

IDENTIFYING AND MANAGING PHARMACEUTICAL COMPLICATIONS

JESSICA STEEN OD, FFAO, DIPL ABO



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JESSICA STEEN OD FINANCIAL DISCLOSURES

- Speakers Bureau-Carl Zeiss Meditec, Bausch and Lomb, Viatriis, Thea Pharma, Alcon, Allergan, Astellas, Dompé
- Consultant-Bausch and Lomb, Balance Ophthalmics, Carl Zeiss Meditec, Opus Genetics, Viatriis, Allergan, Astellas, Alcon, Radius XR, iCare, Glaukos, EyeNovia, Tarsus, Orasis, Topcon, Envision Health Technologies, LKC
- Shareholder-Clearside Biomedical, Annexon Bio (<0.01% ownership)

▪ All relevant relationships have been mitigated

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CHARACTERISTICS OF THE EYE

- Highly vascularized, small mass
 - Retinal and choroidal blood supply
 - Results in 'unusually high' susceptibility to ADRs
- Drugs present in systemic circulation can reach ocular structures through choroidal or retinal circulation

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THE EYE AND OCULAR ADRS

- Choroid and ciliary body have thin, fenestrated walls through which drug molecules can pass
- Small, lipid soluble molecules can pass into the aqueous
 - Diffuse into avascular structures: lens,
- Most common sites for drug deposition and functional disruption:
 - **Cornea, lens, retina, optic nerve**


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OCULAR ADVERSE DRUGS REACTIONS

- As few as 1% of ALL ADRs may be reported
- Ocular adverse effects range from mild to vision threatening
 - Optometrists are often the first to assess OADR

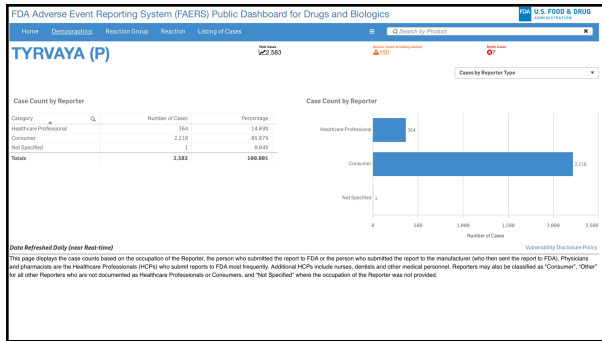
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FDA MedWatch

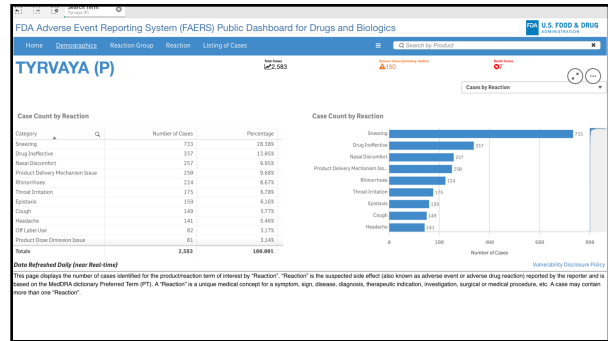


www.fda.gov/medwatch

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LONG TERM SAFETY

- Following approval, the manufacturer continued to monitor adverse effects and clinical benefit
 - May be through a formal phase four trial
- Under reporting has been a significant concern

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Recruiting

Ocular Assessments in Patients Treated With Tivdak® in Recurrent or Metastatic Cervical Cancer

ClinicalTrials.gov ID NCT06952660
Study Start (Actual) 2025-05-07
Sponsor Pfizer
Primary Completion (Estimated) 2028-12-13
Information provided by Pfizer (Responsible Party)
Last Update Posted 2026-02-17
Study Completion (Estimated) 2028-12-13
Brief Summary
 TIVDAK is used for the treatment of cervical cancer that has come back after chemotherapy. Chemotherapy is a treatment that uses medicines to stop the growth of cancer cells. This is done either by killing the cells or by stopping them from growing. The purpose of this study is to learn about possible side effects of TIVDAK, especially to any side effect that is related to the eye. A side effect is anything a medicine does to your body that is not part of how the medicine treats disease.
Enrollment (Estimated) 100
Study Type Interventional
Phase Phase 4

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DETERMINANTS OF ADVERSE DRUG REACTIONS

- Nature of the drug
- Amount of drug administered; dose
- Route of administration
- Age, sex
- Confounding drugs
- History of allergy to drugs
- Individual idiosyncrasy

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DETAILED DRUG HISTORY

- How do you ask your patients about the medications that they take?
 - Medication name, dosage, frequency of use
 - How long they have used it for?

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RISK ASSESSMENT

- While gathering medication history, you will mentally 'red flag' drugs which you know have potential for ocular effects
- May determine test selection
 - e.g. color vision, automated visual field (what type?)
- As clinicians, you'll examine a patient, identify findings which may be due to toxicity, then will 'back track' to determine offending drug

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Drugs which may cause dry eye

Anticholinergics	Oral contraceptives
Atropine, scopolamine	Beta blockers
Antihistamines	Propranolol
Diphenhydramine	Timolol
Vitamin A analogs	Phenothiazines
Isotretinoin	Chlorpromazine
Vitamins	Thioridazine
Niacin	Antianxiety agents
Tricyclic antidepressants	Diazepam
Amitriptyline	Biologics
	Dupilumab, etanercept, infliximab, vedolizumab

