

Caring for Your Patient with Cancer



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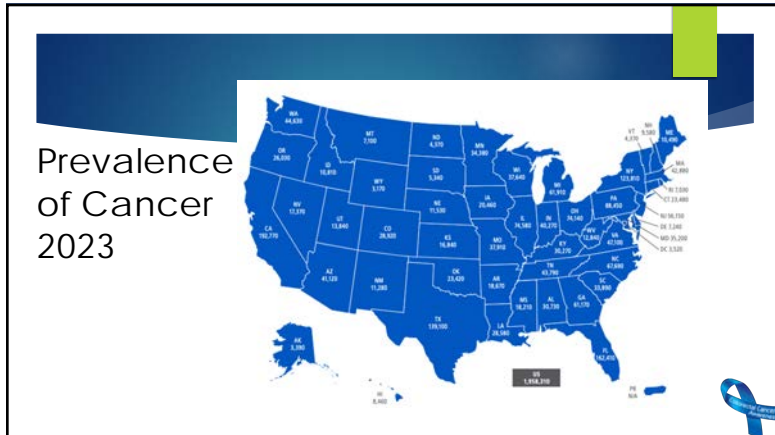
Cecelia Koetting Financial Disclosures

"All relevant relationships have been mitigated."

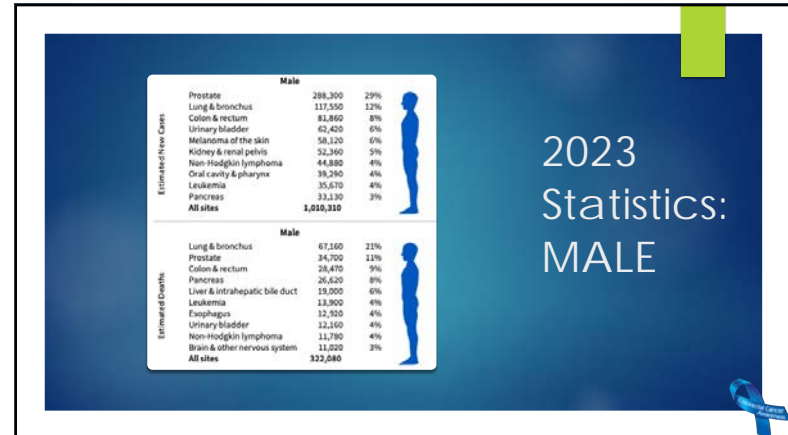
- Horizon-C
- Ivantis-C
- Orasis-C, S, R
- Trukera (B+L) -C
- LENZ-C
- PRN-C,S
- Kala-R
- Tarsus-C,S,R
- Topcon-C
- Glaukos-C
- B +L- C, S, R
- Iveric Bio-C
- Azura-C
- Aldeyra-C
- Dompe-C,S,R
- Myze- C
- MOVU- C
- Vital Tears- C
- Oyster Point/Viatris-C,R
- Allergan/Abbvie -C, S, R
- Alcon-C, S, R
- Harrow-C, S
- Thea-C,R
- Bruder-C
- Blinkjoy-C
- SCOPE-C
- Brill- C

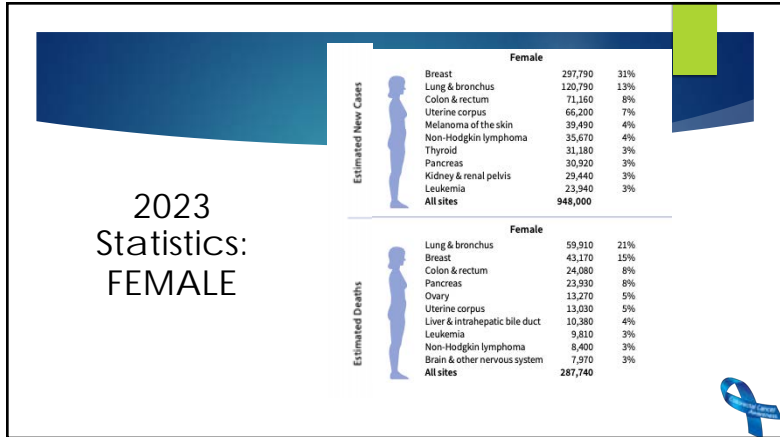
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“In the United States, 1 in 3 people will be diagnosed with cancer during their lifetime”

