Best Practices for the Management of Ocular Events with ADCs

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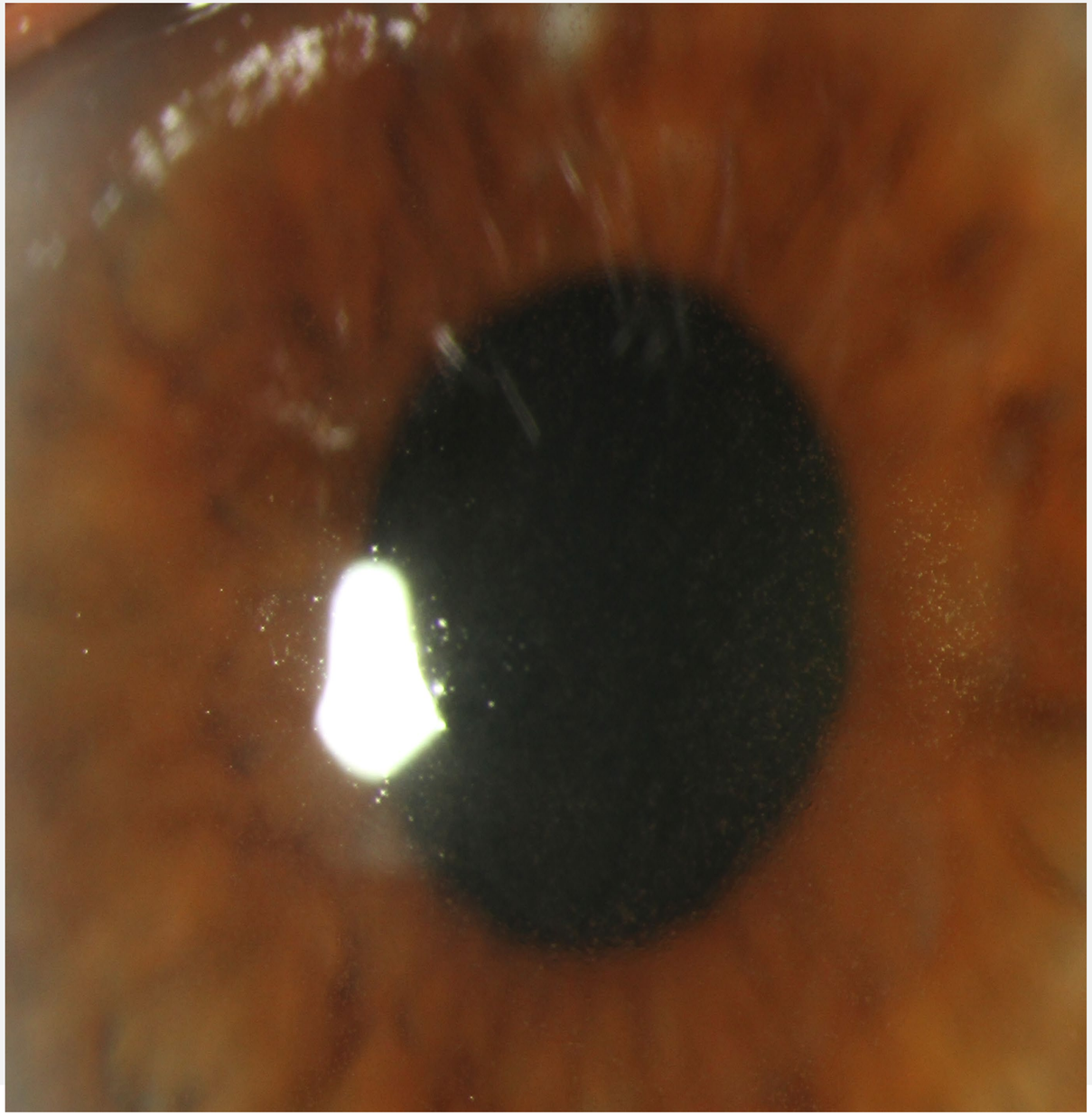

56-year-old female with metastatic cervical cancer

- Grade 1 and 2 keratitis during treatment
- Normal baseline ophthalmologic exam and she adhered to the required eye care plan
- Received 9 cycles of tisotumab vedotin (4 full doses, 5 reduced doses [1.3 mg/kg])
- After Cycle 3, the patient presented to the oncology clinic for an unscheduled visit due to red eyes
- On the same day, we were consulted, and the patient was prescribed steroid eye drops for a week and artificial tears
- The patient again experienced red eyes 5 days later and was reassessed and diagnosed with Grade 2 keratitis
- Treated with lubricating eye drops
- One week later, the keratitis had improved to Grade 1 and resolved after another week
- The tisotumab dose was again reduced to 1.3 mg/kg, with no new ocular adverse events (AEs) reported during the next four months of treatment