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ISOTRETINOIN

- Vitamin A analog (13-cis-retinoic acid)
- Management of:
 - Psoriasis
 - Cystic acne
- Ocular ADRs
 - Dry eye, corneal neovascularization, keratitis, corneal opacities, lenticular opacities altered dark adaptation
 - Basically, shuts down sebaceous glands-including meibomian glands**
 - Pseudotumor cerebri

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The effect of oral isotretinoin therapy on meibomian gland morphology and dry eye tests

Eyüp Düzgün & Ezgi Özkur

Pages 762-768 | Received 22 Apr 2020, Accepted 16 May 2020, Published online: 08 Jun 2020

Assessments of the ocular surface and meibomian gland morphology in patients with treatment-naïve acne vulgaris

ORIGINAL ARTICLE • Arq. Bras. Oftalmol. 86 (2) • Mar-Apr 2023

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ISOTRETINOIN

- Management
 - Advise patient to return for examination if any symptoms of ocular discomfort, redness, decreased CL tolerability
 - Typically within 1 month of treatment
 - Urgent evaluation if decreased vision, headache, transient visual obscuration
 - Evaluate ocular surface, color vision, optic discs
 - Discontinuation alone typically causes resolution of PTC

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ANTICOAGULATION THERAPY

- Warfarin, Apixaban, rivaroxaban, aspirin
- Reduction of stroke and systemic embolism in Afib, prophylaxis of DVT and PE, treatment of DVT and PE, and reduction of recurrent DVT and PE
- Common: Subconjunctival hemorrhage, retinal hemorrhage
- Never advise a patient to STOP their blood thinning medication after an ocular event**

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MYDRIATIC & CYCLOPLEGIC EFFECTS

- Phenothiazines
- Anticholinergics
- Antihistamines
- Benzodiazepines
- Tricyclic antidepressants
- Glycopyrronium cloth

Caution in patients who are primary angle closure suspects

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JAMA Ophthalmology | Original Investigation

Association of Drugs With Acute Angle Closure

Kyeong Ik Na, MD; Sung Pyo Park, MD, PhD

Korean Health Insurance Review and Assessment Service database

13,531 records of AAC
Sumatriptan, topiramate, duloxetine

Total of 61 drugs identified

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QBREXZA (GLYCOPYRRONIUM CLOTH)

- Anticholinergic agonist for the treatment of axial hyperhidrosis
- 9+ years of age
- Unilateral dilated pupil, unilateral headache
- Most common effect: dry mouth (24.2%)

4 **CONTRAINDICATIONS**

Qbrexza is contraindicated in patients with medical conditions that can be exacerbated by the anticholinergic effect of Qbrexza (e.g., glaucoma, paralytic ileus, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis, myasthenia gravis, Sjogren's syndrome).

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SOFDRA (SOPPIRONIUM TOPICAL GEL)

- Anticholinergic agonist for the treatment of primary axillary hyperhidrosis
- M3 receptor agonist
- 9+ years of age

CONTRAINDICATIONS

Medical conditions that can be exacerbated by the anticholinergic effect of SOFDRA (e.g., glaucoma, paralytic ileus, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis, myasthenia gravis, Sjogren's syndrome) (4).

Table 1: Adverse Reactions Occurring in 32% of Subjects with Primary Axillary Hyperhidrosis Treated with SOFDRA in Trials CARDIGAN 1 and 2

Adverse Reactions	SOFDRA (N = 353) n (%)	Vehicle (N = 347) n (%)
Dry mouth	51 (14%)	2 (0.6%)
Vision blurred	30 (9%)	1 (0.3%)
Mydriasis	23 (7%)	0
Urinary retention	8 (2%)	0

Source: <https://doi.org/10.1001/jamaophthalmol.2020.1234>

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66 year old Black female

History of Present Illness

1. glaucoma follow-up
Patient has moderate POAG OD, OS. She is here for 3 month IOP check, DFE, and disc photos. Patient is currently on latanoprost qhs OU, reports good compliance and no toxicities. She needs a refill and pharmacy is the same as on file. She is going on a cruise in November and is wondering if the scopolamine patch that she wears behind her ear will interfere with her glaucoma.

A1c <6% (3 months ago)

Thoughts?

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Drugs which may affect pupil size

<p>Mydriasis</p> <ul style="list-style-type: none"> Anticholinergics CNS stimulants Amphetamines Cocaine CNS depressants Barbituates Anti-anxiety agents Antihistamines Diphenhydramine Phenothiazines Adderall, Ritalin 	<p>Miosis</p> <ul style="list-style-type: none"> Opiates Heroin Opium Codeine Morphine Anticholinesterases Neostigmine
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Drugs which may cause retinal changes

Interferon	Talc retinopathy
Digoxin	Chloroquine/hydroxychloroquine
Sildenafil	Quinine
Thioridazine	Rosiglitazone
Tamoxifen	Atorvastatin
Elmiron	Fingolimod

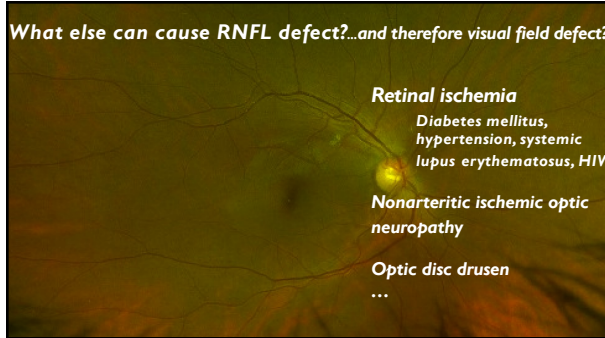
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INTERFERON THERAPY

- Treatment of hepatitis C and multiple sclerosis
- Cotton wool spots, conjunctivitis, dry eye
- Possibly due to upregulation of inflammatory cytokine deposition in vascular walls

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What else can cause RNFL defect?...and therefore visual field defect?



