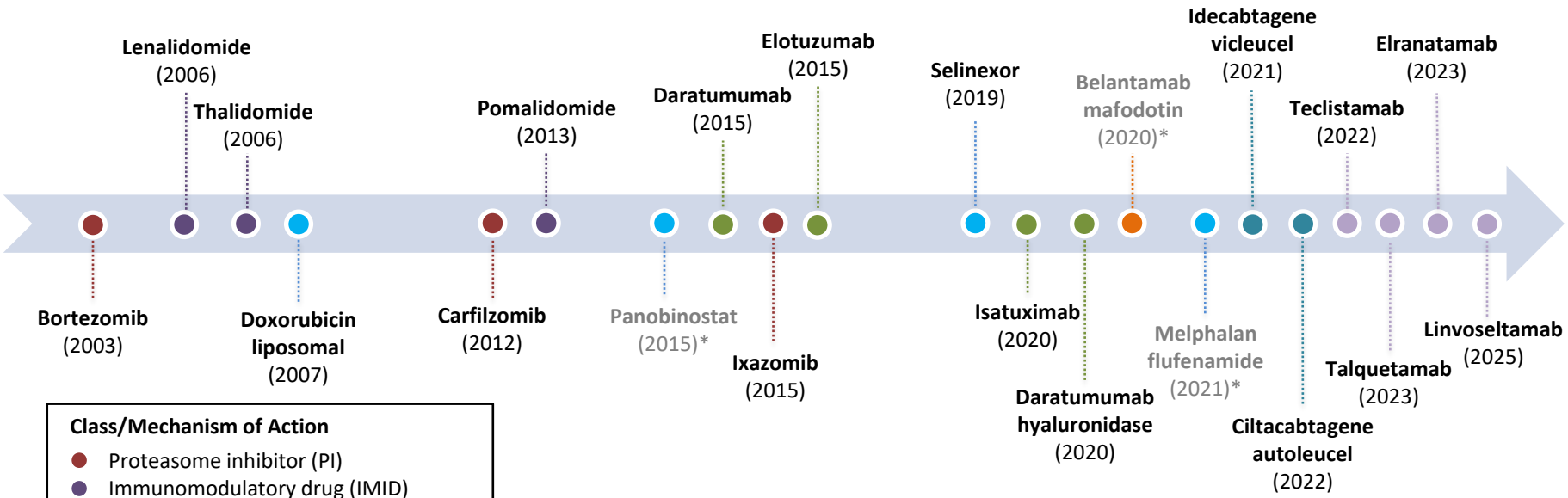
Current RRMM Treatment Landscape

Regimen	Indication
DRd, DVd, IRd, SVd, K	≥1 prior line of therapy
DPd	≥1 prior line of therapy, including lenalidomide and a PI
Ciltacabtagene-autoleucel	≥1 prior line of therapy, including a PI and an IMID and refractory to lenalidomide
DKd, KRd, IsaKd, ERd, Kd	1 to 3 prior lines of therapy
EPd, IsaPd, Pd	≥2 prior lines of therapy including lenalidomide and a PI
Idecabtagene-vicleucel	≥2 prior lines of therapy including an IMID, a PI and an anti-CD38 mAb
Daratumumab	≥3 prior lines of therapy including a PI and an IMID or double-refractory to a PI and an IMID
Teclistamab, Talquetamab, Elranatamab, Linvoseltamab	≥4 prior lines of therapy including an IMID, a PI and an anti-CD38 mAb
Sd	≥4 prior lines of therapy including ≥2 PIs, ≥2 IMIDs, and an anti-CD38 mAb

Abbreviations: RRMM=relapsed or refractory multiple myeloma; Proteasome Inhibitors: V=bortezomib, K=carfilzomib, I=ixazomib; Immunomodulatory Agents: R=lenalidomide, P=pomalidomide; Anti-CD38 Monoclonal Antibodies: D=daratumumab, Isa=isatuximab; Anti-SLAMF7 Monoclonal Antibody: E=elotuzumab; XPO1 Inhibitor: S=selinexor; Chimeric Antigen Receptor T-cell Therapies: ciltacabtagene autoleucel, idecabtagene vicleucel; Bispecific CD3 T-cell Engagers: teclistamab, elranatamab, talquetamab, linvoseltamab; Other: d=dexamethasone.

Source: FDA

Approvals for MM (2003 – 2025)



Class/Mechanism of Action

- Proteasome inhibitor (PI)
- Immunomodulatory drug (IMID)
- Monoclonal antibody (mAb)
- Antibody drug conjugate (ADC)
- Chimeric antigen receptor T-cell (CAR T)
- Bispecific antibody (bsAb)
- Other

*Approval withdrawn

Abbreviations: MM=multiple myeloma

Source: FDA

Improvements in Overall Survival

2000

Lenalidomide (2006)

Thalidomide (2006)

Pomalidomide (2013)

Daratumumab (2015)

Elotuzumab (2015)

2019

Selinexor (2019)

Isatuximab (2020)

Daratumumab hyaluronidase (2020)

Belantamab mafodotin (2020)*

Melphalan flufenamide (2021)*

Idecabtagene vicleucel (2021)

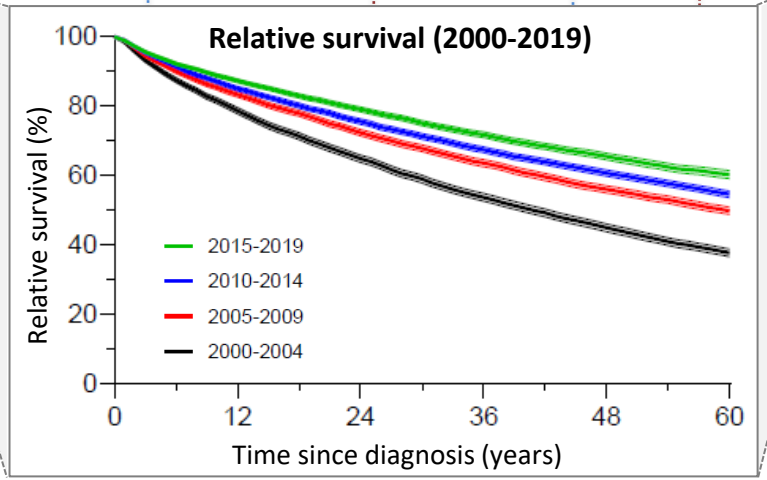
Ciltacabtagene autoleucel (2022)

Teclistamab (2022)

Talquetamab (2023)

Elranatamab (2023)

Linvoseltamab (2025)



Current OS is ~8-10 years

Further improvements in OS are anticipated with the approval of novel therapies

Abbreviations: OS=overall survival

Source: FDA; Dores G. et al, Br J Haematol (2025)

DREAMM-7 Trial Design

DREAMM-7 (Study 207503)

Key Eligibility Criteria
- RRMM
- ≥1 prior line
- Not intolerant or refractory to daratumumab or bortezomib

Stratification
- 1 vs 2/3 vs 4 prior lines
- Prior bortezomib
- R-ISS (I vs II/III)

Randomized 1:1 (N=478)

Arm A: BVd
- Belantamab mafodotin 2.5 mg/kg IV Q3W
- Bortezomib 1.3 mg/m^2 Day 1,4,8,11 (C1-8)
- Dexamethasone 20 mg Day 1,2,4,5,8,9,11,12 (C1-8)

Arm B: DVd
- Daratumumab 16 mg/kg IV QW (C1-3), Q3W (C4-8), Q4W (C9+)
- Bortezomib 1.3 mg/m^2 Day 1,4,8,11 (C1-8)
- Dexamethasone 20 mg Day 1,2,4,5,8,9,11,12 (C1-8)

Primary Endpoint
- PFS (IRC)

Key Secondary Endpoints
- OS
- DOR
- MRD(-)

