Inside the Issue: Managing Ocular Toxicities Associated with Antibody-Drug Conjugates and Other Cancer Therapies

A CME/MOC-Accredited Live Webinar

Thursday, July 17, 2025
5:00 PM – 6:00 PM ET

Faculty

Rebecca A Dent, MD, MSc
Hans Lee, MD
Neel Pasricha, MD
Tiffany A Richards, PhD, ANP-BC, AOCNP

Moderator

Neil Love, MD

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Senior Consultant
National Cancer Centre Singapore
Singapore

Hans Lee, MD
Director, Multiple Myeloma Research
Sarah Cannon Research Institute
Nashville, Tennessee

Neel Pasricha, MD
Assistant Professor of Ophthalmology
University of California, San Francisco
San Francisco, California

Tiffany A Richards, PhD, ANP-BC, AOCNP
Nurse Practitioner
Department of Lymphoma/Myeloma
The University of Texas
MD Anderson Cancer Center
Houston, Texas

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, and GSK.

Dr Love — Disclosures

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Research To Practice CME Planning Committee Members, Staff and Reviewers

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Prof Dent — Disclosures

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Dr Lee — Disclosures

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Data and Safety Monitoring Boards/ Committees	Allogene Therapeutics, Takeda Pharmaceuticals USA Inc

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Dr Pasricha — Disclosures

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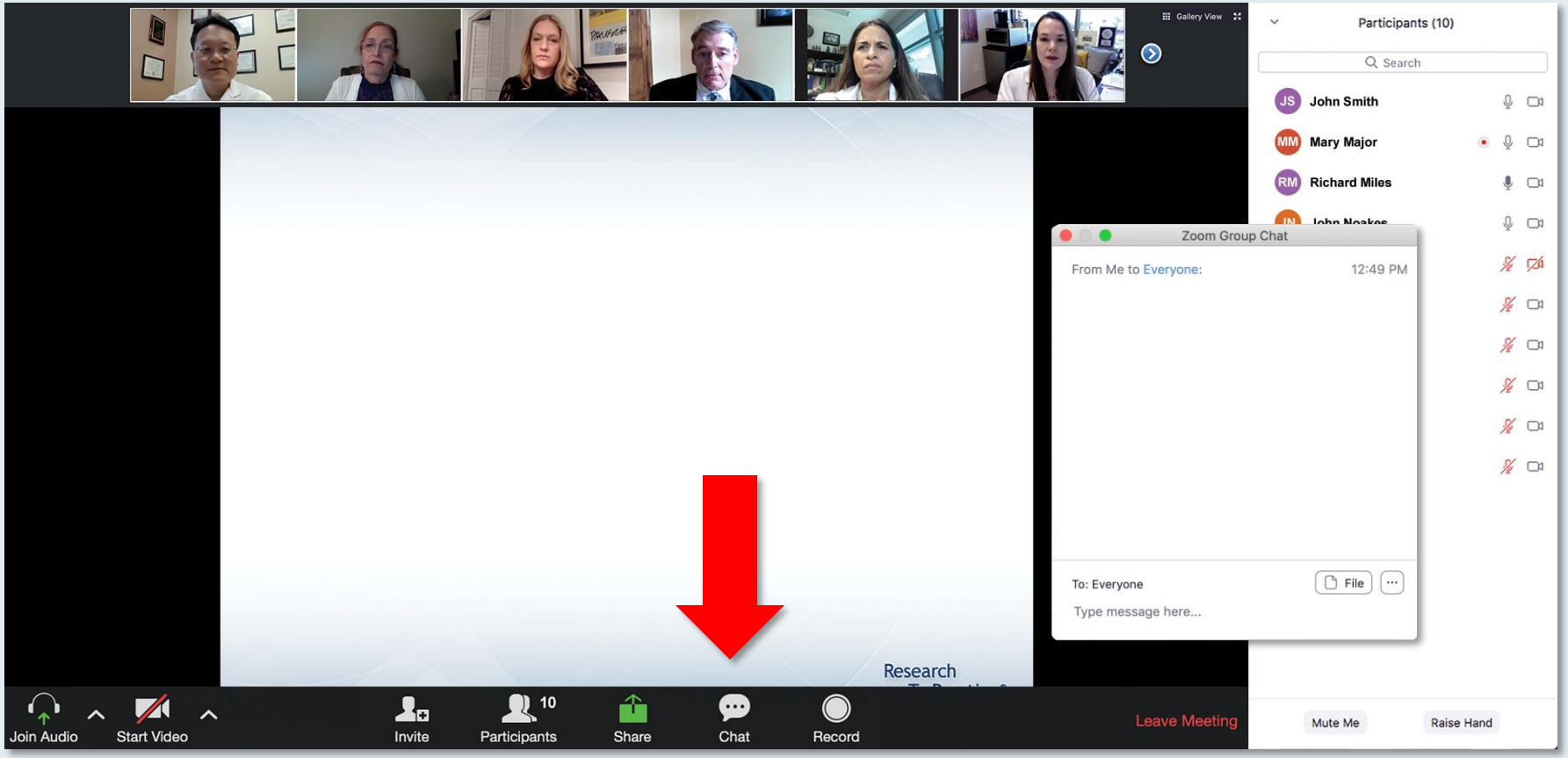

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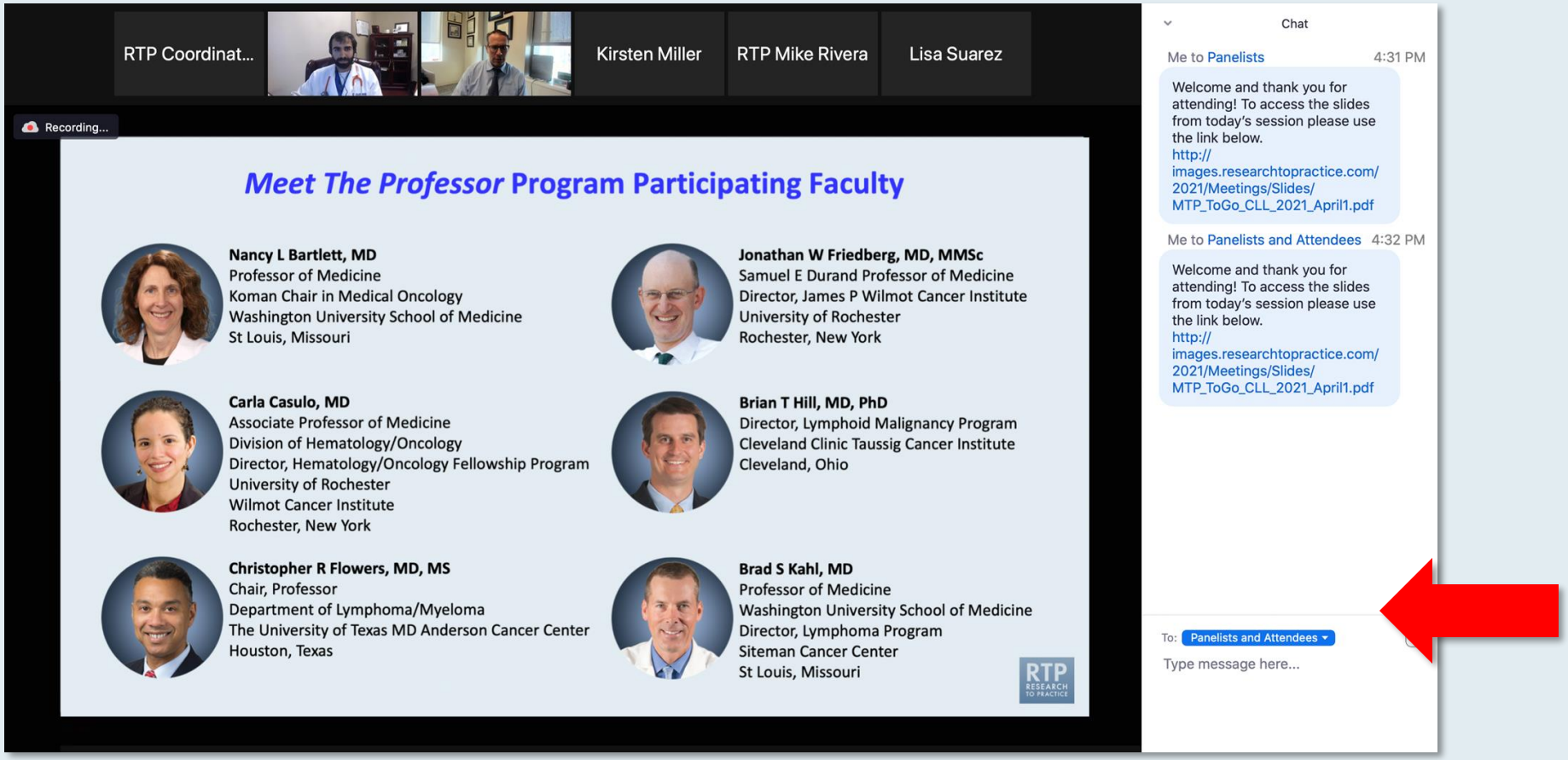

Drag the white line above the submission box up to create more space for your message.

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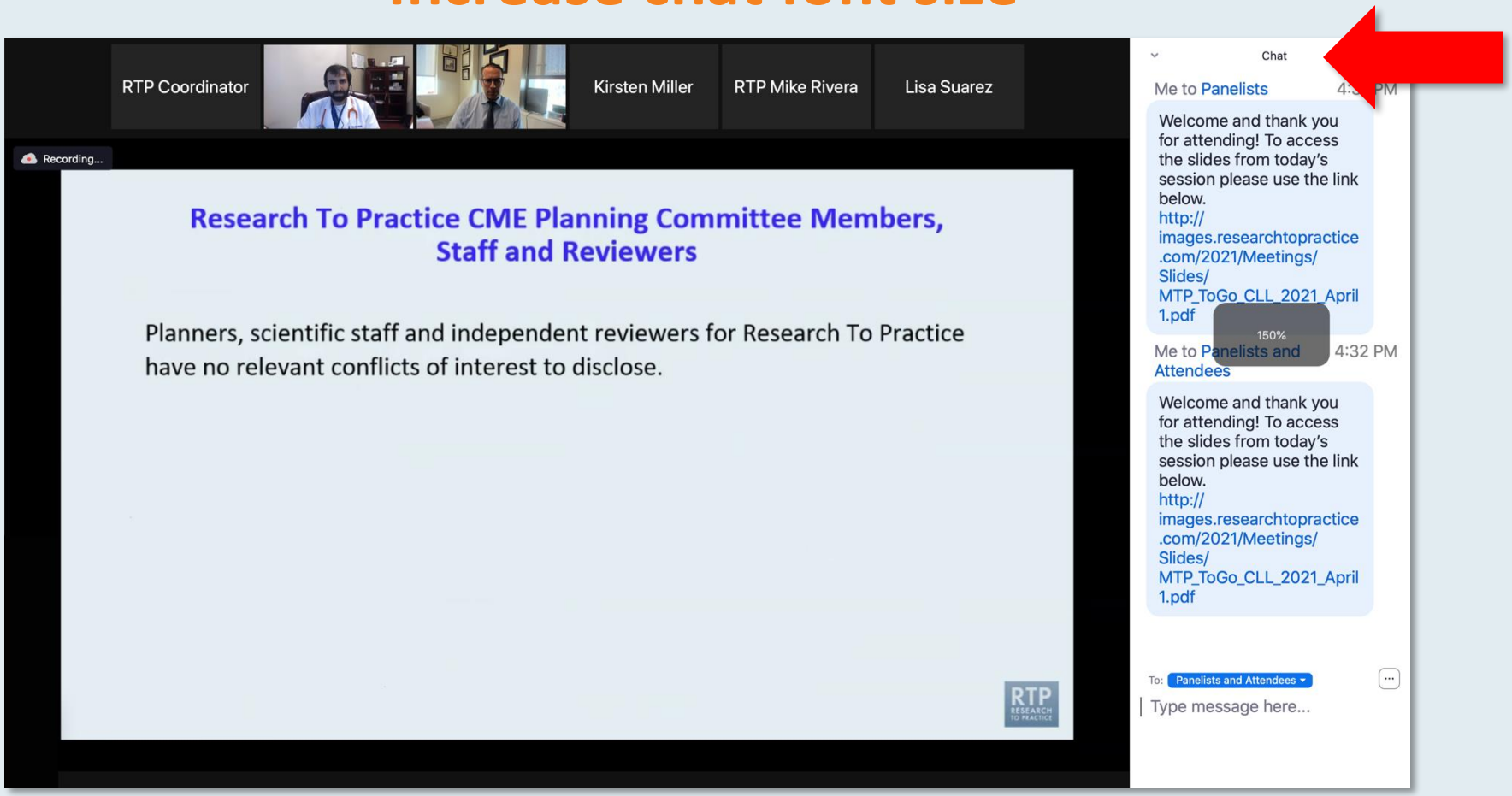

Press Command (for Mac) or Control (for PC) and the + symbol.
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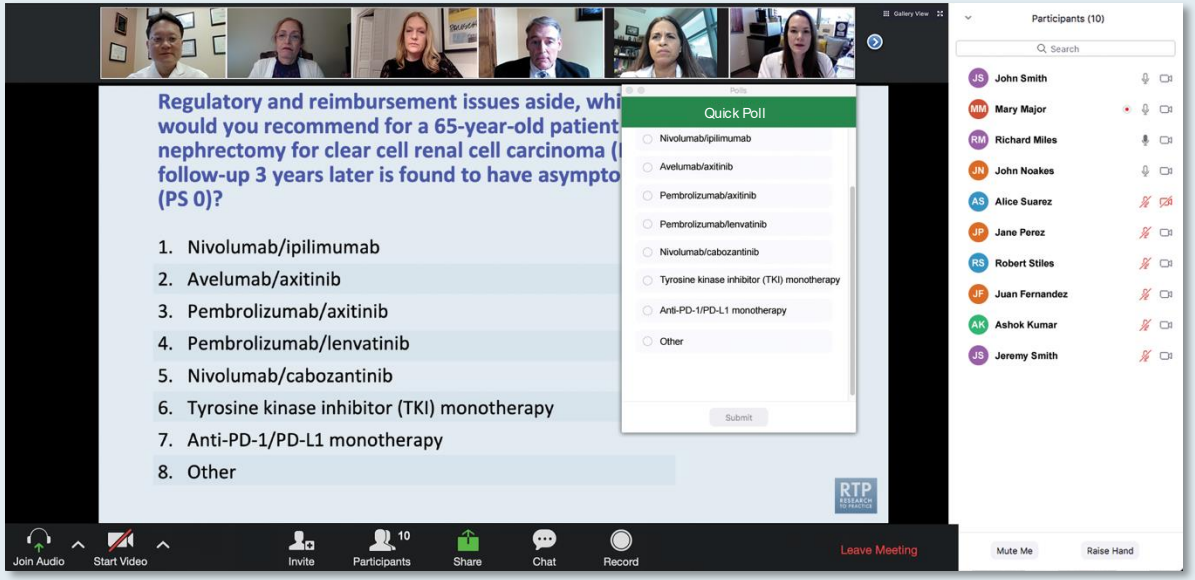

Multiple Myeloma — Proceedings from a Webinar Held in Conjunction with the 2025 ASCO Annual Meeting

DR AJAY K NOOKA
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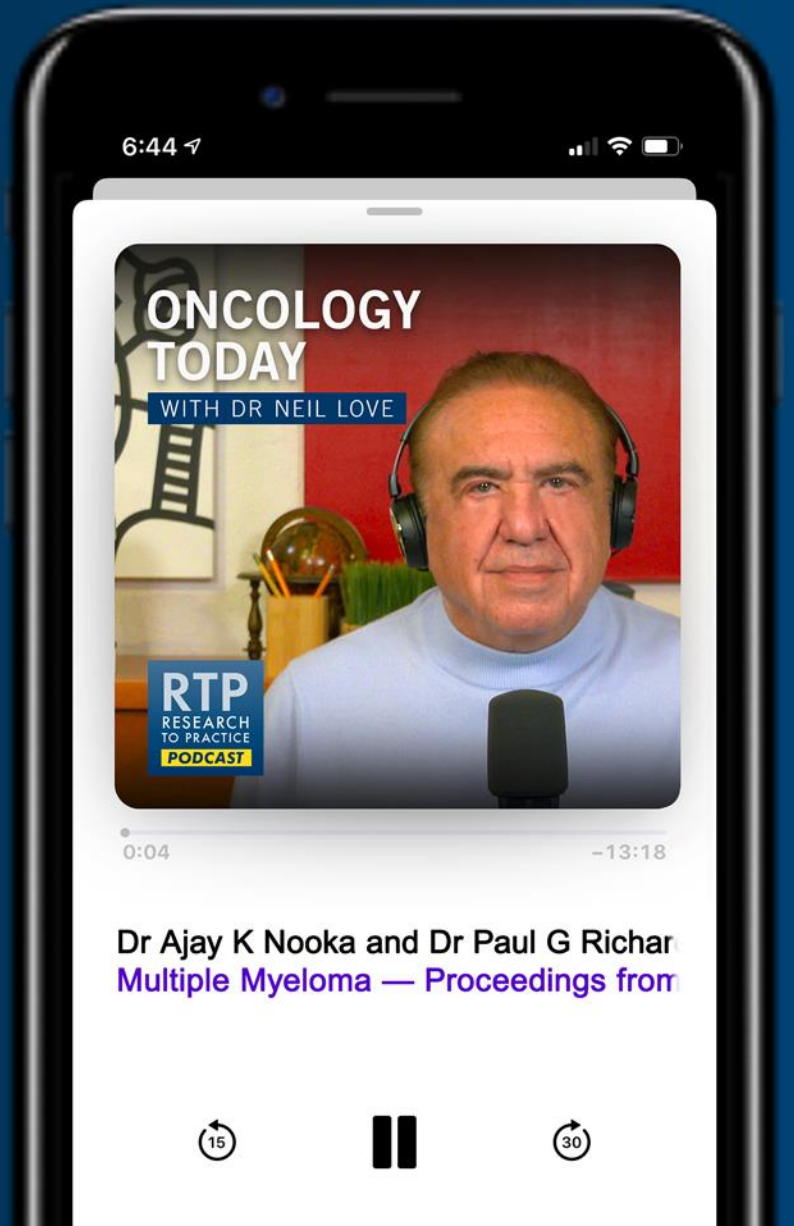
DR PAUL G RICHARDSON
DANA-FARBER CANCER INSTITUTE



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Cancer Q&A: Addressing Common Questions Posed by Patients with Relapsed/Refractory Multiple Myeloma

A Webinar Series for Clinicians and Patients,
Developed in Partnership with Cancer*Care*®

Patients	Clinicians
Wednesday, July 23, 2025	**Thursday, August 7, 2025**
6:00 PM – 7:00 PM ET	**5:00 PM – 6:00 PM ET**

Faculty

Natalie S Callander, MD
Sagar Lonial, MD, FACP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Knowledge and Practice Gaps in the Community — Optimizing the Use of Oral Selective Estrogen Receptor Degraders for Metastatic Breast Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, July 29, 2025

5:00 PM – 6:00 PM ET

Faculty

Komal Jhaveri, MD, FACP

Virginia Kaklamani, MD, DSc

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Practical Perspectives: Experts Review
Actual Cases of Patients with Biliary Tract Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, August 6, 2025
5:00 PM – 6:00 PM ET

Faculty

Haley Ellis, MD
James J Harding, MD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Selection and Sequencing of Therapy for Metastatic Triple-Negative Breast Cancer

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SOHO SYMPOSIUM SERIES

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Follicular Lymphoma

Friday, September 5, 2025

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(12:47 PM – 1:47 PM ET)

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Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us.

Information on how to obtain CME and ABIM MOC credit will be provided at the conclusion of the activity in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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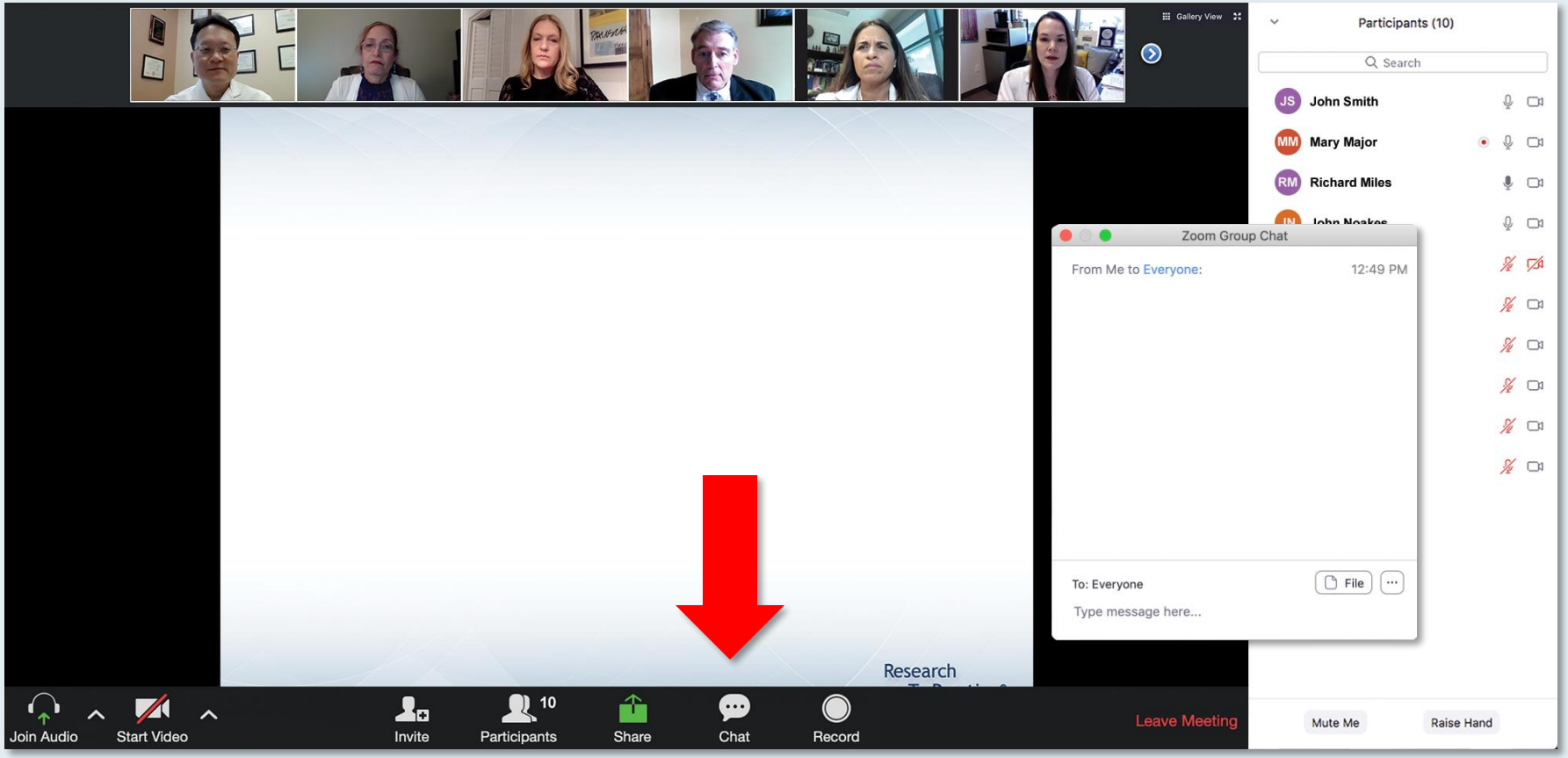

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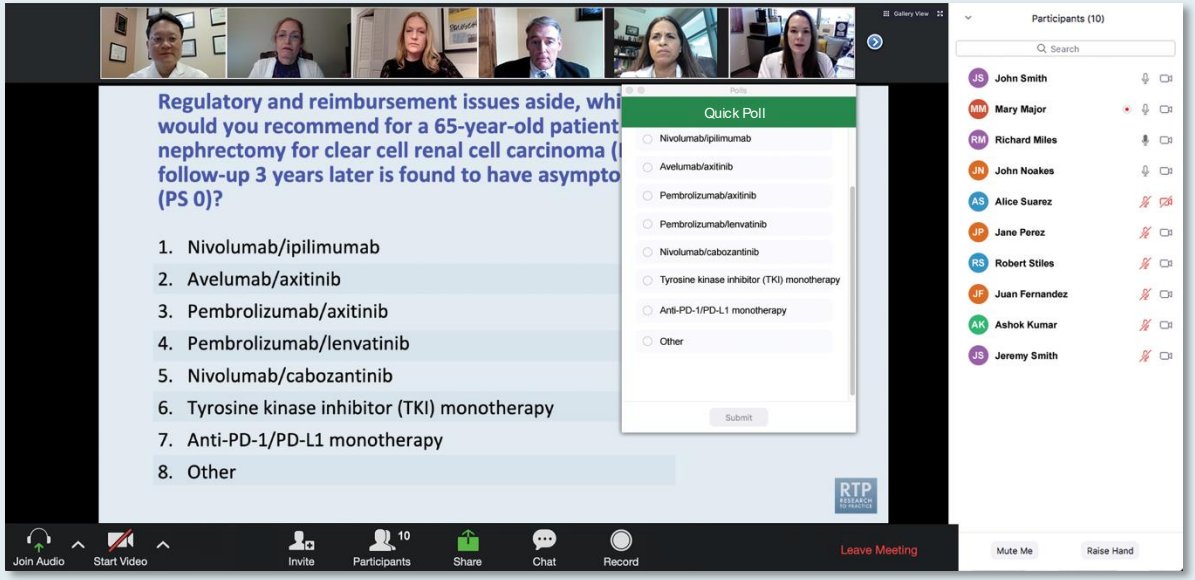

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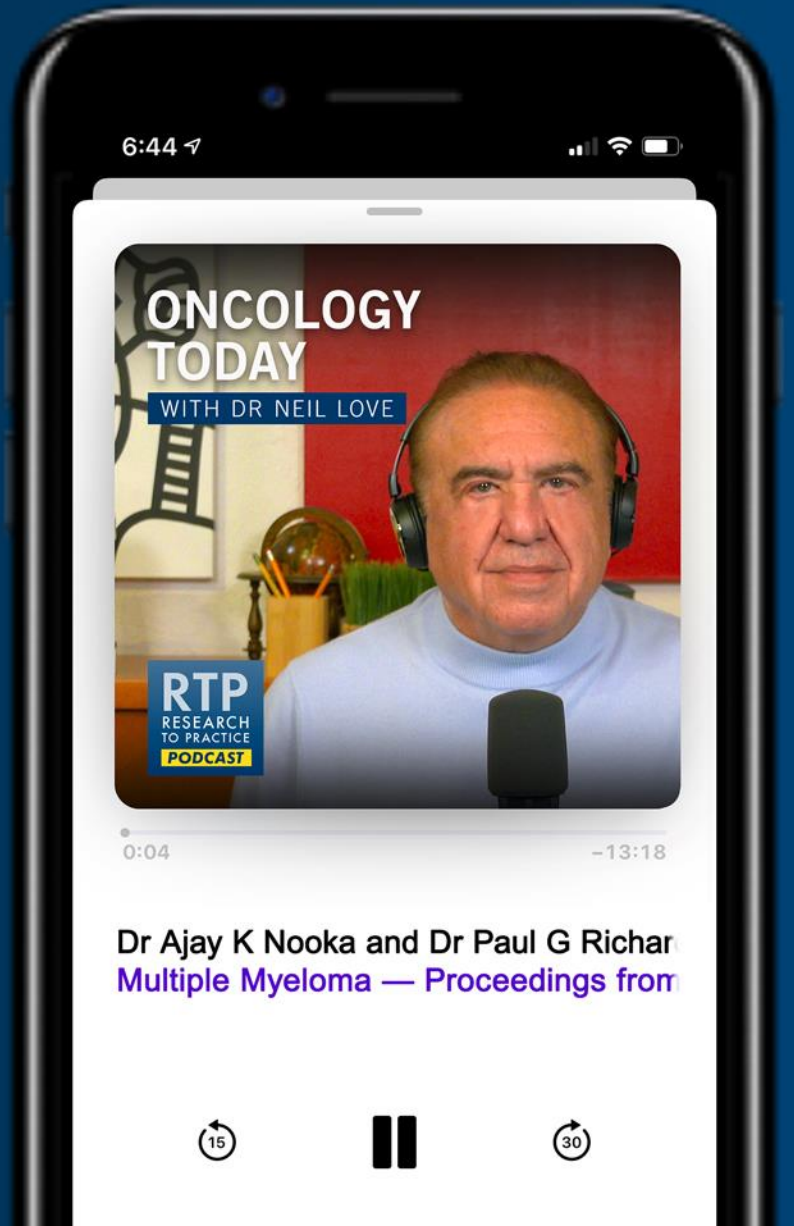

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Agenda

Introduction: The Patient Experience

Module 1: Managing Ocular Toxicities Associated with Antibody-Drug Conjugates and Other Cancer Therapies — Dr Pasricha

Module 2: Ocular Toxicities in Multiple Myeloma

Module 3: Ocular Toxicities in Breast Cancer

Agenda

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FDA Flags Eye Safety Concerns with Belantamab Mafodotin Ahead of Advisory Committee Meeting

Press Release: July 15, 2025

“A new FDA briefing document indicates the [manufacturer] may need to address some of the agency's lingering concerns in order to reintroduce [belantamab mafodotin] in the U.S. market.

