

NEW CANCER DRUGS AND WHY OPTOMETRISTS SHOULD PAY ATTENTION

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DISCLOSURES

- PECAA, Speaker

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ANTIBODY DRUG CONJUGATES

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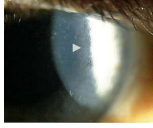
CASE #1

48 y/o M, no complaints

PMH:

- Psoriasis
- Multiple myeloma: starting Blenrep

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	1 month		3 weeks	
Baseline		1st follow-up		2nd follow-up
BCVA: 20/20 20/20 IOP: 18/20 Slit lamp: K's clear OU Fundus examination: normal OU				BCVA: 20/25-1 20/25+2 IOP: 18/19 Slit lamp: diffuse MECs OU (-) staining Fundus examination: normal OU
Rx OD: -2.75-0.75x75 OS: -2.75-0.50x90		Rx OD: -1.25-1.75x14 OS: pl-1.75x160		Rx OD: -2.75-1.25x90 OS: -3.50-1.50x145
		Tx: preservative-free ATs		Tx: preservative-free ATs

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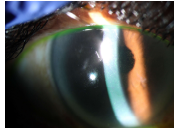
CASE #2

65 y/o M, no complaints

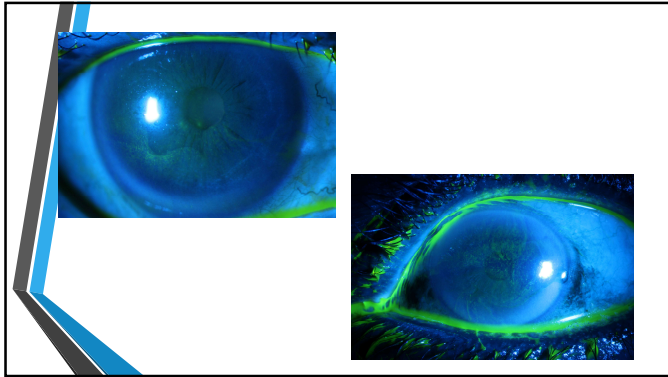
PMH:

- Gastritis
- HLD
- Multiple myeloma s/p SCT, now relapsed: set to start Blenrep

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	1 month		3 months	
Baseline		1st follow-up		4th follow-up
BCVA: 20/25 20/25 IOP: 9/9 Slit lamp: K's clear OU Fundus examination: normal OU		BCVA: 20/50 20/70 IOP: 7/6 Slit lamp: peripheral MECs OU (+) gr 1+ diffuse fl staining Fundus examination: normal OU		
Rx OD: +1.50-0.75x95 OS: +1.50-0.75x75		Rx OD: +5.50-2.00x80 OS: +4.25-0.50x100		Rx OD: +0.50-0.75x90 OS: +0.75-0.75x135
		Tx: preservative-free ATs, Restasis BID		Tx: preservative-free ATs, Restasis BID

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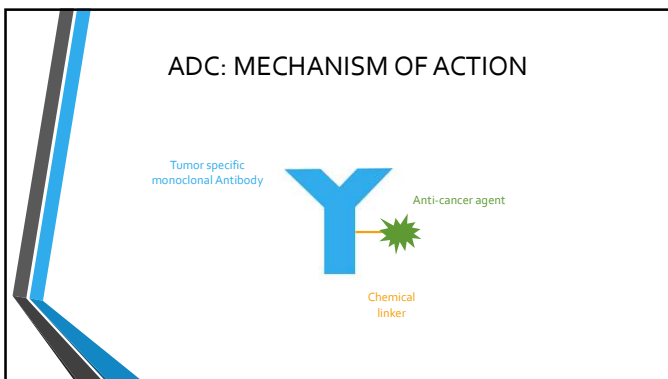
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A NEW FRONTIER IN CANCER TREATMENT Antibody Drug Conjugates