- Retinal ischemia**
Diabetes mellitus, hypertension, systemic lupus erythematosus, HIV
- Nonarteritic ischemic optic neuropathy**
- Optic disc drusen**
- ...

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SILDENAFIL

- Inhibitor of phosphodiesterase type 5 (PDE 5) and type 6 (PDE 6)
- PDE 6 is involved in retinal transduction
- Also includes Cialis and Levitra
- Treatment of erectile dysfunction
- Visual effects in about 10% of patients taking 100mg dose
 - Blue tinged vision, photophobia
- Dose related incidence
 - 40-50% at 200mg
- Possible: anterior ischemic optic neuropathy (NAION)

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What about GLP-1 receptor agonists?!

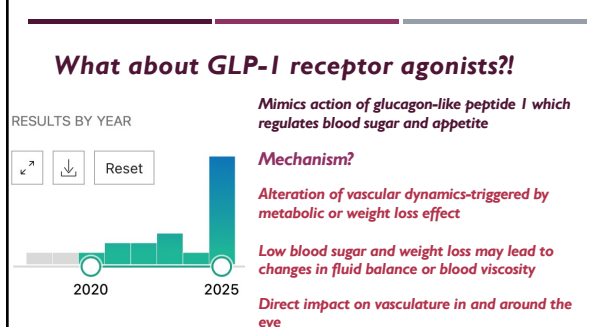
Mimics action of glucagon-like peptide 1 which regulates blood sugar and appetite

Mechanism?
Alteration of vascular dynamics-triggered by metabolic or weight loss effect

Low blood sugar and weight loss may lead to changes in fluid balance or blood viscosity

Direct impact on vasculature in and around the eye

RESULTS BY YEAR



2020 2025

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Original Investigation

July 3, 2024

Risk of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide

What environment were these patients evaluated in? Retrospective...

Jimena Tatiana Hathaway, MD, MPH^{1,2,3}, Madhura P. Shah, BS^{2,3}, David B. Hathaway, MD¹, et al.

Author Affiliations | Article Information

JAMA Ophthalmol. 2024;142(8):732-739. doi:10.1001/jamaophthalmol.2024.2296

The cumulative incidence of NAION for the semaglutide vs non-GLP-1 RA cohorts over 36 months was 6.7% (95% CI, 3.6%-9.7%) and 0.8% (95% CI, 0%-1.8%), respectively. A Cox proportional hazards regression model showed a higher risk of NAION for patients prescribed semaglutide (HR, 7.64; 95% CI, 2.21-26.36; P<.001).

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Association between Semaglutide and Nonarteritic Anterior Ischemic Optic Neuropathy

A Multinational Population-Based Study

Chien-Chih Chou, MD, PhD^{1,2,3} Ssu-Yu Pan, MD^{1,2} Yi-Jing Sheen, MD, PhD^{1,3,4,5} Jun-Fu Lin, MS⁶
 Ching-Heng Lin, PhD^{6,7,8,9} Hui-Ju Lin, MD, PhD^{10,11} I-Jong Wang, MD, PhD^{12,13}
 Chien-Hsiang Weng, MD, MPH^{9,13}

37,314 T2DM
 129,690 obesity
 130,216 T2DM + obesity

Conclusions: The findings suggest that semaglutide may not be associated with an increased risk of NAION in the general population. Therefore, avoidance of semaglutide based solely on concerns regarding the risk of NAION may not be warranted because its potential benefits for blood glucose control and cardiovascular health likely outweigh its potential risks.

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Glucagon-like peptide 1 (GLP1) receptor agonists and risk for ischemic optic neuropathy: A meta-analysis of randomised controlled trials

Giovanni Antonio Silveri MD¹ | Laura Pala PhD² | Barbara Cresci MD² |
 Edoardo Mannucci MD³

A relevant increase of the relative risk for a very rare, although severe, condition does not modify the overall risk-benefit ratio of effective drugs, at least when appropriately prescribed.

effective drugs, at least when appropriately prescribed. In fact, if we assume a difference in incidence between GLP1 RA and placebo of 2.6 cases per 100 000 patient-years, the 1-year number needed to harm would be 38 460—well above the number needed to treat to avoid a major cardiovascular event in cardiovascular outcome trials.^{2,15}

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Semaglutide and the Risk of Nonarteritic Ischemic Optic Neuropathy

2026

A Systematic Review and Certainty of Evidence Meta-Analysis

Abdelaziz Abdelaziz, MD,^{1,2,*} Hashem Abu Serhan, MD,^{3,*} Mustafa Alsaadi, MD,⁴ Luke Yaldo, BS,⁵
 Eric D. Gaier, MD, PhD,^{6,7} Abdelrahman M. Elhousseiny, MD, MS,^{5,6,8}

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MEK INHIBITORS

- Mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK)
 - Non-small cell lung cancer, melanoma
- Serous retinal detachment, retinal vein occlusion
 - Oxidative stress and breakdown of the blood-retinal barrier
- Dry eye disease, panuveitis
- Does not typically require discontinuation of therapy

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CHECKPOINT INHIBITORS

- PD-1 (programmed cell death) inhibitors
 - Pembrolizumab
- CTLA-4 (cytotoxic T-lymphocyte antigen 4) inhibitors
- PD-L1 (programmed cell death ligand 1)
- LAG-3 (lymphocytic activation gene 3)
- **Encourage T-cell activation**
 - Dry eye disease, panuveitis—downstream inflammation!
- Immunotherapy-
- *Is it the cancer? Is it the treatment?*