Abbreviations: RRMM=relapsed or refractory multiple myeloma; R-ISS=Revised International Staging System; BVd=belantamab mafodotin, bortezomib, dexamethasone; Q#W=every # weeks; C=cycle; DVd=daratumumab, bortezomib, dexamethasone; PFS=progression-free survival; IRC=Independent Review Committee; OS=overall survival; DOR=duration of response; MRD(-)=minimal residual disease negativity

Source: FDA

DREAMM-8 Trial Design

DREAMM-8 (Study 207499)

Key Eligibility Criteria

- RRMM
- ≥1 prior line including lenalidomide
- Pomalidomide-naïve

Stratification

- 1 vs 2/3 vs 4 prior lines
- Prior bortezomib
- ISS (I vs II/III); Prior anti-CD38 mAb*

Randomized 1:1 (N=300)

Arm A: BPd

- Belantamab mafodotin 2.5 mg/kg IV (C1); 1.9 mg/kg IV Q4W (C2+)
- Pomalidomide 4 mg PO Day 1-21
- Dexamethasone 40 mg Day 1, 8, 15, 22

Arm B: PVd

- Pomalidomide 4 mg PO Day 1-14
- Bortezomib 1.3 mg/m^2 Day 1, 4, 8, 11 (C1-8); Day 1 and 8 (C9+)
- Dexamethasone 20 mg Day 1, 2, 4, 5, 8, 9, 11, 12 (C1-8); Day 1, 2, 8, 9 (C9+)

Primary Endpoint

- PFS (IRC)

Key Secondary Endpoints

- OS
- DOR
- MRD(-)

*Changed from ISS to prior anti-CD38 mAb in Amendment 1

Abbreviations: RRMM=relapsed or refractory multiple myeloma; ISS=International Staging System; BPd= belantamab mafodotin, pomalidomide, dexamethasone; Q#W=every # weeks; C=cycle; PVd=pomalidomide, bortezomib, dexamethasone; PFS=progression-free survival; IRC=Independent Review Committee; OS=overall survival; DOR=duration of response; MRD(-)=minimal residual disease negativity

Source: FDA

Key Demographics

	DREAMM-7		DREAMM-8	
Demographic Category, n (%)	**BVd N=243**	**DVd N=251**	**BPd N=155**	**PVd N=147**
Age				
Median (range), in years	65 (35, 87)	65 (33, 89)	66 (40, 82)	68 (34, 86)
18 to <65	121 (50)	126 (50)	64 (41)	53 (36)
65 to <75	85 (35)	95 (38)	72 (47)	59 (40)
>=75	37 (15)	30 (12)	19 (12)	35 (24)
Ethnicity				
Hispanic or Latino	30 (12)	41 (16)	10 (6)	17 (12)
Not Hispanic or Latino	213 (88)	208 (83)	145 (94)	139 (95)
Race				
White	203 (81)	206 (85)	133 (86)	127 (86)
Black/African American	12 (5)	8 (3)	0	0
Asian	33 (13)	28 (12)	20 (13)	17 (12)
Native Hawaiian/Pacific Islander	0	0	1 (<1)	2 (1)
Region				
Europe	126 (52)	120 (48)	105 (68)	109 (74)
North America	10 (4)†	18 (7)†	4 (3)	1 (<1)
Northeast Asia	26 (11)	28 (11)	18 (12)	14 (10)
Rest of the World*	81 (33)	85 (40)	28 (18)	23 (16)

†Includes U.S. (N=14) and Canada
*Includes Australia, Brazil, Israel, New Zealand

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; DVd=daratumumab, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone; PVd=pomalidomide, bortezomib, dexamethasone

Source: FDA Analysis

Prior Therapies

	DREAMM-7		DREAMM-8	
Category, %	**BVd N=243**	**DVd N=251**	**BPd N=155**	**PVd N=147**
Prior Lines of Therapy				
Median (range)	1 (1, 7)	2 (1, 7)	1 (1, 6)	1 (1, 9)
1	51	50	53	52)
2 or 3	36	39	35	33)
>=4	12	11	12	15)
Prior PI				
Y	90	86	90	93
N	10	14	10	7
Prior IMID				
Y	81	86	100	100
N	19	14	0	0
Prior Anti-CD38 mAb				
Y	1	2	25	29
N	99	98	75	71
Prior Transplant				
Y	67	69	64	56
N	33	31	36	44

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; DVd=daratumumab, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone; PVd=pomalidomide, bortezomib, dexamethasone

Source: FDA Analysis

Efficacy Overview

- Primary PFS endpoint was met in both trials
  - DREAMM-7: HR=0.41 (95% CI: 0.31, 0.53); p-value < 0.0001
  - DREAMM-8: HR=0.52 (95% CI: 0.37, 0.73); p-value = 0.0001
- DREAMM-7 OS was statistically significant
  - OS IA2: HR=0.58 (95% CI: 0.43, 0.79); p-value = 0.0005
- DREAMM-8 OS did not reach statistical significance
  - OS IA1: HR 0.77 (95% CI: 0.53, 1.14)

Abbreviations: PFS=progression-free survival; HR=hazard ratio; CI=confidence interval; OS=overall survival; IA=interim analysis

Source: FDA Analysis

Safety Overview

	DREAMM-7		DREAMM-8	
Adverse Event Category, %	**BVd N=242**	**DVd N=246**	**BPd N=150**	**PVd N=145**
Any Grade TEAEs	100	100	99	96
Grade 3 or 4 TEAEs	95	76	92	74
Serious TEAEs	50	37	63	45
Fatal (Grade 5) TEAEs	10	8	11	11
TEAEs leading to any dose modification	98	89	91	86
TEAEs leading to dose interruption	94	75	91	75
TEAEs leading to dose reduction	75	59	61	61
TEAEs leading to discontinuation	31	19	15	12

Abbreviations: TEAE=treatment-emergent adverse event; BVd=belantamab mafodotin, bortezomib, dexamethasone; DVd= daratumumab, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone; PVd=pomalidomide, bortezomib, dexamethasone

Source: FDA Analysis

Issues for Discussion

- High Rates of Ocular Toxicity
  - Similar incidence and severity of ocular toxicity despite different dosing regimens
  - High rates of dose modifications due to ocular toxicity
- Uncertainty Regarding the Proposed Dosages
  - Poor tolerability of belantamab mafodotin in both dosing regimens
  - Limited data to support dose selection for DREAMM-7 and DREAMM-8

Issues for Discussion

- **High Rates of Ocular Toxicity**
  - **Similar incidence and severity of ocular toxicity despite different dosing regimens**
  - **High rates of dose modifications due to ocular toxicity**
- Uncertainty Regarding the Proposed Dosages
  - Poor tolerability of belantamab mafodotin in both dosing regimens
  - Limited data to support dose selection for DREAMM-7 and DREAMM-8

Grading of Corneal Toxicity

	Grade 1	Grade 2	Grade 3	Grade 4
Keratopathy and Visual Acuity (KVA) Scale Grading				
Corneal exam findings	Mild superficial keratopathy	Moderate superficial keratopathy	Severe superficial keratopathy	Corneal epithelial defect
Change in BCVA (from baseline)	Decline of 1 line	Decline of 2 or 3 lines and not worse than 20/200	Decline by >3 lines and not worse than 20/200	Worse than 20/200