– American Cancer Society

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Understanding the Journey of Diagnosis

- Physical Exam
- Laboratory testing
- Imaging
- Biopsy

- ▶ CT
- ▶ MRI
- ▶ PET
- ▶ Ultrasound
- ▶ Mammogram
- ▶ X ray
- ▶ Endoscopy
- ▶ Colonoscopy

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TNM Classification System


Primary Tumor (T)	TX	Primary tumor cannot be measured
	T0	No evidence of primary tumor
	Tis	Carcinoma in situ (has not spread to neighboring tissue)
	T1, T2, T3, T4	Size and/or extent of primary tumor
Regional Lymph Nodes (N)	NX	Regional lymph nodes cannot be measured
	N0	No regional lymph node involvement
	N1, N2, N3	Involvement of regional lymph nodes (number and/or extent of spread)
Metastasis (M)	MX	Distant metastasis cannot be measured
	M0	No distant metastasis
	M1	Distant metastasis (cancer has spread to distant parts of the body)

Adapted from: What is cancer staging? American Joint Committee on Cancer. www.americanoncology.com/askoncologybooks/Pages/What-is-cancer-staging.aspx. Accessed September 9, 2020.

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Discussing the Diagnosis with Patients

- ▶ Patients may not understand why you are asking so many questions regarding their diagnosis.
- ▶ It can feel invasive to have so many doctors continue to prod.



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Being Empathetic/Sympathetic

- ▶ Can you relate to your patient?
- ▶ Is now a good time to try to lend an ear?
- ▶ Remember, your patients ARE NOT statistics
- ▶ Don't ask about prognosis unless it is offered

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Treatments for Cancer



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Options

- **Surgery**
- **Chemotherapy.**
- **Radiation therapy.**
- **Bone marrow transplant.** Bone marrow transplant is also known as a stem cell transplant.
 - Donor or from self
 - Allows your doctor to use higher doses of chemotherapy to treat your cancer
 - It may also be used to replace diseased bone marrow.
- **Immunotherapy aka Biologic therapy**
- **Hormone therapy.**
 - Some types of cancer are fueled by your body's hormones.
 - Removing those hormones from the body or blocking their effects may cause the cancer cells to stop growing.
- **Targeted drug therapy.**
 - Focuses on specific abnormalities within cancer cells that allow them to survive.
- **Clinical trials.**


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Radiation

- ▶ *Radiation* is an area-targeted treatment
- ▶ Uses high-powered energy beams, such as X-rays and protons, to kill cancer cells
- ▶ Radiation treatment can come from a machine outside your body (external beam radiation), or it can be placed inside your body (brachytherapy).
- ▶ Unless the area treated is near the eye, it is unlikely there will be ocular effects.
 - ▶ Pigmentation changes, peeling of the skin, blisters, and skin photosensitivity



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Interferon treatment

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Interferon

- ▶ A natural substance made by our white blood cells that helps our body's immune system fight infection and disease.
- ▶ Interferon can also be made in a lab
- ▶ It is used to help control the growth of cancer or to kill cancer cells
- ▶ Considered a type of immunomodulatory agent.

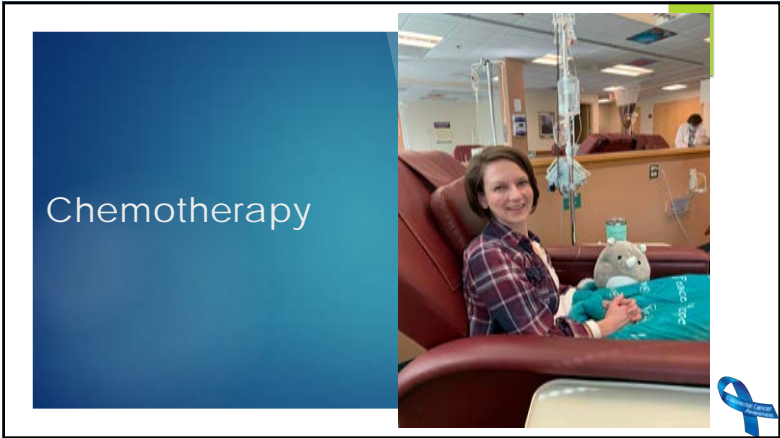
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Possible Ocular Side Effects