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MIRVETUXIMAB SORAVTANSINE (ELAHERE)

- Folate receptor alpha-directed antibody and microtubule inhibitor conjugate (intravenous infusion) on label for the treatment of **ovarian**, fallopian tube, or primary peritoneal cancer
- Who have received one to three prior treatments with platinum resistance
- FDA approved in 2022; full approval March 22, 2024; permanent J-code July 1, 2023

- WARNING: OCULAR TOXICITY**
- ELAHERE can cause severe ocular toxicities, including visual impairment, keratopathy, dry eye, photophobia, eye pain, and uveitis [see *Warnings and Precautions (5.1)* and *Adverse Reactions (6.1)*].
 - Conduct an ophthalmic exam including visual acuity and slit lamp exam prior to initiation of ELAHERE, every other cycle for the first 8 cycles, and as clinically indicated [see *Dosage and Administration (2.3)*].
 - Administer prophylactic artificial tears and ophthalmic topical steroids [see *Dosage and Administration (2.3)* and *Warnings and Precautions (5.1)*].
 - Withhold ELAHERE for ocular toxicities until improvement and resume at the same or reduced dose [see *Dosage and Administration (2.3)* and *Warnings and Precautions (5.1)*].
 - Discontinue ELAHERE for Grade 4 ocular toxicities [see *Dosage and Administration (2.3)* and *Warnings and Precautions (5.1)*].

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Phase 3 MIRASOL

453 patients; 227 randomized to MIRV, 226 chemotherapy

Progression-free survival:
Elahere: 5.6 months
Chemotherapy: 3.98 months

Overall survival:
Elahere: 16.5 months
Chemo: 12.8 months

Response rate:
Elahere: 42%
Chemo: 16%

Mirvetuximab Soravtansine in FRα-Positive, Platinum-Resistant Ovarian Cancer

Authors: Kathleen N. Moore, M.D., Antonio Angariger, M.D., Catriona E. Konecny, M.D., Yolanda Garcia, M.D., Susana Barajas, Ph.D., Dominica Lencinas, M.D., Jung-Yun Lee, M.D., [88], for Gynecologic Oncology Group Partners and the European Network of Gynecological Oncological Trial Groups†. Author Inks & Alliances
 Published December 6, 2023 | N Engl J Med 2023;389:2162-2174 | DOI: 10.1056/NEJMoa2309169

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Work with an eye care provider (ophthalmologist or optometrist) to manage ocular events that may occur

BEFORE STARTING ELAHERE

Prednisolone acetate 1% 6x daily beginning the day before therapy; through day 4 of the cycle (5 days); then QID for 4 days



You will visit an eye doctor for a baseline eye exam, and eye exams throughout your treatment on ELAHERE, or about every 6 weeks during the first 8 cycles of treatment. This will help your healthcare team keep track of any potential changes to your vision or eyes during treatment.*

*There may be additional costs associated with eye exams. Please check with your insurance provider for more information.



Your eye doctor may recommend 2 different types of eye drops to help reduce the risk of developing eye-related side effects:

- Prescription steroid eye drops, filled by a pharmacist
- Preservative-free lubricating eye drops, which can be purchased over the counter

Apply the eye drops as directed by your doctor.

Avoid wearing contact lenses during treatment with ELAHERE unless your doctor tells you that you can

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TO BE COMPLETED AND SUBMITTED TO THE PRESCRIBING ONCOLOGIST BY THE EYE CARE PROVIDER

Please select the appropriate option:
 Baseline exam Scheduled follow-up exam Follow-up due to patient-reported symptoms
 Note: As part of their treatment with ELAHERE, your patient is being prescribed topical steroids that may elevate intraocular pressure.**

Baseline assessment:
 Patient reports the following new or ongoing ocular symptom(s) No symptoms reported

Visual Acuity*

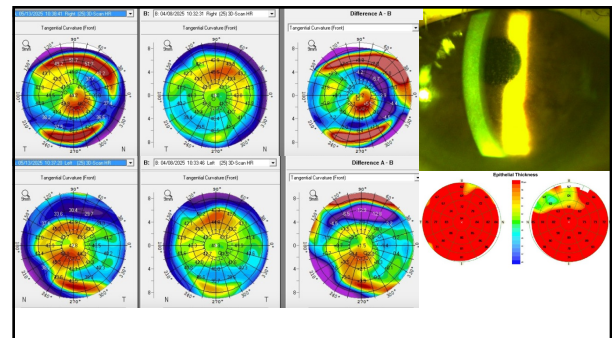
	Baseline exam		Current exam	
	Right eye	Left eye	Right eye	Left eye
Best corrected distance visual acuity	20/	20/	20/	20/
Entering distance visual acuity were corrective lenses worn during the assessment? <input type="checkbox"/> Yes <input type="checkbox"/> No	20/	20/	20/	20/