Abbreviations: BCVA=best corrected visual acuity

Source: FDA

Dose Modifications for KVA Events

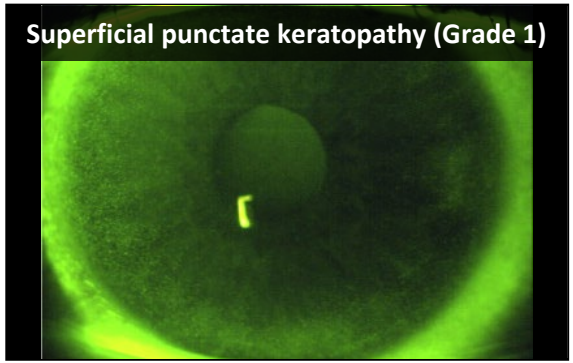
	Grade 1	Grade 2	Grade 3	Grade 4
Keratopathy and Visual Acuity (KVA) Scale Grading				
Corneal exam findings	Mild superficial keratopathy	Moderate superficial keratopathy	Severe superficial keratopathy	Corneal epithelial defect
Change in BCVA (from baseline)	Decline of 1 line	Decline of 2 or 3 lines and not worse than 20/200	Decline by >3 lines and not worse than 20/200	Worse than 20/200
Recommended Dosage Modifications for Belantamab Mafodotin				
DREAMM-7	Continue current dose	Hold until Grade ≤1; resume at current dose	Hold until Grade ≤1; resume at reduced dose (1.9 mg/kg Q3W)	Permanently discontinue
DREAMM-8	Continue current dose	Hold until Grade ≤1; resume at reduced dose: • Prior to Cycle 2: 1.9 mg/kg Q4W • Cycle 2+: reduce to 1.9 mg/kg Q8W		Hold until Grade ≤1; discuss B/R; resume at reduced dose (1.4 mg/kg Q8W)

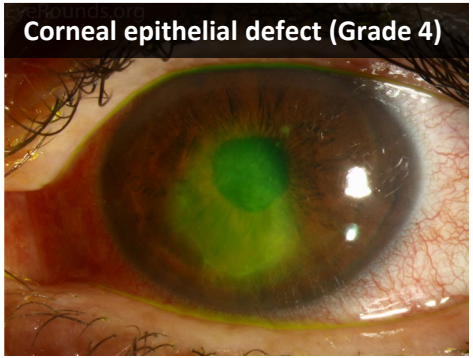
Abbreviations: BCVA=best corrected visual acuity; Q#W=once every # weeks; B/R=benefit-risk

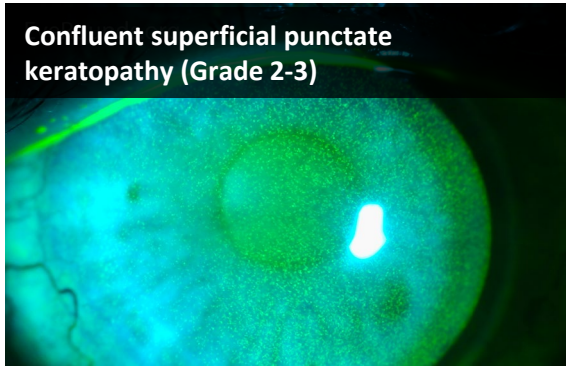
Source: FDA

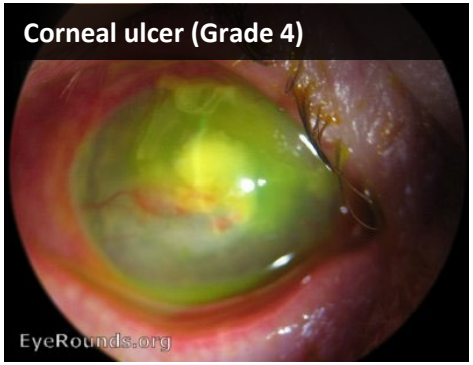
Clinical Perspective on Ocular Toxicity

Keratopathy Clinical Considerations









Key Considerations:

- May be asymptomatic in earlier stages
- Epithelial defects are typically painful
- Compromise to barrier can increase risk of infection
- Increased infection risk with increasing confluence

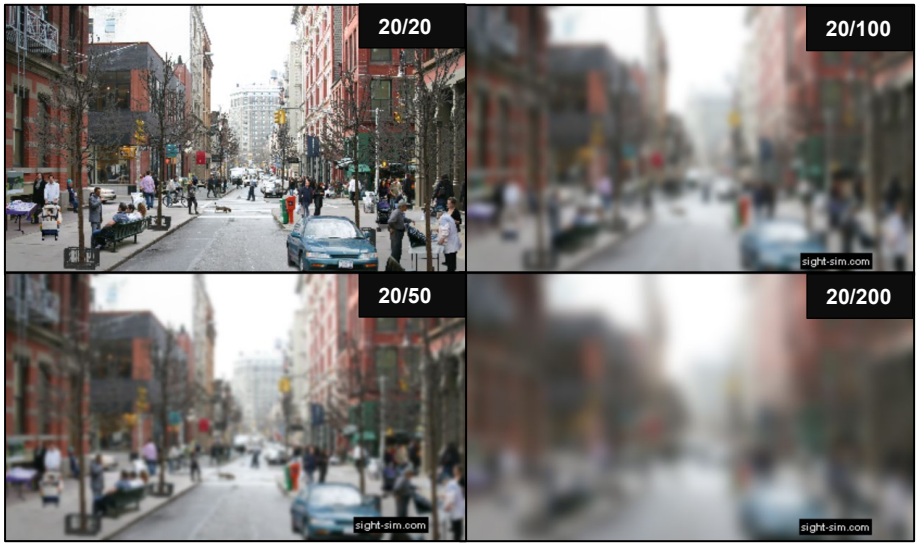
Source: ScienceDirect.com; University of Iowa, Ophthalmology and Visual Sciences, EyeRounds.org

BCVA Clinical Considerations

Snellen Eye Chart for Visual Acuity

1	20/200
2	20/100
3	20/70
4	20/50
5	20/40
6	20/30
7	20/25
8	20/20
9	
10	
11	

Simulations of Visual Acuity Changes



- BCVA is the ***best possible visual acuity that an individual can achieve*** when wearing corrective lenses (such as glasses or contact lenses)
- Clinically significant change: 20/20 → 20/50; driving restrictions may be required at 20/70 or worse

Abbreviations: BCVA=best corrected visual acuity

Source: Sight-Sim ™ Software Tool

Ocular Toxicity: Clinical Impression

- Potential for lower grade corneal toxicities to be asymptomatic
- Higher-grade KVA scale toxicities are more confluent, more likely to have inflammatory infiltrates, more likely 3 or more lines of vision loss
- Prompt management is essential to minimize progression to corneal thinning and perforation
- Managing lower/intermediate grade toxicities may minimize progression to higher grade toxicities with dose modifications as indicated

Abbreviations: KVA=keratopathy and visual acuity

Overview of KVA Events

	DREAMM-7	DREAMM-8
Adverse Event Category, %	**BVd N=242**	**BPd N=150**
Any Grade KVA event	92	93
Grade 1	5	6
Grade 2	9	10
Grade 3	56	69
Grade 4	21	9
	77%	78%
Any dose modification due to KVA event	76	78
Dose interruption due to KVA event	74	75
Dose reduction due to KVA event	30	57
Discontinuation due to KVA event	6	7

Abbreviations: KVA=keratopathy and visual acuity; BVd=belantamab mafodotin, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone

Source: FDA Analysis

Onset and Duration of KVA Events

	DREAMM-7	DREAMM-8
	BVd N=242	BPd N=150
Grade ≥2 KVA event, n (%)	209 (86)	131 (87)
Onset (1st event), median (range), in days	43 (15, 611)	32 (18, 533)
Duration (all events), median (range), in days	85 (5, 813)	85 (15, 746)

- Majority of 1st Grade ≥2 KVA events occurred within 1-2 months after starting treatment
- Median duration of all events was approximately 3 months

Abbreviations: KVA=keratopathy and visual acuity; BVd=belantamab mafodotin, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone

Source: FDA Analysis

Recurrent KVA Events

	DREAMM-7	DREAMM-8
	BVd N=242	BPd N=150
Grade ≥2 KVA event, n (%)	209 (86)	131 (87)
Number of occurrences, n (%)†		
1	63 (30)	36 (27)
2	35 (17)	20 (15)
3 or more	111 (53)	75 (57)
Median (range)	3 (1, 11)	3 (1, 10)