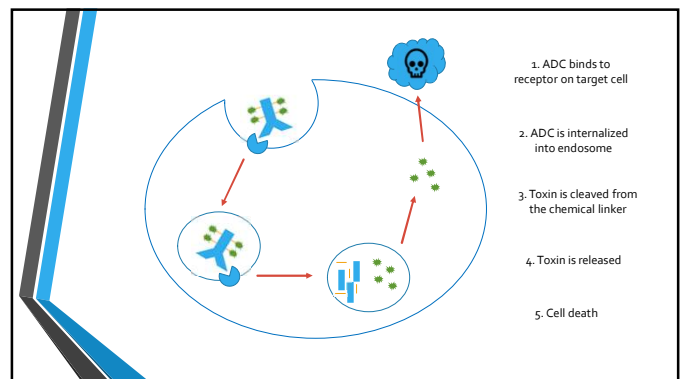
ADC	Target	mAb	Payload/Payload Class	Payload Action	Disease Indication (Four of Approval)
Myostatin (apitolizumab) (CG030)	CD33	lgG4	Cologemycin/Cytotoxication	DNA cleavage	CD33+ EIV AML (2020)
Enfortumab vedotin (EV)	CD30	lgG1	MMAE/karastatin	Microtubule inhibitor	RL-HLCL or cHL (2021); R-PMALCL or CD30+ MP (2021); cHL, HLCL, or CD30+PTCL (2018)
Enfortumab vedotin (EV)	HER2	lgG1	DM1/irreversible	Microtubule inhibitor	HER2+ metastatic breast cancer previously treated with trastuzumab & a taxane (2021); HER2+ early breast cancer after neoadjuvant taxane & trastuzumab-based treatment (2021)
Enfortumab vedotin (EV)	CD22	lgG4	Cologemycin/Cytotoxication	DNA cleavage	FL & ALL (2021)
Trinectin (CD79b) (CD79b)	CD79b	lgG1	MMAE/karastatin	Microtubule inhibitor	FL (2021, 2023)
Paclitaxel (paclitaxel) (paclitaxel)	Neuropilin-1	lgG1	MMAE/karastatin	Microtubule inhibitor	Locally advanced or metastatic urothelial cancer after a PD-1 or PD-L1 inhibitor and a platinum-based regimen (2023) or as a component of a platinum-based regimen (2023)
Enfortumab vedotin (EV)	HER2	lgG1	DM1/irreversible	Microtubule inhibitor	Locally advanced or metastatic HER2+ breast cancer after 2 or more anti-HER2 regimens (2021); locally advanced or metastatic HER2+ gastric or gastroesophageal junction adenocarcinoma after a trastuzumab-based regimen (2021)
Enfortumab vedotin (EV)	TROP2	lgG1	SN-38/irinotecan	TOP1 inhibitor	Locally advanced or metastatic TNBC after at least two prior therapies (2021); locally advanced or metastatic urothelial cancer after a Pt-containing chemotherapy and a PD-1 or PD-L1 inhibitor (2021)
Enfortumab vedotin (EV)	CD30	lgG1	MMAE/karastatin	Microtubule inhibitor	Locally advanced or metastatic TNBC after at least two prior therapies including an anti-CD30 mAb, a taxane, and an immunomodulatory agent (2021)
Enfortumab vedotin (EV)	CD19	lgG1	MMAE/karastatin	Microtubule inhibitor	Asymptomatic after 2 or more lines of systemic therapy, including DLBCL, primary DLBCL arising from low-grade lymphoma and high-grade B-cell lymphoma (2021)
Enfortumab vedotin (EV)	CD30	lgG1	MMAE/karastatin	Microtubule inhibitor	Relapsed or refractory CD30+ Hodgkin lymphoma (2021)
Enfortumab vedotin (EV)	CD30	lgG1	MMAE/karastatin	Microtubule inhibitor	Relapsed or refractory CD30+ Hodgkin lymphoma (2021)
Enfortumab vedotin (EV)	CD30	lgG1	MMAE/karastatin	Microtubule inhibitor	Relapsed or refractory CD30+ Hodgkin lymphoma (2021)
Enfortumab vedotin (EV)	CD30	lgG1	MMAE/karastatin	Microtubule inhibitor	Relapsed or refractory CD30+ Hodgkin lymphoma (2021)

Black box warning: FDA's most stringent warning for drugs on the market

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WHY CORNEAL TOXICITY?