Interferons	Cancer Type	Ocular Side Effects
Interferon-alpha Interferon-beta Interferon-gamma	Haematological malignancies Chronic myeloid leukemia Bladder cancer, melanoma, multiple myeloma, hairy cell leukemia, Kaposi sarcoma, follicular non-Hodgkins lymphoma, condyloma acuminata, kidney, carcinoid syndrome, islet cell	<ul style="list-style-type: none"> • Alopecia • Trichiasis • Corneal allograft rejection • Retinopathy • Retinal vein/artery occlusions • Anterior ischemic optic neuropathy • Myasthenia gravis • Cranial nerve palsy

Ho W, Wang H, Yau T. The ophthalmological complications of targeted agents in cancer therapy: what do we need to know as ophthalmologists? *Acta Ophthalmol*. 2013;91(7):604-609.


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Chemo Overview


- ▶ Chemotherapy is a drug treatment that uses powerful chemicals to kill fast-growing cells in your body.
 - ▶ Cancer cells grow and multiply much more quickly than most cells in the body.
- ▶ Many times chemotherapy drugs are not used alone
 - ▶ multiple drugs are used at the same time and are coupled with steroids.
- ▶ Delivered either intravenously or orally in pill form
 - ▶ May or may not be used in conjunction with radiation



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Chemotherapy Agents		
Alkylating Agents		
Cisplatin	Head and neck, lung, cervical, ovarian, testicular, upper gastrointestinal, osteogenic sarcoma, neuroblastoma, brain tumor in children, bladder cancer	Ocular Side Effects <ul style="list-style-type: none"> • Optic Neuritis • Papilledema • Transient cortical blindness • Homonymous hemianopia • Central scotoma • Masquerade pigment changes • CRAO
Carboplatin	Lung cancer, head and neck, ovarian, breast, gastro-intestinal, and osteogenic sarcoma	<ul style="list-style-type: none"> • Optic neuropathy • Maculopathy • Limitation of ocular motility
Oxaliplatin	Colon cancer, esophageal, pancreatic, epithelial ovarian, non-hodgkin's lymphoma, testicular cancer	<ul style="list-style-type: none"> • Blurred vision • Eye pain • Epiphora • Conjunctivitis • Visual field defects • Keratitis • Diplopia • Papilledema • Retinal hemorrhages
Chlorambucil	Hodgkin's and non-hodgkin's disease, adult chronic lymphocytic leukemia	<ul style="list-style-type: none"> • Blurred vision • Keratoconjunctivitis sicca • Blepharocconjunctivitis • Epiphora
Cyclophosphamide	Breast cancer, lymphomas, leukemias, retinoblastoma, small cell lung cancer, ovarian, sarcoma, multiple myeloma	<ul style="list-style-type: none"> • Blurred vision • Conjunctivitis
Ifosfamide	Soft tissue sarcoma, osteosarcoma, non-hodgkin's lymphoma, small cell lung cancer, ovarian, testicular, cervical	<ul style="list-style-type: none"> • Blurred vision • Conjunctivitis
Busulfan	Chronic myeloid leukemia	<ul style="list-style-type: none"> • Posterior sub-capsular cataract • Blurred vision • Keratoconjunctivitis sicca
Camustine	Brain neoplasms, multiple myeloma, hodgkin's and non hodgkin's lymphoma, cutaneous T-cell lymphoma, malignant melanoma	<ul style="list-style-type: none"> • Optic neuro-retinitis • Optic neuritis • Blurred vision • Diplopia • Optic Atrophy • Retinopathy

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Adjunct Medications Commonly Used