†Denominator based on number of patients with a Grade ≥2 KVA event

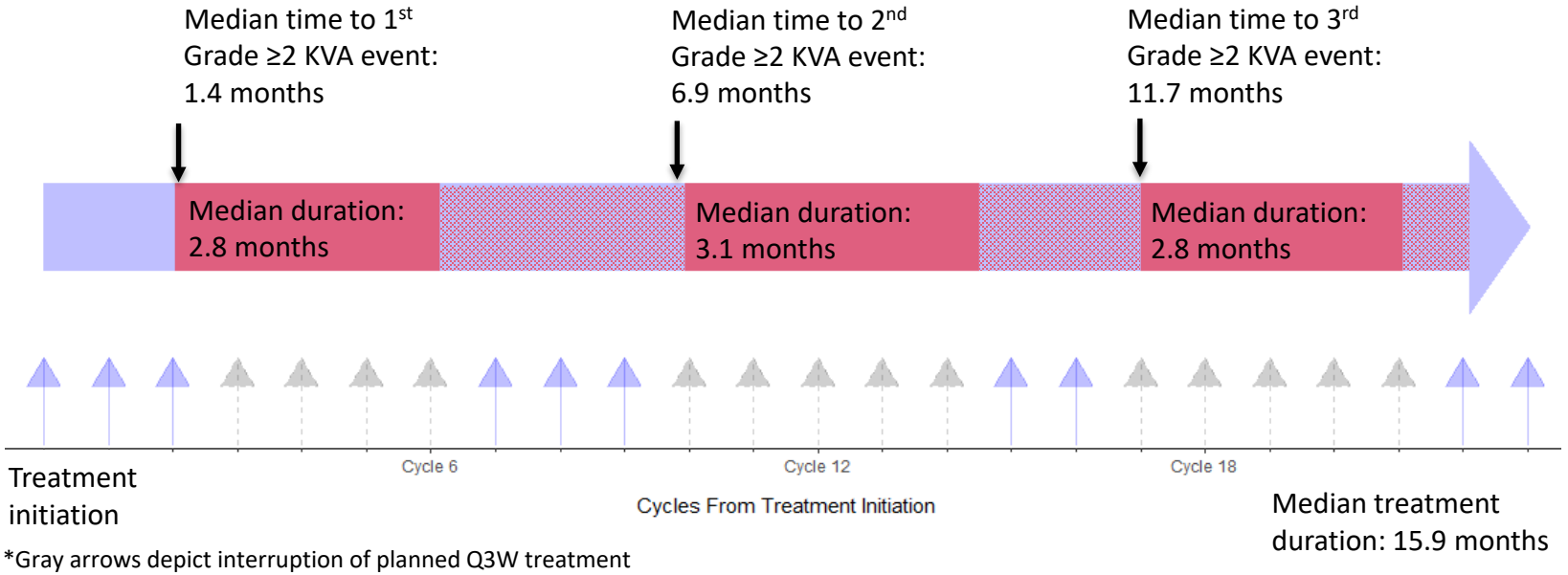
Most patients experienced recurrent Grade ≥2 KVA events (median of 3)

Abbreviations: KVA=keratopathy and visual acuity; BVd=belantamab mafodotin, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone

Source: FDA Analysis

Hypothetical Patient Experience

DREAMM-7: BVd (Q3W cycles)



*Gray arrows depict interruption of planned Q3W treatment

Patients had active Grade ≥2 KVA events for a substantial proportion of time on treatment

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; Q3W=every 3 weeks; KVA=keratopathy and visual acuity

Source: FDA Analysis

Outcomes of KVA Events

	DREAMM-7	DREAMM-8
	BVd N=242	BPd N=150
Grade ≥2 KVA event, n (%)	212 (88)	132 (88)
Outcome (last event), n (%)†		
Resolved (to baseline or better)	52 (25)	40 (30)
Ongoing	160 (75)	92 (70)
Treatment ongoing	52 (25)	36 (27)
Discontinued, follow-up ongoing	48 (23)	21 (16)
Discontinued, follow-up ended	60 (28)	35 (27)

†Denominator based on number of patients with a Grade ≥2 KVA event as of the 4-Month Safety Update (07 Oct 2024 data cut-off)

- More than 70% of patients had ongoing toxicity as of the data cut-off
- Of the patients with ongoing events ~2/3 had discontinued study treatment

Abbreviations: KVA=keratopathy and visual acuity; BVd=belantamab mafodotin, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone

Source: Applicant's Response to FDA Information Request

Clinically Meaningful Changes in BCVA

	DREAMM-7	DREAMM-8
	BVd N=242	BPd N=150
BCVA (Unilateral Changes)	**20/50 or Worse**	**20/50 or Worse**
Patients with event, n (%)	155 (64)	95 (63)
Duration of any event, median (Range), in days	23 (3-766)	29 (5-302)

- Over 60% of patients experienced a change in *best-corrected visual acuity* to 20/50 or worse
- Median duration approximately 3 weeks in DREAMM-7 and 4 weeks in DREAMM-8

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone; BCVA=best corrected visual acuity

Source: FDA Analysis; Applicant's Response to FDA Information Request; Sight-Sim ™ Software Tool

Clinically Meaningful Changes in BCVA

	DREAMM-7	DREAMM-8
	BVd N=242	BPd N=150
BCVA (Unilateral Changes)	**20/100 or Worse**	**20/100 or Worse**
Patients with event, n (%)	68 (28)	41 (27)
Duration of any event, median (Range), in days	22 (5-766)	29 (3-338)

- Over 25% of patients experienced a change in *best-corrected visual acuity* to 20/100 or worse
- Median duration approximately 3 weeks in DREAMM-7 and 4 weeks in DREAMM-8

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone; BCVA=best corrected visual acuity

Source: FDA Analysis; Applicant's Response to FDA Information Request; Sight-Sim ™ Software Tool

Clinically Meaningful Changes in BCVA

	DREAMM-7	DREAMM-8
	BVd N=242	BPd N=150
BCVA (Unilateral Changes)	**20/200 or Worse**	**20/200 or Worse**
Patients with event, n (%)	27 (11)	19 (13)
Duration of any event, median (Range), in days	22 (4-766)	58 (26-450)

- Over 10% of patients experienced a change in *best-corrected visual acuity* to 20/200 or worse
- Median duration approximately 3 weeks in DREAMM-7 and 8 weeks in DREAMM-8

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone; BCVA=best corrected visual acuity

Source: FDA Analysis; Applicant's Response to FDA Information Request; Sight-Sim ™ Software Tool

DREAMM-7: Ocular Toxicity by CTCAE

	DREAMM-7			
	BVd N=242		DVd N=246	
Adverse Event Term, %†	All Grades	Grades 3-4	All Grades	Grades 3-4
Vision blurred	66	22	11	<1
Dry eye*	51	7	7	0
Photophobia	47	2	2	0
Foreign body sensation*	44	3	4	0
Eye irritation	43	5	5	0
Eye pain*	33	<1	4	<1

†Graded by Common Terminology Criteria for Adverse Events (CTCAE); events with >30% incidence in either arm
*Includes grouped related adverse events terms

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; DVd=daratumumab, bortezomib, dexamethasone