- Inappropriate binding of the antibody to an off-target site
- Unstable linker
- Highly toxic payload

Most of these drugs represent **off-target** toxicity, except for **Kadcyla** and **Enhertu** which target HER2

HER2 is expressed in corneal cells, therefore keratopathy is likely a combination of **off** and **on-target** toxicity

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DIFFERENT PAYLOAD = DIFFERENT TOXICITY?

DNA CLEAVAGE

- Ozogamicin
- Mylotarg
- Besponsa

TOP1 INHIBITOR

- DXd
- Enhertu (HER2 target)
- SN-38
- Trodely

MICROTUBULE INHIBITOR

- MMAE
- Adcetris
- Polivy
- Tivdak
- Padcev
- DM4
- Elahere
- DM1
- Kadcyla (HER2 target)
- MMAF

Isolated case report of grade 3 keratitis¹

Clinical trial: Keratitis in 11% of patients² (3-2% with severe ulcerative keratitis)

Conjunctivitis in 26% of patients³

Isolated case report of "corneal epitheliopathy"⁴

Clinical trial: keratopathy in 37% of patients (uveitis in 4%)⁵

Clinical trial: MECs in 69-71% of patients^{1,6,8}

"10 patients with corneal cysts"⁷

Phase 3 and 2 studies: 31-40% incidence of "ocular adverse events"⁹

Isolated report of "corneal lesions"¹⁰

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MICR CHANGES

- ADC enter
- Start peric cycle

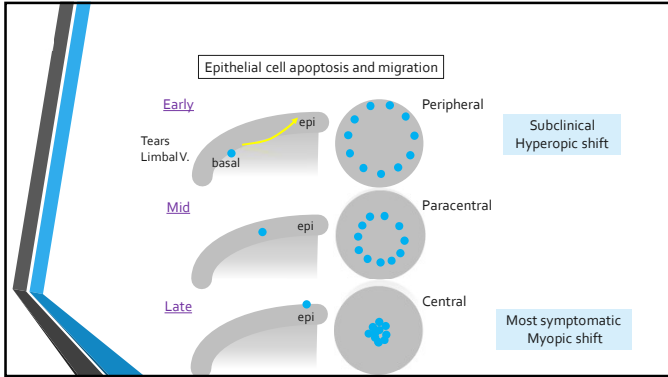
through its life

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Refractive Shifts and Changes in Corneal Curvature Associated With Antibody-Drug Conjugates
Cornea: The Journal of Cornea and External Disease
Canestraro, Julia, Hultcrantz, Malin, Modi, Shanu, Ham...
Vol. 41 Issue 6, pp. 792-801, 2022.

- Refractive error fluctuates while on and off drug, largest shift is myopic in nature (up to -4.75D) = steepening of K's (up to 3.9D)
- Mean change in VA of 2 Snellen lines
- Peripheral MECs = hyperopic shifts, paracentral/central MECs = myopic shifts

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WHAT DOES THIS MEAN FOR THE PATIENT?

- Drug affects the cornea and may cause blurred vision or dry eye
- Your need for glasses may change, often week-to-week. This may affect your ability to read fine print (or drive)
- Once treatment is complete, paused, or with dose reduction: changes are reversible

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TREATMENT/MANAGEMENT

Keratopathy:

- Preservative-free artificial tears
- Restasis/Xiidra to treat concomitant dry eye disease
- Treat concomitant blepharitis
- Predifone?
 - Moutafonis et al., 2019: lower incidence of keratopathy in patients who received steroid prophylaxis
 - Farooq et al., 2020: Steroid drops ineffective in treating MEC

Refractive error:

- At-home trial lenses
- OTC readers
- Contact lenses should be **AVOIDED** (unless advised by your doctor)

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• CTCA

Eye disorders		Grade			
Adverse Event	1	2	3	4	
Keratitis		Symptomatic; medical intervention indicated (e.g., topical agents); limiting instrumental ADL	Decline in vision (worse than 20/40 but better than 20/200); limiting self care ADL	Perforation or blindness (20/200 or worse) in the affected eye	

Definition: A disorder characterized by inflammation to the cornea of the eye.