In a document posted ahead of the July 17 meeting of the Oncologic Drugs Advisory Committee (ODAC), FDA reviewers flagged ‘high rates of ocular toxicity’ and ‘uncertainty regarding the proposed dosages’ as key issues for discussion.

On the ocular toxicity issue, FDA reviewers said the majority of patients in [the] pivotal DREAMM-7 and DREAMM-8 trials experienced Keratopathy and Visual Acuity (KVA) events. KVA events at any grade occurred in 92% and 93% of patients in the trials, respectively, while grade 3-4 events happened in 77% and 78% of patients in the studies.

In addition, treatment with [belantamab] was ‘associated with severe ocular toxicities, including corneal ulcers and clinically significant decline in visual acuity, including severe vision loss,’ the document reads.”

https://www.fiercepharma.com/pharma/gsk-eyes-blenreps-us-return-fda-flags-eye-safety-concerns-ahead-advisory-committee-meeting

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81-Year-Old Man with Recurrent Multiple Myeloma on Belantamab Mafodotin for 3 Years

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Management of Ocular Toxicity in Patients Receiving Belantamab Mafodotin

REBECCA LU, MSN, FNP-C, ASHLEY MORPHEY, RN, MSN, CCRP, FELICIA DIAZ, MSN, APRN, FNP-BC, AOCNP®, JESSICA CHEN, RN, MSN, OCN®, FNP-C, AZADEH RAZMANDI, OD, FAAO, and TIFFANY RICHARDS, PhD, ANP-BC, AOCNP®

J Adv Pract Oncol 2023;14(4):300-6.

Ocular Toxicity Management with Belantamab Mafodotin

Table 1. Dose Modifications for Ocular Toxicities

Grade	Keratopathy findings on cornea	Snellen change	Dose modification
1	Mild superficial keratopathy	Worsening vision by one line	Continue treatment.
2	Moderate superficial keratopathy	Worsening vision by 2–3 lines and not worse than 20/200	Hold treatment until keratopathy returns to grade 1 and visual acuity returns to grade 1. Resume at prior dose.
3	Severe superficial keratopathy	Worsening visual acuity by more than 3 lines	Hold treatment until keratopathy returns to grade 1 and visual acuity returns to grade 1 or better. Reduce dose by one dose level (1.9 mg/kg).
4	Corneal epithelial defect	Visual acuity worse than 20/200	Consider permanent discontinuation. If treatment continues, hold until corneal exam and visual acuity return to baseline. Reduce dose by one dose level.

Note. Information from US Food and Drug Administration (2020b).

Lu R et al. *J Adv Pract Oncol* 2023;14(4):300-6.

Approved Antibody-Drug Conjugates (ADCs) in Oncology

Name	Tumor type	Year approved
Gemtuzumab ozogamicin	Acute myeloid leukemia	2000
Brentuximab vedotin	Hodgkin lymphoma	2011
Trastuzumab emtansine	HER2-positive breast cancer	2013
Inotuzumab ozogamicin	Acute lymphoblastic leukemia	2017
Moxetumomab pasudotox	Hairy cell leukemia	2018
Polatuzumab vedotin	DLBCL	2019
Trastuzumab deruxtecan	HER2-positive metastatic breast cancer	2019
Enfortumab vedotin	Urothelial bladder cancer	2019
Sacituzumab govitecan	Breast cancer	2020
Belantamab mafodotin*	Multiple myeloma	2020
Tisotumab vedotin	Cervical cancer	2021
Loncastuximab tesirine	DLBCL	2021
Mirvetuximab soravtansine	Ovarian cancer	2022
Datopotamab deruxtecan	Breast cancer; EGFR-mutated NSCLC	2025
Telisotuzumab vedotin	NSCLC	2025

* not currently FDA approved

https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

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UCSF School of Medicine

Managing Ocular Toxicities Associated with Antibody-Drug Conjugates (ADCs) and Other Cancer Therapies

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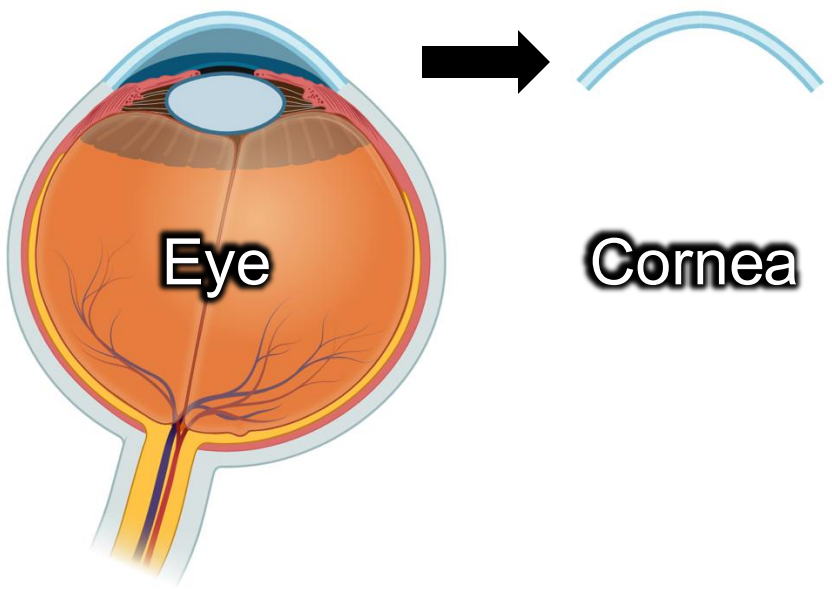
Neel Pasricha, MD
Assistant Professor of Ophthalmology
University of California San Francisco
Francis I. Proctor Foundation

July 17, 2025



Key Takeaway Points

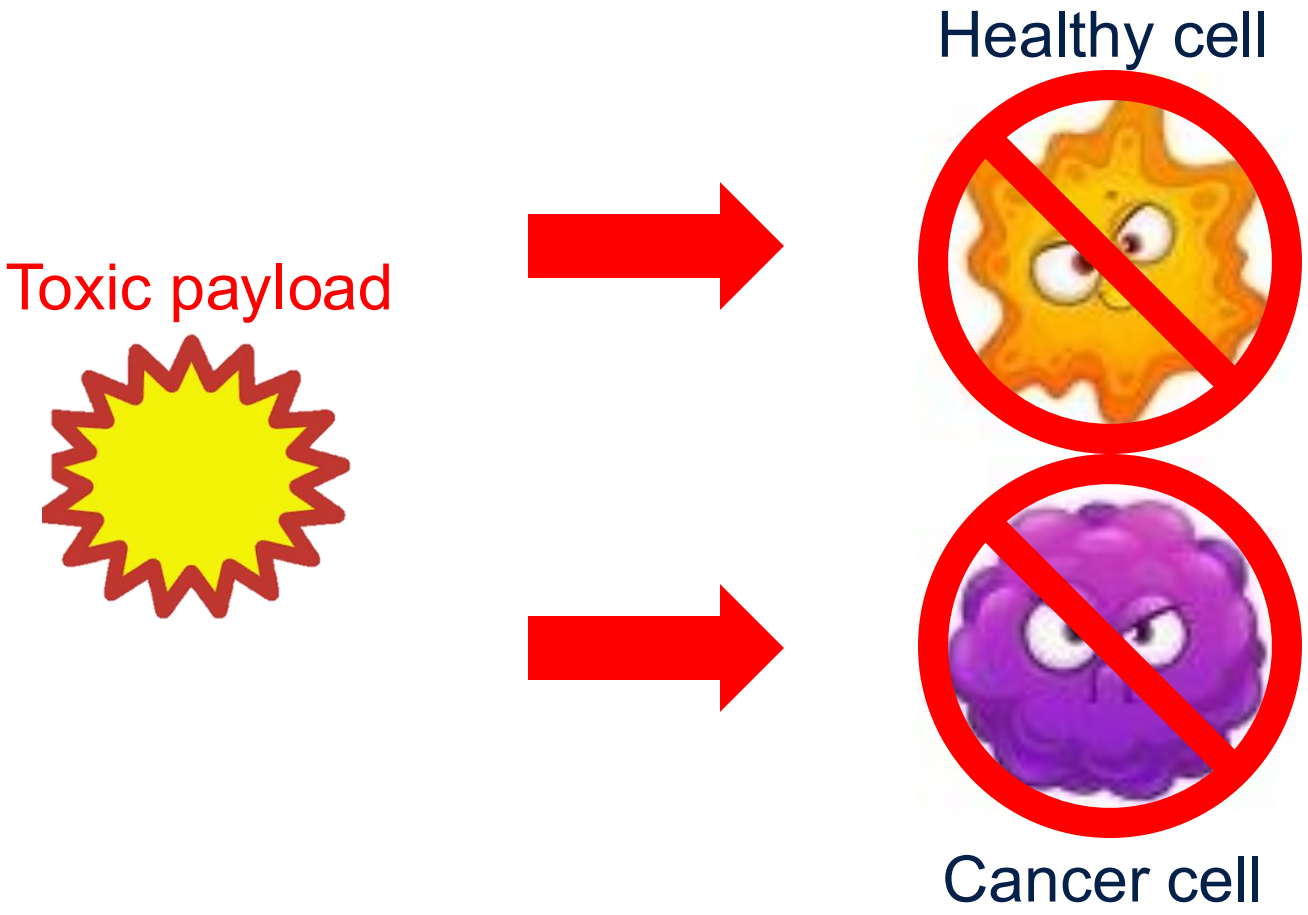
1. Explain ocular adverse events (OAEs) from antibody-drug conjugates (ADCs)
2. Improve grading and screening of cancer therapy-induced OAEs
3. Develop effective preventative therapy for ADC corneal toxicity

Key Takeaway Points

1. **Explain ocular adverse events (OAEs) from antibody-drug conjugates (ADCs)**
2. Improve grading and screening of cancer therapy-induced OAEs
3. Develop effective preventative therapy for ADC corneal toxicity

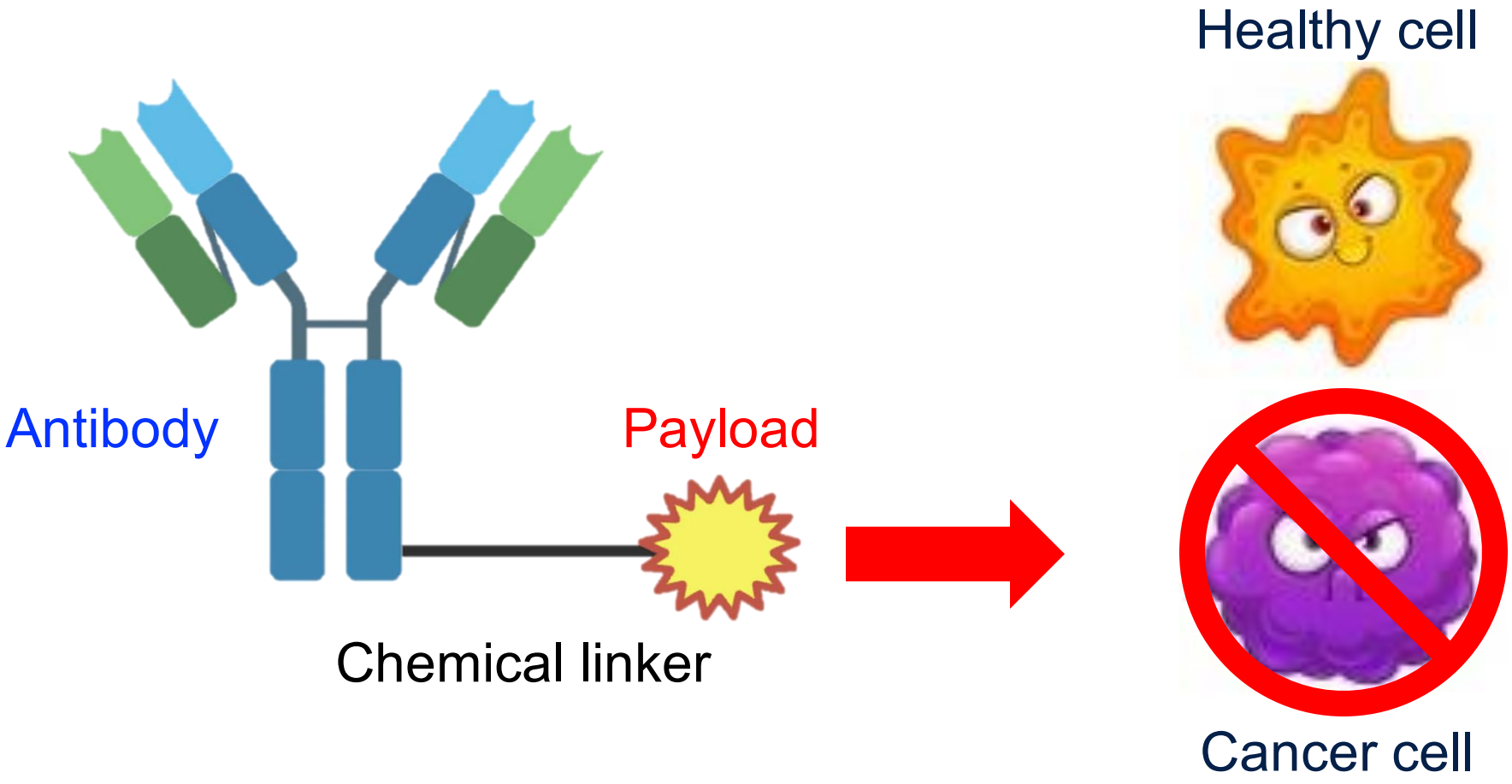
Background: ADCs

Traditional chemotherapies are non-specific



Background: ADCs

Antibody-drug conjugates (ADCs) are targeted cancer therapies

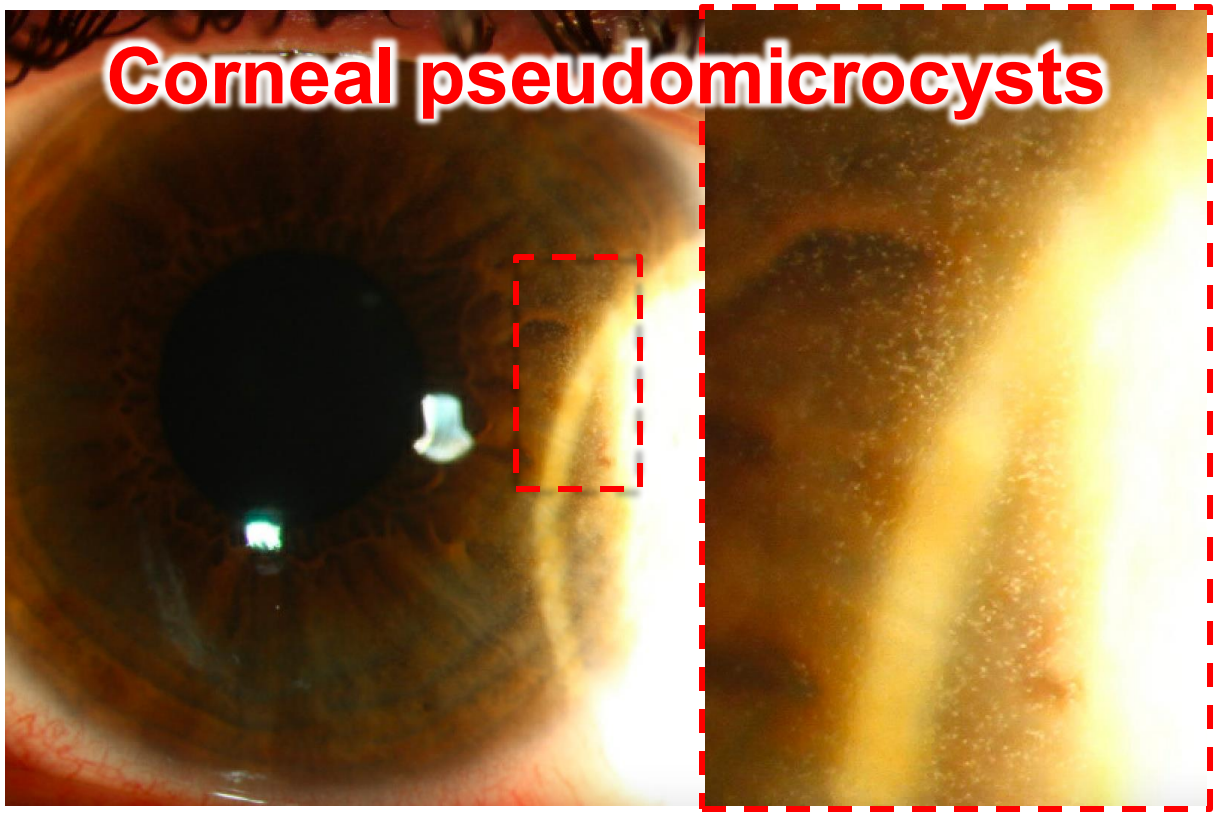


15 FDA-approved

>150 in clinical trials

Background: ADC OAEs

ADC corneal toxicity is a common ocular adverse event (OAE)



- **20%** (3/15*) of ADCs have FDA black box warning for ocular toxicity
- Develop **~3 weeks** after ADC infusion
- Reversible **2 weeks-8 months** after ADC discontinuation
- Causes **eye pain** and **blurry vision**

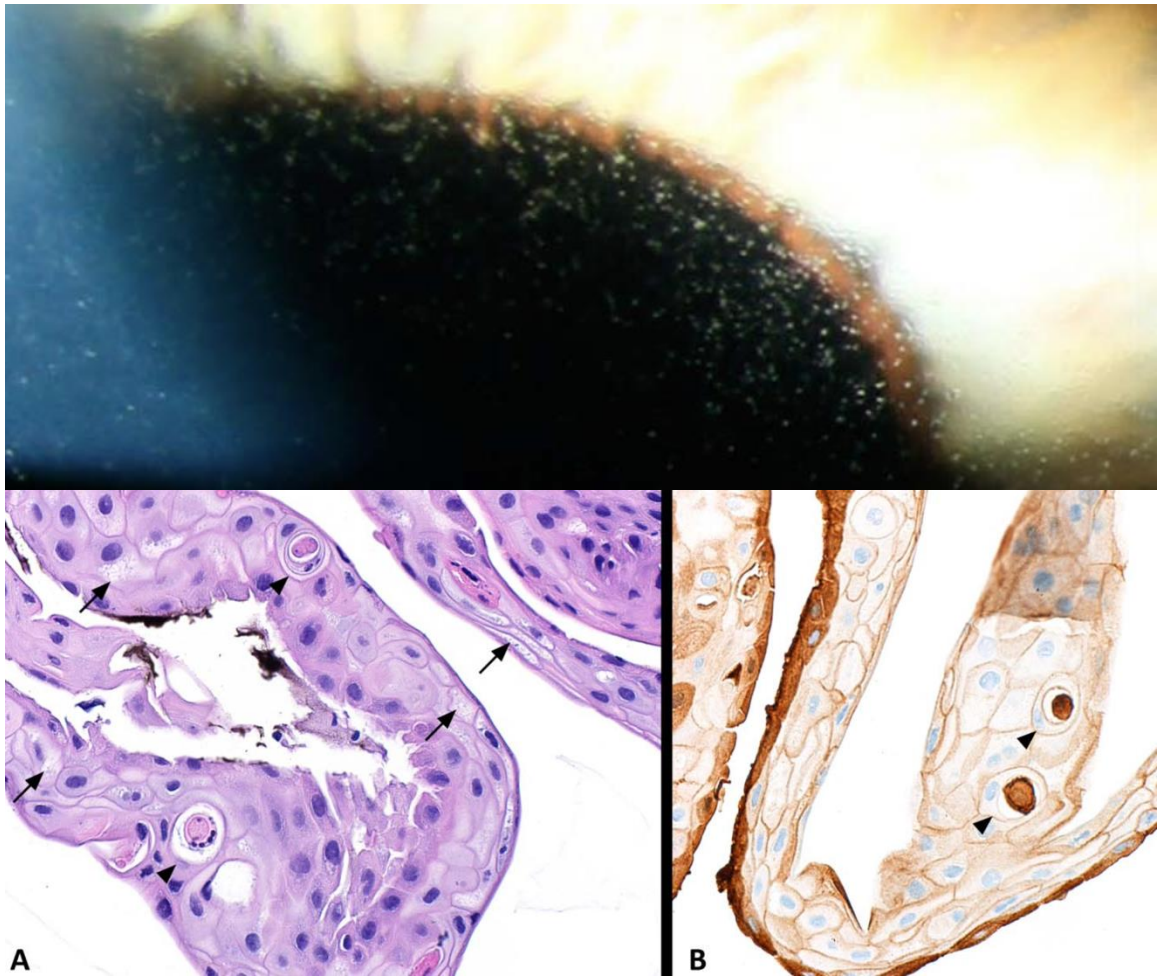
Lindgren ES…**Pasricha ND**. Incidence and Mitigation of Corneal Pseudomicrocysts Induced by Antibody–Drug Conjugates (ADCs). *Curr Ophthalmol Rep*. 2024

Background: ADC OAEs

Corneal pseudomicrocysts = Apoptosis of corneal epithelial cells

H&E: Vacuolar and granular cytoplasm with **apoptosis** in epithelial layers

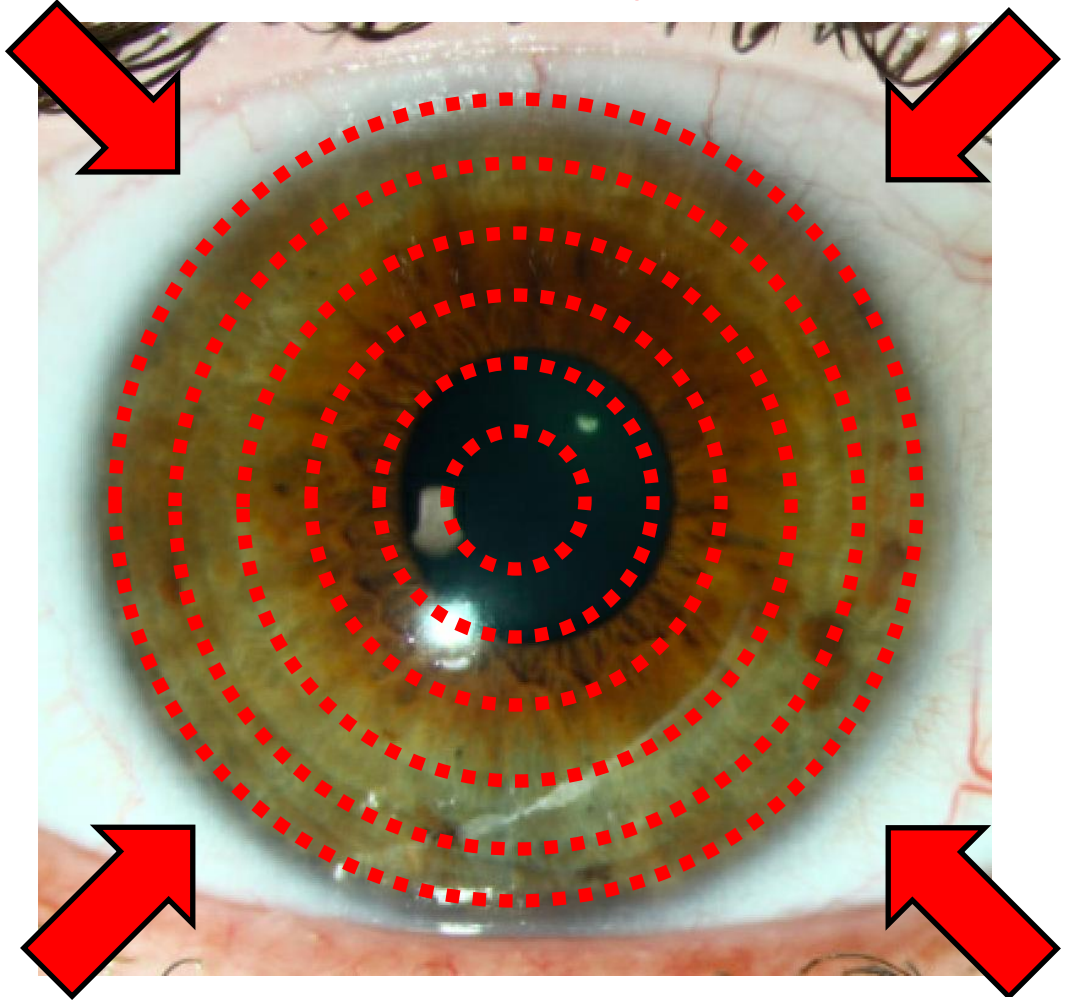
IHC: IgG+ basal epithelial cytoplasm and engulfed **apoptotic** cells

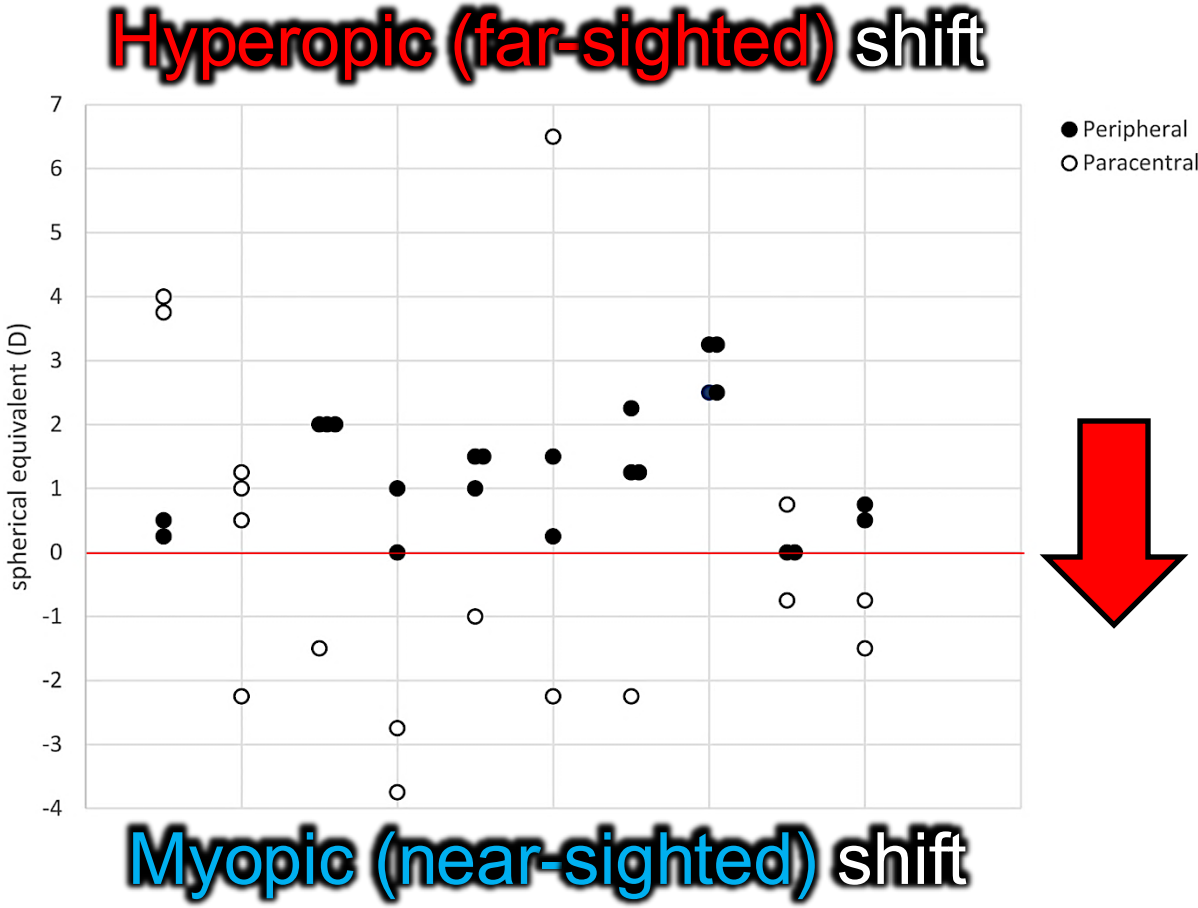


Lee BA et al. Clinical and Histological Characterization of Toxic Keratopathy From Depatuxizumab Mafodotin (ABT-414), an Antibody-Drug Conjugate. *Cornea*. 2021