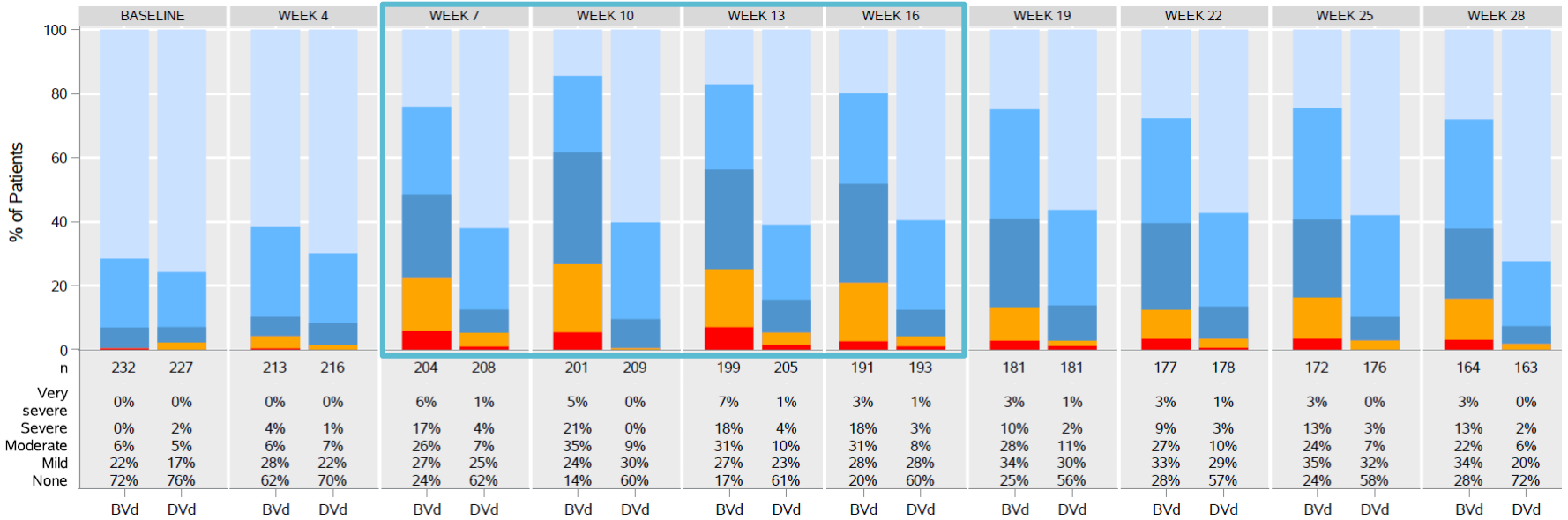
Source: FDA Analysis

Patient-Reported Outcomes

- Tolerability assessed using **PRO-CTCAE** (symptomatic toxicity), **OSDI** (visual symptoms and function) and **FACT-GP5** (overall side-effect bother)
  - Applicant also used a non-validated qualitative 2-item questionnaire to assess reading and driving
- At each assessed timepoint, a group of patients reported severe visual side effects related to belantamab mafodotin
  - Progressive worsening from baseline through ~Week 13-17
  - ~5-15% of respondents reported severe visual symptoms at most timepoints
- PRO results demonstrate the impact of ocular toxicity and support the clinician-reported ocular toxicity findings

Abbreviations: PRO-CTCAE=Patient-Reported Outcomes version of Common Terminology Criteria for Adverse Events; OSDI=Ocular Surface Disease Index; FACT-GP5=Functional Assessment of Cancer Therapy – General Population Item #5

DREAMM-7: PRO-CTCAE Blurred Vision



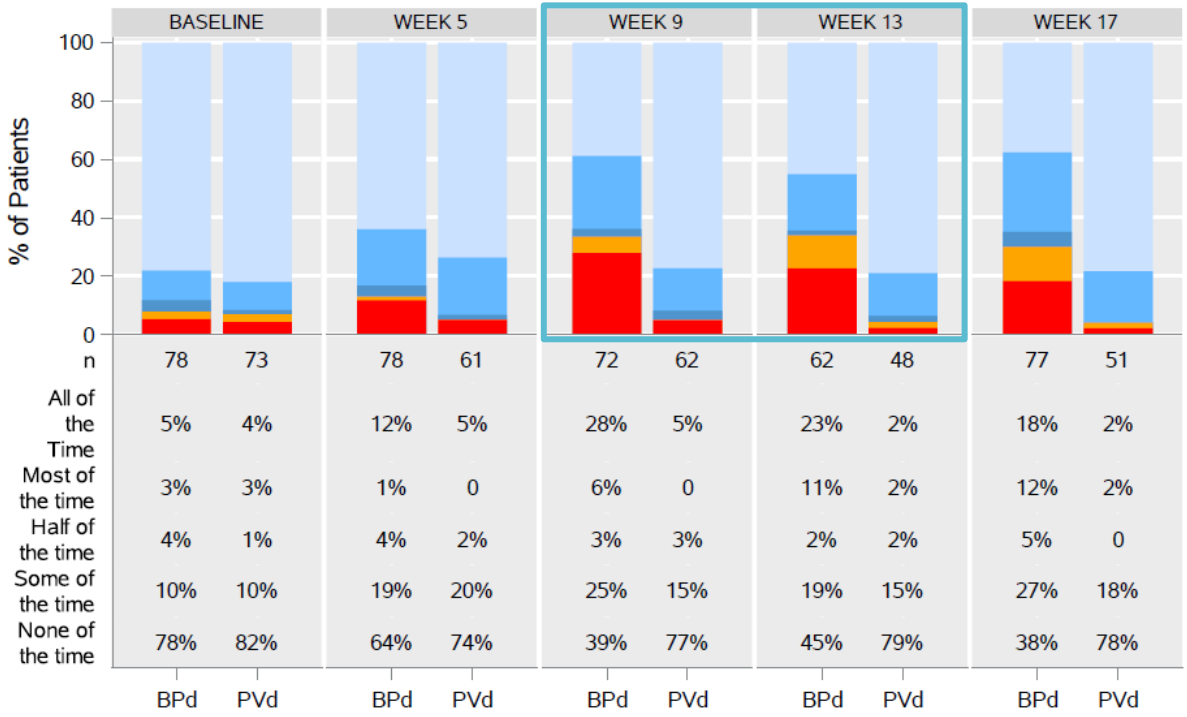
Question: "In the last 7 days, what was the severity of your blurry vision at its worst?"

- High rates of blurred vision reported, with a peak between Weeks 7-16

Abbreviations: PRO-CTCAE=Patient Reported Outcomes – Common Terminology Criteria for Adverse Events; BVd=belantamab mafodotin, bortezomib, dexamethasone; DVd=daratumumab, bortezomib, dexamethasone

Source: Applicant's Response to FDA Information Request

DREAMM-8: OSDI Driving at Night



	BASELINE		WEEK 5		WEEK 9		WEEK 13		WEEK 17	
	BPd	PVd	BPd	PVd	BPd	PVd	BPd	PVd	BPd	PVd
n	78	73	78	61	72	62	62	48	77	51
All of the Time	5%	4%	12%	5%	28%	5%	23%	2%	18%	2%
Most of the time	3%	3%	1%	0	6%	0	11%	2%	12%	2%
Half of the time	4%	1%	4%	2%	3%	3%	2%	2%	5%	0
Some of the time	10%	10%	19%	20%	25%	15%	19%	15%	27%	18%
None of the time	78%	82%	64%	74%	39%	77%	45%	79%	38%	78%

- OSDI assesses dry eye symptoms and impact on vision-related functions (e.g., reading, driving at night, using a computer)
- At Weeks 9 and 13, 34% of respondents in the BPd arm reported limitations in driving at night “all of the time” or “most of the time”

Abbreviations: OSDI=Ocular Surface Disease Index; BPd=belantamab mafodotin, pomalidomide, dexamethasone; PVd=pomalidomide, bortezomib, dexamethasone

Source: Applicant’s Response to FDA Information Request

Summary: High Rates of Ocular Toxicity

Ocular Toxicity

- High rates of KVA events, including Grade 3-4 events in both trials
- Recurrent events
- Not all events resolved

Dose Modifications

- High rates of dose modifications in both trials, primarily due to KVA events
- Prolonged and recurrent treatment interruptions

Changes in BCVA

- Clinically significant changes in BCVA in >60% of patients
- Likely to have a significant impact considering MM is primarily a disease of older adults

Patient-Reported Outcomes

- Impact on visual symptoms and interference with usual/daily activities
- Impact on vision-related functions (e.g., driving, reading, using a computer)