Ophthalmic Exam*
 No abnormal findings

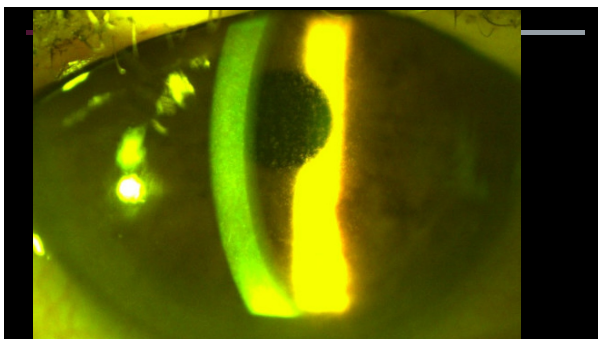
Finding	Severity of finding	Right eye		Left eye		Action
		<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	<input type="checkbox"/> Yes	
Keratitis/keratopathy	Nonconfluent superficial keratitis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Monitor
	Confluent superficial keratitis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Corneal epithelial defect	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Keratitis/keratopathy	S-line or more loss in best corrected visual acuity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If yes for either eye, notify prescribing oncologist*
	Corneal ulcer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Stromal opacity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Uveitis	Best corrected distance visual acuity of 20/200 or worse	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Monitor
	Grade 1/2 flare cell in anterior chamber	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Grade 2/3+ cell or flare in anterior chamber	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
	Grade 3/4 cell or flare in anterior chamber	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Uveitis	Grade 4/5 cell or flare in anterior chamber	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	If yes for either eye, notify prescribing oncologist*
	Grade 4/5 hypopyon	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Monitor your patient in the hospital setting if you detect any of the following: severe ocular pain, severe photophobia, or severe vision loss.

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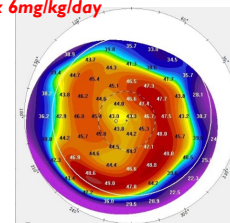
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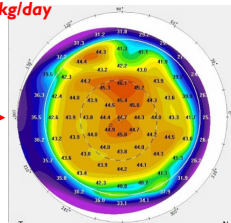
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65 year old with primary peritoneal cancer

2 x 6mg/kg/day



2 x 5mg/kg/day



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Tisotumab vedotin-tftv, for injection 40 mg, Eye Care Consult Form	
<p>This patient has been prescribed tisotumab vedotin-tftv. Tisotumab vedotin-tftv can cause changes in the corneal epithelium and conjunctiva resulting in changes in vision, including severe vision loss, and corneal ulceration. Conduct an ophthalmic exam at baseline, prior to each dose, and as clinically indicated.</p> <p>The information in this form is important to the prescriber of tisotumab vedotin-tftv to make treatment and dose modification decisions in the event of an ocular adverse reaction.</p>	<p>INSTRUCTIONS: Please complete this form and promptly provide it to the prescribing physician. The completed form may be carried by the patient, faxed, or included in electronic medical records.</p>
<p>WARNING: OCULAR TOXICITY <i>See full prescribing information for complete boxed warning.</i></p> <ul style="list-style-type: none"> • TIVDAK caused changes in the corneal epithelium and conjunctiva resulting in changes in vision, including severe vision loss, and corneal ulceration. (5.1) • Conduct an ophthalmic exam at baseline, prior to each dose, and as clinically indicated. (2.2, 5.1) • Adhere to premedication and required eye care before, during, and after infusion. (2.3) • Withhold TIVDAK until improvement and resume, reduce the dose, or permanently discontinue, based on severity. (2.3, 5.1) 	<p>Brimonidine-3 drops prior to each infusion</p> <p>Prednisolone acetate 1% TID x 3 days beginning prior to the infusion</p>

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Phase 3 innovaTV301

Second- or third-line agent in patients with recurrent or metastatic cervical cancer; 502 patients, 253 received TV

Overall survival:
TV: 11.5 months
Chemo: 9.5 months

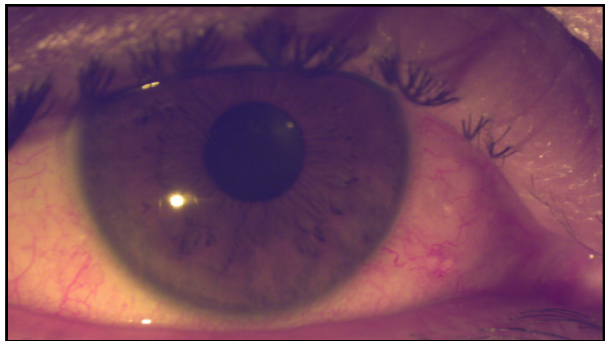
Median progression-free survival:
TV: 4.2 months
Chemo: 2.9 months

Response rate:
TV: 17.8%
Chemo: 5.2%

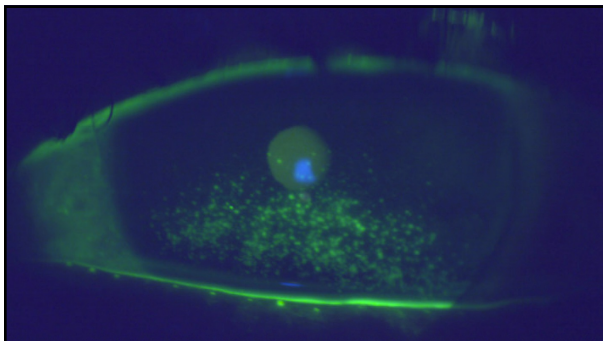
Tisotumab Vedotin as Second- or Third-Line Therapy for Recurrent Cervical Cancer

Authors: Ignacio Vergara, M.D., Ph.D., Antonio González-Martín, M.D., Ph.D., Kaichi Fujwara, M.D., Ph.D., Elva Kubota, M.D., Andrea Bagner, M.D., Sherali Ghauri, M.D., Jing-Yan Liu, M.D., Ph.D., [DOI: 10.1093/annonc/ndz131](#)
30/ENCO-013/COG-3057 Collaborators* Author Info & Affiliations
Published July 3, 2024 | N. Engl. J. Med. 2024;371:44-55 | DOI: 10.1056/NEJMoa2313111 | VOL. 381 NO. 1