Background: ADC OAEs

Corneal pseudomicrocysts start peripherally then migrate centrally

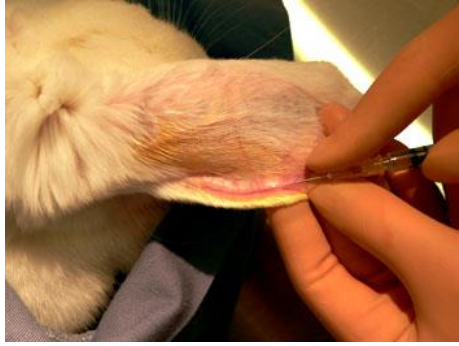




Canestraro J et al. Refractive Shifts and Changes in Corneal Curvature Associated with Antibody-Drug Conjugates. *Cornea*. 2021

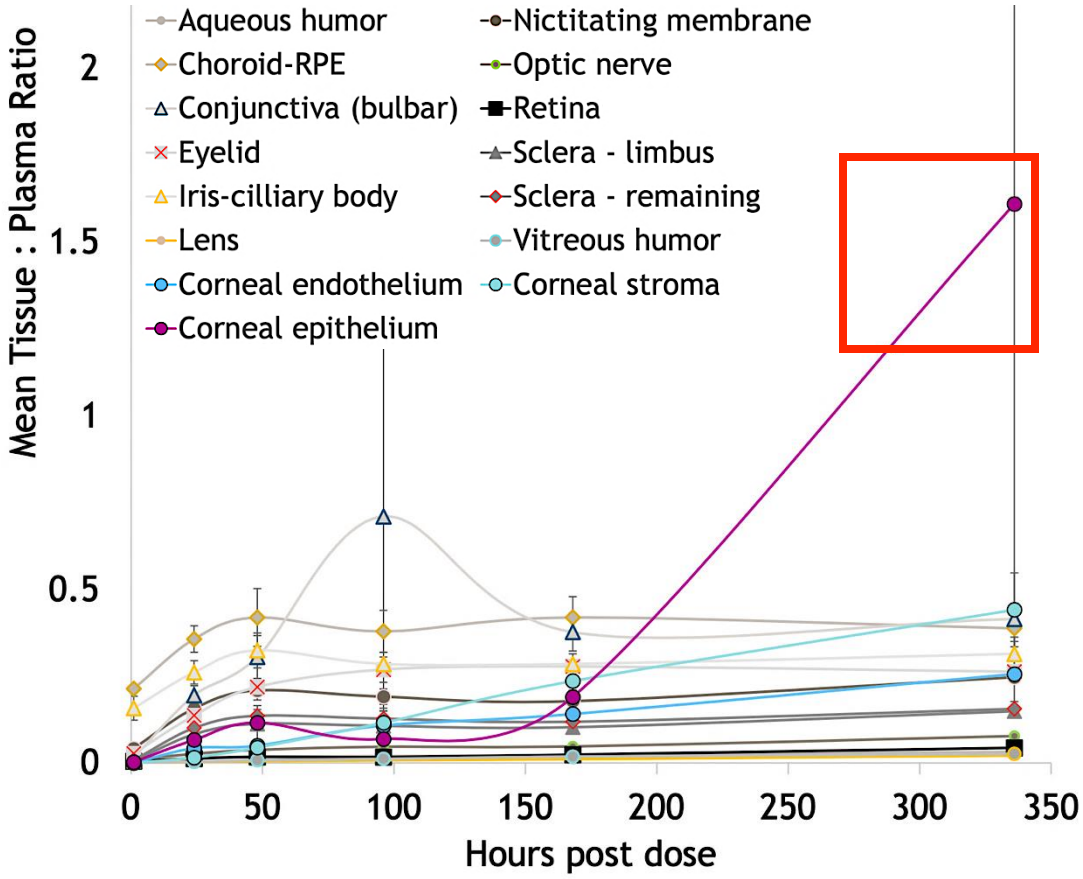
Background: ADC OAEs

ADCs selectively accumulate in the corneal epithelium



- Rabbits administered radiolabeled ADC and ocular tissues collected over 14 days

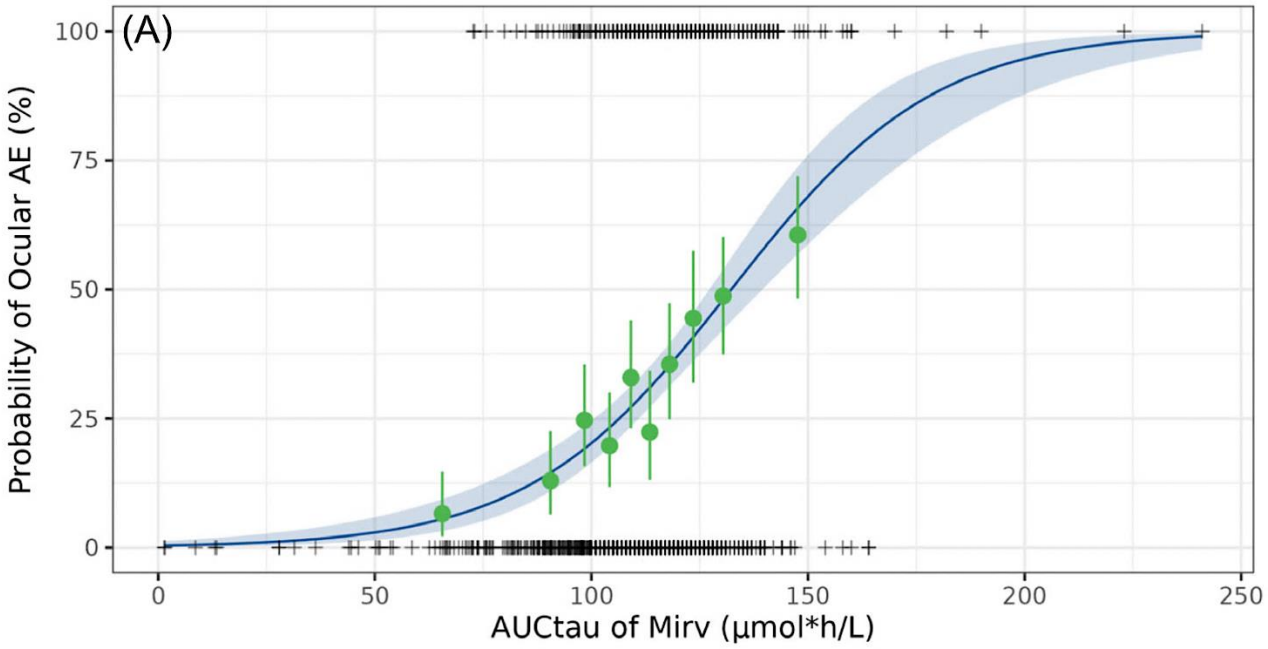
- Results:
  - ADC in ocular tissues (except corneal epithelium) similar to blood/plasma elimination **($T_{1/2}$ = 4.5-7.5 days)**
  - Corneal epithelium:
    - Absorption phase followed by **stable concentration plateau through 14 days**
    - High tissue-to-plasma ratio **(1.6 vs <0.5)**

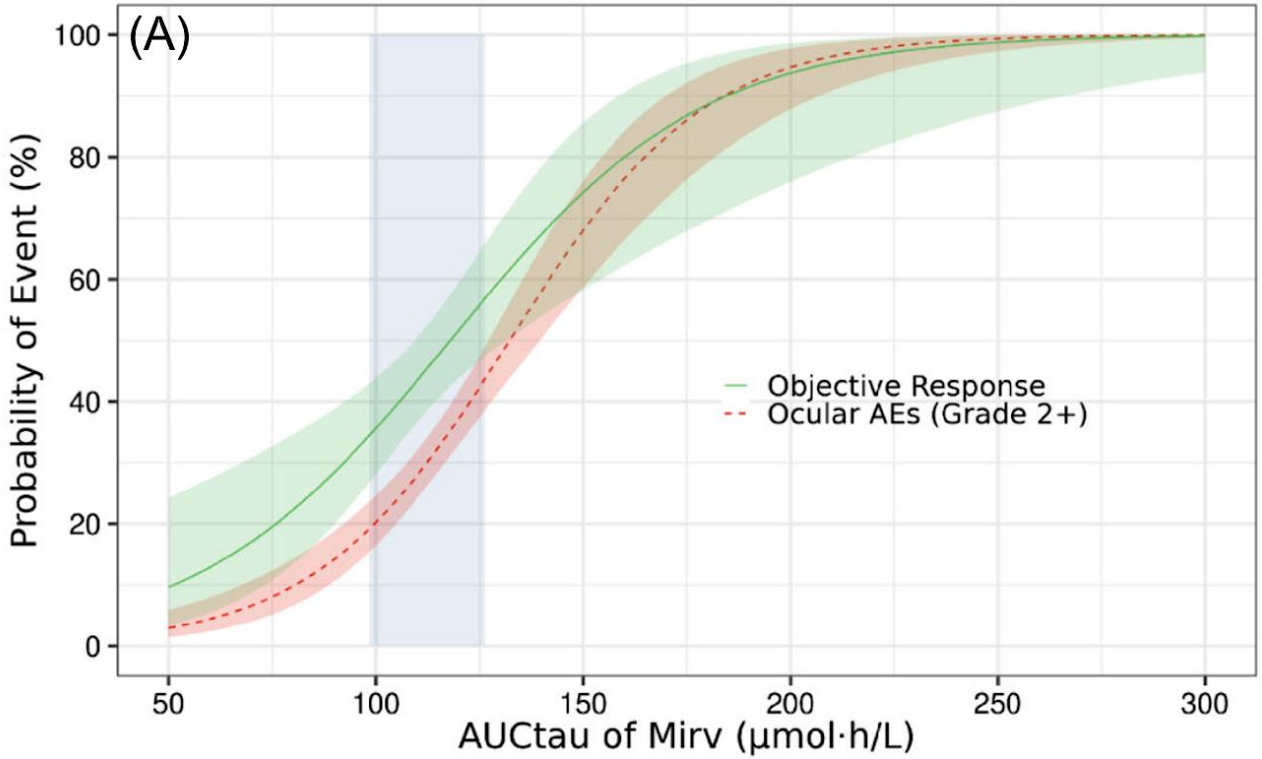


Warbington A et al. Nonclinical ocular toxicity of a maytansinoid payload-antibody drug conjugate: Ocular tissue distribution, lesion pathogenesis, and mitigation. *AACR Annual Meeting*. 2024

Background: ADC OAEs

OAEs can be dose-limiting for ADC efficacy





Tu YP et al. Exposure-response relationships of mirvetuximab soravtansine in patients…*Br J Clin Pharmacol.* 2025

UCSF

Background: ADC OAEs

Off-target toxicity occurs with a wide variety of ADCs

1. Off-target
2. Various linkers
3. Various payloads

ADC	Indication	Antibody	Linker	Payload	DAR	OAE
Belantamab mafodotin	Multiple myeloma	BCMA	Non-cleavable	MMAF	4	71%
Mirvetuximab soravtansine	Ovarian cancer	FRα	Cleavable	DM4	3.5	61%
Tisotumab vedotin	Cervical cancer	Tissue factor	Enzyme-cleavable	MMAE	4	60%
Datopotamab deruxtecan	Breast cancer	TROP2	Cleavable	TOP1i	4	51%
Enfortumab vedotin	Bladder cancer	Nectin-4	Enzyme-cleavable	MMAE	3.8	40%
Trastuzumab deruxtecan	Breast cancer	HER2	Enzyme-cleavable	TOP1i	8	11%
Trastuzumab emtansine	Breast cancer	HER2	Non-cleavable	DM1	3.5	6%

Lindgren ES…**Pasricha ND**. Incidence and Mitigation of Corneal Pseudomicrocysts Induced by Antibody–Drug Conjugates (ADCs). *Curr Ophthalmol Rep*. 2024

Questions?

Background: Prevention Strategies

Current therapies have limited efficacy to prevent ADC corneal toxicity

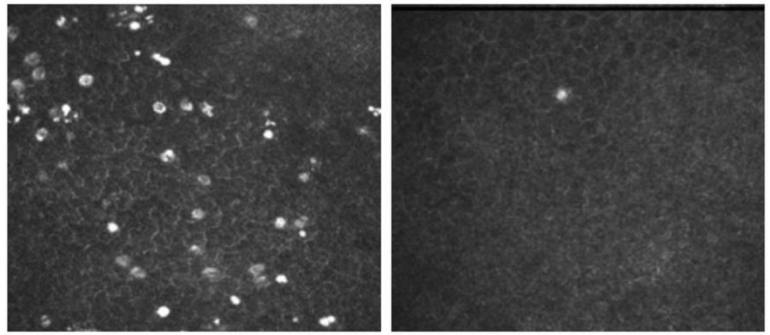
- Occurs in **>75%** of patients on select ADCs despite ocular prophylaxis regimen
- Leads to ADC dose interruptions:
  - Up to **50%** dose delays
  - Up to **35%** dose reductions
  - Up to **25%** discontinuation

Lindgren ES…**Pasricha ND**. Incidence and Mitigation of Corneal Pseudomicrocysts Induced by Antibody–Drug Conjugates (ADCs). *Curr Ophthalmol Rep*. 2024

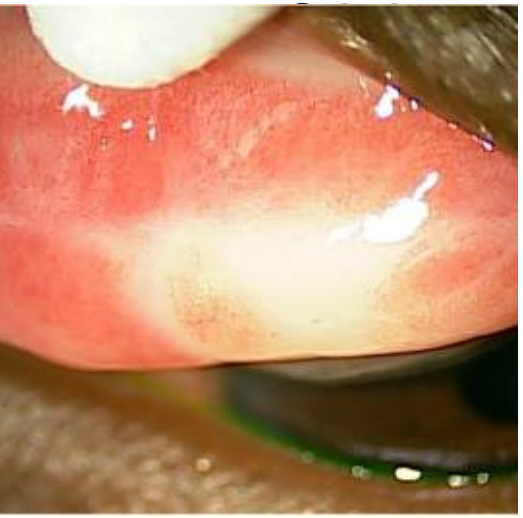
Background: Prevention Strategies

Vasoconstriction: Some efficacy

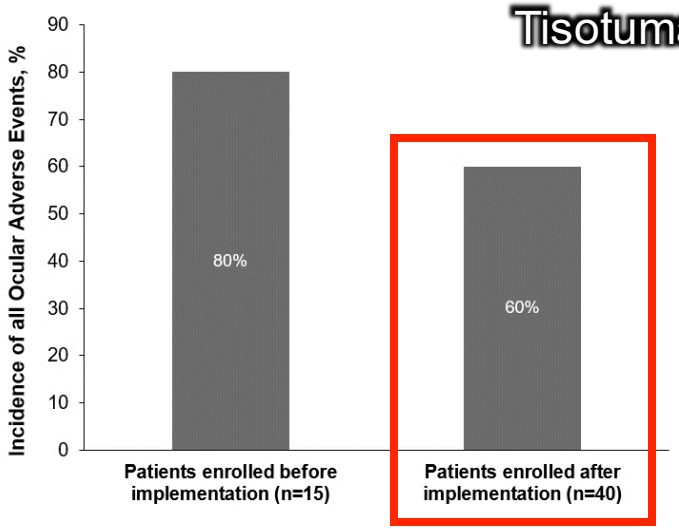
- Preclinical:
  - Decreases **severity** of corneal epitheliopathy
  - Delays **onset** of corneal pseudomicrocysts:
    - 40% vs 100% at 10 days
    - **100% at 14 days!**

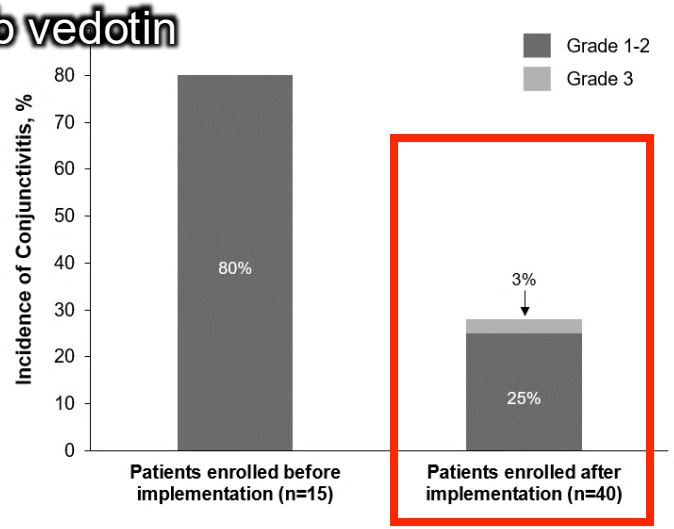


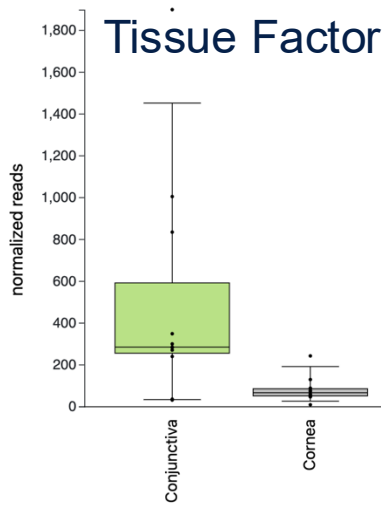
No eye drop treatment | Brimonidine tartrate, 0.2%



Tisotumab vedotin







Warbington A et al. Nonclinical ocular toxicity of a maytansinoid payload-antibody drug conjugate: Ocular tissue distribution, lesion pathogenesis, and mitigation. *AACR Annual Meeting*. 2024
Kim SK et al. Mitigation and management strategies for ocular events associated with tisotumab vedotin. *Gynecol Oncol*. 2022
Lent-Schochet D et al. Ocular surface disease related to tisotumab vedotin-tftv. *Gynecol Onc Rep*. 2025

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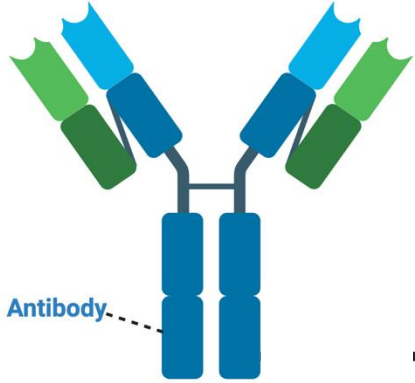
Background: Prevention Strategies

Systemic or topical antibody saturation: No efficacy

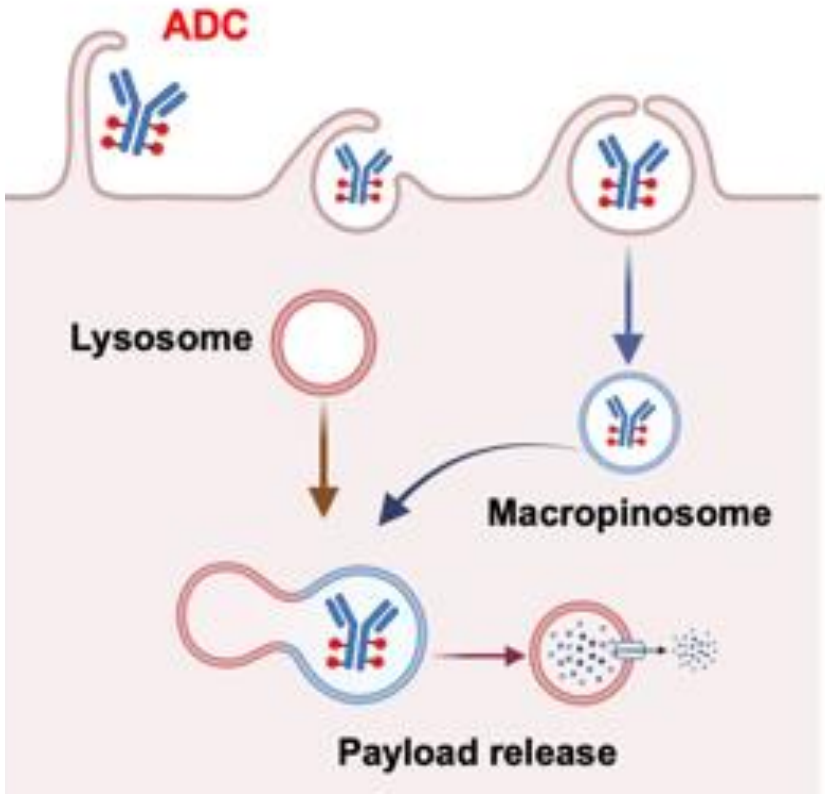


- Non-human primates administered an anti-EGFR ADC (depatuxizumab mafodotin) showed **no benefit** in corneal toxicity prevention from:
  - Systemic depatuxizumab (30 mg/kg) 4-24 hours before ADC
  - Topical depatuxizumab 2x/day
  - Topical rhEGF 2x/day

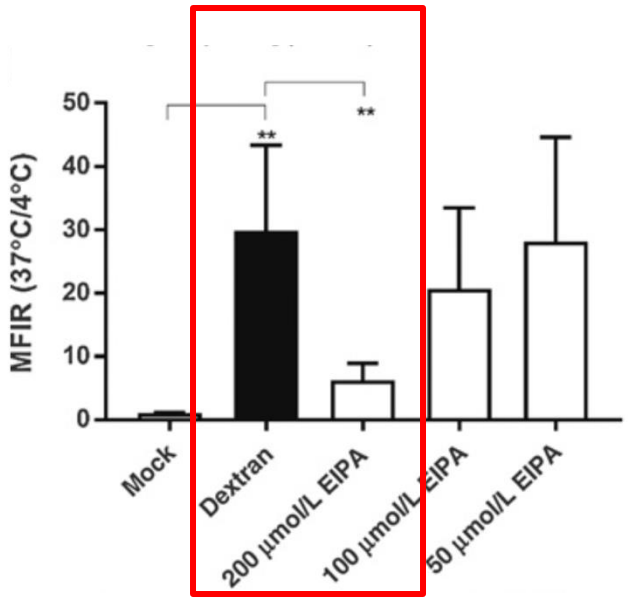
Loberg LI et al. Characterization and Potential Mitigation of Corneal Effects in Nonclinical Toxicology Studies in Animals Administered Depatuxizumab Mafodotin. *J Ocul Pharmacol Ther*. 2022

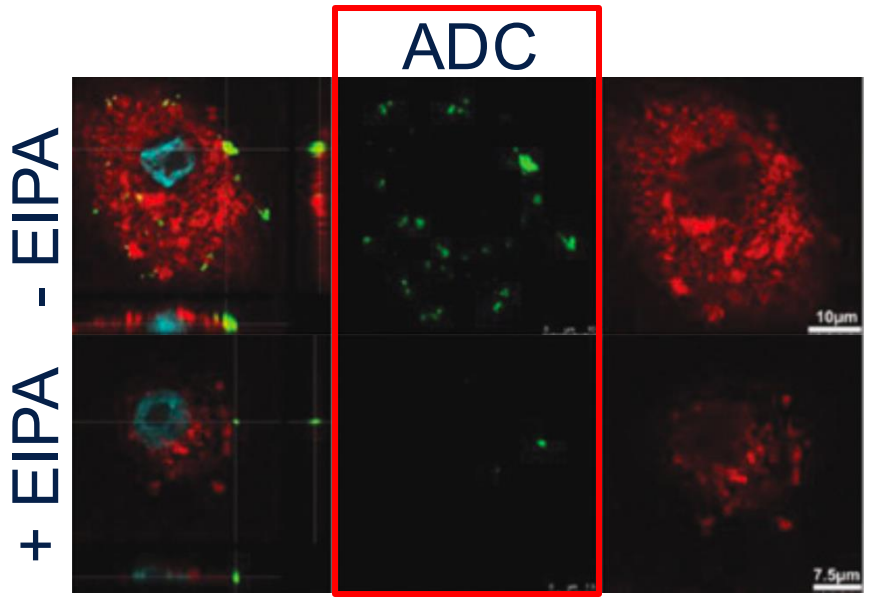
Background: Proposed Mechanism

Macropinocytosis (actin-dependent non-selective endocytosis) off-target toxicity



Ethylisopropylamiloride (EIPA):
Gold standard macropinocytosis inhibitor





Zhao H et al. *Cancer Res*. 2018

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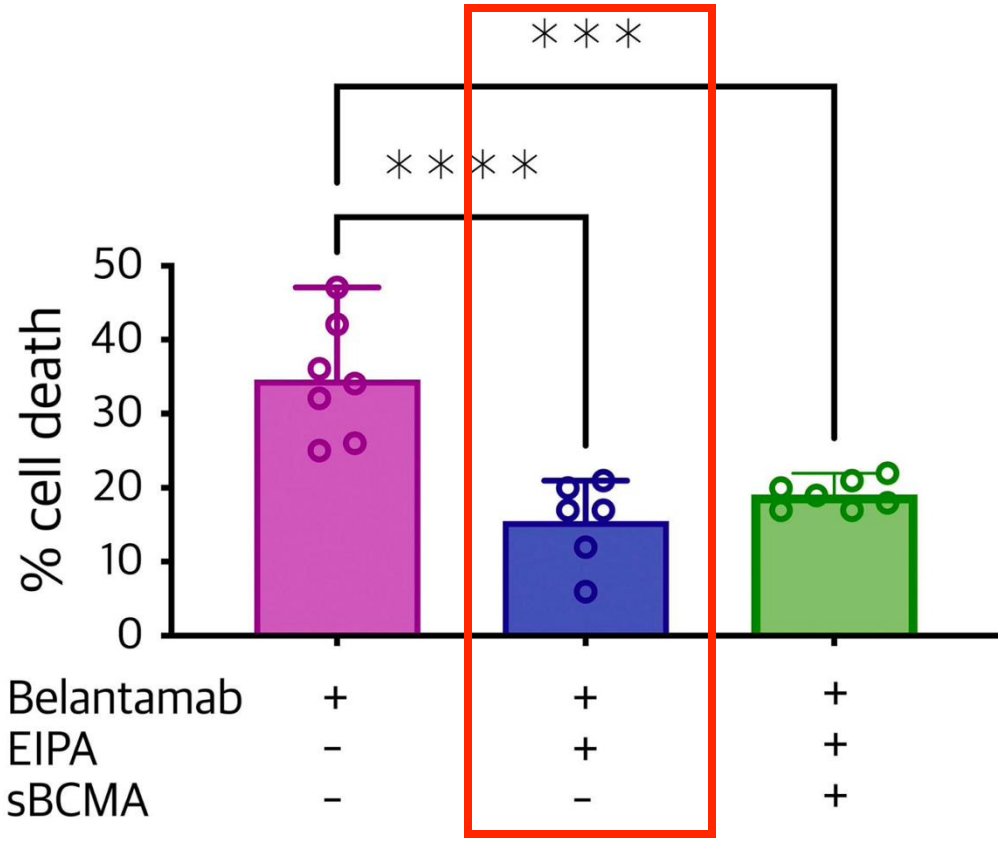
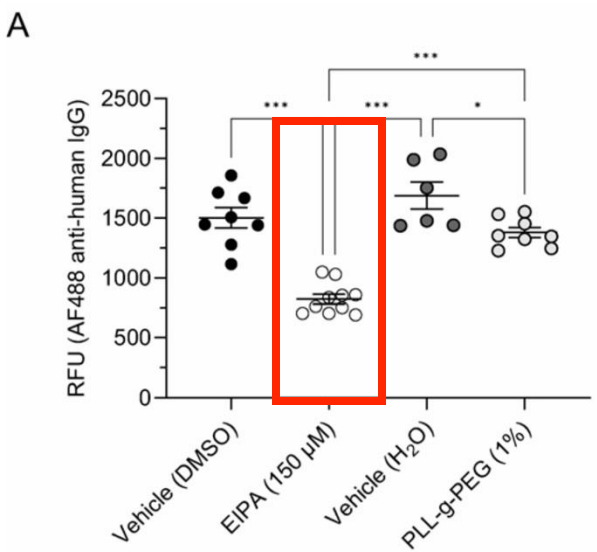
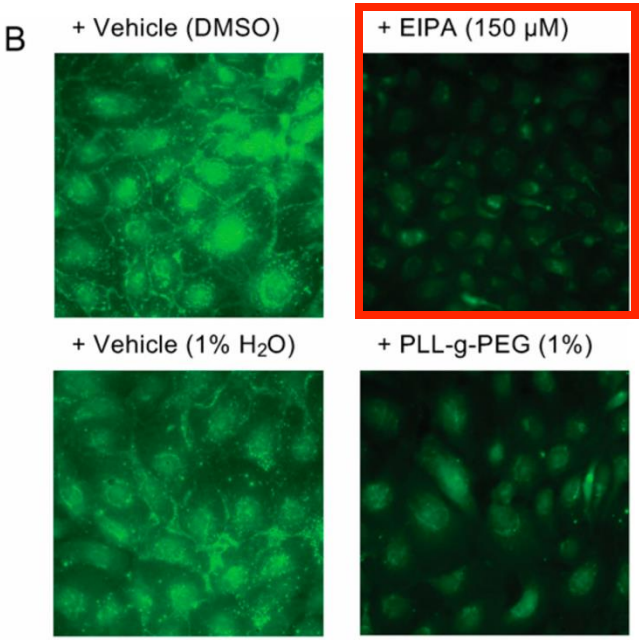
Background: Proposed Mechanism

Macropinocytosis inhibition: Promising in vitro efficacy





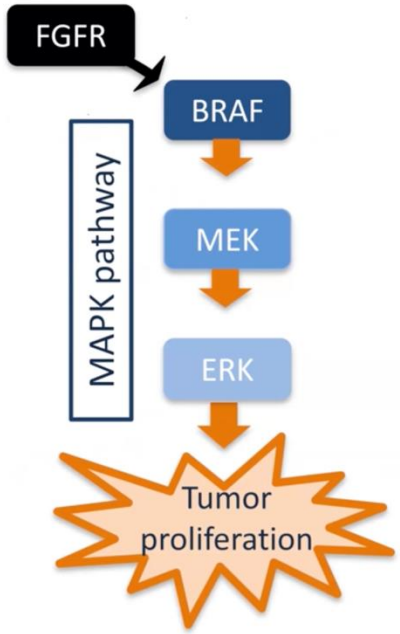


Munawar U et al. Soluble B-cell maturation antigen in lacrimal fluid as a potential biomarker and mediator of keratopathy in multiple myeloma. *Haematologica*. 2024

Kleinman D et al. PLL-g-PEG Polymer Inhibits Antibody-Drug Conjugate Uptake into Human Corneal Epithelial Cells In Vitro. *J Ocul Pharmacol Ther*. 2024

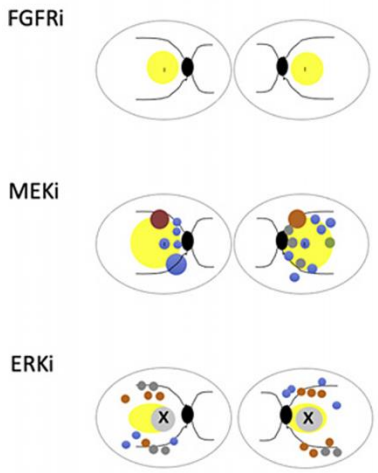
Background: Other Cancer Therapies

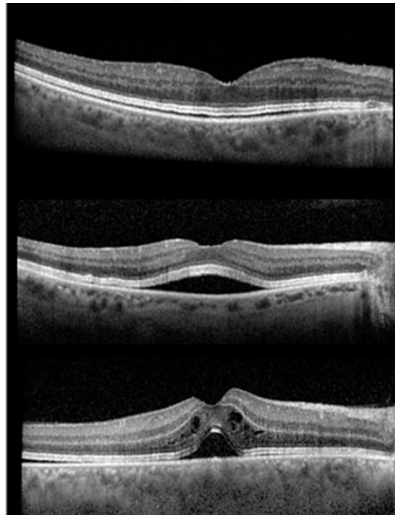
Differentiated OAEs compared to ADCs



- Immune Checkpoint Inhibitors (e.g. Pembrolizumab): 1-3%
  - Dry eye: ~60%
  - **Uveitis (intraocular inflammation): ~15%**
    - ~90% can be managed with topical/local corticosteroids

- MAPK Inhibitors
  - BRAF (e.g. Dabrafenib) → Uveitis: ~5%
  - ERK>MEK>FGFR (e.g. Erdafitinib) → **Retinopathy: ~15%**
    - ~50% symptomatic
    - Improves over time (can resolve while remaining on drug)





Fortes Bh et al. Ophthalmic adverse effects of immune checkpoint inhibitors: the Mayo Clinic experience. *Br J Ophthalmol*. 2021
Francis JH et al. Mitogen-Activated Pathway Kinase Inhibitor-Associated Retinopathy: Do Features Differ with Upstream versus Downstream Inhibition? *Ocul Oncol Path*. 2023

Questions?