- Baseline exam
- Prior to each dose
- As clinically indicated

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ELAHERE
 Today's where tomorrow begins. **Ocular Assessment Form**
 This is an optional form to help support eye care for patients prescribed ELAHERE.

THIS FORM IS TO BE COMPLETED BY THE PRESCRIBING ENDOCRINOLOGIST OR PROVIDER

THIS FORM IS TO BE COMPLETED AND SUBMITTED TO THE PRESCRIBING ENDOCRINOLOGIST OR THE EYE CARE PROVIDER

Please select the appropriate option:
 • Baseline exam • Scheduled follow-up exam • Follow-up due to patient-reported symptoms
 Make a copy of this report to send to ELAHERE, your patient is being prescribed synthetic topical steroids that may increase the risk of ocular infections.
 • 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/...
Uncorrected distance visual acuity	20/...	20/...	20/...	20/...
Were corrective lenses worn during the assessment?	Yes / No	Yes / No	Yes / No	Yes / No

Finding	Severity of finding	Right eye		Left eye	Action
		Yes	No	Yes	
Conjunctival hyperemia		Yes	No	Yes	Monitor
Corneal epithelial defect		Yes	No	No	
Is tear or more tears in best corrected visual acuity?		Yes	No	No	If yes for either eye, notify prescribing ophthalmologist
Corneal ulcer		Yes	No	No	
Intraocular pressure		Yes	No	No	
Best corrected distance visual acuity of 20/200 or worse		Yes	No	No	
Corneal perforation		Yes	No	No	
Opaque film cast in anterior chamber		Yes	No	No	Monitor
Grade 2+ or more of keratic precipitates		Yes	No	No	
Grade 2+ or more of vitreous inflammation		Yes	No	No	
Grade 2+ or more of vitreous hemorrhage		Yes	No	No	
Grade 2+ or more of vitreous floaters		Yes	No	No	
Grade 2+ or more of vitreous debris		Yes	No	No	
Grade 2+ or more of vitreous strands		Yes	No	No	
Grade 2+ or more of vitreous membranes		Yes	No	No	

Additional Information Eye Care Provider: Name and contact information

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- Baseline exam
- Every other cycle for first 8 cycles
- As clinically indicated

PREVENTION?

- Brimonidine (alpha-agonist) (Tivdak)
- Cold compresses during infusion (Tivdak)
- Steroid prophylaxis (Tivdak and Elahere)

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IMMUNOTHERAPY

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CASE #3

54 y/o F with complaints of blurred vision OS>OD

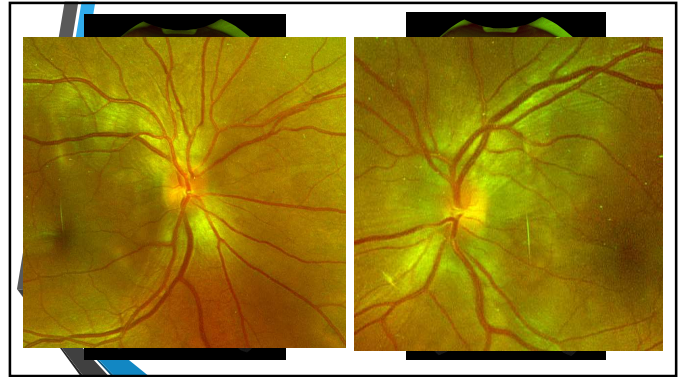
PMH:

- Metastatic NSCLC s/p chemotherapy, now on ipilimumab and nivolumab x 2 months

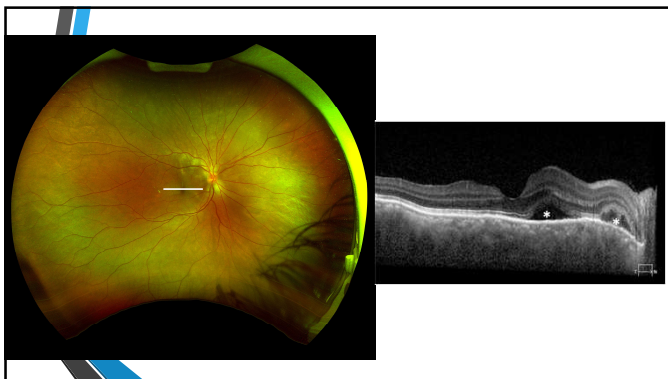
Exam:

- BCVA 20/40 OS 20/300 OD
- IOPs: 18/13
- Pupils: sluggish OU
- Slit lamp: unremarkable OU

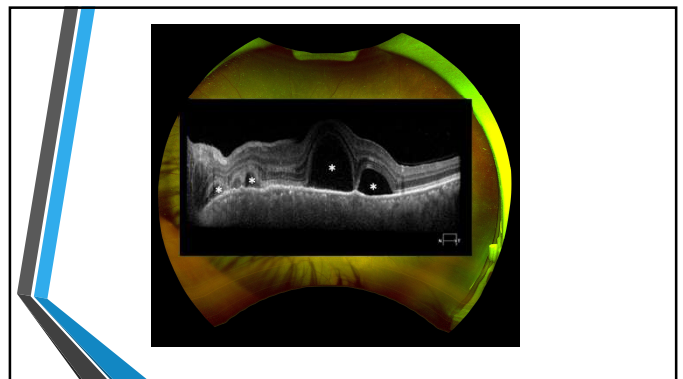
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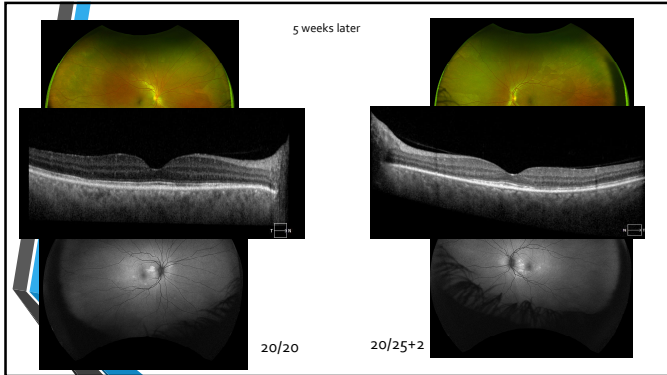
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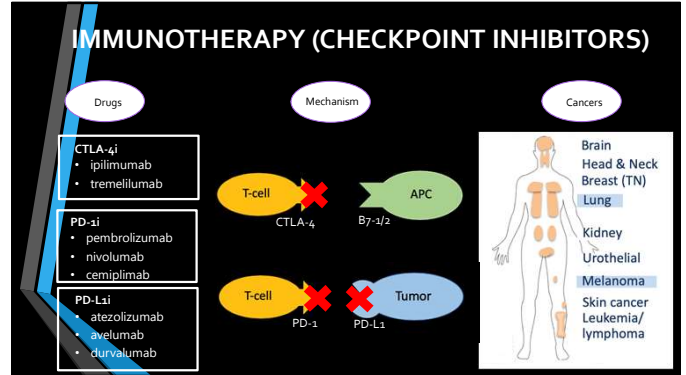
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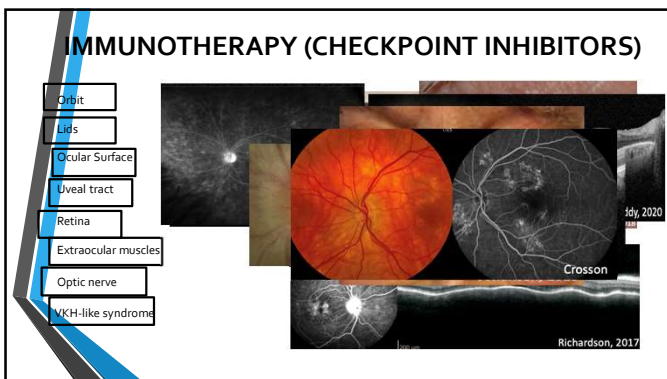
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CASE #4