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Antimetabolites		
Cytosine arabinoside	Acute myeloid leukemia, lymphocytic leukemia, lymphomatous meningitis, chronic myeloid leukemia	Ocular Side Effects <ul style="list-style-type: none"> • Ocular pain • Epiphora • Foreign body sensation • Photophobia • Blurred vision • Conjunctival hyperemia • Corneal punctate opacities • Optic neuropathy
5-Fluorouracil and Capecitabine	Skin, head and neck, breast, gastrointestinal, colorectal, cervical cancer	<ul style="list-style-type: none"> • Blurred vision • Ocular pain • Photophobia • Epiphora • Conjunctivitis • Periorbital edema • Ectropion • Keratitis • Peri-orbital edema
Methotrexate	Breast cancer, choriocarcinoma, osteogenic sarcoma, acute leukemia, cutaneous lymphoma, head and neck	<ul style="list-style-type: none"> • Blurred vision • Photophobia • Conjunctivitis • Blepharitis • Optic neuropathy • INO • Macular edema* • RPE changes*
Pemetrexed	Pleural mesothelioma, small cell lung cancer	<ul style="list-style-type: none"> • Epiphora • Conjunctivitis
Fludarabine	B cell chronic lymphocytic leukemia, non-hodgkins lymphoma, acute leukemias, mycosis fungoides	<ul style="list-style-type: none"> • Diplopia • Photophobia • Optic neuritis • Blurred vision • Conjunctivitis • Epiphora • Dry eye • Photophobia • Retinopathy
Pentostatin	Hairy cell leukemia, cutaneous T-cell lymphoma, chronic lymphocytic leukemia	<ul style="list-style-type: none"> • Epiphora • Conjunctivitis • Epiphora • Dry eye • Photophobia • Retinopathy

Ho WL, Wong H, Yau T. The ophthalmological complications of targeted agents in cancer therapy: what do we need to know as ophthalmologists? Acta Ophthalmol. 2013;91(7):604-609.



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Mitotic Inhibitors		
	Cancer Type	Ocular Side Effects
Paclitaxel	Breast cancer, ovarian cancer	<ul style="list-style-type: none"> Scintillating scotoma Visual field impairment Photopsia Ischemic optic neuropathy
Docetaxel	Breast cancer, gastric, gastro- esophageal adenocarcinoma, head and neck, prostate cancer, non small cell lung carcinoma	<ul style="list-style-type: none"> Erosive conjunctivitis Punctual stenosis Canalicular narrowing Naso-lacrimal duct obstruction
Vincristine	Lymphoblastic leukemia, ewing's sarcoma, hodgkin's disease, non- hodgkin's disease, lung, breast, soft tissue sarcomas	<ul style="list-style-type: none"> Cranial nerve palsies (ptosis, lagophthalmos, INO, corneal hyperesthesia) Optic neuropathy Optic atrophy Cortical blindness Night blindness
Topoisomerase Inhibitor II	Retinoblastoma	<ul style="list-style-type: none"> CRAO Retinal toxicity

*in conjunction with cyclophosphamide when administered intra-caroid
Ho WL, Wong H, Yau T. The ophthalmological complications of targeted agents in cancer therapy: what do we need to know as ophthalmologists? Acta Ophthalmol. 2013;91(7):604-609.

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Biologics

- Adoptive cell transfer
- Angiogenesis inhibitors
- Bacillus Calmette-Guerin therapy
- Biochemotherapy
- Cancer vaccines
- Chimeric antigen receptor (CAR) T-cell therapy
- Cytokine therapy
- Gene therapy
- Immune checkpoint modulators
- Immunocjugates
- Monoclonal antibodies
- Oncolytic virus therapy
- Targeted drug therapy

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Biologics for Cancer

Biologics as a category

- ▶ a diverse group of medicines which includes vaccines, growth factors, immune modulators, monoclonal antibodies, as well as products derived from human blood and plasma.

In general, biological therapies work by:

1. Getting the immune system to attack cancer cells.
2. Making cancer cells easier for the immune system to see.

Benefit: Possibly fewer side effects

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Biologic Agents		
Inhibitor of Epidermal Growth Factor Receptor		
	Cancer Type	Ocular Side Effects
Gefitinib	Non-small cell lung cancer	<ul style="list-style-type: none"> Corneal erosion Corneal perforation Trichiasis Dry eye syndrome Blepharitis conjunctivitis
Erlotinib	Non-small cell lung cancer, pancreatic	<ul style="list-style-type: none"> Corneal erosion Corneal perforation Infectious keratitis Trichiasis Periorbital rash Periorbital swelling Ectropion Conjunctivitis
Cetuximab	Colorectal, head and neck squamous cell carcinoma	<ul style="list-style-type: none"> Corneal epithelium toxicity Corneal erosion Corneal perforation Trichiasis Dry eye syndrome Mebomian gland dysfunction Blepharitis conjunctivitis
Panitumumab		<ul style="list-style-type: none"> Corneal perforation Conjunctivitis Hyperemia Epiphora Trichiasis

Ho WL, Wong H, Yau T. The ophthalmological complications of targeted agents in cancer therapy: what do we need to know as ophthalmologists? Acta Ophthalmol. 2013;91(7):604-609.