Key Takeaway Points

1. Explain ocular adverse events (OAEs) from antibody-drug conjugates (ADCs)
2. **Improve grading and screening of cancer therapy-induced OAEs**
3. Develop effective preventative therapy for ADC corneal toxicity

Ocular Adverse Event (OAE) Grading

Limitations of the Common Terminology Criteria for Adverse Events (CTCAE)

Eye disorders					
CTCAE Term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Dry eye	Asymptomatic; clinical or diagnostic observations only; symptoms relieved by lubricants	Symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better or 3 lines or less decreased vision from known baseline)	Symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or more than 3 lines of decreased vision from known baseline, up to 20/200); limiting self care ADL	-	-
Definition: A disorder charact **Navigational Note:** If corneal					
Keratitis		baseline)	known baseline, up to 20/200); corneal ulcer; limiting self care ADL	; best corrected y of 20/200 or e affected eye	-
Definition: A disorder characterized by inflammation to the cornea of the eye. **Navigational Note:** Also consider Eye disorders: Corneal ulcer					

1. Mixes visual acuity with clinical findings
2. No photos
3. Ambiguous terms

Ocular Adverse Event (OAE) Grading

Limitations of the FDA modified OAE scales

Adverse Reaction	Severity	Grade	Change in dosing
Corneal keratitis	Clear cornea, no epithelial defects	Grade 0	Dosing not interrupted
Corneal keratitis	Nonconfluent superficial keratitis	Grade 1	Dosing not interrupted
Corneal keratitis	Confluent superficial keratitis, a cornea epithelial defect, or 3-line or more loss in best corrected distance visual acuity.	Grade 2	Delay dose until resolved to nonconfluent superficial keratitis, then maintain dose.
Corneal keratitis	Corneal ulcer or stromal opacity or best corrected distance visual acuity 20/200 or worse.	Grade 3	Delay dose until resolved, then reduce dose by 1 level.
Corneal keratitis	Corneal perforation	Grade 4	Discontinue participant from study
Iritis/Uveitis	Clear anterior chamber	Grade 0	Dosing not interrupted
Iritis/Uveitis	Rare cell in anterior chamber	Grade 1	Dosing not interrupted
Iritis/Uveitis	1-2+ Cell or Flare in anterior chamber	Grade 2	Delay dose until resolved to Grade 0 or 1 and then maintain dose.
Iritis/Uveitis	3+ Cell or Flare in anterior chamber	Grade 3	Delay dose until resolved to Grade 0 or 1, then reduce dose by 1 level.
Iritis/Uveitis	Hypopyon	Grade 4	Discontinue participant from study treatment

~50% of patients

1. Mixes visual acuity with clinical findings
2. No photos
3. Unnecessary dose delays

Ocular Adverse Event (OAE) Grading

Multicenter interspecialty consensus

+

+

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Hope Rugo, MD (UCSF)
Laura Huppert, MD (UCSF)
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Alexa Glencer, MD (UCSF)
Janice Lu, MD, PhD (Northwestern)
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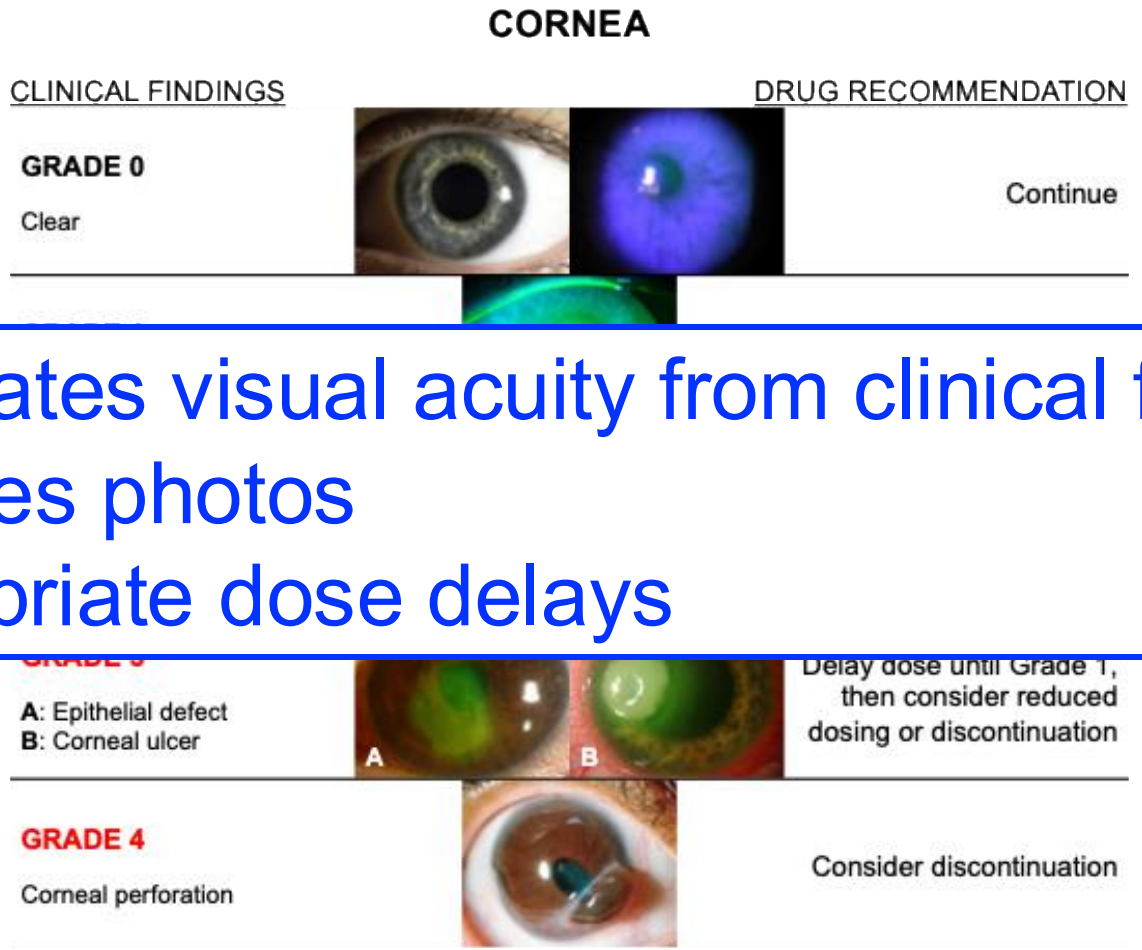
Kathy Colby, MD, PhD (NYU)
Deb Goldstein, MD (Northwestern)
Lucia Sobrin, MD (MEEI)
Ivana Kim, MD (MEEI)
Kuldev Singh, MD (Stanford)

Wiley Chambers, MD
William Boyd, MD

Pasricha ND et al. Multicenter Interspecialty Consensus on Experimental Oncology Drug-Related Ocular Adverse Event Reporting. *JAMA Ophthalmol*. Under review

Ocular Adverse Event (OAE) Grading

New consensus experimental oncology drug-related OAE scales



1. Separates visual acuity from clinical findings
2. Includes photos
3. Appropriate dose delays

Pasricha ND et al. Multicenter Interspecialty Consensus on Experimental Oncology Drug-Related Ocular Adverse Event Reporting. *JAMA Ophthalmol*. Under review

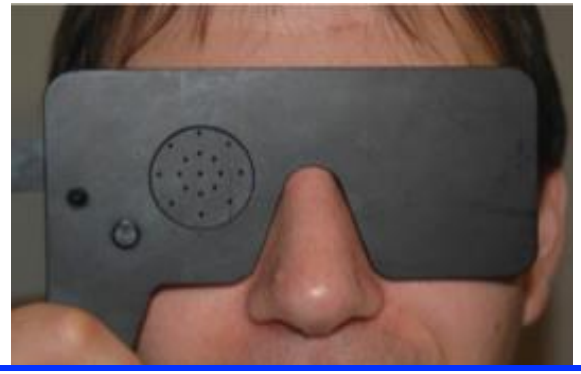
Eye Exam Screening

Scheduling delays are common for eye exams in the ophthalmology clinics

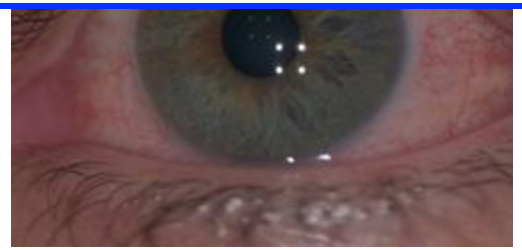
Ophthalmologists

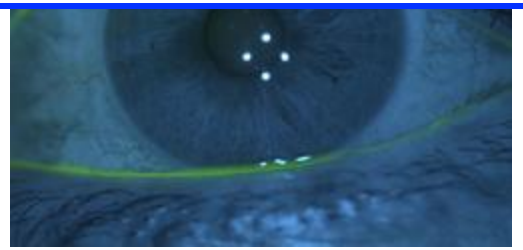
Portable Eye Exam Screening

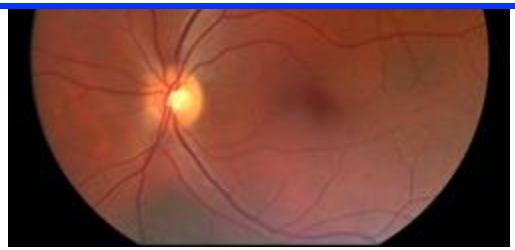
Expedites clinical trial enrollment in the oncology clinic



1. Efficient (~20 minutes)
2. Effective (comparable to eye clinic)
3. Easy (high patient and technician satisfaction)







Landzberg R…**Pasricha ND**. Portable Eye Examinations in the Oncology Clinic: An Innovative Pilot for Clinical Trial Screening. *CERSI Summit*. 2025

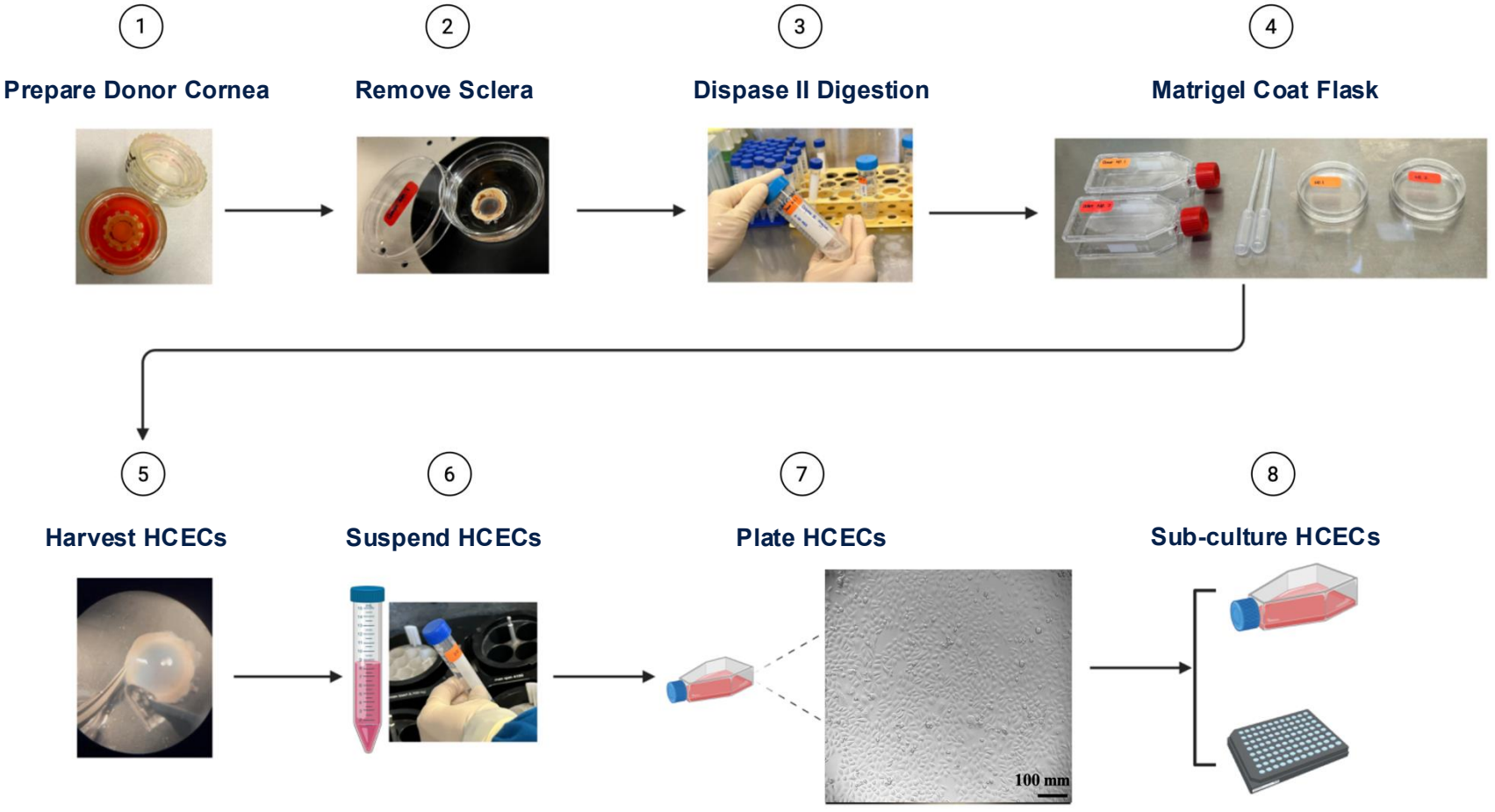
Questions?

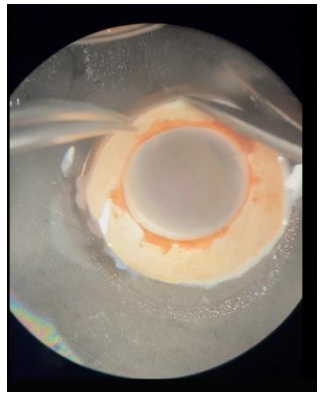
Key Takeaway Points

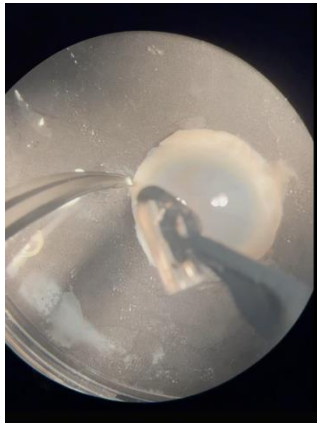
1. Explain ocular adverse events (OAEs) from antibody-drug conjugates (ADCs)
2. Improve grading and screening of cancer therapy-induced OAEs
3. **Develop effective preventative therapy for ADC corneal toxicity**

In Vitro Setup

Patient-derived primary human corneal epithelial cells (HCECs)







Yan R…**Pasricha ND**. Optimized Protocol for Isolation and Culture of Primary Human Corneal Epithelial Cells. *Transl Vis Sci Technol*. Under review

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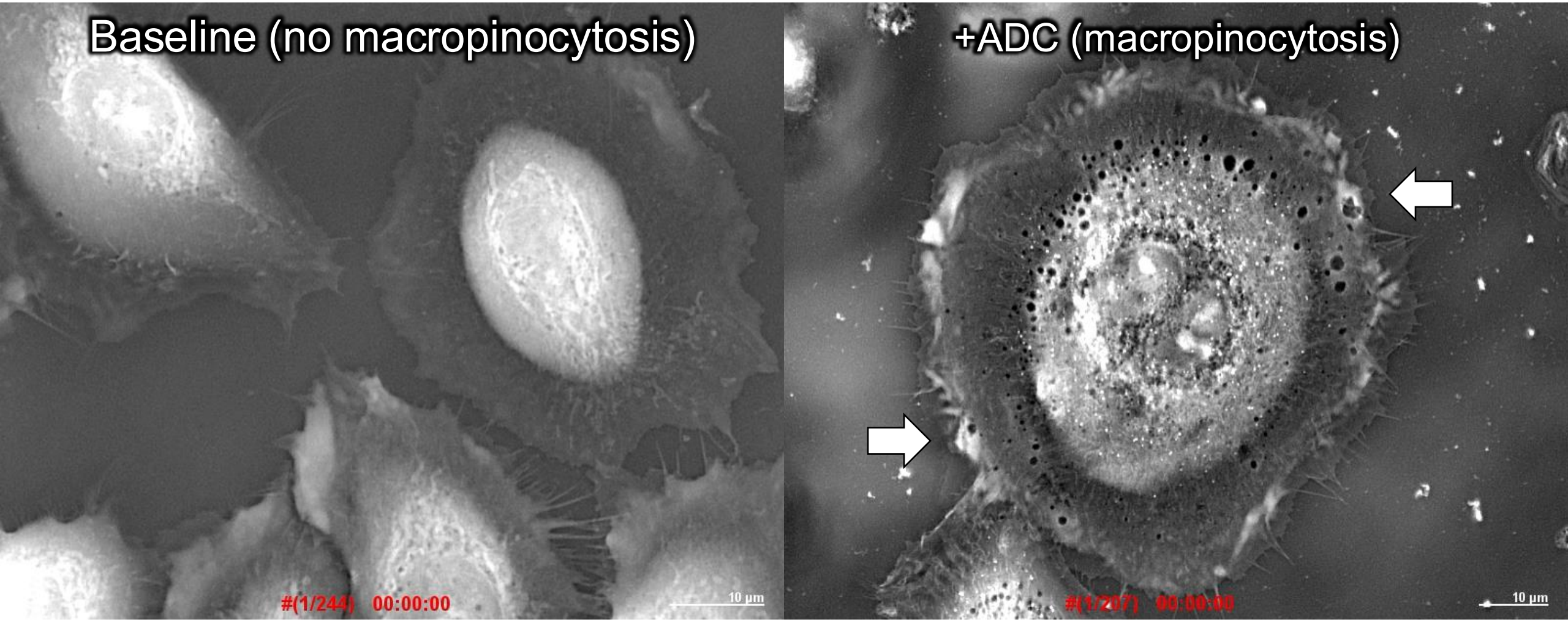
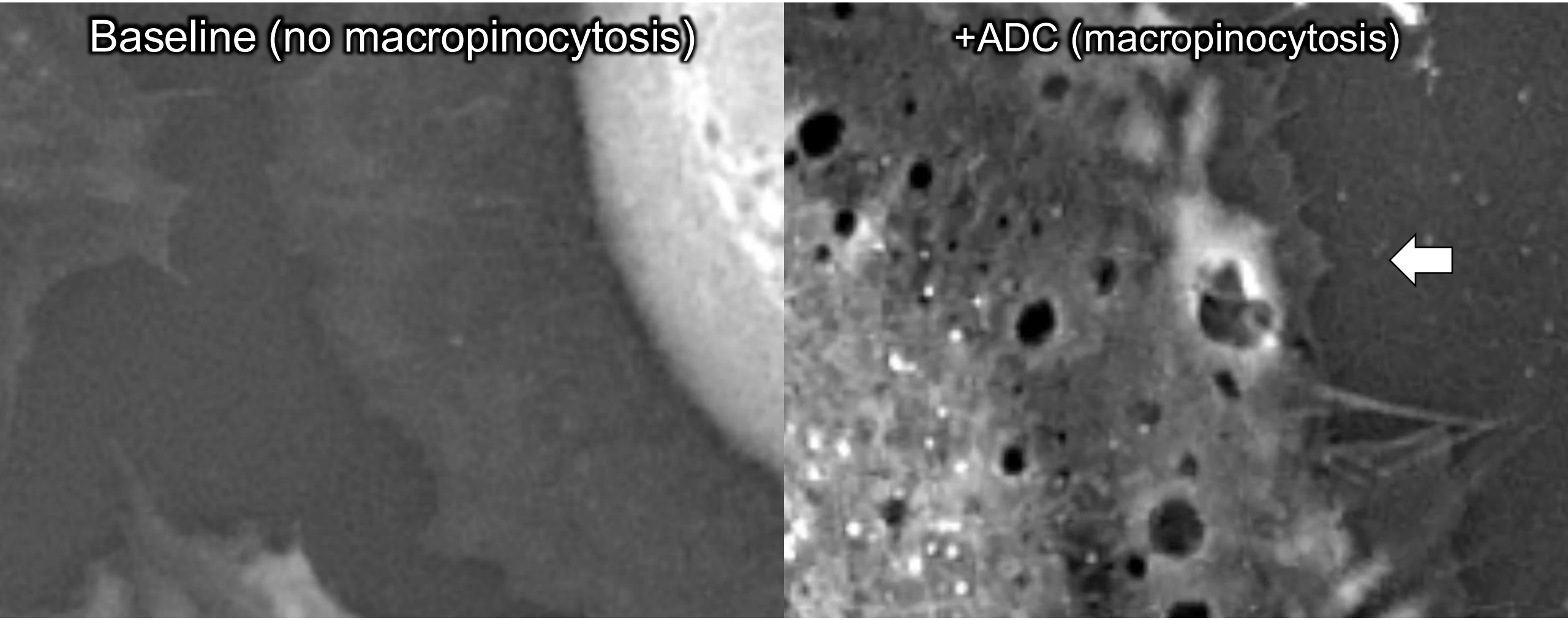
ADC Internalization

Primary HCECs demonstrate macropinocytosis after ADC addition



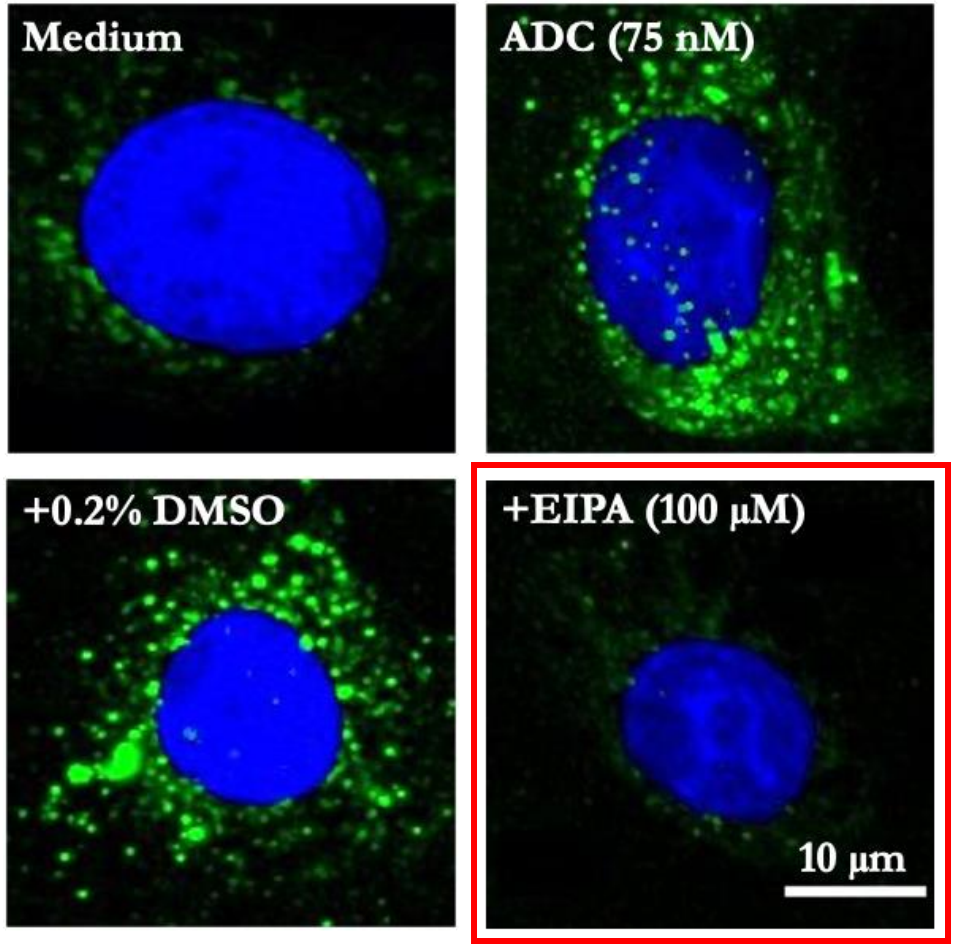
ADC Internalization

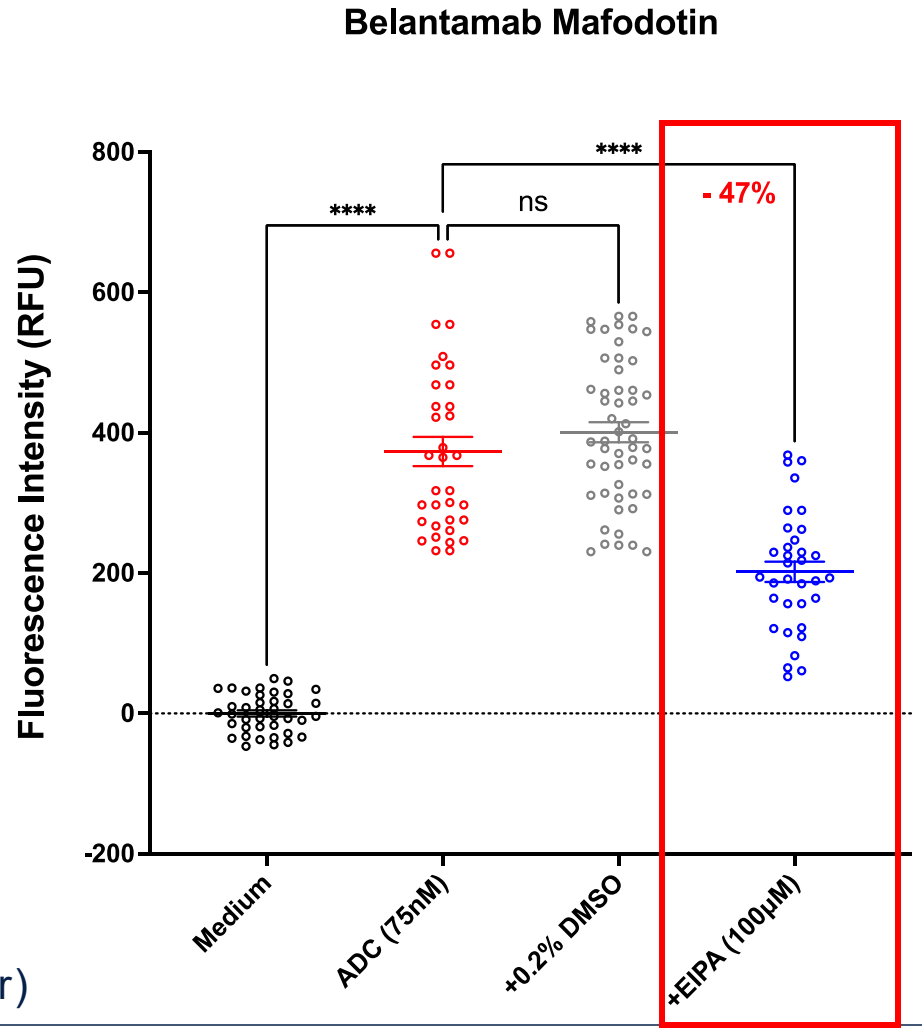
Primary HCECs demonstrate macropinocytosis after ADC addition



ADC Internalization

EIPA inhibits ADC internalization in primary HCECs





❖ **EIPA:** Ethylisopropylamiloride (macropinocytosis inhibitor)

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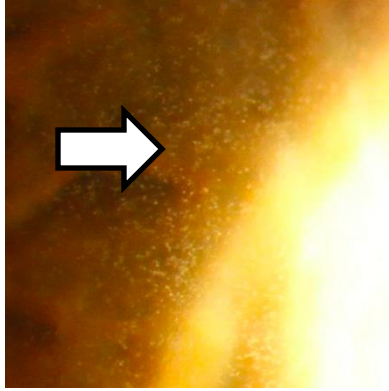
Key Takeaway Points



1. Explain ocular adverse events (OAEs) from antibody-drug conjugates (ADCs)

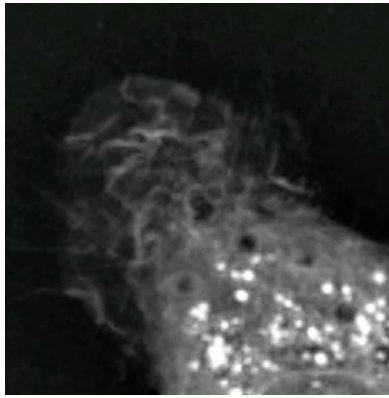
Cause reversible corneal pseudomicrocysts leading to eye pain and blurry vision

2. Improve grading and screening of cancer therapy-induced OAEs

Consensus OAE grading scales and portable eye exam screenings

3. Develop effective preventative therapy for ADC corneal toxicity

Inhibit macropinocytosis (off-target ADC internalization)



Thank You!