70 y/o M with complaints of blurred vision OS x 4 days

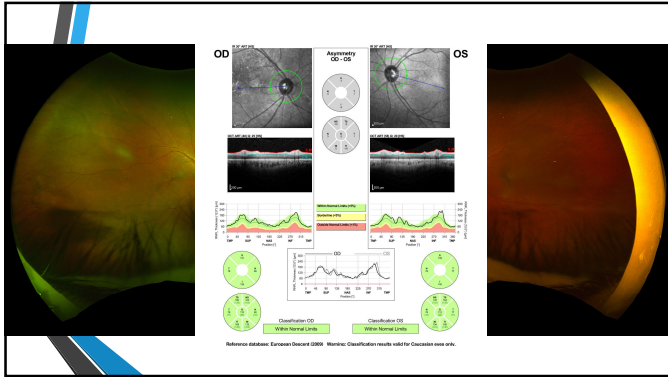
PMH:

- Non-metastatic prostate cancer on pembrolizumab since 9/2021

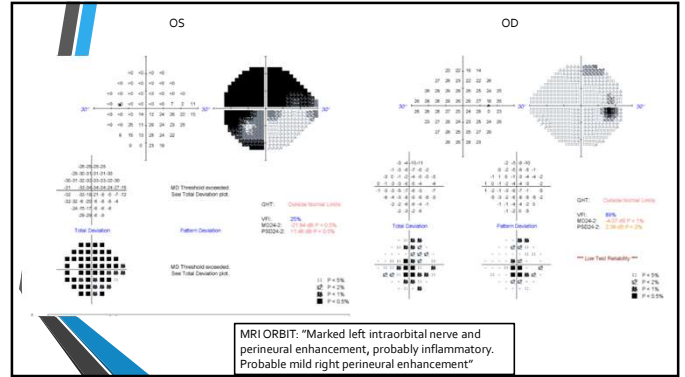
Exam:

- BCVA 20/20 20/30 (with effort, he reports part of the line is missing)
- IOPs: 19/16
- Pupils: sluggish OU
- Slit lamp: unremarkable OU
- Color vision: 8/8 OD and 6/8 OS

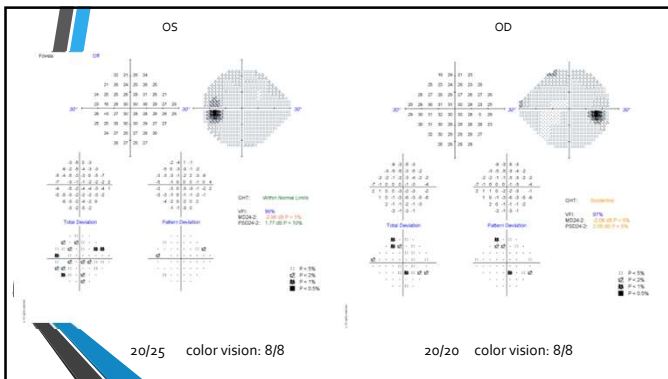
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WHAT DOES THIS MEAN FOR THE PATIENT?

- 1% of patients can get inflammation of the eye
- Things you may notice: blurred vision, redness, photosensitivity. If this happens, come in for evaluation
- Once treatment is complete, paused, or with dose reduction: changes can be reversible (depending on part of eye that is involved)

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TREATMENT/MANAGEMENT

- Steroids (topical or oral, depending on location of inflammation)
- Pause or cessation of therapy

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MAP K INHIBITORS

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CASE #5

55 y/o M with complaints of intermittent blurred vision after each cancer treatment, that resolves within a few days