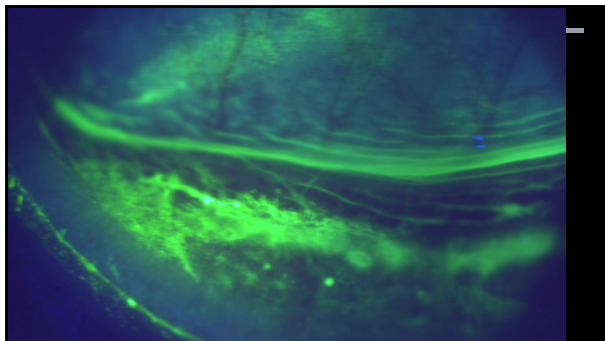
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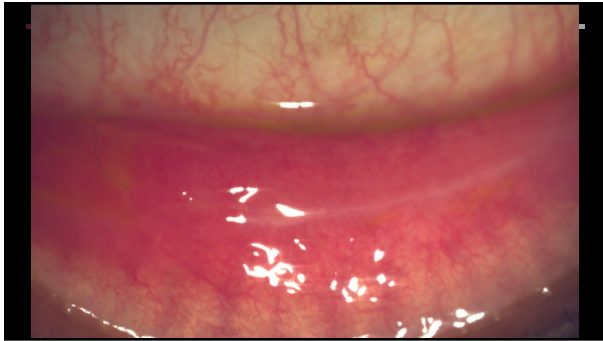
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PENTOSAN POLYSULFATE SODIUM (ELMIRON)

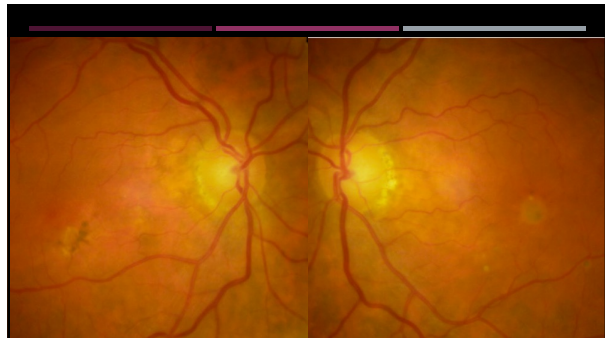
- Semi-synthetic analogue of glycosaminoglycan
 - Regulate cellular permeability at the level of the epithelium of the bladder
- Treatment of interstitial cystitis
 - Chronic regional pain syndrome of the bladder and pelvis
- Median duration of PPS intake 16-17 years
 - Average 14,067 capsules
- Prolonged dark adaptation, metamorphopsia, blurred vision while reading
- Annual eye examinations are recommended; cumulative exposure 500 grams = greater risk
 - 100mg TID = 109.5g/year

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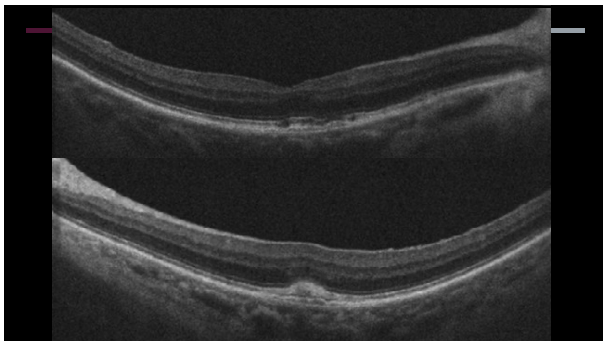
76 YEAR OLD HISPANIC FEMALE

- Presents for evaluation of suspicion of glaucoma
- BCVA 20/30 OD 20/40 OS
- IOP 14mmHg OD and OS

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Medications reconciled today:

Adherence	Medication Name	Sig Desc	Elsewhere	Status
taking as directed	pregabalin 75 mg capsule	take 1 capsule by oral route 2 times every day	Y	Verified
taking as directed	atenolol 100 mg tablet	take 1 tablet by oral route every day	Y	Verified
taking as directed	atorvastatin 20 mg tablet	take 1 tablet by oral route every day	Y	Verified
taking as directed	amlodipine 5 mg tablet	take 1 tablet by oral route every day	Y	Verified
taking as directed	clopidogrel 75 mg tablet	take 1 tablet by oral route every day	Y	Verified
taking as directed	lisinopril 5 mg tablet	take 1 tablet by oral route 3 times every day	Y	Verified
taking as directed	arnica flower (bull) tincture		Y	Verified
taking as directed	Multi Vitamin 9 mg iron/15 mL oral liquid		Y	Verified
taking as directed	melatonin 10 mg capsule		Y	Verified
taking as directed	cranberry concentrate-ascorbic acid 4,200 mg-20 mg capsule		Y	Verified
taking as directed	aspirin 325 mg tablet	take 1 tablet by oral route every day for post-angioplasty	Y	Verified
taking as directed	escitalopram 10 mg tablet	take 1 tablet by oral route every day	Y	Verified
taking as directed	timolol maleate 0.5 % eye drops	apply 1 by Ophthalmic route OU BID	N	Verified
taking as directed	Elmiron 100 mg capsule	take 1 capsule by oral route 3 times every day with water, 1 hour before or 2 hours after a meal	Y	Verified

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2016 GUIDELINES FOR PLAQUENIL MONITORING

- Marmor et al. 2016
- Major risk factors: dose >5mg/kg/day, >5 years of use, reduced glomerular filtration rate, concomitant retinal disease, **concomitant tamoxifen use**
 - Age and liver disease no longer considered to be major risk factors
- Dosage: recommended maximum daily dose of 5mg/kg/day
 - Typical dosage 200mg BID po
 - For a patient who is 130 lbs = 59kg = 6.80mg/kg/day
- At recommended doses, risk of toxicity up to 5 years is under 1% and up to 10 years is 2%
 - Almost 20% after 20 years of treatment