Pasricha Lab

- Rongshan Yan, PhD
- Ethan Lindgren
- Josh Radlow
- Renée Landzberg

Cil Lab

- Onur Cil, MD, PhD
- Taskin Tas, MD, PhD
- Fernanda Carmona

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- Hope Rugo, MD
- Laura Huppert, MD

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- NEI P30 EY002162
- 1S10OD036282-01
- RPB Career Development Award
- All May See Foundation
- UCSF Catalyst Award
- Lindonlight Collective
- QLHC I-SPY 2 Trial
- Sierra Donor Services Eye Bank
- Nanolive
- Tomocube

Agenda

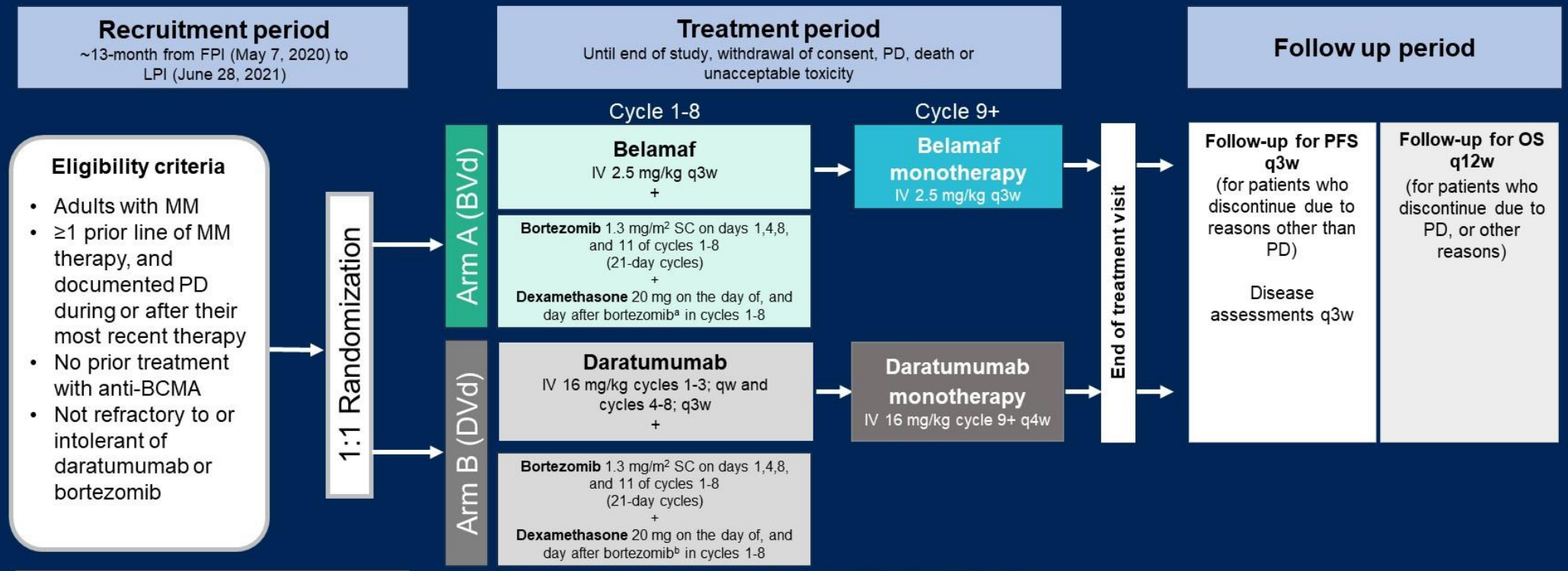
Introduction: The Patient Experience

Module 1: Managing Ocular Toxicities Associated with Antibody-Drug Conjugates and Other Cancer Therapies — Dr Pasricha

Module 2: Ocular Toxicities in Multiple Myeloma

Module 3: Ocular Toxicities in Breast Cancer

DREAMM-7: study design

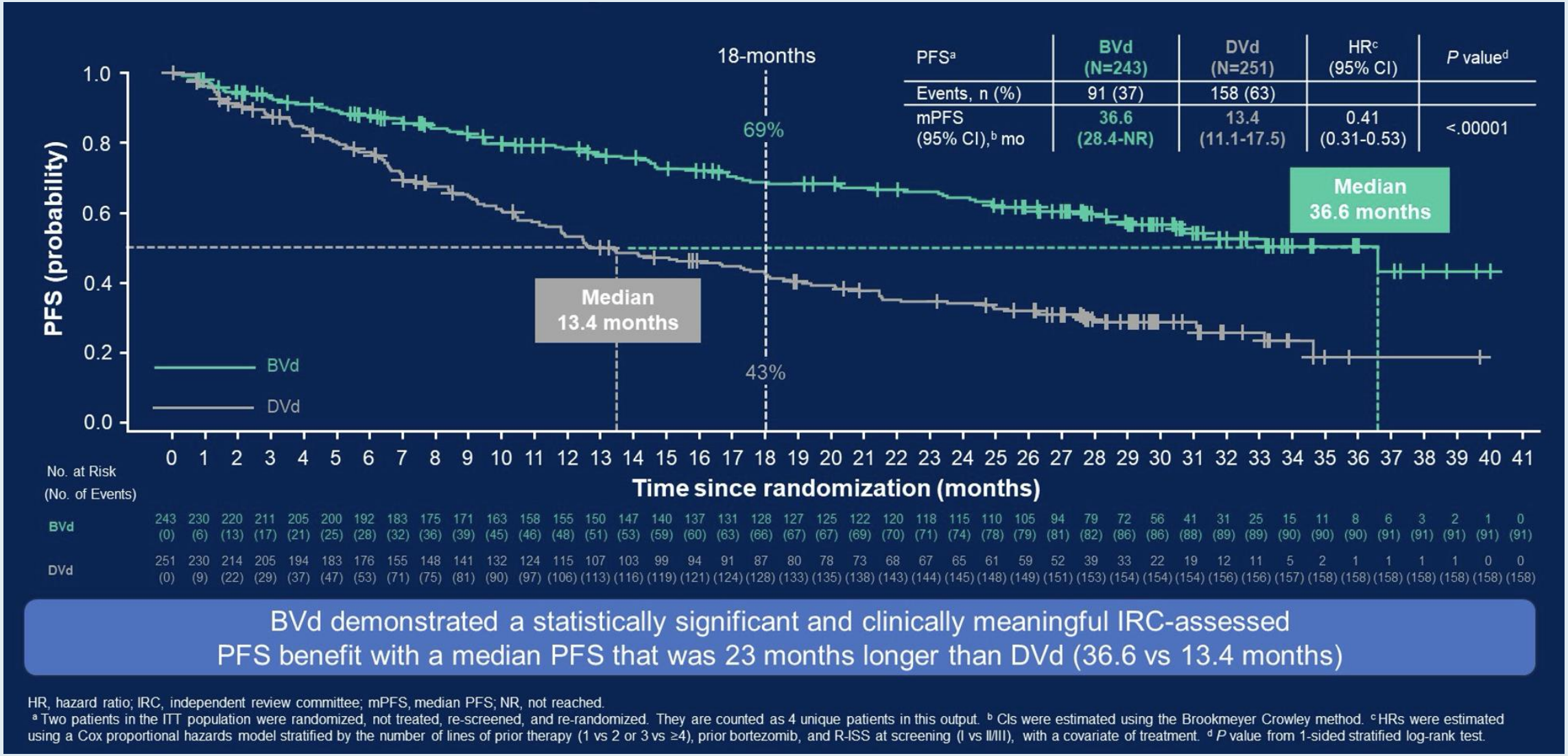


AE, adverse event; CBR, clinical benefit rate; CRR, complete response rate; DOR, duration of response; FPI, first-patient-in; IV, intravenous; LPI, last-patient-in; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; q3w, every 3 weeks; q4w, every 4 weeks; q12w, every 12 weeks; qw, every week; QOL, quality of life; R-ISS, Revised International Staging System; SC, subcutaneous; TTP, time to progression; TTR, time to response.

[a] Reduce starting dose of dexamethasone to 10 mg for patients >75 years of age, who have a body-mass index <18.5, who had previous unacceptable side effects associated with glucocorticoid therapy, or who are unable to tolerate the starting.

Mateos M-V et al. ASCO 2024;Abstract 439572.

DREAMM-7: Progression-Free Survival (PFS) Outcomes



PFS[a]	BVd (N=243)	DVd (N=251)	HR[c] (95% CI)	*P* value[d]
Events, n (%)	91 (37)	158 (63)		
mPFS (95% CI),[b] mo	36.6 (28.4-NR)	13.4 (11.1-17.5)	0.41 (0.31-0.53)	<.00001

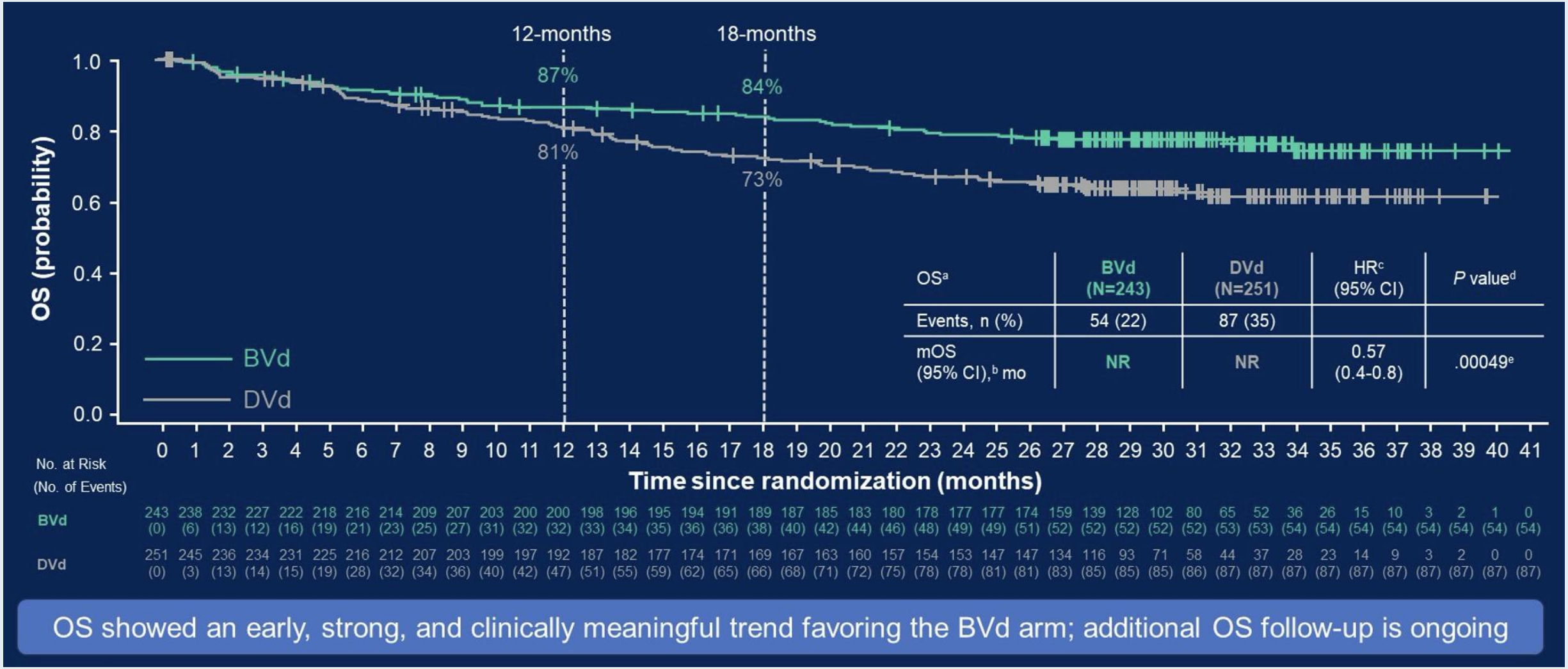
BVd demonstrated a statistically significant and clinically meaningful IRC-assessed PFS benefit with a median PFS that was 23 months longer than DVd (36.6 vs 13.4 months)

HR, hazard ratio; IRC, independent review committee; mPFS, median PFS; NR, not reached.
[a] Two patients in the ITT population were randomized, not treated, re-screened, and re-randomized. They are counted as 4 unique patients in this output. [b] CIs were estimated using the Brookmeyer Crowley method. [c] HRs were estimated using a Cox proportional hazards model stratified by the number of lines of prior therapy (1 vs 2 or 3 vs ≥4), prior bortezomib, and R-ISS at screening (I vs II/III), with a covariate of treatment. [d] *P* value from 1-sided stratified log-rank test.

BVd = belantamab mafodotin/bortezomib/dexamethasone; DVd = daratumumab/bortezomib/dexamethasone

Mateos M-V et al. ASCO 2024;Abstract 439572.

DREAMM-7: OS Outcomes



OS[a]	BVd (N=243)	DVd (N=251)	HR[c] (95% CI)	*P* value[d]
Events, n (%)	54 (22)	87 (35)		
mOS (95% CI),[b] mo	NR	NR	0.57 (0.4-0.8)	.00049[e]

OS showed an early, strong, and clinically meaningful trend favoring the BVd arm; additional OS follow-up is ongoing

Belamaf = belantamab mafodotin

Mateos M-V et al. ASCO 2024;Abstract 439572.

DREAMM-7: Visual Acuity

DREAMM-7: changes in best corrected visual acuity

Normal Vision (20/20)

Blurred Vision (20/50)

Vision Impaired (20/200)

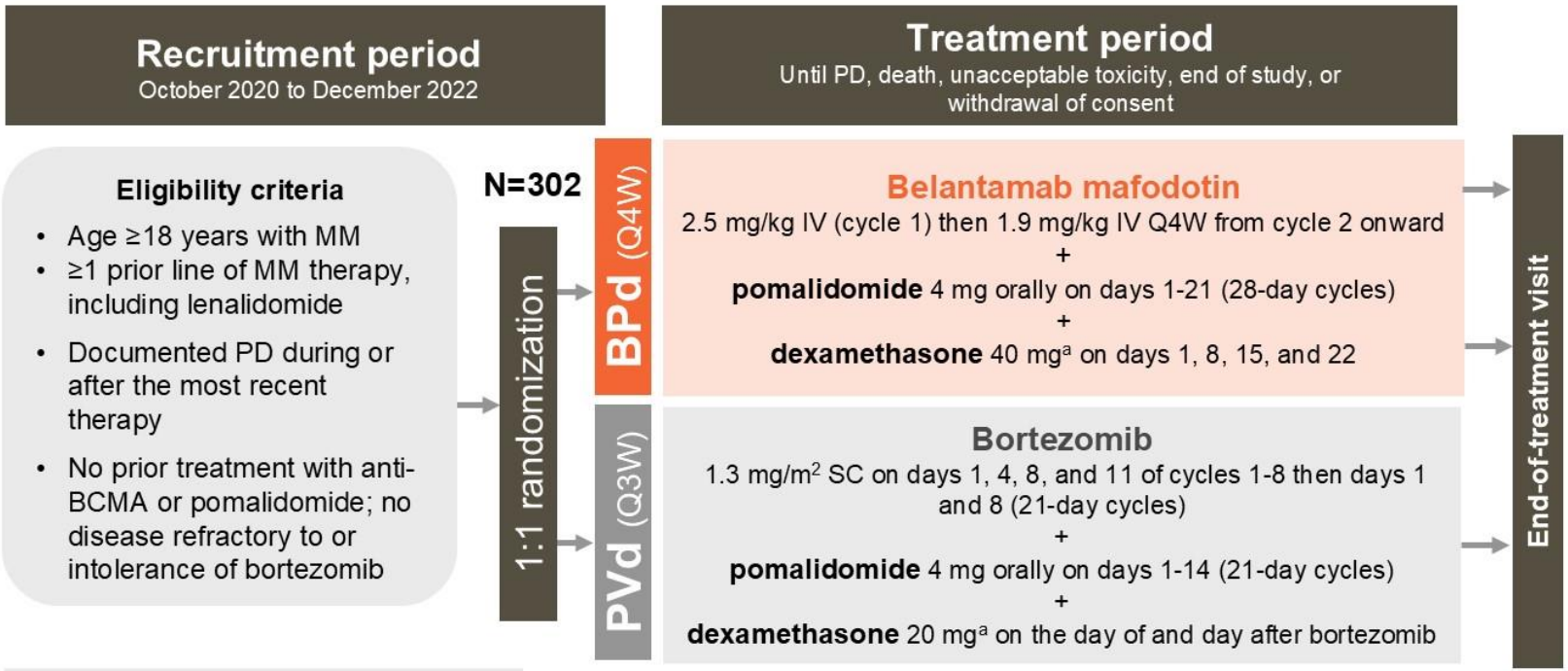
BVd	Blurred Vision (20/50)[a]	Vision Impaired (20/200)[a]
Patients, n/N (%)	82/242 (34)	5/242 (2)
Time to onset of first event, median (range), days	73.5 (16-753)	105 (47-304)
Duration of first event, median (range), days	22 (6-257)	19 (8-26)
First event resolved,[b] n (%)	80 (98)	5 (100)

44% of patients had dose reductions, 78% had dose delays/interruptions, and 9% discontinued due to any ocular event

BPd = belantamab mafodotin/pomalidomide/dexamethasone

Mateos M-V et al. ASCO 2024;Abstract 439572.

DREAMM-8: Trial Design

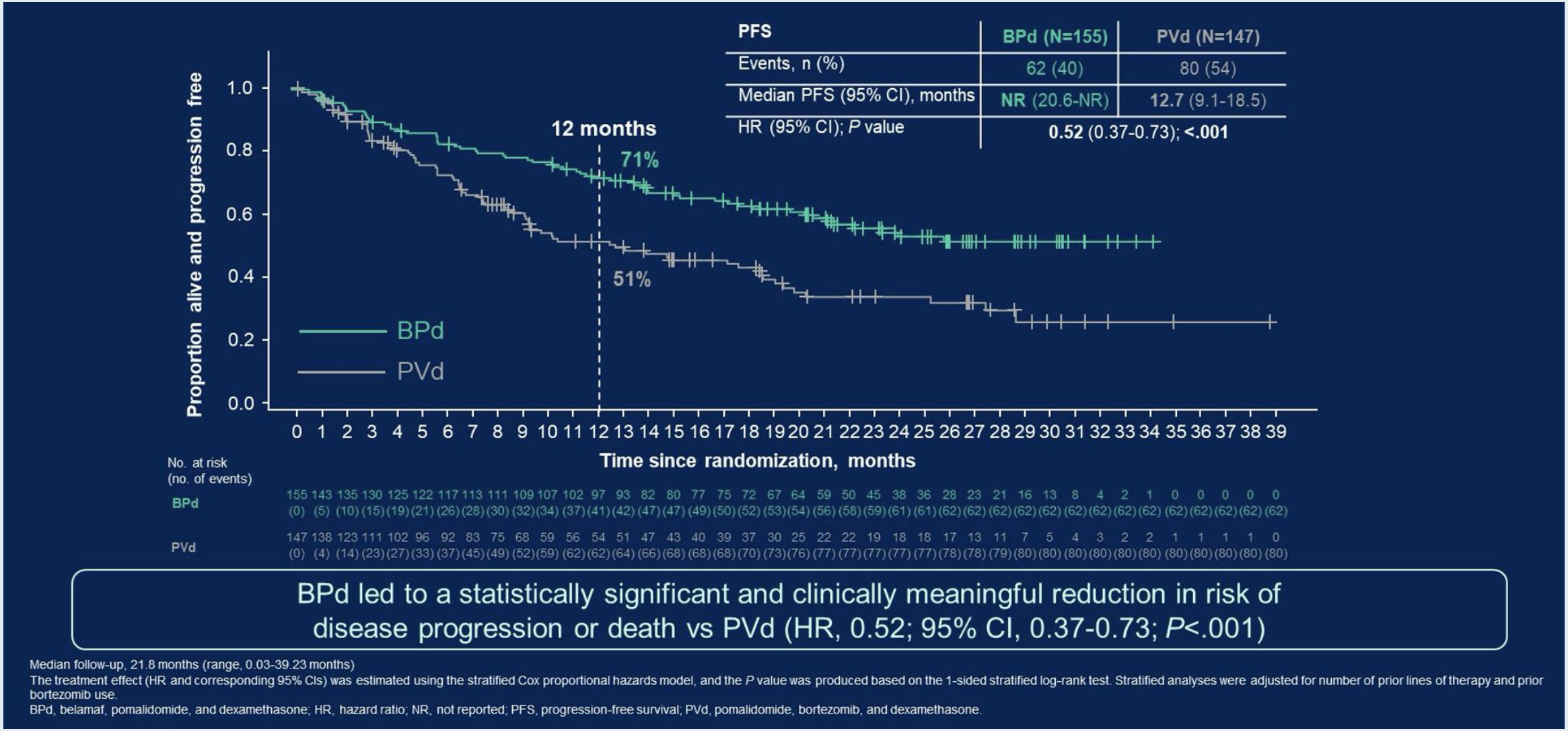


AE, adverse event; BCMA, B-cell maturation antigen; BPd, belantamab mafodotin, pomalidomide, and dexamethasone; CD, cluster of differentiation; CRR, complete response rate; DOR, duration of response; HRQOL, health-related quality of life; IMWG, International Myeloma Working Group; IRC, independent review committee; ISS, International Staging System; IV, intravenous; MM, multiple myeloma; MRD, minimal residual disease; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival on subsequent line of therapy; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; Q3W, every 3 weeks; Q4W, every 4 weeks; SC, subcutaneous; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.

[a] Patients aged >75 years with comorbidities or intolerance of the 40-mg dose in arm A or 20-mg dose in arm B could have dose level reduced to half per investigator discretion. [b] Some patients were stratified by ISS stage (I vs II/III); the protocol was amended on April 20, 2021, to replace this randomization factor with prior anti-CD38 treatment (yes vs no).

Trudel S et al. ASCO 2025;Abstract 7515.

DREAMM-8: PFS Outcomes



BPd led to a statistically significant and clinically meaningful reduction in risk of disease progression or death vs PVd (HR, 0.52; 95% CI, 0.37-0.73; *P*<.001)

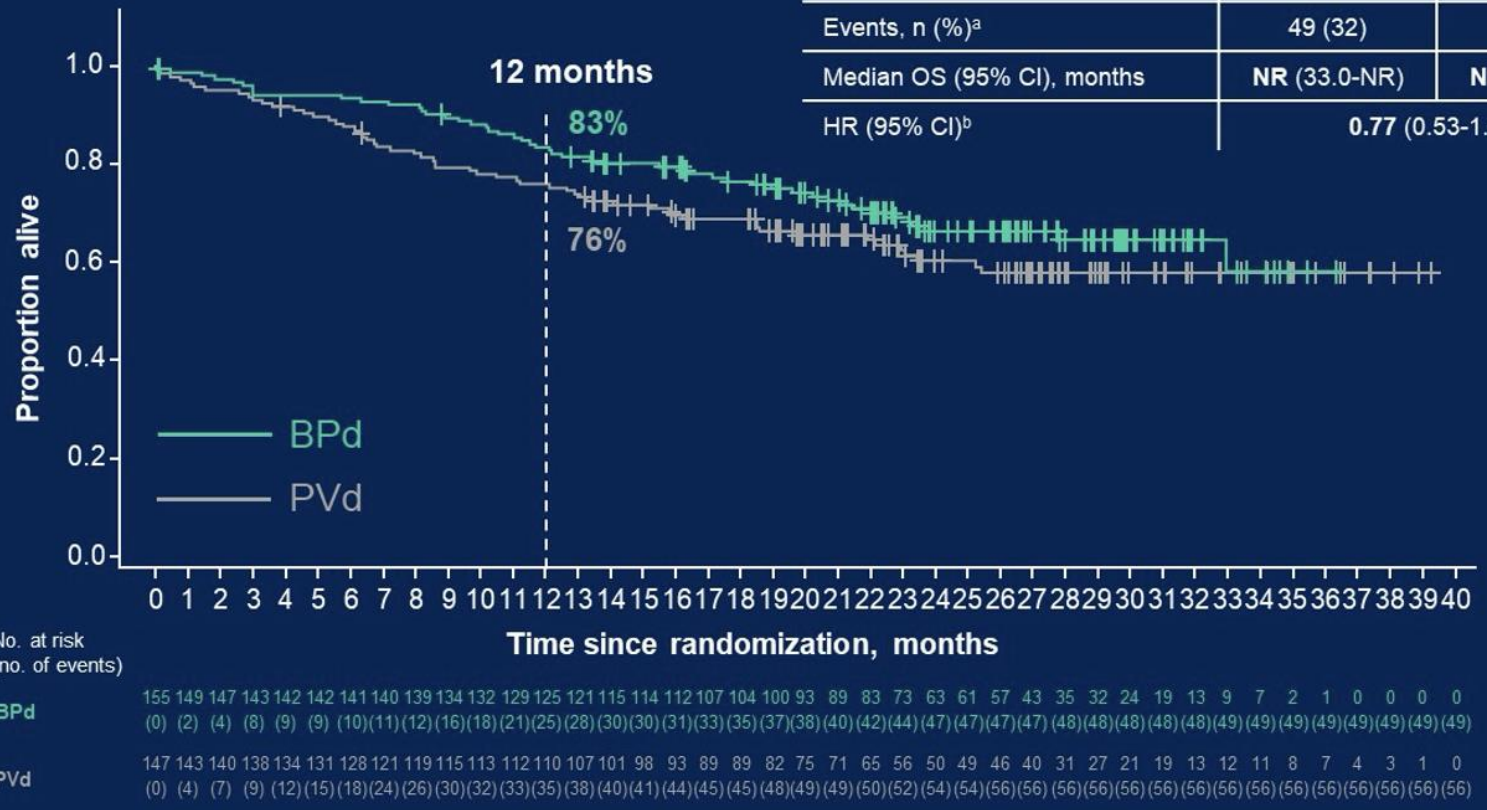
Median follow-up, 21.8 months (range, 0.03-39.23 months)

The treatment effect (HR and corresponding 95% CIs) was estimated using the stratified Cox proportional hazards model, and the *P* value was produced based on the 1-sided stratified log-rank test. Stratified analyses were adjusted for number of prior lines of therapy and prior bortezomib use.