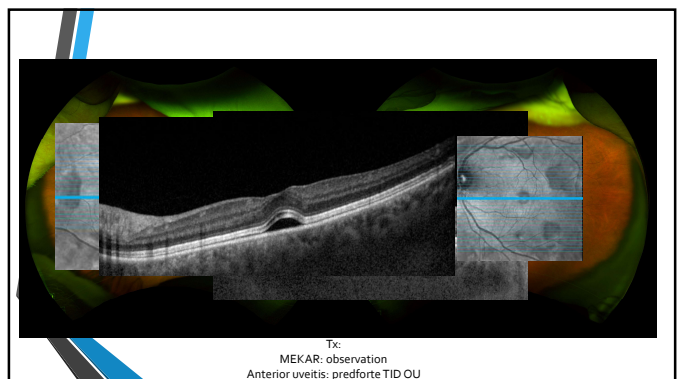
PMH:

- Recurrent cutaneous melanoma on dabrafenib and trametinib

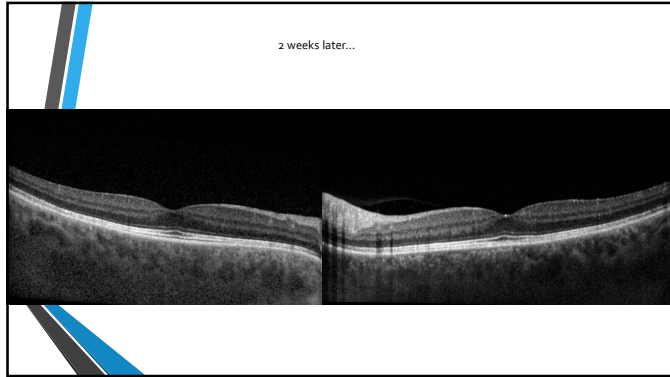
Exam:

- BCVA 20/40 20/25-2
- IOPs: 11/12
- Slit lamp: tr conjunctival injection, tr cells in AC OU

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CASE #6

61 y/o F with complaints of sudden blurred vision OS

PMH:

- Recurrent ovarian cancer s/p surgery, now on trametinib
- Atrial fibrillation
- HLD
- HTN

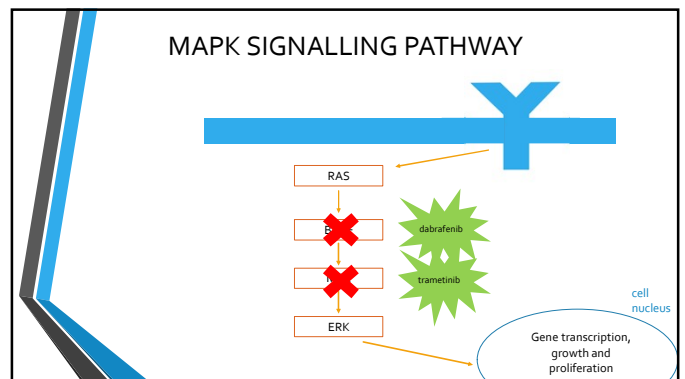
Exam:

- BCVA 20/25 CF@2ft
- IOPs: 16/14
- Slit lamp: unremarkable OU

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WHAT DOES THIS MEAN FOR THE PATIENT?

MEKi

- 15% of patients can get fluid behind the retina, which may cause blurred vision. The fluid resolves on its own but sometimes dose-holds are required
- <0.3% of patients may develop bleeding behind the eye, which may cause more drastic changes to vision

BRAFi

- 5% of patients may develop inflammation of the eye, which can be treated with a steroid drop
- Patients may develop squamoproliferative eyelid lesions

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TREATMENT/MANAGEMENT

MEKAR

- Observation/dose-hold as deemed by drug company

Retinal Vein Occlusion

- Anti-VegF intravitreal injection
- Topical drops to control IOP

Uveitis

- Steroid drops

Squamoproliferative Lesions

- Surgical excision

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TAKE-HOME POINTS

- Always check medication list (google is your friend)
- If your systemic work-up is negative and things don't make sense, don't forget about drugs!!

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REFERENCES

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