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Inhibitors of Vascular Endothelial Growth Factor Receptor		
Sunitinib	Renal cell carcinoma, gastrointestinal stromal tumors	<ul style="list-style-type: none"> Central visual field defect Cortical blindness Retinal detachment/tear Blurred vision Periocular edema
Pazopanib	Renal cancer	<ul style="list-style-type: none"> Ptosis Corneal toxicity Retinal detachment/tear Retinal artery/vein occlusion Papilledema Optic neuropathy Uveitis Macular edema Conjunctival hemorrhage Retinal/vitreous hemorrhage
Bevacizumab	Colorectal, non small cell lung cancer, renal cell carcinoma, glioblastoma, cutaneous melanoma	<ul style="list-style-type: none"> Cortical blindness Optic neuritis Optic neuropathy

Fraunfelder FT, Fraunfelder FW. Oral anti-vascular endothelial growth factor drugs and ocular adverse events. J Ocul Pharmacol Ther. 2018;34(6):432-435.

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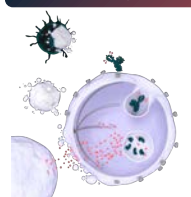
Inhibitors of tumor specific proteins		
Crizotinib	Non-small cell lung cancer	<ul style="list-style-type: none"> Flashes Light trails Image persistence Light Dark adaptation abnormality
Imatinib	Chronic myeloid leukemia, Gastrointestinal stromal tumors	<ul style="list-style-type: none"> Periorbital edema Subconjunctival hemorrhage Conjunctival chemosis Epiphora Ulcerative keratitis Dry eye syndrome Blurred vision Optic neuritis Optic disc edema Retinal edema Cystoid macular edema
Vandetanib	Melanoma	<ul style="list-style-type: none"> Uveitis Iritis Retinal vein occlusion
Ipilimumab	Malignant melanoma	<ul style="list-style-type: none"> Dry eye syndrome Proptosis Swelling of EOM Diplopia Iridocyclitis
Ganglioside GD2	Neuroblastoma	<ul style="list-style-type: none"> Photophobia Accommodative deficiency Mydriasis

Ho WL, Wong H, Yau T. The ophthalmological complications of targeted agents in cancer therapy: what do we need to know as ophthalmologists? Acta Ophthalmol. 2013;91(7):604-609.

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Mirvetuximab Soravtansine

Mirvetuximab soravtansine (MIRV) is the first biomarker-directed agent showing antitumor activity in patients with FR α -positive^a platinum-resistant ovarian cancer (PROC)¹



- MIRV is an antibody-drug conjugate (ADC) comprising an FR α -binding antibody, cleavable linker, and maytansinoid DM4 payload¹
- A phase 3 clinical study, SORAYA, evaluated MIRV in patients with FR α -high PROC who had received 1 to 3 prior therapies, including required bevacizumab^{1,3}

AEs, adverse events; DM4, NZ-[4-(3-carboxypropyl)idithio]-4-methyl-1-oxo-2-sulfopentyl]-N-(2'-deoxy-5'-methyluracil)mytansine; FR α , folate receptor alpha.
^aMirvetuximab actively with MIRV has been demonstrated with single-agent MIRV in FR α -high PROC ($\geq 75\%$ tumor cells FR α -positive by P52¹) and in combination with other agents in FR α -low to high PROC ($\geq 25\%$ tumor cells FR α -positive by P52¹).

1. Matulonis UA, et al. Presented at: 2022 American Society of Clinical Oncology Annual Meeting; June 3-7, 2022; Chicago, IL. Poster 391. 2. Matulonis UA, et al. Clin Cancer Res. 2019;25(6):1727-1736.
 3. ClinicalTrials.gov Identifier: NCT04296990. Updated April 21, 2022. Accessed August 8, 2022. <https://clinicaltrials.gov/ct2/show/NCT04296990>. 4. Matulonis UA, et al. Presented at: 2018 European Society for Medical Oncology Congress; October 19-23, 2018; Munich, Germany. Abstract 949P.