BPd, belamaf, pomalidomide, and dexamethasone; HR, hazard ratio; NR, not reported; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone.

Trudel S et al. ASCO 2024;Abstract LBA105.

DREAMM-8: OS Outcomes



Interim OS	BPd (N=155)	PVd (N=147)
Events, n (%)[a]	49 (32)	56 (38)
Median OS (95% CI), months	**NR** (33.0-NR)	**NR** (25.2-NR)
HR (95% CI)[b]	**0.77** (0.53-1.14)	

Subsequent antimyeloma therapy, n (%)[c]	ITT population	
	BPd (N=155)	PVd (N=147)
Steroids	37 (24)	59 (40)
Anti-CD38 antibodies	23 (15)	49 (33)
Proteasome inhibitor	26 (17)	36 (24)
Immunomodulator	14 (9)	29 (20)
BCMA-targeting therapy[d,e]	1 (<1)	20 (14)
Chemotherapy	16 (10)	25 (17)
Transplant	1 (<1)	5 (3)

Positive OS trend favoring BPd was seen despite the use of effective anti-MM therapies after progression with PVd; additional OS follow-up is ongoing

Trudel S et al. ASCO 2024;Abstract LBA105.

DREAMM-8: Visual Acuity

DREAMM-8

Belantamab Mafodotin + Pd

Bilateral Worsening in Best Corrected Visual Acuity

20/20

20/50

20/200

Reprinted from Shi C, et al. *bioRxiv*. 2018;doi:doi.org/10.1101/328443. Copyright © 2018 the Author.

BPd	Bilateral worsening of BCVA in patients with normal baseline (20/25 or better in ≥1 eye)	
	20/50 or worse[a]	20/200 or worse[a]
Patients, n/N (%)	51/150 (34)	2/150 (1)
Time to onset of first event, median (range), days	112 (28-761)	351 (29-673)
Time to resolution of first event to normal baseline, median (range), days[b,c]	57 (14-451)	NA[d]
Time to improvement of first event, median (range), days[e]	29 (7-196)	25.5 (22-29)
First event resolved to normal baseline, n/N (%)[c]	43/51 (84)	1/2 (50)
First event improved, n/N (%)[e]	47/51 (92)	2/2 (100)
Follow-up ended with event ongoing, n/N (%)[c,f]	4/51 (8)	1/2 (50)

Visual acuity changes that could affect activities of daily living were reversible in most patients

Trudel S et al. ASCO 2024;Abstract LBA105.

Abstract # 12040: Incidence of ocular toxicities in patients with relapsed/refractory multiple myeloma treated with belantamab mafodotin: A systemic review and meta-analysis of phase 3 randomized controlled trials

Riccesha Hattin, DO[1], Hazem Aboaid, MD[1], Daniel Thomas Jones, OMS-IV[2], Abbas Hussain, MD[1], Savannah Schauer, MS-III[3], Tal Schlesinger, MS-III[3], Rory Twells, MS-III[3], Karl Aharonian, MS-III[3], Ryan Parto, MD[1], Rodd Rahmani, MD[1], Chalette Lambert-Swainston, MD[1], Ramaditya Srinivasmurthy, OMS-IV[2] Kyaw Zin Thein, MD[1,2,3,4], Thura Win Htut, MBBS, MRCP, FRCPath[5]

ASCO 2025.

RTP RESEARCH TO PRACTICE

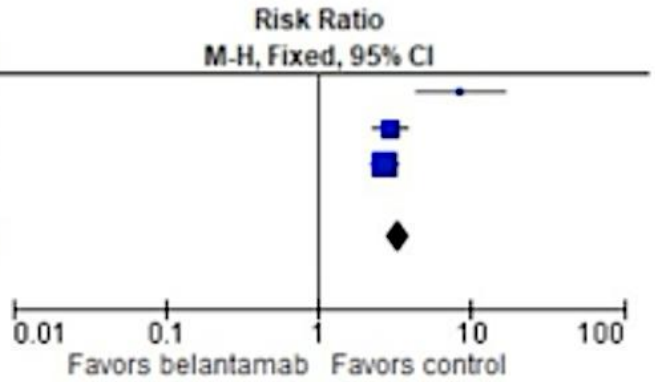
Meta-Analysis of Ocular Events in DREAMM Studies

Ocular adverse events – Any Grade

Study or Subgroup	Belantamab Events	Belantamab Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Dimopoulos 2023 DREAMM-3	143	217	8	102	8.6%	8.40 [4.29, 16.45]
Dimopoulos 2024 DREAMM-8	134	150	44	145	35.5%	2.94 [2.29, 3.79]
Hungria 2024 DREAMM-7	191	242	71	246	55.9%	2.73 [2.22, 3.36]
Total (95% CI)		**609**		**493**	**100.0%**	**3.30 [2.80, 3.89]**
Total events	468		123			

Heterogeneity: $Chi^2 = 11.37$, $df = 2$ ($P = 0.003$); $I^2 = 82\%$

Test for overall effect: $Z = 14.28$ ($P < 0.00001$)

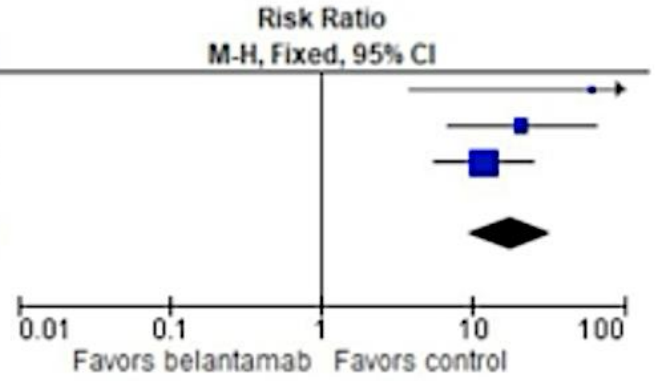


Ocular adverse events – High Grade

Study or Subgroup	Belantamab Events	Belantamab Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Dimopoulos 2023 DREAMM-3	64	217	0	102	6.4%	60.95 [3.81, 975.25]
Dimopoulos 2024 DREAMM-8	65	150	3	145	28.6%	20.94 [6.73, 65.14]
Hungria 2024 DREAMM-7	82	242	7	246	65.1%	11.91 [5.62, 25.24]
Total (95% CI)		**609**		**493**	**100.0%**	**17.61 [9.40, 33.00]**
Total events	211		10			

Heterogeneity: $Chi^2 = 1.90$, $df = 2$ ($P = 0.39$); $I^2 = 0\%$

Test for overall effect: $Z = 8.95$ ($P < 0.00001$)



Hattin R et al. ASCO 2025;Abstract 12040.

Baseline ocular conditions and incidence of ocular events in patients with relapsed/refractory multiple myeloma from the DREAMM-7 and DREAMM-8 trials of belantamab mafodotin

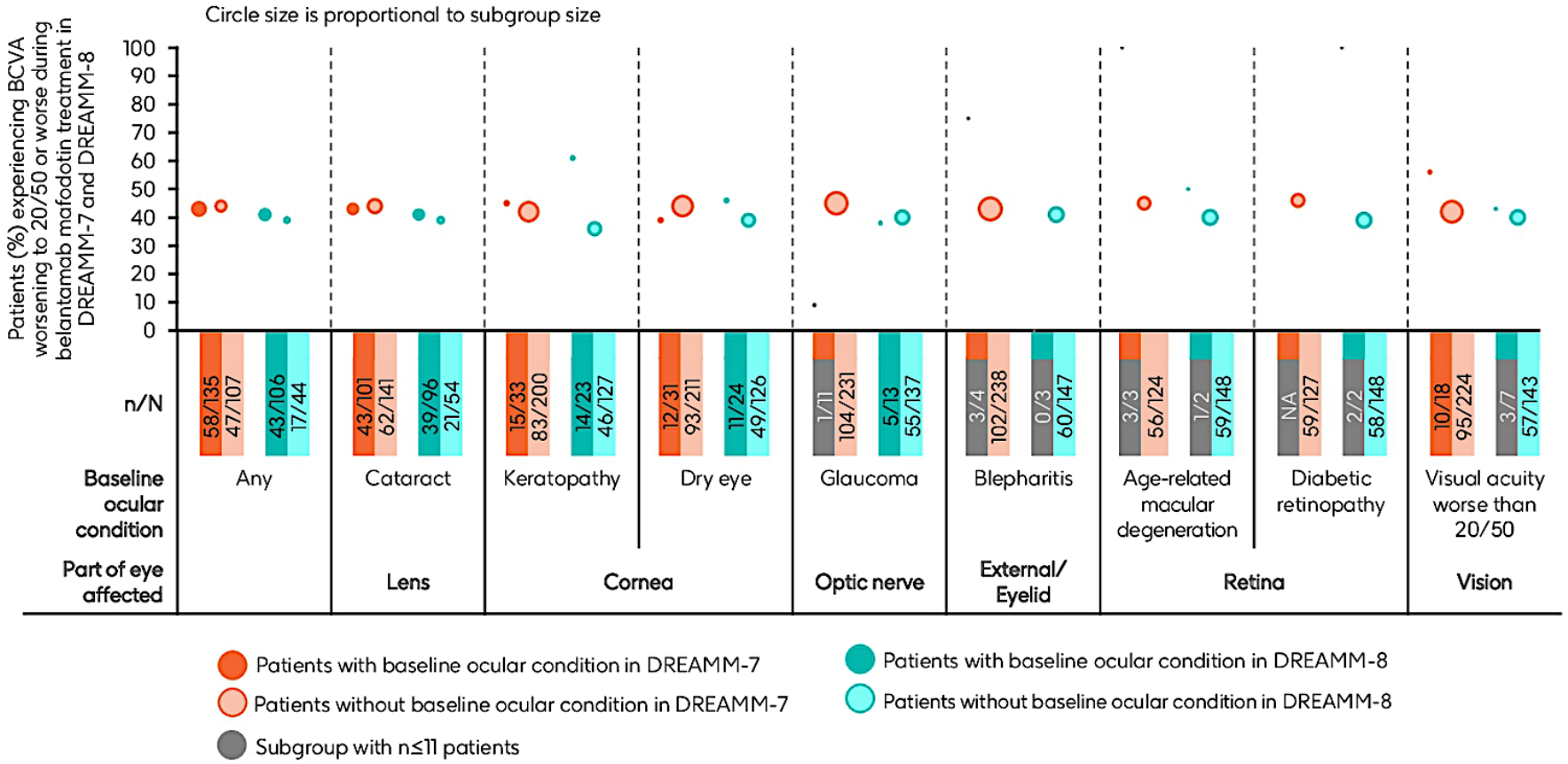
Meral Beksac[1], Hang Quach[2], Vania Hungria[3], Ludek Pour[4], Kihyun Kim[5], Sergey Voloshin[6], Hanlon Sia[7], Esther Gonzalez Garcia[8], Chang Ki Min[9], Marcelo Pitonbeira de Lacerda[10], Anna Maria Sureda[11], Ivan Spicka[12], Marek Hus[13], Vera Zherebtsova[14], Margaret Polinkovsky[15], Sybil Varghese[15], Joe Lee[16], Elisabet E. Manasanch[15], Pawel Robak[17], Meletios Dimopoulos[18]

ASCO 2025;Abstract 7544.

Visual Acuity in Patients with Baseline Ocular Conditions

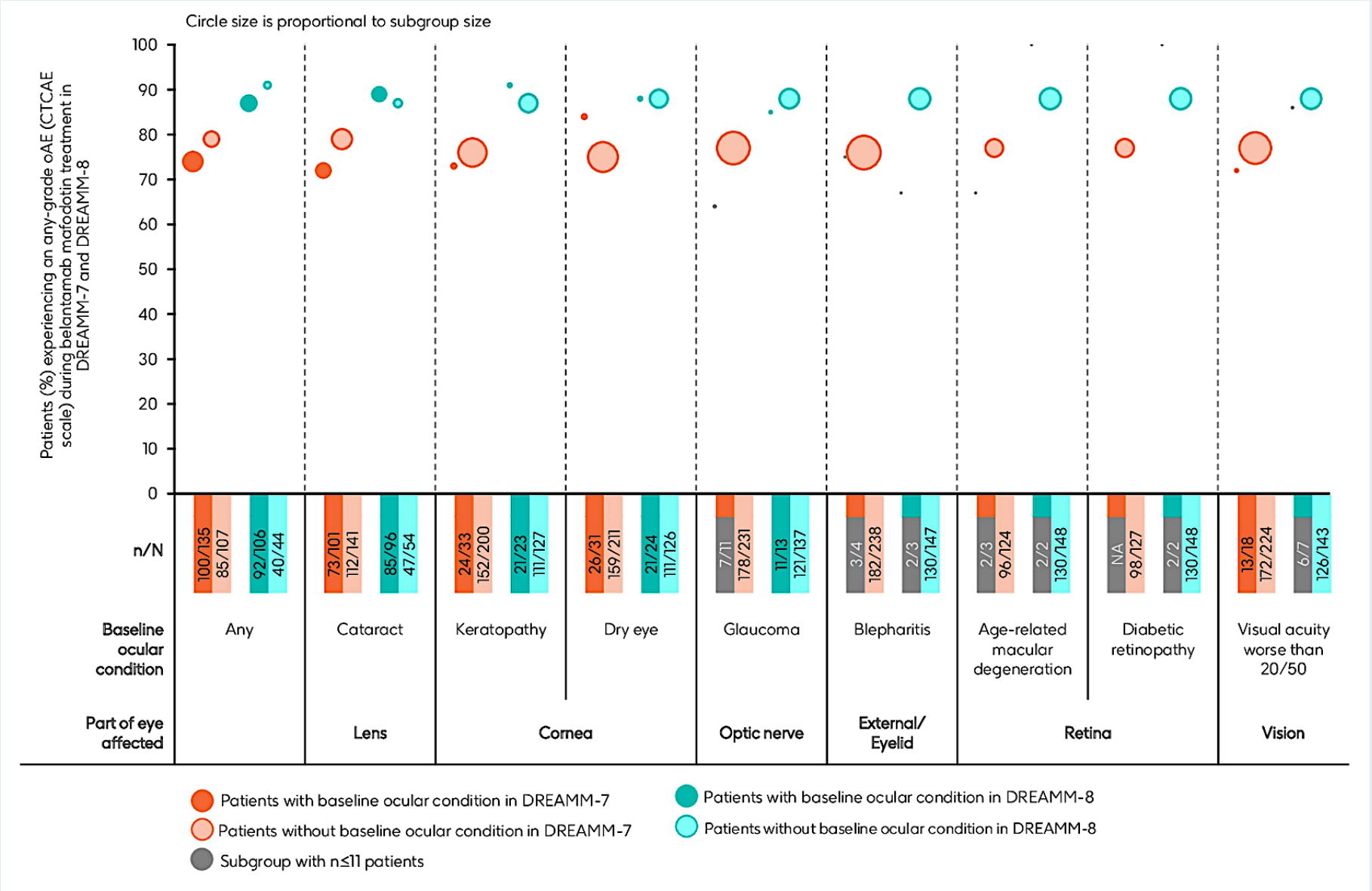
Figure 2: **Reduction of BCVA to 20/50 or worse was generally similar in patients with and without ocular conditions at baseline**

- Differences of >20 percentage points were observed between those with and without some baseline ocular conditions, but the size of the subgroups with baseline conditions were too small (n ≤11) for meaningful interpretation; these included baseline glaucoma (DREAMM-7), blepharitis (DREAMM-7 and -8), age-related macular degeneration (DREAMM-7), and diabetic nephropathy (DREAMM-8)



Beksac M et al. ASCO 2025;Abstract 7544.

Ocular Events in Patients with Baseline Ocular Conditions



Beksac M et al. ASCO 2025;Abstract 7544.

FDA Briefing Document

BLA 761440

Belantamab mafodotin

Oncologic Drugs Advisory Committee Meeting

July 17, 2025

Incidence of Ocular Toxicities with Belantamab Mafodotin

Table 17: DREAMM-7 and DREAMM-8 Overview of KVA Events

	DREAMM-7	DREAMM-8
Adverse Event Category, n (%)	**BVd N=242**	**BPd N=150**
Any Grade KVA event	222 (92)	140 (93)
Grade 1	13 (5)	9 (6)
Grade 2	22 (9)	15 (1)
Grade 3	136 (56)	103 (69)
Grade 4	51 (21)	13 (9)
Any dose modification due to KVA event	185 (76)	117 (78)
Dose interruption due to KVA event	179 (74)	113 (75)
Dose reduction due to KVA event	72 (30)	86 (57)
Discontinuation due to KVA event	15 (6)	11 (7)

Abbreviations: KVA=keratopathy and visual acuity (i.e., event per KVA scale).
Source: FDA Analysis

FDA Briefing Document: Oncologic Drugs Advisory Committee Meeting on July 17, 2025. https://www.fda.gov/media/187578/download

Timing and Duration of Ocular Toxicities with Belantamab Mafodotin

Table 20: Timing and Duration of Grade ≥2 KVA Events

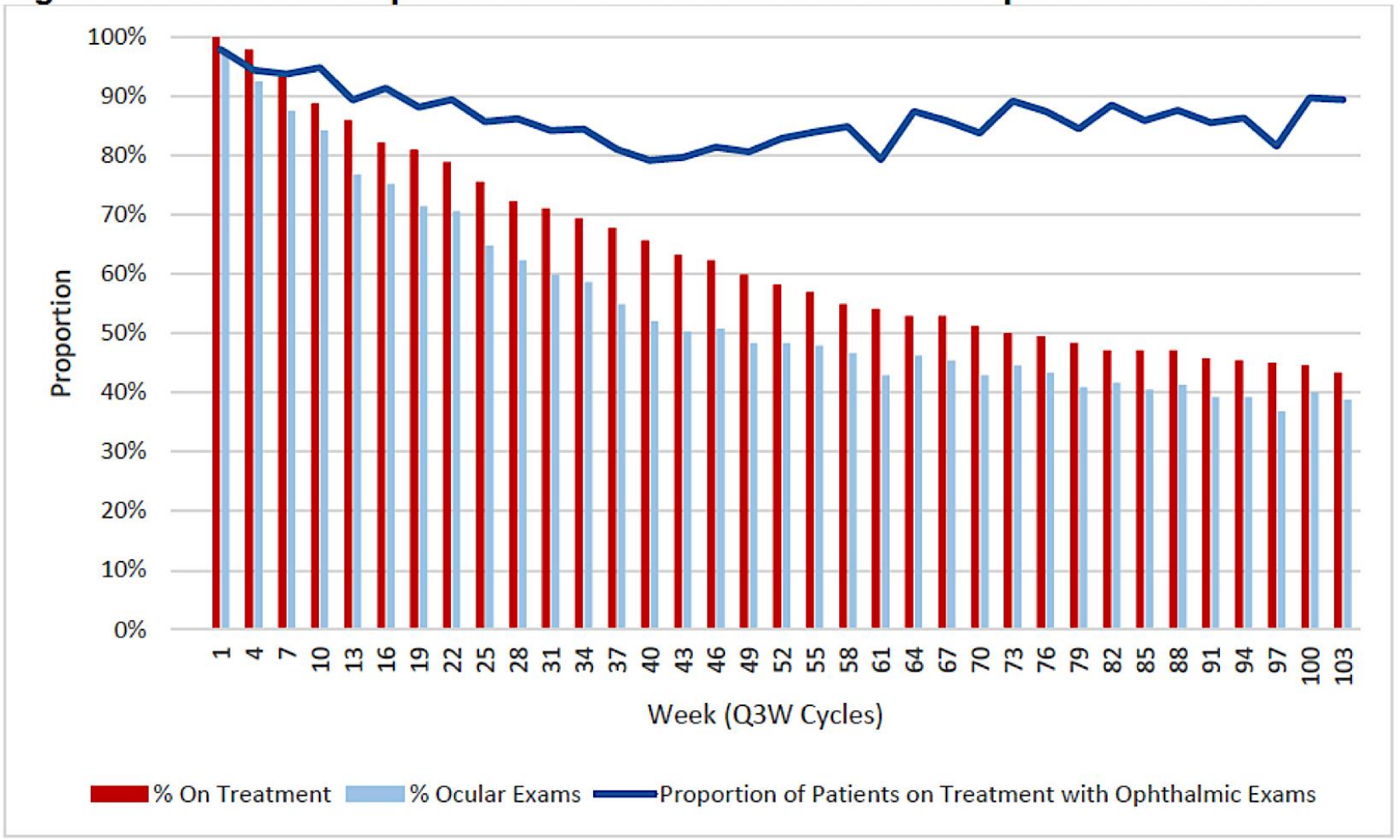
	DREAMM-7	DREAMM-8
	BVd N=242	BPd N=150
Grade ≥2 KVA event, n (%)	209 (86)	131 (87)
Onset (1st event), median (range), in days	43 (15, 611)	32 (18, 533)
0-2 months	154 (74)*	102 (78)
2-4 months	38 (18)	19 (14)
4-6 months	7 (3)	4 (3)
6 months and beyond	10 (5)	6 (5)
Duration (all events), median (range), in days	85 (5, 813)	85 (2, 746)

*Includes 1 patient with Grade 2 KVA findings at baseline.
Abbreviations: KVA=keratopathy and visual acuity (i.e., event per KVA scale).
Source: FDA analysis

FDA Briefing Document: Oncologic Drugs Advisory Committee Meeting on July 17, 2025. https://www.fda.gov/media/187578/download

DREAMM-7: Ophthalmic Exams

Figure 8: DREAMM-7 Proportion of Patients on Treatment with Ophthalmic Exams



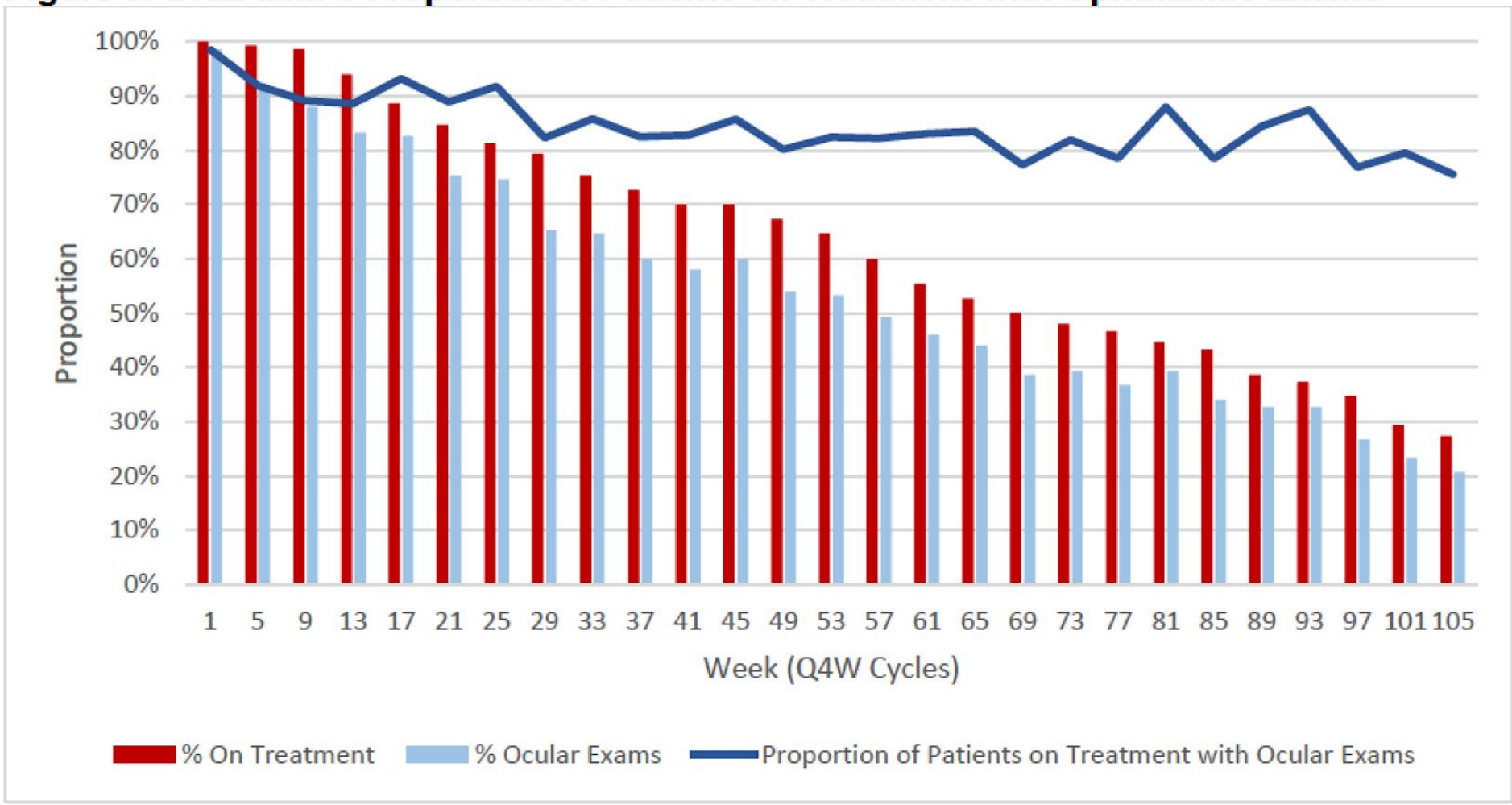
Abbreviations: Q3W=once every 3 weeks.

Source: FDA analysis; Applicant's Response to FDA Information Request dated February 7, 2025

FDA Briefing Document: Oncologic Drugs Advisory Committee Meeting on July 17, 2025. https://www.fda.gov/media/187578/download

DREAMM-8: Ophthalmic Exams

Figure 9: DREAMM-8 Proportion of Patients on Treatment with Ophthalmic Exams



Abbreviations: Q4W=once every 4 weeks.

Source: FDA analysis; Applicant's Response to FDA Information Request dated February 7, 2025

FDA Briefing Document: Oncologic Drugs Advisory Committee Meeting on July 17, 2025. https://www.fda.gov/media/187578/download

RTP RESEARCH TO PRACTICE

Outcome of Ocular Toxicities with Belantamab Mafodotin

Table 21: Outcome of Current or Last Grade 2 KVA Event

	DREAMM-7	DREAMM-8
	BVd N=242	BPd N=150
Grade ≥2 KVA event, n (%)	209 (86)	131 (87)
Outcome (last event), n (%)		
Resolved (Grade ≤1)	87 (42)	56 (43)
Ongoing	122 (58)	75 (57)
Ongoing study treatment	56 (27)	38 (29)
Discontinued treatment, follow-up ongoing	31 (15)	12 (9)
Discontinued treatment, follow-up ended	35 (17)	25 (19)

Abbreviations: KVA=keratopathy and visual acuity (i.e., event per KVA scale).

Source: FDA analysis

FDA Briefing Document: Oncologic Drugs Advisory Committee Meeting on July 17, 2025. https://www.fda.gov/media/187578/download

FDA Briefing Document: Belantamab Ocular Toxicity Summary

7.1.7 Ocular Toxicity Summary

The key safety issue with belantamab mafodotin is ocular toxicity, with specific findings that include keratopathy, clinically significant changes in visual acuity, and other ocular TEAEs such as blurred vision, photophobia, and dry eye. Despite the differences in the dosing regimens of belantamab mafodotin in DREAMM-7 and DREAMM-8, with a reduction in dose from Cycle 2 onward in DREAMM-8, the ocular toxicity findings were generally similar across studies.

In both DREAMM-7 and DREAMM-8, there were high rates of KVA events, including Grade 3 and higher KVA events. The majority of patients experienced recurrent KVA events throughout the duration of treatment and a substantial percentage of patients experienced clinically significant unilateral changes in visual acuity. While data regarding reversibility of ocular toxicity is limited by the duration of follow up and missing eye exams following study treatment, it is notable that not all KVA events, including visual acuity changes, resolved and that a subset of patients who discontinued study treatment continued to have stable or worsening KVA events at the time of follow up examinations. These findings raise questions regarding the reversibility of the ocular toxicity seen with belantamab mafodotin, particularly towards the end of study treatment, when a patient may have already experienced multiple ocular toxicity events.