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Recommendation on Screening for Hydroxychloroquine Retinopathy (2025 Revision)

- OCT and FAF are primary screening tests
- Renal disease and tamoxifen use are key risk factors for retinopathy
- 5mg/kg/day dosing rule remains
 - Maybe HCQ blood levels to evaluate true exposure? But not practical in the US
- Visual fields should screen for pericentral and parafoveal patterns of disease
- There's a tipping point for development of retinopathy

Marmor MF, Ahn JS, Elvers PJ, Melles RB, Meier WF, Sarraf D, Youf H, American Academy of Ophthalmology. Special AAO Report: Recommendations on Screening for Hydroxychloroquine Retinopathy (2025 Revision). Ophthalmology. 2025 Nov 11;50(11):6420-5(00709-2).

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Epidemiology and outcomes

LUPUS SCIENCE & MEDICINE

Rheumatologists' perspective on hydroxychloroquine guidelines

James Winebrake,¹ Leila Khalili,² Julia Weiner,² Yevgeniya Gartshteyn,² Lisa Park,³ Anca D Askanase,²

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American College of Rheumatology, American Academy of Dermatology, Rheumatologic Dermatology Society, and American Academy of Ophthalmology 2020 Joint Statement on Hydroxychloroquine Use With Respect to Retinal Toxicity

James T. Rosenbaum,¹ Karen H. Costenbader,² Julianna Desmarais,³ Ellen M. Ginzler,⁴ Nicole Fett,³ Susan M. Goodman,² James R. O'Dell,⁴ Gabriela Schmajuk,⁵ Victoria P. Werth,⁶ Ronald B. Melles,⁷ and Michael F. Marmor^{2*}

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Statins in General

May cause diplopia or ptosis
Average time to adverse effect was 8 months

Can cause myositis
Seems to be a localized myositis in the extraocular muscles and levator

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JAMA Ophthalmology | Original Investigation

Systemic Drugs Associated With Maculopathy

Jiyeon Kim, PhD, Seong Joon Ahn, MD, PhD, Jiyeon Park, MS, Emily W. Gower, PhD, Jee-Eun Chung, RPh, PhD

FAERS analysis from 2014-2023

Table 1. Top 30 Candidate Drugs With the Highest Number of Reported Maculopathy Adverse Events (December 2023)

Rank	Medication	No. of reports	Reporting odds ratio (95% CI)
1	Pentosan polysulfate	2627	1081.8 (1030.8-1135.3)
2	Rambuzumab	1021	83.2 (78.1-88.8)
3	Insulin	879	4.5 (4.2-4.8)
4	Adalimumab	799	1.3 (1.3-1.4)
5	Fingolimod	788	8.1 (7.6-8.8)
6	Aflibercept	524	29.0 (26.5-31.6)
7	Bevacizumab	285	4.9 (4.3-5.5)
8	Apixaban	262	2.5 (2.2-2.8)
9	Paclitaxel	248	7.6 (6.7-8.6)
10	Hydroxychloroquine	230	9.5 (8.3-10.8)

5 drugs with underrecognized macular toxicity

- Fingolimod
- Apixaban-15.7%
- Paclitaxel-6.6%
- Ibrutinib-9.9%
- Sildenafil-6%

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Drugs which may cause optic nerve changes

Ethambutol	Oral contraceptives
Isoniazid	Amiodarone
Vigabatrin	Vitamin A analogs
NSAID (indomethacin)	Tetracyclines
	Tamoxifen

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ETHAMBUTOL

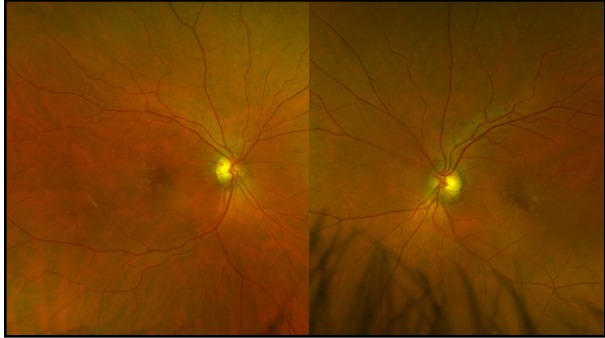
- Treatment of mycobacterium
 - Interferes with mycobacterium nucleic acid structure
- Toxic optic neuropathy
 - Reduced visual acuity, visual field, color vision (R/G)
- Stop treatment as soon as vision affected
 - Vision rarely recovers
- Dose-related response
 - 50% for 60-100mg/kg/day
 - 5-6% for 25mg/kg/day
 - 1% <15mg/kg/day

88

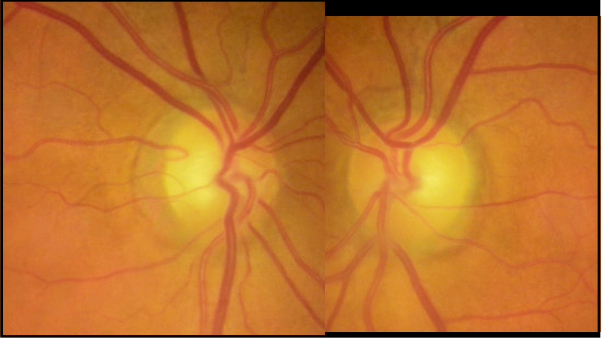
59 YEAR OLD HISPANIC MALE

- History of mycobacterium tuberculosis (resolved)
- Development of MAC fibrocavitary disease
- Treatment with:
 - Ethambutol 15mg/kg/day
 - Rifampin
 - Azithromycin