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Ocular AEs and Grading

Eye Disorders

CTCAE term	Grade 1	Grade 2	Grade 3	Grade 4
Blurred vision	Intervention not indicated	Symptomatic; moderate decrease in visual acuity; limiting instrumental ADL ^a	Symptomatic, with marked decrease in visual acuity; limiting self-care ADL ^a	Best corrected visual acuity of $\leq 20/200$ or worse in the affected eye
Keratitis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; moderate decrease in visual acuity	Symptomatic, with marked decrease in visual acuity; corneal ulcer ^b ; limiting self-care ADL ^a	Perforation; best corrected visual acuity of $\leq 20/200$ or worse in the affected eye
Dry eye ^c	Asymptomatic; clinical or diagnostic observations only; symptoms relieved by lubricants	Symptomatic; moderate decrease in visual acuity	Symptomatic, with marked decrease in visual acuity; limiting self-care ADL ^a	NA
Photophobia ^d	Symptomatic but not limiting ADL	Limiting instrumental ADL ^a	Limiting self-care ADL ^a	NA

Best corrected visual acuity $\geq 20/40$ and better or ≤ 3 lines of decreased vision from known baseline ← Moderate decrease in visual acuity → Marked decrease in visual acuity → Best corrected visual acuity worse than $20/40$ or ≥ 3 lines of decreased vision from known baseline, up to $20/200$

ADL, activities of daily living; AEs, adverse events; CTCAE, Common Terminology Criteria for Adverse Events; NA, not available.
^aInstrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc. ^bSelf-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not driving. ^cDisorder characterized by inflammation to the cornea and conjunctiva. ^dDisorder characterized by dryness of the cornea and conjunctiva.
 National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE), Version 5. US Department of Health and Human Services; 2017. Published November 27, 2017. Accessed July 30, 2022. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5v7.pdf

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Most common Anterior segment and Adnexal Side Effects

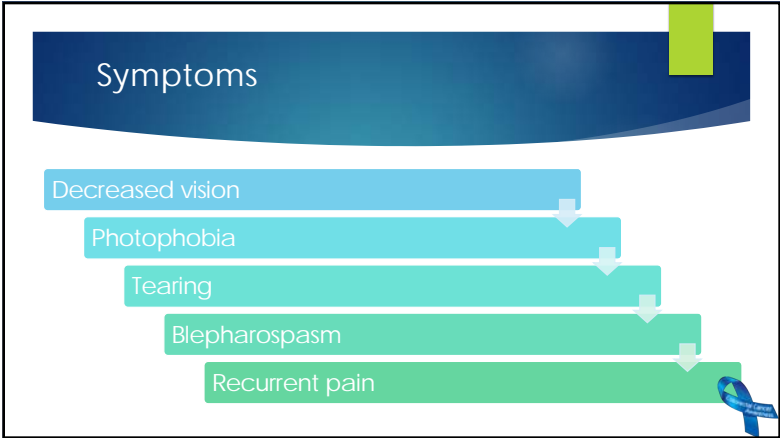
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- ## Ocular Surface Disease
- ▶ Ocular Surface disease
 - ▶ Dry eye Disease
 - ▶ Conjunctivitis
 - ▶ Blepharitis
 - ▶ Demodex
 - ▶ Meibomian gland damage
 - ▶ Limbal stem cell deficiency
 - ▶ Neurotrophic keratitis
 - ▶ Epiphora
 - ▶ 2/2 lacrimal gland stenosis or OSD?
 - ▶ Surgical Tx

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- ## Limbal Stem Cell Deficiency
- ▶ When limbal stem cells begin to struggle and poorly function, the epithelial cell layer and its reproduction becomes compromised
 - ▶ Loss or deficiency of stem cells in the limbus which are vital for re-population of the corneal epithellum and to the barrier function of the limbus
 - ▶ Once limbal stem cells are damaged the epithellum will be replaced by conjunctival goblet cells

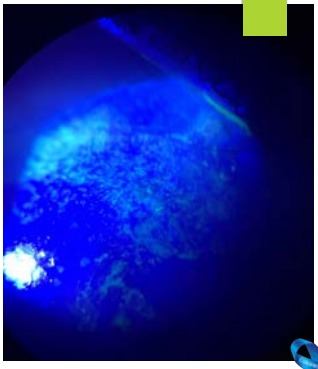
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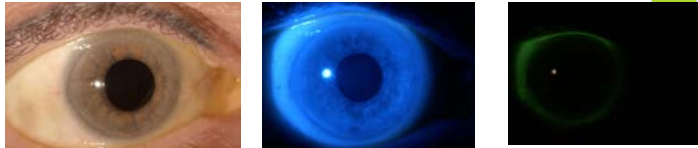
Signs