FDA Briefing Document: Oncologic Drugs Advisory Committee Meeting on July 17, 2025. https://www.fda.gov/media/187578/download

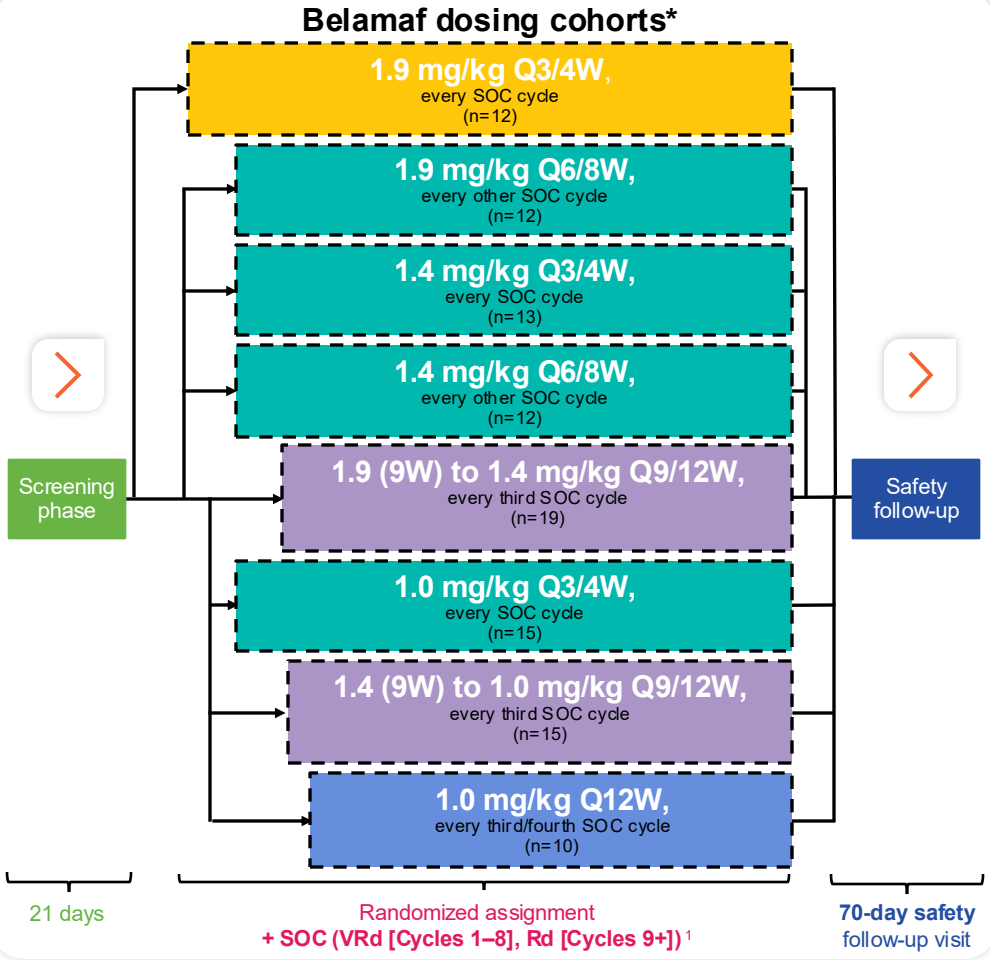
DREAMM-9: Study design

Inclusion criteria

- MM diagnosis per IMWG criteria
- ECOG performance status of 0–2
- Not a candidate for HDT with ASCT due to frailty and/or significant comorbid condition(s)
- Measurable disease per IMWG criteria

Exclusion criteria

- Prior systemic therapy for MM or SMM
- Current corneal epithelial disease



Primary endpoint:

- Safety (DLTs and AEs)

Secondary endpoints

- Efficacy (ORR, ≥CR, ≥VGPR per IMWG criteria)
- RDI of lenalidomide and bortezomib after 4 cycles
- Cumulative administered belamaf dose after 4 cycles with VRd
- Incidence and titers of ADAs
- PK

Exploratory endpoint

- MRD negativity (assessed in bone marrow aspirate samples using next-generation sequencing [10^{-5}]).

- Cohorts with lower doses and longer schedules were opened to assess the potential to improve tolerability while maintaining efficacy
- All cohorts received belamaf with VRd for Cycles 1–8 (21-day cycle), followed by belamaf with Rd for Cycles 9+ (28-day cycle)
- Ocular events were managed by dose modifications or extending the dosing interval

*Cohorts of the same color opened at the same time. Cohorts with longer rectangles opened earlier.
ADA, anti-drug antibodies; AE, adverse event; ASCT, autologous stem cell transplant; belamaf, belantamab mafodotin; CR, complete response; DLT, dose-limiting toxicities; ECOG, Eastern Cooperative Oncology Group; HDT, high-dose chemotherapy; IMWG, International Myeloma Working Group; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; PK, pharmacokinetics; PR, partial response; QxW, every x weeks; RDI, relative dose intensity; SMM, smouldering MM; SOC, standard of care; VGPR, very good partial response

Courtesy of Thanos C Dimopoulos, MD

Usmani S, et al. ASH 2024;Abstract 497.

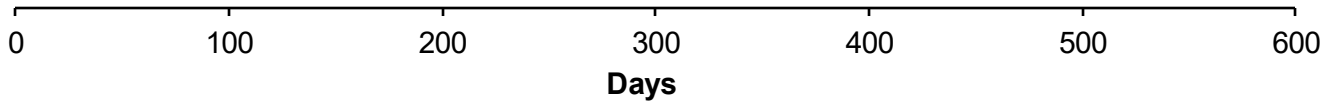
DREAMM-9: Best corrected visual acuity

Dose and schedule affected the time to, and resolution of, BCVA decreases

- Extending the dosing interval between the 1.9 mg/kg or 1.4 mg/kg doses from Q3/4W to Q6/8W was associated with longer time to BCVA decrease to 20/50 or worse*
- Resolution of BCVA decreases was generally faster in cohorts with lower initial doses of belamaf

First occurrence of decrease in BCVA score from baseline (20/25 or better) to 20/50 or worse

Belamaf schedule	Number of patients, n (%)	Time to onset	Median (range), days
1.9 mg/kg Q3/4W	6 (50)		76 (42–439)
1.9 mg/kg Q6/8W	6 (50)		246 (106–472)
1.4 mg/kg Q3/4W	3 (23)		128 (113–409)
1.4 mg/kg Q6/8W	6 (50)		264 (92–546)
		Time to resolution	
1.9 mg/kg Q3/4W			163 (36–230)
1.9 mg/kg Q6/8W			135 (29–246)
1.4 mg/kg Q3/4W			36 (22–85)
1.4 mg/kg Q6/8W			70 (43–421)



*In the 4 cohorts shown, 2 patients had a BCVA change from 20/25 or better to 20/200 or worse. These patients both had bilateral cataracts.
†Image adapted from Shi C, et al. bioRxiv. 2018;doi:doi.org/10.1101/328443. Copyright © 2018 the Author.
belamaf, belantamab mafodotin; BCVA, best corrected visual acuity; QxW, every x weeks.

Courtesy of Thanos C Dimopoulos, MD

Usmani S, et al. ASH 2024;Abstract 497.

LETTER TO THE EDITOR

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

Hultcrantz M et al. *Haematologica* 2025 March 1;110(3):753-7.

Assessment of Ocular Events During Follow-Up

Ocular events	Patients N=184
N of belantamab mafodotin administrations prior to first event, median (mean ± SD)	2.0 (2.1±1.1)
By number of belantamab mafodotin administrations prior to first event, N (%)	
1	30 (16.3)
2	40 (21.7)
≥3	22 (12.0)
N of events in patients with ≥1 event, median (mean ± SD)	2.0 (1.7±0.9)
By number of events, N (%)	
1	44 (23.9)
>1	48 (26.1)
2	34 (18.5)
≥3	14 (7.6)

Hultcrantz M et al. *Haematologica* 2025 March 1;110(3):753-7.

Assessment of Ocular Events During Follow-Up (Continued)

Ocular events	Patients N=184
Type of event, N (%)	
Keratopathy	76 (41.3)
Patients with multiple keratopathy events	6 (7.9)
Keratopathy severity of first event	
Patients with ≥1 ocular examination on or after the keratopathy onset date	72 (94.7)
BCVA score assessment	63 (82.9)
Slit lamp examination	71 (93.4)
Blurred vision	52 (28.3)
Dry eye	32 (17.4)
Keratitis	18 (9.8)
Action taken	
Therapy hold*, N (%)	57 (31.0)
Patients subsequently administered belantamab mafodotin, N (%)	41 (22.3)
Time from last administration before the onset date to subsequent administration† in days, median (mean ± SD)	42.0 (48.4±27.2)
Hold >28 days, N (%)	26 (14.1)
Treatment for adverse event, N (%)	55 (29.9)
Therapy dose or schedule change, N (%)	18 (9.8)
None, N (%)	14 (7.6)
Therapy discontinuation, N (%)	13 (7.1)

BCVA = best corrected visual acuity

Hultcrantz M et al. *Haematologica* 2025 March 1;110(3):753-7.

Assessment and Management of Keratopathy Events During Follow-Up

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

Hultcrantz M et al. *Haematologica* 2025 March 1;110(3):753-7.

Assessment and Management of Keratopathy Events During Follow-Up (Continued)

Keratopathy severity, N=62	Mild N=38	Moderate N=19	Severe N=5
Therapy dose or schedule change, N (%)	7 (18.4)	6 (31.6)	1 (20.0)
Therapy discontinuation, N (%)	3 (7.9)	4 (21.1)	1 (20.0)

Hultcrantz M et al. *Haematologica* 2025 March 1;110(3):753-7.

Ophthalmic Monitoring During Follow-Up

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

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

Hultcrantz M et al. *Haematologica* 2025 March 1;110(3):753-7.

Ophthalmic Monitoring During Follow-Up (Continued)

Ophthalmic examinations before each belantamab mafodotin administration	Patients N=184
First administration	
Patients with ≥1 ophthalmic examination before first administration, N (%)	169 (91.8)
≤14 days prior to administration, N (%)	142 (77.2)
≤28 days prior to administration, N (%)	164 (89.1)
Ocular treatments, N (%)	
Any	157 (85.3)
Preservative-free artificial tears	130 (70.7)
Eye drops	34 (18.5)
Other	16 (8.7)

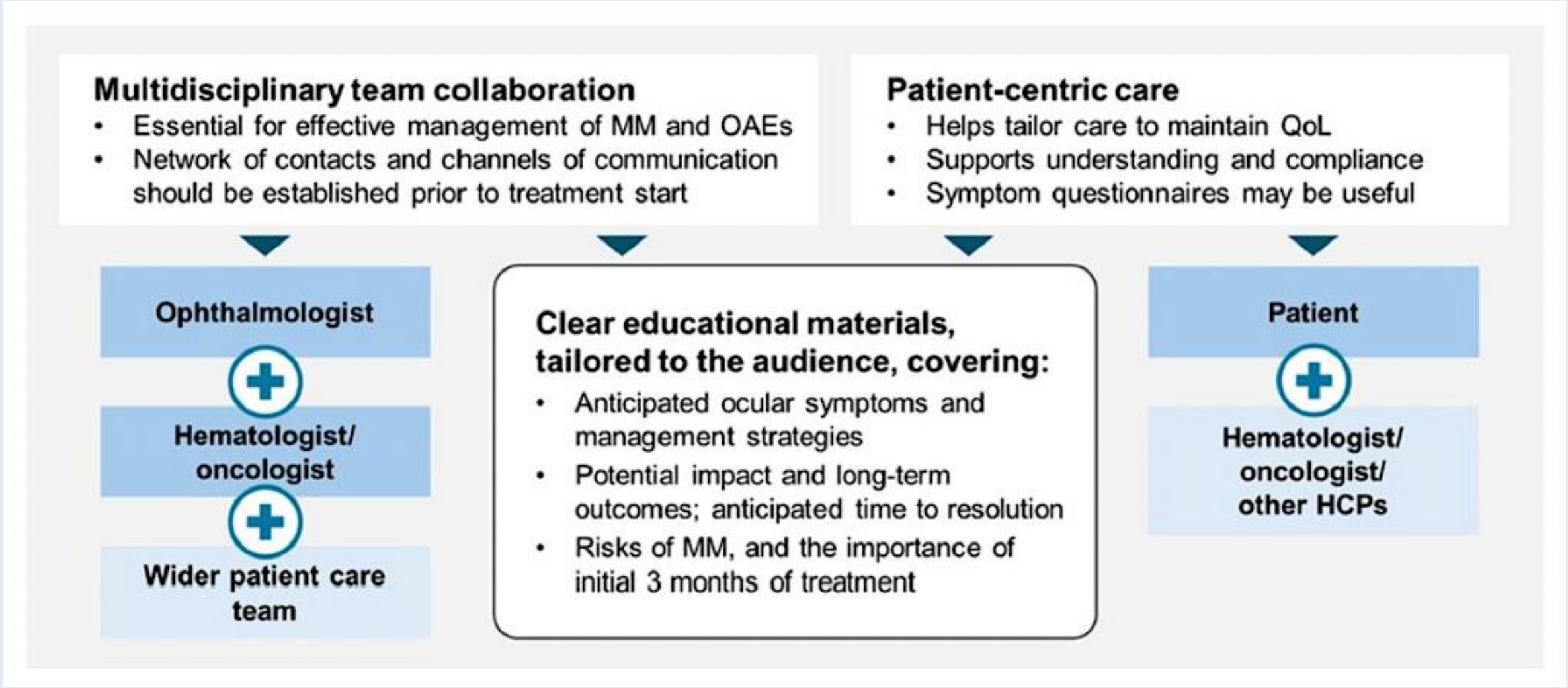
Hultcrantz M et al. *Haematologica* 2025 March 1;110(3):753-7.

Practical Guidance on the Clinical Management of Ocular Adverse Events Associated with Belantamab Mafodotin for Patients with Relapsed/Refractory Multiple Myeloma: Latin American Expert Panel Recommendations

Vânia Hungria · Virginia Abello Polo · Ariel Corzo · Edvan Q. Crusoe · Michel E. Farah · Natália A. Iutaka · Gracia A. Martinez · Aline G. Ramírez Alvarado · Simón Romano-Bucay · Patricio G. Schlottmann · Cristian M. Seehaus · Jorge C. Torres Flores · Angelo Maiolino

Oncol Ther 2025;[Online ahead of print].

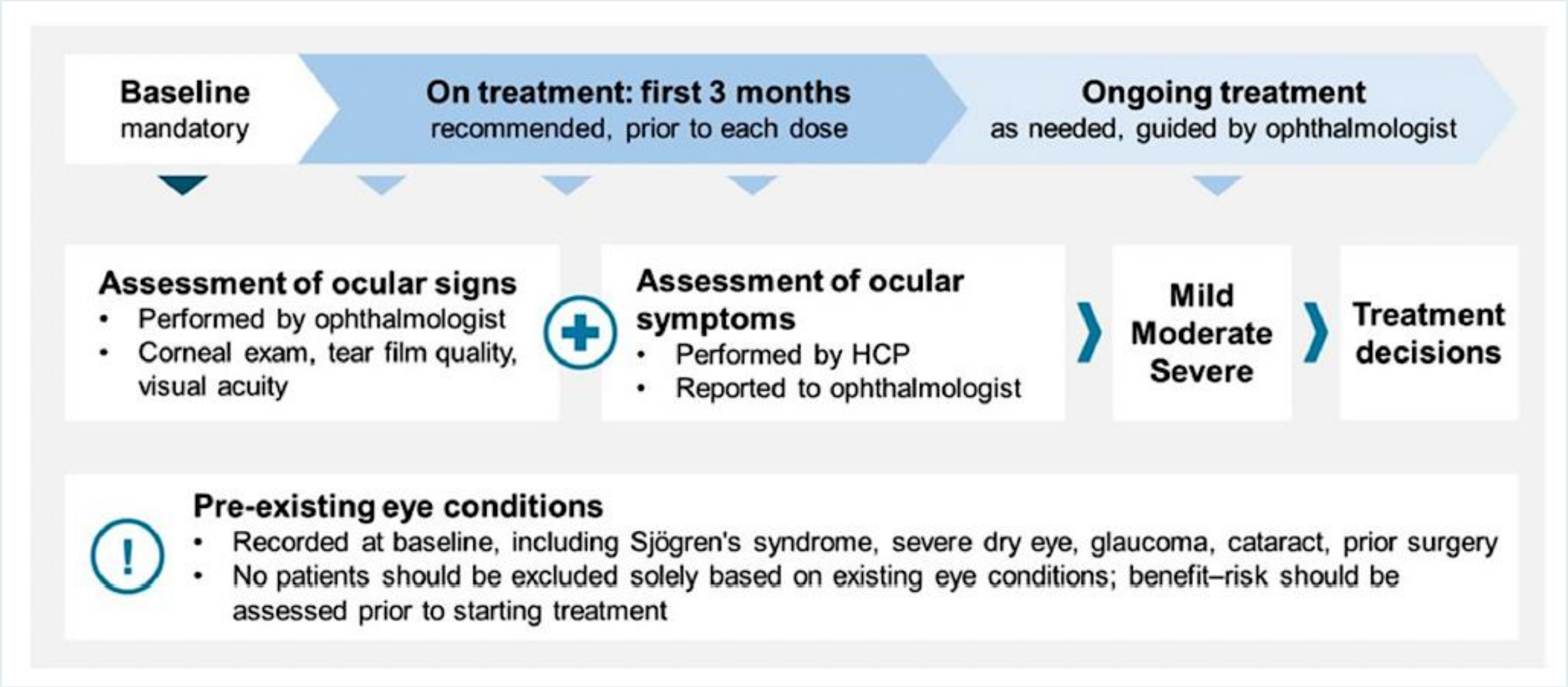
Belantamab: Latin American Expert Panel Recommendations



MM = multiple myeloma; OAEs = ocular adverse events

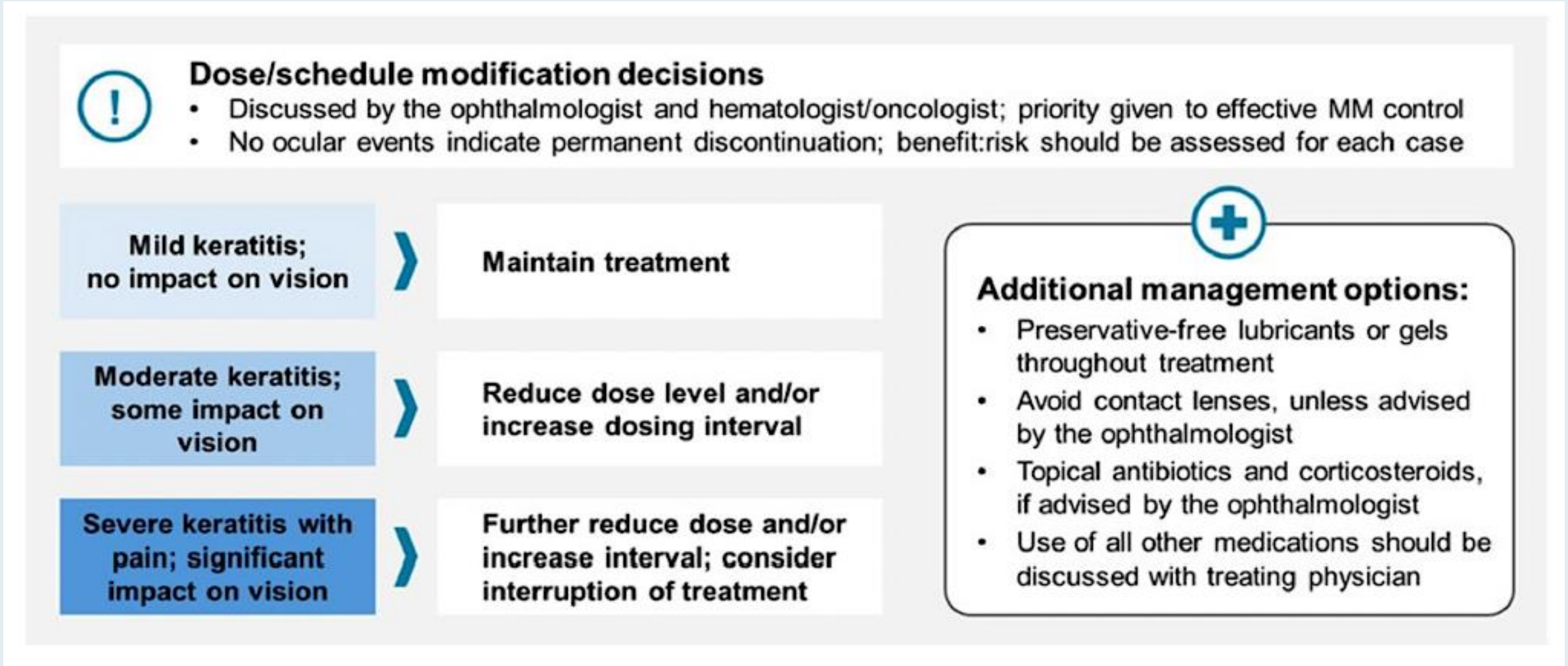
Hungria V et al. *Oncol Ther* 2025;[Online ahead of print].

Belantamab: Latin American Panel – Ocular Assessments



Hungria V et al. *Oncol Ther* 2025;[Online ahead of print].

Belantamab: Latin American Expert Panel – Dose Modifications



Hungria V et al. *Oncol Ther* 2025;[Online ahead of print].

Agenda

Introduction: The Patient Experience

Module 1: Managing Ocular Toxicities Associated with Antibody-Drug Conjugates and Other Cancer Therapies — Dr Pasricha

Module 2: Ocular Toxicities in Multiple Myeloma

Module 3: Ocular Toxicities in Breast Cancer

2024 ESMO BREAST CANCER
Annual Congress

Datopotamab deruxtecan (Dato-DXd) vs chemotherapy in pretreated, inoperable/metastatic HR+/HER2– breast cancer: Additional safety analysis from TROPION-Breast01

Komal Jhaveri,[1] Aditya Bardia,[2] Seock-Ah Im,[3] Sonia Pernas,[4] Michelino De Laurentiis,[5] Shusen Wang,[6] Noelia Martínez Jañez,[7] Giuliano Borges,[8] David W. Cescon,[9] Masaya Hattori,[10] Yen-Shen Lu,[11] Erika Hamilton,[12] Junji Tsurutani,[13] Kevin Kalinsky,[14] Darlington Mapiye,[15] Rick Fairhurst,[16] Manjunatha Ankathatti Munegowda,[17] Binghe Xu,[18] Barbara Pistilli,[19] Hope S. Rugo[20]

[1]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA, and Department of Medicine, Weill Cornell Medical College, New York, NY, USA; [2]Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA (formerly Massachusetts General Cancer Center, Harvard Medical School, Boston, MA, USA); [3]Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul National University, Seoul, Republic of Korea; [4]Institut Català d'Oncologia, IDIBELL, L'Hospitalet, Barcelona, Spain; [5]Istituto Nazionale Tumori Napoli IRCCS "Fondazione Pascale", Napoli, Italy; [6]Cancer Center of Sun Yet-sen University, Guangzhou, China; [7]Ramón y Cajal University Hospital, Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain; [8]Catarina Pesquisa Clínica, Santa Catarina, Brazil; [9]Princess Margaret Cancer Centre/UHN, Toronto, ON, Canada; [10]Aichi Cancer Center, Nagoya, Japan; [11]National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan; [12]Sarah Cannon Research Institute, Nashville, TN, USA; [13]Showa University Hospital, Tokyo, Japan; [14]Winship Cancer Institute at Emory University, Atlanta, GA, USA; [15]AstraZeneca, Cambridge, UK; [16]AstraZeneca, Gaithersburg, MD, USA; [17]AstraZeneca, Mississauga, ON, Canada; [18]National Cancer Center / National Clinical Research Center for Cancer / Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [19]Gustave Roussy Cancer Center, Villejuif, France; [20]University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA

TROPION-Breast01 Study Design

Randomised, phase 3, open-label, global study (NCT05104866)

Key inclusion criteria:

- Patients with HR+/HER2– breast cancer* (HER2– defined as IHC 0/1+/2+; ISH negative)
- Previously treated with 1–2 lines of chemotherapy (inoperable/metastatic setting)
- Experienced progression on ET and for whom ET was unsuitable
- ECOG PS 0 or 1

1:1

Dato-DXd
6 mg/kg IV Day 1 Q3W
(n=365)

Investigator's choice of chemotherapy (ICC)
as per protocol directions†
(eribulin mesylate D1,8 Q3W; vinorelbine D1,8 Q3W; gemcitabine D1,8 Q3W; capecitabine D1–14 Q3W)
(n=367)

Endpoints:

- **Dual primary:** PFS by BICR per RECIST v1.1, and OS
- **Key secondary:** ORR, PFS (investigator assessed) and **safety**

Randomisation stratified by:

- **Lines of chemotherapy** in unresectable/metastatic setting (1 vs 2)
- **Geographic location** (USA/Canada/Europe vs other geographic regions)
- **Previous CDK4/6 inhibitor** (yes vs no)

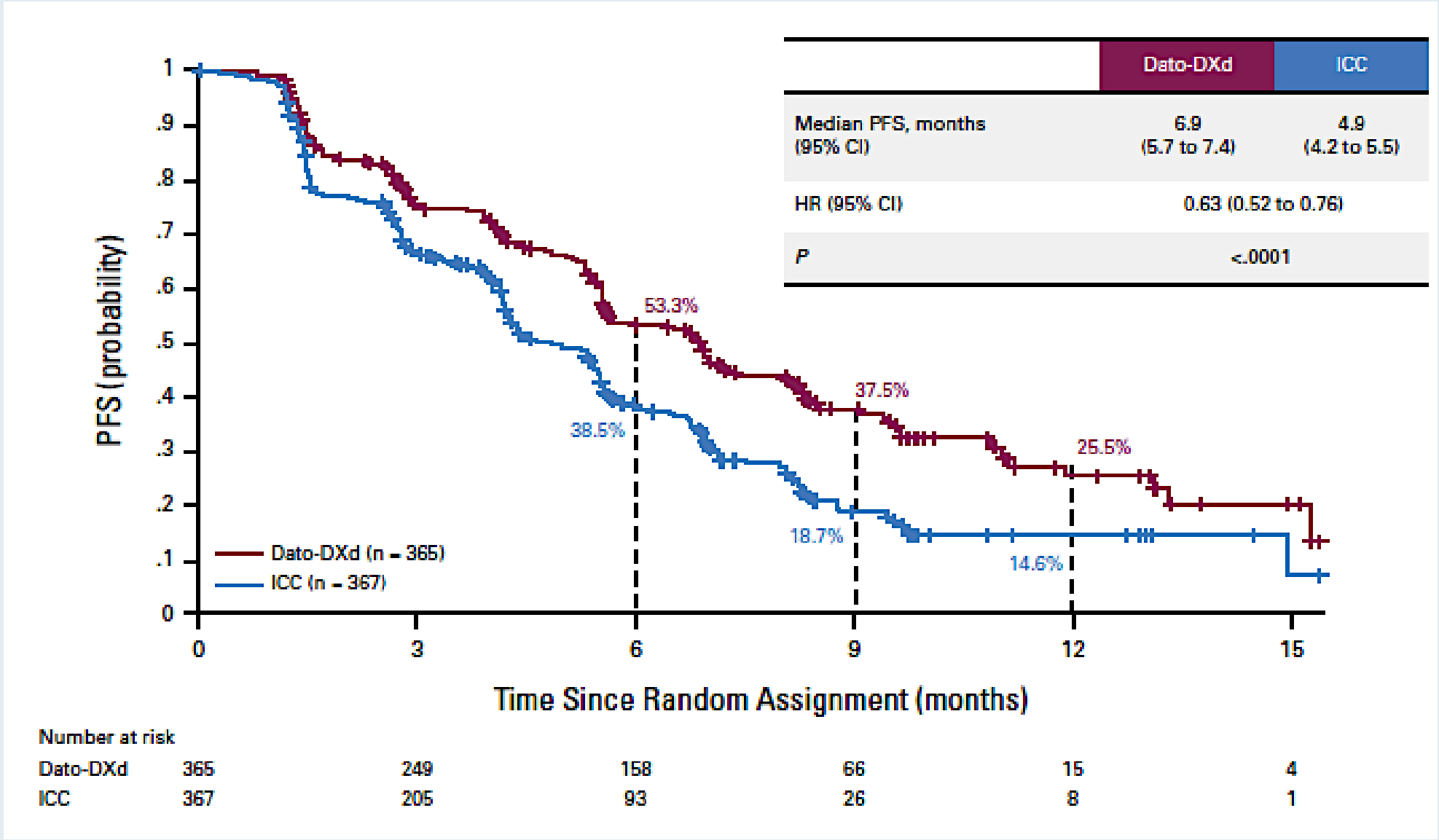
- Treatment continued until PD, unacceptable tolerability, or other discontinuation criteria

Detailed description of the statistical methods published previously.[1] *Per American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines. †ICC was administered as follows: eribulin mesylate, 1.4 mg/m^2 IV on Days 1 and 8, Q3W; vinorelbine, 25 mg/m^2 IV on Days 1 and 8, Q3W; gemcitabine, 1000 mg/m^2 IV on Days 1 and 8, Q3W; or capecitabine, 1000 or 1250 mg/m^2 orally twice daily on Days 1 to 14, Q3W (dose per standard institutional practice). CDK4/6, cyclin-dependent kinase 4/6; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; IHC, immunohistochemistry; ISH, in situ hybridisation; IV, intravenous; ORR, objective response rate; OS, overall survival; PD, progressive disease; Q3W, once every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

1. Bardia A, et al. *Future Oncol* 2024;20:423–36.

Jhaveri K et al. ESMO Breast 2024;Abstract LBA2.