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91



92

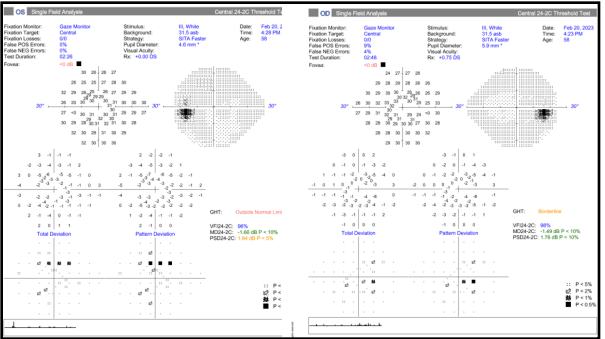
Medication Reconciliation

Medications reconciled today.

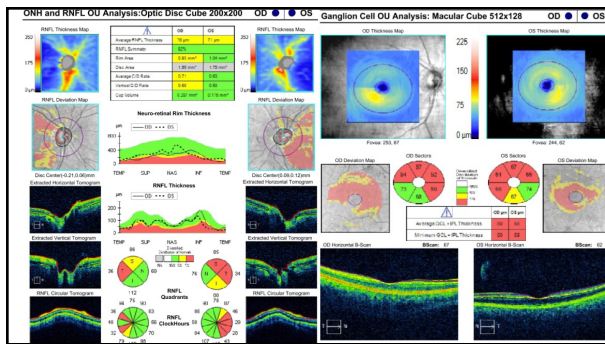
Adherence	Medication Name	Sig Desc	Elsewhere	Status
taking as directed	Centrum 0.4 mg-162 mg-18 mg Tab	Use as needed	Y	Verified
taking as directed	Omega-3	as needed	Y	Verified
taking as directed	Ankayce 590 mg/8.4 mL suspension for inhalation via nebulization	inhale 8.4 milliliter by inhalation route every day via nebulizer for MAC lung infection	Y	Verified
taking as directed	PreserVision AREDS-2 250 mg-90 mg-40 mg-1 mg capsule	Take one capsule twice daily with food	N	Verified
taking as directed	isoniazid	take 1 tablet by oral route every day	Y	Verified
taking as directed	rifampin	take by oral route every day up to 600 mg 1 hour before a meal or 2 hours after a meal	Y	Verified
taking as directed	ethambutol	take by oral route every day	Y	Verified

Systemic Medications

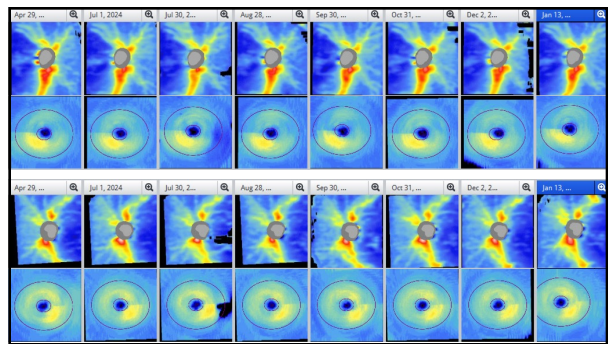
94



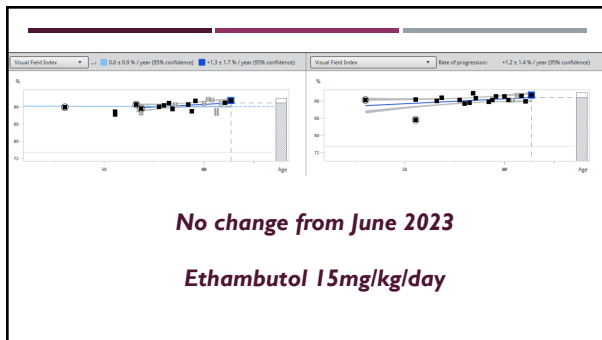
95



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AMIODARONE

- Anti-arrhythmic drug
- 1. Whorl keratopathy
 - Not a reason for drug discontinuation
- 2. Optic neuropathy
 - Blocks axoplasmic flow = optic disc edema
 - Insidious onset, slow progression, bilateral vision loss (usually)
 - Mean duration of treatment before vision loss = 9 months

99



100

BILATERAL OPTIC DISC EDEMA

- Presentation of pseudotumor cerebri
- Back to the medication list:
 - Oral contraceptive
 - Vitamin A derivative (Accutane)
 - Tetracycline
 - Indomethacin
- What symptoms may be present in this patient?

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TETRACYCLINES

- Conjunctival deposits
 - Brownish/greenish/black with tetracycline
 - Bluish discoloration of sclera with minocycline
- Skin discoloration!!

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So you've identified ocular toxicity, now what?

#1 Assess the level of urgency (i.e. risk of vision loss) and communicate with the prescribing physician

...In a way most appropriate for the situation

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BOTTOM LINE

- All medications have adverse effects
- Identifying ocular effects of systemic medications begins with an accurate history
- Potential ocular effects of systemic medications improves with familiarity
- Known adverse effects of systemic medications may be the "lowest hanging fruit"; but are not always the answer
- Communication with the patient's other managing physicians is integral!

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Bottom Line

All medications have adverse effects

Identifying ocular effects of systemic medications begins with an accurate history

Potential ocular effects of systemic medications improves with familiarity

Known adverse effects of systemic medications may be the "lowest hanging fruit"; but are not always the answer

Communication with the patient's other managing physicians is integral!

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jessicaa.steen@gmail.com

480.289.0613

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