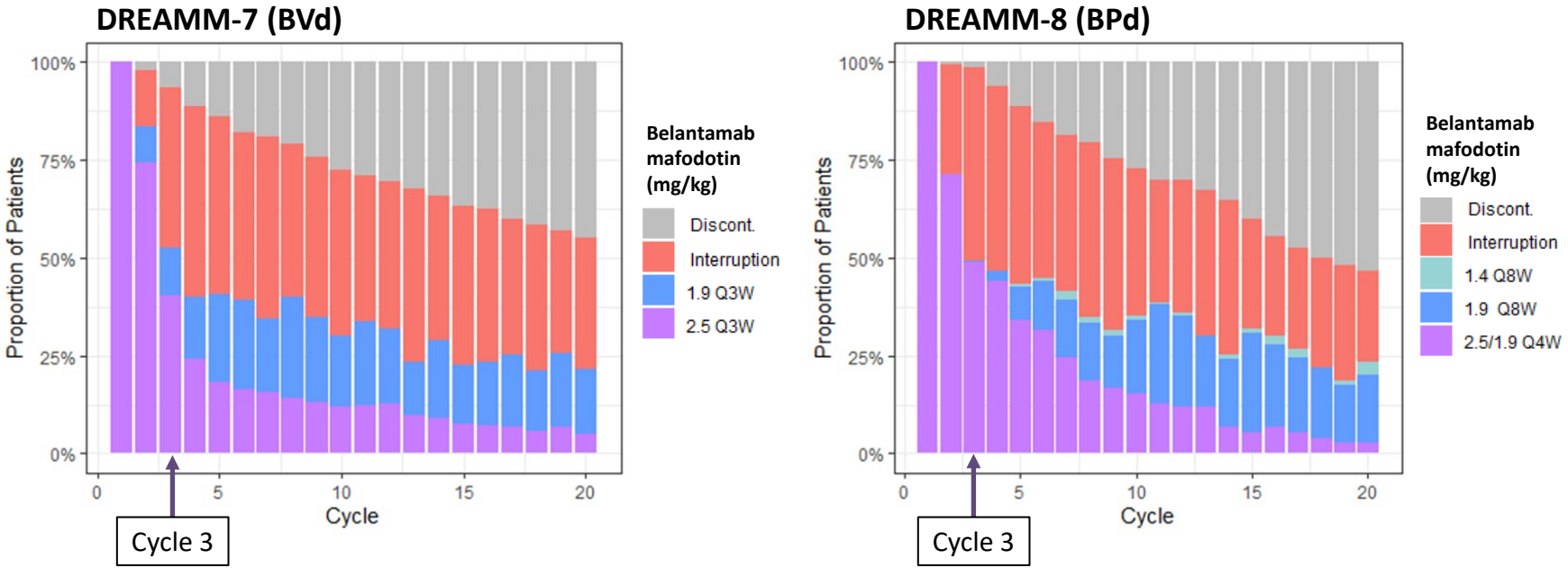
Abbreviations: KVA=keratopathy and visual acuity; BCVA=best corrected visual acuity; MM=multiple myeloma

Source: FDA

Issues for Discussion

- High Rates of Ocular Toxicity
  - Similar incidence and severity of ocular toxicity despite different dosing regimens
  - High rates of dose modifications due to ocular toxicity
- **Uncertainty Regarding the Proposed Dosages**
  - **Poor tolerability of belantamab mafodotin in both dosing regimens**
  - **Limited data to support dose selection for DREAMM-7 and DREAMM-8**

Poor Tolerability of Intended Dose



DREAMM-7 (BVd): Starting dosage 2.5 mg/kg Q3W

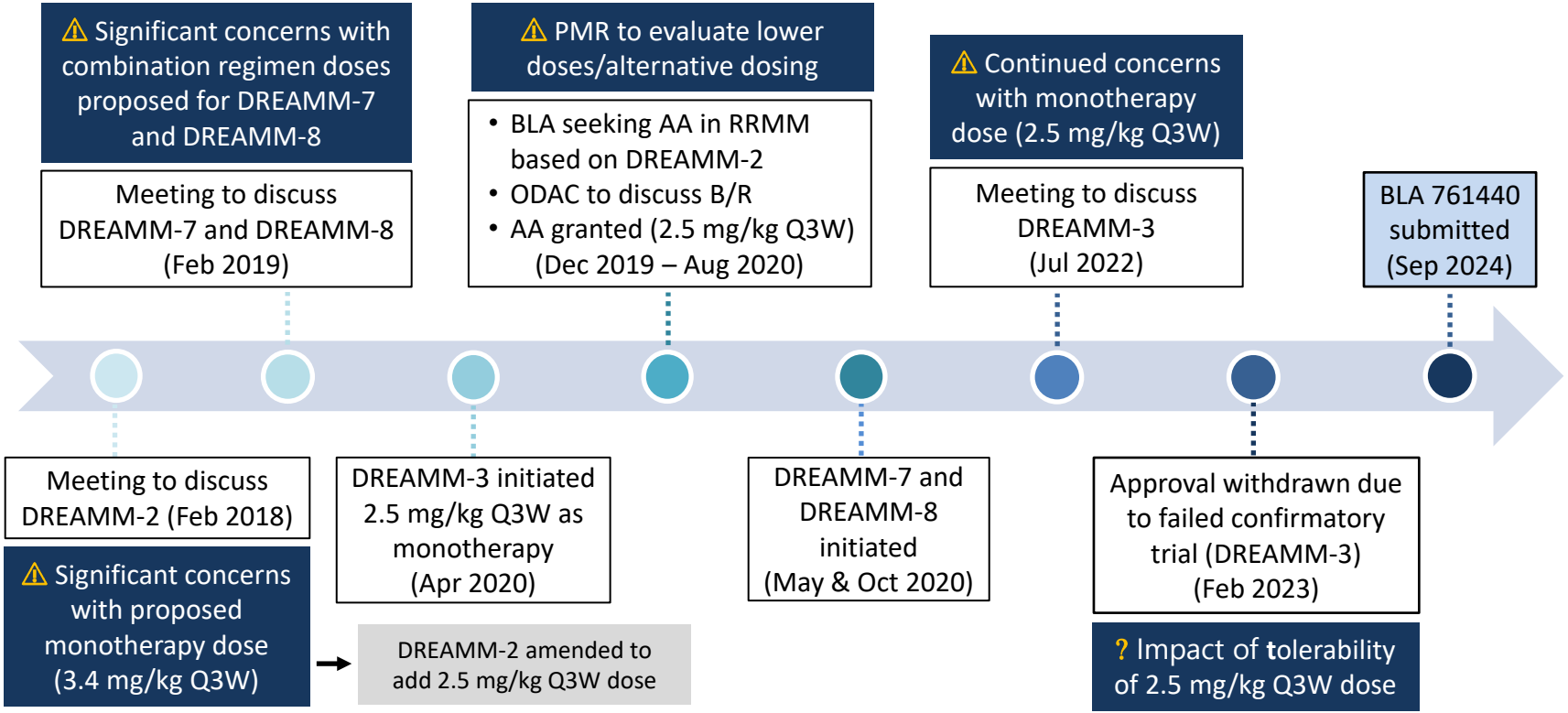
DREAMM-8 (BPd): Starting dosage 2.5 mg/kg on Cycle 1 Day 1 → 1.9 mg/kg Q4W from Cycle 2+

By Cycle 3, more than 50% of patients were not receiving the intended dose

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; BPd=belantamab mafodotin, pomalidomide, dexamethasone; Q#W=every # weeks; Discont=discontinuation

Source: FDA Analysis

Dosing Concerns Throughout Development



Abbreviations: Q3W=every 3 weeks; BLA=Biologic Licensing Application; AA=Accelerated Approval; ODAC=Oncologic Drugs Advisory Committee; B/R=benefit-risk; PMR=Post-Marketing Requirement

Source: FDA

Limited Dose-Exploration to Support Dosages in DREAMM-7 and DREAMM-8

Dose-Finding for DREAMM-7

DREAMM-6 (Arm B): Dose-exploration for BVd

DREAMM-6 ARM B	1.9 mg/kg	2.5 mg/kg		3.4 mg/kg
	Q3W N=12	Q3W† N=18	Q6W N=12	Q3W N=16
Overall response rate (ORR)	10 (83%)	14 (78%)	9 (75%)	11 (69%)
Grade ≥2 corneal AE (GSK scale)*				
Dose interruption due to corneal AE				
Dose reduction due to corneal AE				