TROPION-Breast01: Progression-Free Survival



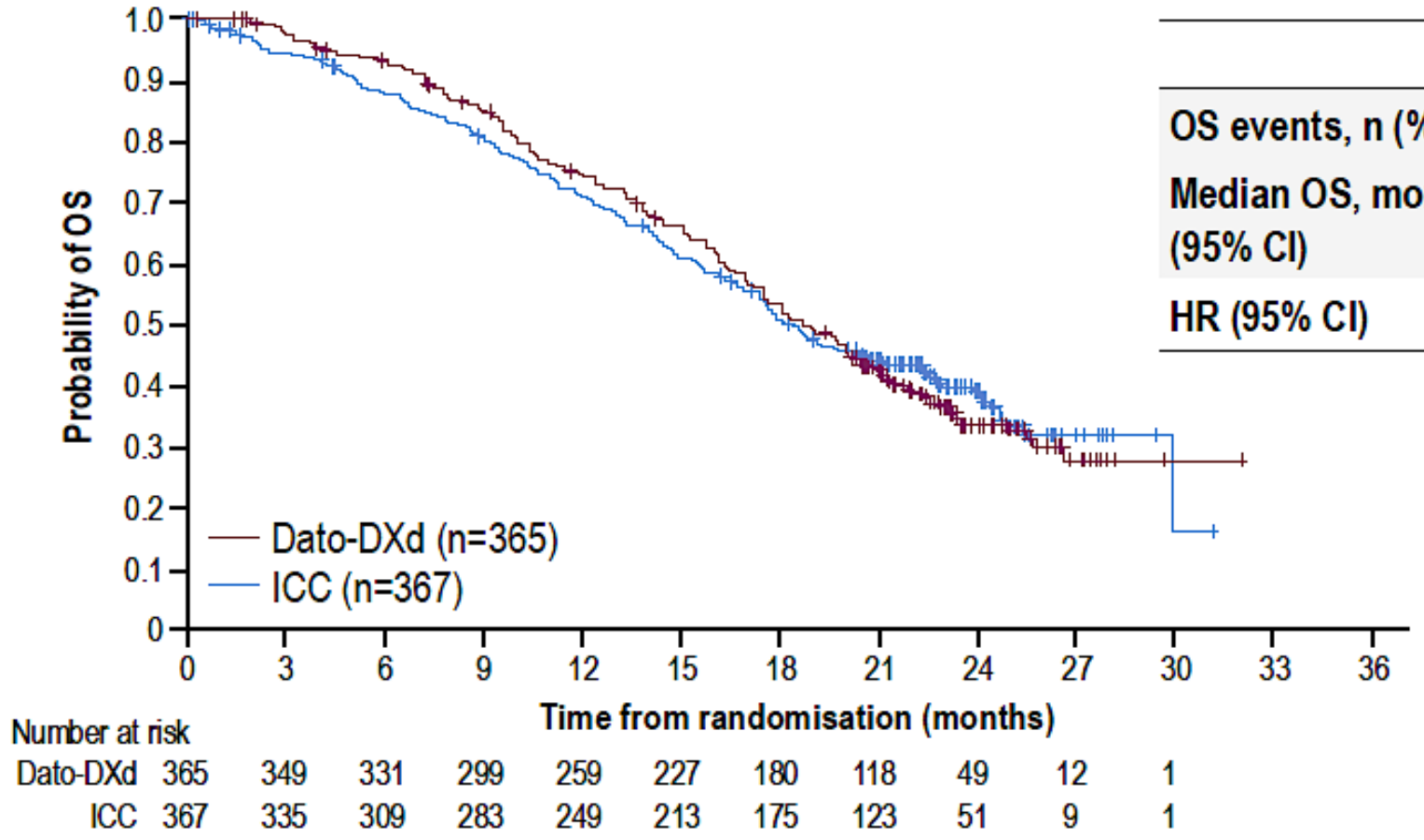
	Dato-DXd	ICC
Median PFS, months (95% CI)	6.9 (5.7 to 7.4)	4.9 (4.2 to 5.5)
HR (95% CI)	0.63 (0.52 to 0.76)	
P	<.0001	

Number at risk

Dato-DXd	365	249	158	66	15	4
ICC	367	205	93	26	8	1

Bardia A et al. *J Clin Oncol* 2025;43(3):285-96.

TROPION-Breast01: Overall Survival



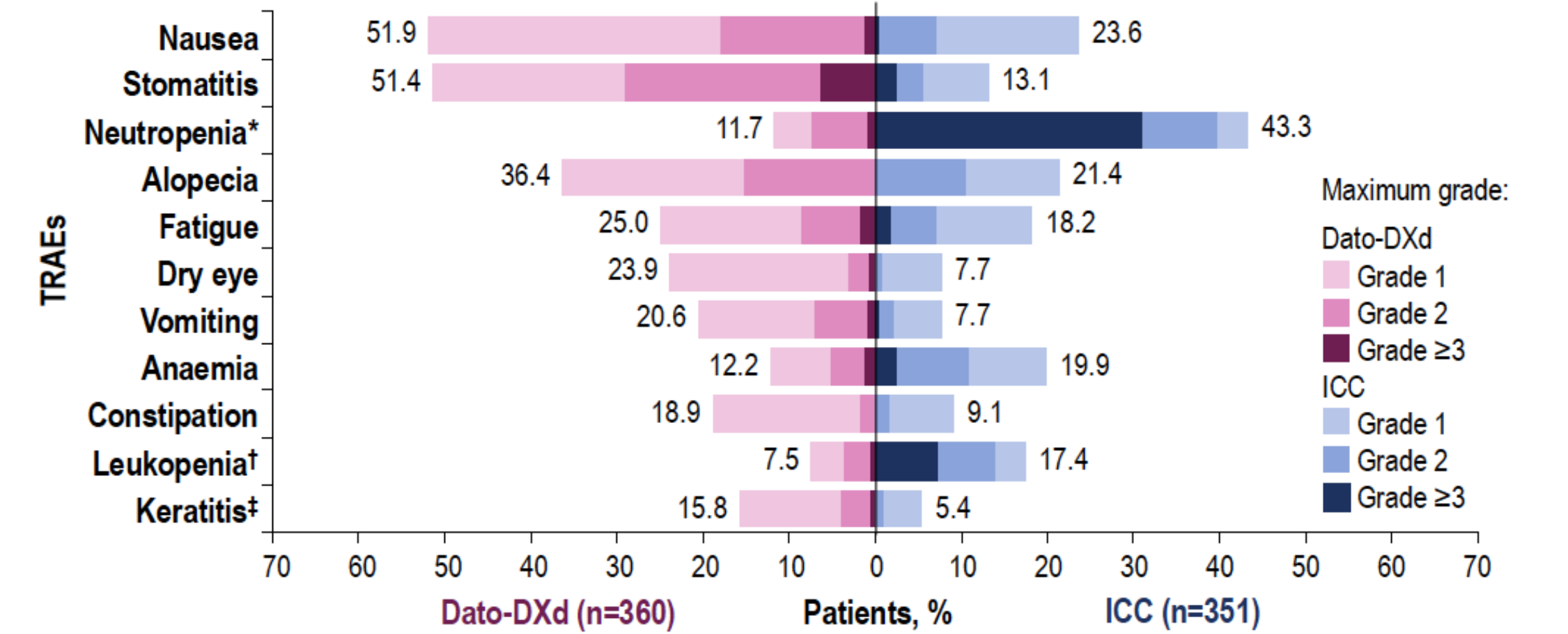
	Dato-DXd	ICC
OS events, n (%)	223 (61)	213 (58)
Median OS, months (95% CI)	18.6 (17.3–20.1)	18.3 (17.3–20.5)
HR (95% CI)	1.01 (0.83–1.22)	

- Maturity: 59.6%
- Median follow-up: 22.8 months
- Protocol prespecified OS sensitivity analysis based on the stratification factors according to the eCRF*: **HR 0.99 (95% CI: 0.82–1.20)**

Data cutoff: 24 July 2024. Pre-specified P-value boundary for OS analysis: α=0.0427.
*Mis-stratification between interactive response technology (where data entered could not be changed by the site) and eCRF (where data could be corrected by sites) was <5%.
eCRF, electronic case report form.

Pistilli B et al. ESMO Virtual Plenary, February 12, 2025.

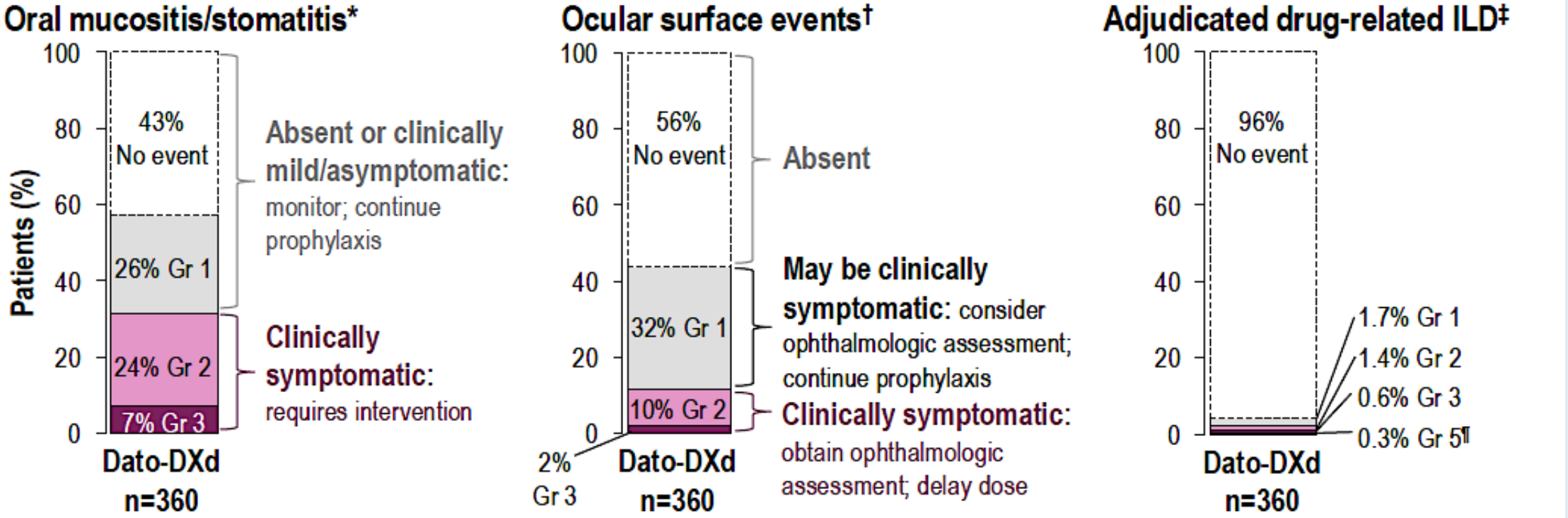
TROPION-Breast01: Treatment-Related Adverse Events Occurring in ≥15% of Patients



Data cutoff: 24 July 2024. Data are ordered according to frequency in either the Dato-DXd or ICC arms.
*Grouped term comprising neutropenia and neutrophil count decreased. †Grouped term comprising white blood cell count decreased and leukopenia. ‡Grouped term comprising keratitis, punctate keratitis, ulcerative keratitis.

Pistilli B et al. ESMO Virtual Plenary, February 12, 2025.

TROPION-Breast01: Treatment-Related Adverse Events of Special Interest



- Oral mucositis/stomatitis events were recovered/resolved or recovering/resolving in 178/206 patients (86%)
- Grade 3 ocular surface events were either recovered/resolved or recovering/resolving in 6/7 patients (86%)§

Data cutoff: 24 July 2024. Details of Toxicity Management Guidelines published previously.[1]

*Comprising PTs of aphthous ulcer, dysphagia, glossitis, mouth ulceration, odynophagia, oral mucosal blistering, oral pain, oropharyngeal pain, pharyngeal inflammation, stomatitis. †Comprising selected PTs from Corneal Disorder standard MedDRA query and select relevant preferred terms from Eye Disorder system organ class. ‡Comprising the PTs of ILD and pneumonitis; an independent adjudication committee reviewed all potential cases to assess whether the event was ILD/pneumonitis and, if so, whether it was related to the study drug. ¶The gr 5 event was characterised by the investigator as gr 3 pneumonitis, with death attributed to disease progression. §The patient with the gr 3 ocular surface event that was not recovered died before resolution. AESIs, adverse events of special interest; ILD, interstitial lung disease; PT, preferred term.

1. Bardia A, et al. J Clin Oncol 2025;43:285–96.

Pistilli B et al. ESMO Virtual Plenary, February 12, 2025.

Incidence of Ocular Toxicities with Datopotamab Deruxtecan (Dato-DXd)

Treatment-related ocular surface events*, n (%)	Dato-DXd (n=360)
All grades†	144 (40.0)
Grade 1	115 (31.9)
Grade 2	26 (7.2)
Grade 3	3 (0.8)
Leading to dose reduction and/or interruption	12 (3.3)
Leading to dose discontinuation	1 (0.3)

Toxicity management guidelines

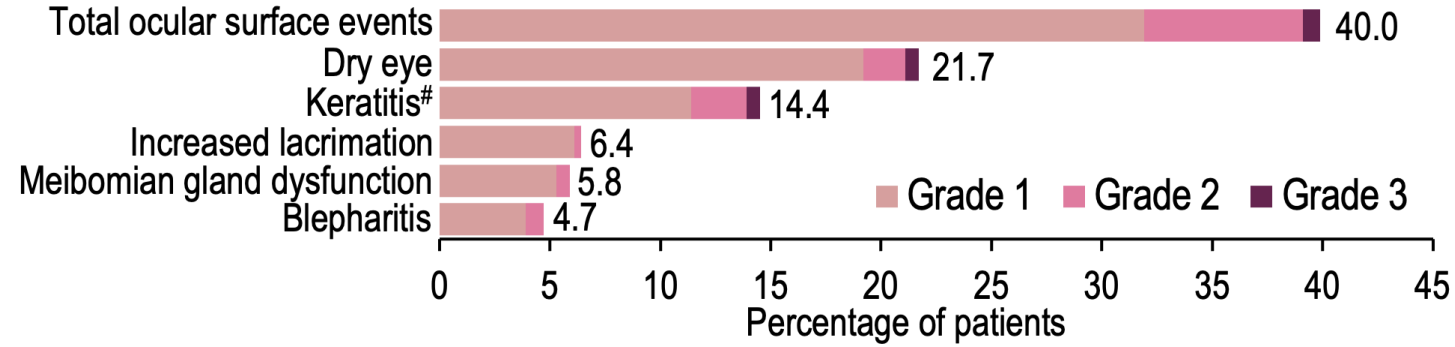
Daily use of **artificial tears** and **avoidance of contact lenses** recommended

- Most events were grade 1, with low rates of grade 2/3, low rates of dose reduction/ interruption (3.3%), and discontinuation (0.3%); over half of events were dry eye

Median time to onset: **65 days**

Median time to resolution‡: **67 days**

Most common preferred terms§



Ophthalmologic assessments were mandated during study (per regulatory request) every three 21-day cycles

Frequent assessments likely contributed to high rate of low-grade events in both arms; incidence of ocular surface events with ICC (11.7%) was higher than historic benchmarks.[1]

*Comprising the preferred terms of: blepharitis, conjunctivitis, corneal disorder, corneal erosion, corneal lesion, dry eye, foreign body sensation in eyes, keratitis, keratopathy, lacrimation increased, limbal stem cell deficiency, meibomian gland dysfunction, ocular toxicity, photophobia, punctate keratitis, superior limbic keratoconjunctivitis, ulcerative keratitis, vision blurred, visual impairment, and xerophthalmia. †No grade 4/5 events. ‡For events recovered/resolved at data cutoff. §Reported in ≥15 patients. #Grouped term comprising keratitis, punctate keratitis, and ulcerative keratitis.

1. Canino F, et al. *Clin Breast Cancer* 2022;22:289–99.

Jhaveri K et al. ESMO Breast 2024;Abstract LBA2.

FDA Approves Datopotamab Deruxtecan-dlnk for Unresectable or Metastatic, HR-positive, HER2-negative Breast Cancer

Press Release: January 17, 2025

The Food and Drug Administration approved datopotamab deruxtecan-dlnk, a Trop-2-directed antibody and topoisomerase inhibitor conjugate, for adult patients with unresectable or metastatic, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC1+ or IHC2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

Efficacy was evaluated in TROPION-Breast01 (NCT05104866), a multicenter, open-label, randomized trial. Patients must have experienced disease progression, been deemed unsuitable for further endocrine therapy, and have received one or two lines of prior chemotherapy for unresectable or metastatic disease.

Median PFS was 6.9 months (95% CI: 5.7, 7.4) in the datopotamab deruxtecan-dlnk arm and 4.9 months (95% CI: 4.2, 5.5) in the chemotherapy arm (Hazard ratio 0.63 [95% CI: 0.52, 0.76] two-sided p-value <0.0001). Median OS was 18.6 months (95% CI: 17.3, 20.1) in the datopotamab deruxtecan-dlnk arm and 18.3 months (95% CI: 17.3, 20.5) in the chemotherapy arm (Hazard ratio 1.01 [95% CI: 0.83, 1.22]; two-sided p-value was not statistically significant).

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https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-datopotamab-deruxtecan-dlnk-unresectable-or-metastatic-hr-positive-her2-negative-breast

Dato-DXd Ocular Toxicities – Keratitis – Prophylaxis

Prophylaxis

Advise patients to:

- Use preservative-free lubricant eye drops/ artificial tears several times daily (4 times daily for prevention and up to 8 times daily if clinically needed)
- **Avoid use of contact lenses unless directed by an eye care professional**

EMA = Patients should be promptly referred for appropriate ophthalmologic assessments for any new or worsening ocular signs and symptoms that could suggest keratitis.

FDA = Conduct an ophthalmic exam including visual acuity testing, slit lamp examination (with fluorescein staining), intraocular pressure, and fundoscopy at initiation of DATO, annually while on treatment, at end of treatment, and as clinically indicated.

Courtesy of Rebecca A Dent, MD, MSc

Dato-DXd Ocular Toxicities – Keratitis – Management

Eye disorders			
Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better or 3 lines or less decreased vision from known baseline)	Symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or more than 3 lines of decreased vision from known baseline, up to 20/200); corneal ulcer; limiting self care ADL	Perforation; best corrected visual acuity of 20/200 or worse in the affected eye

Grade 1
- Consider obtaining ophthalmologic assessment
- No change in Dato-DXd dose

Grade 2
- Obtain an ophthalmologic assessment
- Delay dose until event has been resolved to Grade ≤1, then maintain dose

Grade 3
- Obtain an ophthalmologic assessment
- Delay dose until event has been resolved to Grade ≤1, then reduce dose by 1 level

Grade 4
- Obtain an ophthalmologic assessment
- Permanently discontinue

Dose Reductions:
First 4 mg/kg (up to a maximum of 360 mg for patients ≥90 kg)
Second 3 mg/kg (up to a maximum of 270 mg for patients ≥90 kg)
Third Permanently discontinue

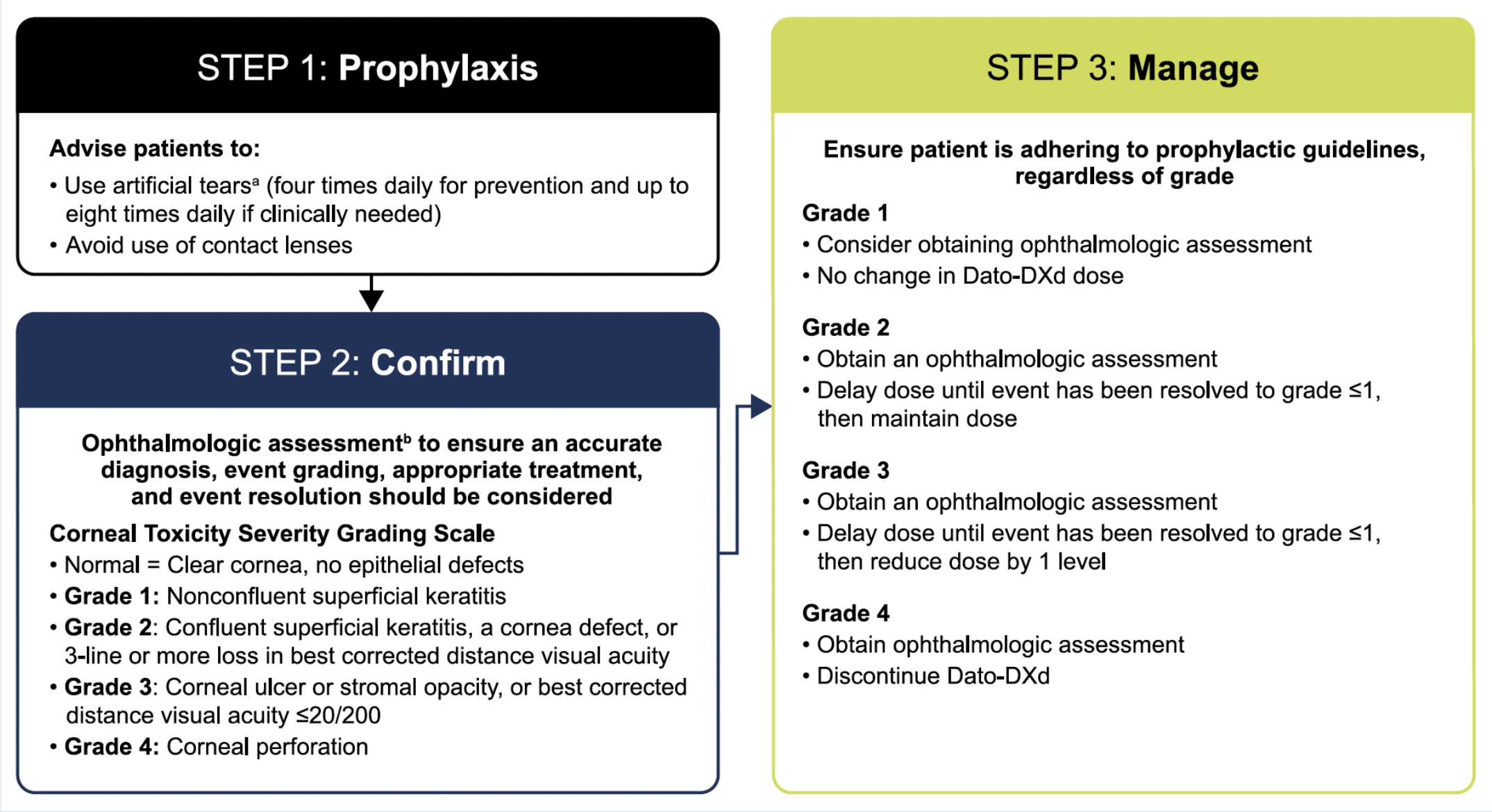
Courtesy of Rebecca A Dent, MD, MSc

Clinical management, monitoring, and prophylaxis of adverse events of special interest associated with datopotamab deruxtecan

Rebecca S. Heist [a,*], Jacob Sands [b], Aditya Bardia [c], Toshio Shimizu [d], Aaron Lisberg [c], Ian Krop [e], Noboru Yamamoto [f], Takahiro Kogawa [g], Saba Al-Hashimi [h], Simon S.M. Fung [h], Anat Galor [i,j], Francesca Pisetzky [k], Priyanka Basak [l], Cindy Lau [l], Funda Meric-Bernstam [m]

Cancer Treat Rev 2024;125:102720.

Clinical Management of Ocular Surface Events with Dato-DXd



Heist RS et al. *Cancer Treat Rev* 2024;125:102720.

STEP 3: **Manage**

Ensure patient is adhering to prophylactic guidelines, regardless of grade

Grade 1
- Consider obtaining ophthalmologic assessment
- No change in Dato-DXd dose

Grade 2
- Obtain an ophthalmologic assessment
- Delay dose until event has been resolved to grade ≤1, then maintain dose

Grade 3
- Obtain an ophthalmologic assessment
- Delay dose until event has been resolved to grade ≤1, then reduce dose by 1 level

Grade 4
- Obtain ophthalmologic assessment
- Discontinue Dato-DXd

Heist RS et al. *Cancer Treat Rev* 2024;125:102720.

Ocular Assessment Form for Dato-DXd

OCULAR ASSESSMENT FORM

This resource should be used to support ocular exams for patients on datopotamab deruxtecan-dink and inform decisions on treatment management.

TO BE COMPLETED BY THE PRESCRIBING ONCOLOGIST

ONCOLOGIST

NAME

FACILITY

PHONE

EMAIL

PATIENT

NAME

DATE OF BIRTH

PATIENT ID

RTP RESEARCH TO PRACTICE

Jhaveri K et al. ESMO Breast 2024;Abstract LBA2.

Ocular Assessment Form for Dato-DXd

INFORMATION FOR EYE CARE PROVIDERS

Your patient is being referred by their oncologist for an ophthalmic exam, as they have been prescribed treatment with Dato-DXd, a Trop-2-directed antibody and topoisomerase inhibitor conjugate.[1]
Dato-DXd can cause ocular adverse reactions, including dry eye, keratitis, blepharitis, meibomian gland dysfunction, increased lacrimation, conjunctivitis, and blurred vision.[1]

OCULAR EXAM DETAILS

When should patients undergo this exam?
Patients are instructed to receive an ocular assessment upon initiation of Dato-DXd, annually while on treatment, at end of treatment, and as clinically indicated! The initial eye exam serves as a reference point to monitor for any signs or symptoms of ocular conditions while on Dato-DXd.

What should the exam include?
Patients are instructed to undergo an ophthalmic exam that can be performed by either an optometrist or ophthalmologist. The exam should include the following[1]:

- ☐ visual acuity testing
- ☐ slit lamp examination (with fluorescein staining)
- ☐ intraocular pressure
- ☐ fundoscopy

Ocular assessment may be covered by medical or vision insurance. Patients may also be eligible for coverage up to $250 for an eye exam related to the use of Dato-DXd through the DATROWAY4U patient savings program.*

What should I be looking for when performing the exams?

- There are **no contraindications** to prescribing Dato-DXd. Patients with clinically significant corneal disease were excluded from clinical studies. **Notify the prescribing oncologist** if you believe your patient falls under this category
- If any new or worsening ocular signs and symptoms could suggest an eye condition, notify the prescribing oncologist (refer to chart on page 2)

RTP RESEARCH TO PRACTICE

Ocular Assessment Form for Dato-DXd

RECOMMENDED PROPHYLAXIS[1]

- Advise patients to **use preservative-free lubricant eye drops at least 4 times daily and as needed**
- Advise patients to **avoid using contact lenses during treatment** unless directed by an eye care professional

DOSAGE MODIFICATIONS OF Dato-DXd FOR SELECT ADVERSE EVENTS: KERATITIS[1]

Please see the table below for recommended management strategies for a common ocular adverse reaction on Dato-DXd, and see the Important Safety Information and accompanying full Prescribing Information for more Intormation.

Severity of Keratitis	Eye Care Provider Action	Oncologist Action for Dosage Modifications
Nonconfluent superficial keratitis	Notify prescribing oncologist*†	Monitor and continue at current dose
Confluent superficial keratitis, a corneal epithelial defect, or 3-line or more loss in best corrected visual acuity		Withhold until improved or resolved, then maintain at same dose level or consider dose reduction
Corneal ulcer or stromal opacity or best corrected distance visual acuity 20/200 or worse		Withhold until improved or resolved, then reduce by one dose level
Corneal perforation		Permanently discontinue

RTP RESEARCH TO PRACTICE

Cancer Q&A: Addressing Common Questions Posed by Patients with Relapsed/Refractory Multiple Myeloma

A Webinar Series for Clinicians and Patients,
Developed in Partnership with Cancer*Care*®

Patients	Clinicians
Wednesday, July 23, 2025	**Thursday, August 7, 2025**
6:00 PM – 7:00 PM ET	**5:00 PM – 6:00 PM ET**

Faculty

Natalie S Callander, MD
Sagar Lonial, MD, FACP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME and ABIM MOC credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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