Ocular Toxicities of ADCs for Gynecologic Cancers

	Tisotumab	Mirvetuximab	Trastuzumab	Upifitamab	Luveltamab (STRO-002-GM2)	Farletuzumab (MORAb-003)
Trade Name	Tivdak	Elahere	T-DXd	UpRi	Luvelta	
Receptor Binding	Tissue Factor	Folate Receptor alpha	HER-2	anti-NaPi2b	Folate Receptor alpha	Folate Receptor alpha
Cancer Target	Cervical	Ovarian	Solid Tumor	Ovarian	Ovarian	Ovarian
Toxicity Site in the Eye	Ocular Surface	Cornea	Cornea, Conjunctiva			
Ocular Findings	• Conjunctival AEs 40% • Dry eye 29% • Corneal AEs 21% • Blepharitis 8% • Severe ulcerative keratitis 3.2%	• Dry eye 25% • Keratopathy 24%	• Dry eye 11%	None	None	None

Ali A, et al. Emergence of ocular toxicities associated with novel anticancer therapeutics: What the oncologist needs to know. **Cancer Treatment Reviews**, Volume 105, April 2022, 102376.

How to Monitor and Mitigate Ocular Adverse Events for ADCs

- Baseline eye exam prior to each infusion and repeated prior to infusion
- No contact lens use during treatment to avoid infectious keratitis or increased surface dryness
- Prophylactic steroid eye drops should be given prior to starting the infusion and continued use for 72 hours after infusion (Tivdak) and through day 10 (Elahere)
  - Patients on steroid drops for symptom management require follow-up to monitor for cataract progression or elevation of the intraocular pressure
- Vasoconstrictor eye drops are given prior to each infusion and cold packs are applied during and after the infusion to decrease blood flow thereby potentially decreasing off-tumor delivery (Tivadak)
- Lubricating eye drops are also prophylactically used throughout treatment to add moisture to the eye
  - For self-use as needed through the day from the infusion until 30 days after the last dose
- If symblepharon or ulcerative keratitis occur (grade 4), discontinuation is required
  - If more than grade 1, hold dose
  - Higher CTCAE score, dose reduction or discontinuation

Tisotumab Mitigation Protocol

Key Resources and Materials for Required Eye Care

An eye care plan based on clinical trial experience was developed to help reduce the risk of ocular adverse events with tisotumab vedotin. With these measures, ocular adverse events may be detected early on, and symptoms can be alleviated prior to impacting vision.

Access to eye care providers

- Conduct ophthalmic exam including visual acuity and slit lamp exam at baseline, prior to each dose and as clinically indicated
- Promptly refer patient to an eye care provider if new or worsening ocular symptoms occur

Eye drops ready for use

1. Topical steroid (Rx): e.g. dexamethasone 0.1%
2. Topical ocular vasoconstrictor (Rx): e.g. brimonidine tartrate 0.2%
3. Topical lubricating (OTC)

Cold packs during infusion

- E.g., standard chemical cold packs which reach approximately 35F
- Apply cold pack fully over eyes following administration of vasoconstrictor eye drops and leave on during the infusion
- Change cold packs as needed throughout infusion to ensure eye area remains cold

Dose modification guidelines have also been developed to manage potential ocular adverse events.

Required eye care description is based on the tisotumab vedotin US Prescribing Information.

Kim SK, Ursell P, Coleman RL, Monk BJ, Vergote I. Mitigation and management strategies for ocular events associated with tisotumab vedotin. *Gynecol Oncol*, 165(2):385-392.

Mirvetuximab Mitigation Protocol

	Management
Severity (CTCAE Grade)	
Grade 1	• Complete eye exam • Monitor for worsening symptoms • No change in mirvetuximab soravtansine dose or schedule of administration
Grade 2	• Complete eye exam • Weekly symptomatic ocular assessments until symptoms resolve or return to baseline • Hold mirvetuximab soravtansine until improvement to Grade 1 or better
Recommended guidelines	
	• Avoid use of contact lenses • Regular cleaning (baby shampoo, soft cloth) • Warm compress before sleep • Sunglasses in direct sunlight
Prophylactic Measures	
Lubricating eye drops (required)	• Daily administration of preservative-free eye drops (Days 1-21)
Corticosteroid eye drops (expansion cohort)	• 1% prednisolone acetate during active study treatment • Administered six times daily (Days 1-5) • Administered four times daily (Days 6-10)

Moore et al. Fut Oncol 2018

Coordination of Care is Key

- Always refer to the current prescribing information for the most up-to-date dose modification and AE management guidance as additional data become available
- The oncology care team should monitor patients for ocular signs and symptoms
  - Reduced visual acuity, blurred vision, light sensitivity, redness, dryness, and irritation
- Ocular AEs observed result in conjunctival or corneal inflammation
  - Detectable before becoming severe, allowing for early referral for management
- **Close communication between oncologists and eye care providers are needed**
  - Many ophthalmologists are not familiar with grading ocular examinations using the CTCAEs applicable for oncology trials.
  - Any change in dosing needs to be conveyed