*GSK scale was an earlier version of the KVA scale
†2.5 mg/kg Q3W dosing regimen was selected for DREAMM-7

- Response rates were comparable across the dose levels and dosing schedules
- Small number of patients in each dose cohort

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; Q#W=every # weeks; AE=adverse event

Source: DREAMM-6 Clinical Study Report

Dose-Finding for DREAMM-7

DREAMM-6 ARM B (BVd)	1.9 mg/kg	2.5 mg/kg		3.4 mg/kg
	Q3W N=12	Q3W† N=18	Q6W N=12	Q3W N=16
Overall response rate (ORR)	10 (83%)	14 (78%)	9 (75%)	11 (69%)
Grade ≥2 corneal AE (GSK scale)*	10 (83%)	18 (100%)		16 (100%)
Dose interruption due to corneal AE	9 (75%)	15 (83%)		15 (94%)
Dose reduction due to corneal AE	0	14 (78%)		7 (44%)

*GSK scale was an earlier version of the KVA scale
†2.5 mg/kg Q3W dosing regimen was selected for DREAMM-7

Fewer dose modifications occurred at the lower dose level among Q3W dosing regimens

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; Q#W=every # weeks; AE=adverse event

Source: DREAMM-6 Clinical Study Report

Dose-Finding for DREAMM-7

DREAMM-6 ARM B (BVd)	1.9 mg/kg		2.5 mg/kg		3.4 mg/kg
	Q3W N=12	Q6W N=12	Q3W† N=18	Q6W N=12	Q3WΔ N=16
Overall response rate (ORR)	10 (83%)	6 (50%)	14 (78%)	9 (75%)	11 (69%)
Grade ≥2 corneal AE (GSK scale)*	10 (83%)	8 (67%)	18 (100%)	12 (100%)	16 (100%)
Dose interruption due to corneal AE	9 (75%)	7 (58%)	15 (83%)	10 (83%)	15 (94%)
Dose reduction due to corneal AE	0	0	14 (78%)	3 (25%)	7 (44%)

*GSK scale was an earlier version of the KVA scale
†2.5 mg/kg Q3W dosing regimen was selected for DREAMM-7
ΔQ6W interval not explored due to 3.4 mg/kg dose being determined too high for further exploration

- Lower incidence of Grade ≥2 corneal AEs and fewer dose modifications at the longer dosing interval (Q6W)
- **Lower dose** with **longer dosing interval** may improve safety while maintaining ORR

Abbreviations: BVd=belantamab mafodotin, bortezomib, dexamethasone; Q#W=every # weeks; AE=adverse event

Source: DREAMM-6 Clinical Study Report

Dose-Finding for DREAMM-8

- ALGONQUIN (BPd):
  - 1.92, 2.5, or 3.4 mg/kg at Q4W, Q8W, and Q12W
  - **Small number of patients** in each cohort (N=5-12/arm)
  - Fewer missed doses, and higher relative dose intensity with **lower doses** and **longer intervals**
  - Similar response rates across the dosages

- **2.5 mg/kg Cycle 1 Day 1 → 1.9 mg/kg Q4W from Cycle 2+** dosing regimen was selected for DREAMM-8

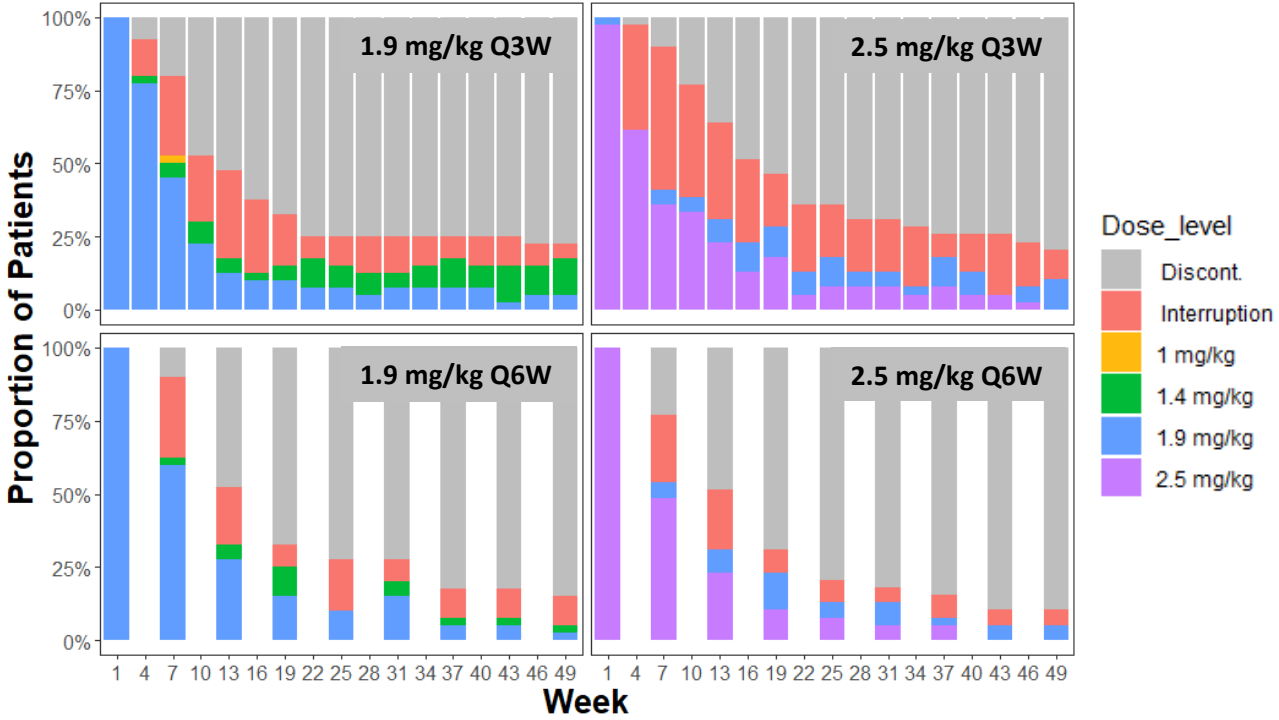
FDA did not agree with the proposed dosage and recommended evaluating more patients at lower dosages in the combination trials

Abbreviations: BPd=belantamab mafodotin, pomalidomide, dexamethasone; Q#W=every # weeks

Source: End-of-Phase 2 Meeting (Feb 2019)

DREAMM-14 PMR Study

Belantamab Mafodotin Monotherapy



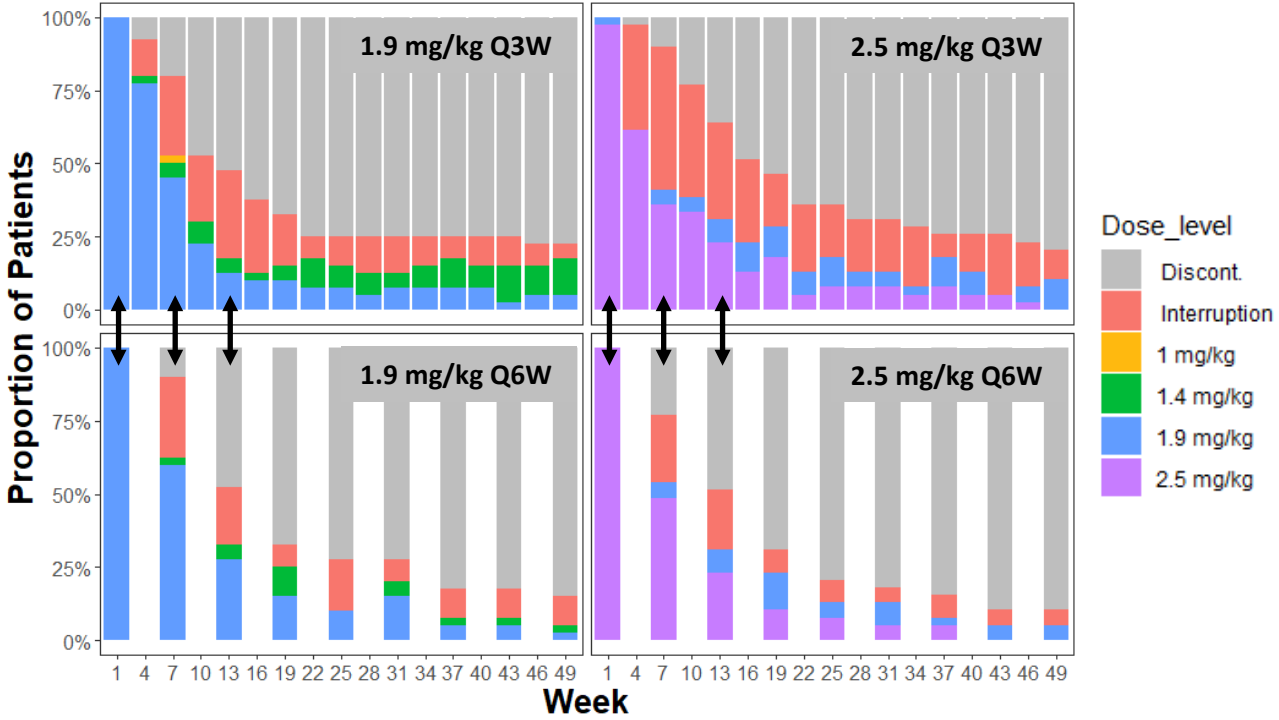
Fewer dose modifications with **lower dose of 1.9 mg/kg**

Abbreviations: PMR=post-marketing requirement; Q#W=every # weeks

Source: FDA Analysis

DREAMM-14 PMR Study

Belantamab Mafodotin Monotherapy



Fewer dose modifications with **lower dose/longer dosing interval**

Abbreviations: PMR=post-marketing requirement; Q#W=every # weeks

Source: FDA Analysis

DREAMM-14 PMR Study

Belantamab Mafodotin Monotherapy

DREAMM-14	1.9 mg/kg		2.5 mg/kg	
	Q3W N=40	Q6W N=40	Q3W N=40	Q6W N=40
ORR (95% CI)	25% (12.7, 41.2)	25% (12.7, 41.2)	33% (18.6, 49.1)	25% (12.7, 41.2)
Grade ≥ 2 KVA (GSK)	40%	38%	64%	44%
Dose interruption/delay – KVA (GSK)	35%	33%	59%	28%
$C_{avg,42day}$ (ADC)* (µg/mL)	5.8 (56%)	3.8 (38%)	7.3 (48%)	4.6 (50%)
C_{max} (ADC)* (µg/mL)	34.8 (26%)	33.4 (19%)	46.3 (23%)	42.4 (26%)

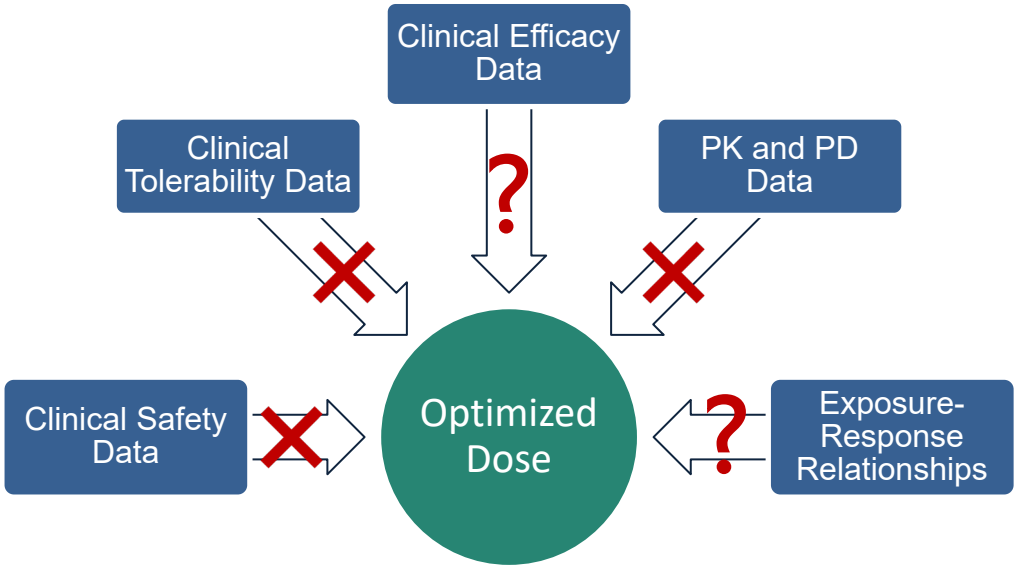
*The exposure parameters are expressed as geometric mean (%CV)

- Similar efficacy across the doses and exposures
- Lower incidence of grade ≥2 corneal adverse events and dose-modifications at lower dose levels and exposures

Abbreviations: PMR=post-marketing requirement; Q#W=every # weeks; ORR=overall response rate; CI=confidence interval; KVA=keratopathy and visual acuity; GSK=GlaxoSmithKline; C=concentration; ADC=antibody-drug-conjugate

Source: DREAMM-14 Clinical Study Report; FDA analysis

Summary: Uncertainty Regarding Proposed Dosages



- Safety and tolerability data suggest that current dosages may not be optimized
- Efficacy may be maintained at lower doses/less frequent dosing intervals

Abbreviations: PK=pharmacokinetics; PD=pharmacodynamics

Source: FDA

Benefit-Risk Considerations: DREAMM-7

Benefit	DREAMM-7 met the primary endpoint of progression-free survival (PFS)
	DREAMM-7 showed a statistically significant improvement in overall survival (OS)
Risk	Ocular toxicity: • Unique toxicity not seen with other therapies for MM • High rates of KVA events, including high-grade events, frequent recurrences, and unresolved events
	Uncertainty regarding proposed dosage: • Poor tolerability; high rates of dose modifications • Limited dose exploration; same dose as prior monotherapy regimen • Available data suggest improved tolerability with lower doses and longer dosing intervals • Significant challenges with post-approval dose optimization
	Applicability to U.S. patient population: • Questionable relevance of DVd control arm; low U.S. enrollment

Abbreviations: MM=multiple myeloma; KVA=keratopathy and visual acuity; DVd=daratumumab, bortezomib, dexamethasone

Benefit-Risk Considerations: DREAMM-8

Benefit	DREAMM-8 met the primary endpoint of progression-free survival (PFS)
Risk	Ocular toxicity: • Unique toxicity not seen with other therapies for MM • High rates of KVA events, including high-grade events, frequent recurrences, and unresolved events • Similar incidence/severity compared to DREAMM-7 despite lower dose
	Uncertainty regarding proposed dosage: • Poor tolerability; high rates of dose modifications despite lower dose • Limited dose exploration; same starting dose as prior monotherapy regimen • Available data suggest improved tolerability with lower doses and longer dosing intervals • Significant challenges with post-approval dose optimization
	Applicability to U.S. patient population: • Questionable relevance of PVd control arm; not an approved regimen in the U.S.

Abbreviations: MM=multiple myeloma; KVA=keratopathy and visual acuity; PVd=pomalidomide, bortezomib, dexamethasone

Discussion Topic

Discuss whether appropriate dosages of belantamab mafodotin have been identified for the proposed patient population with relapsed or refractory multiple myeloma

Voting Questions

1. Is the overall benefit-risk of belantamab mafodotin in combination with bortezomib and dexamethasone favorable at the proposed dosage in the proposed patient population?

2. Is the overall benefit-risk of belantamab mafodotin in combination with pomalidomide and dexamethasone favorable at the proposed dosage in the proposed patient population?


FDA
U.S. FOOD & DRUG
ADMINISTRATION