- ▶ Stippled superficial punctate late fluorescein staining
 - ▶ Stained cells are more elongated and pill shaped than in SPK from DED
 - ▶ Early LSCD staining more concentrated peripheral near limbal area
 - ▶ More progressed LSCD staining spread central and becomes more diffuse
 - ▶ Natural migration of epithelial cells
 - ▶ Whorl like pattern staining
- ▶ Ingrowth of opaque epithelium
- ▶ Superficial neovascularization

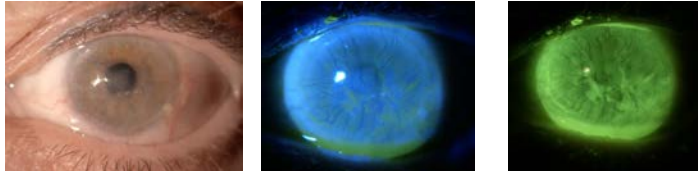


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NORMAL EYE

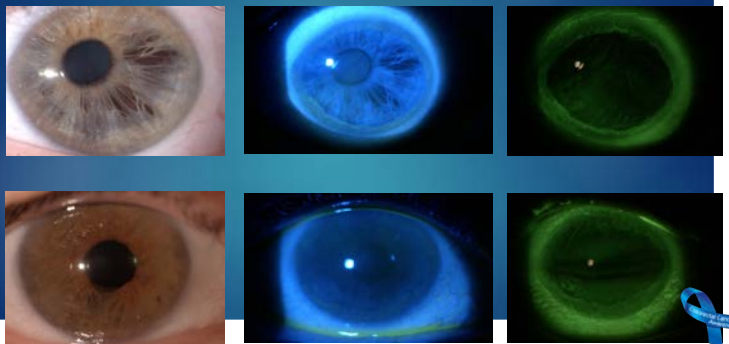


TOTAL LSCD

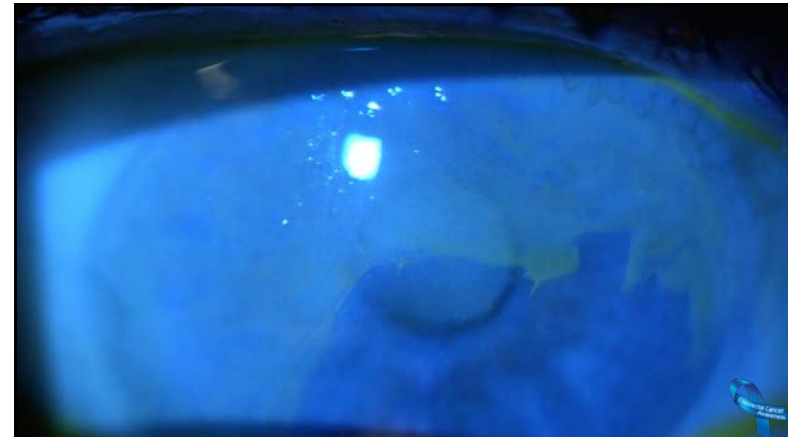


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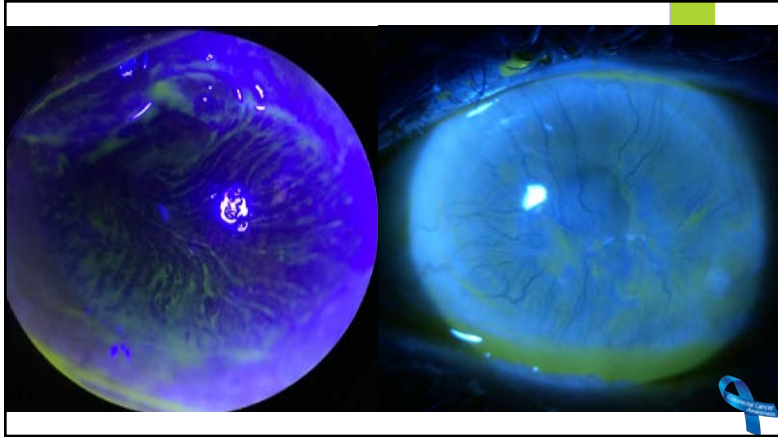
LATE STAINING FLUORESCCEIN PATTERN



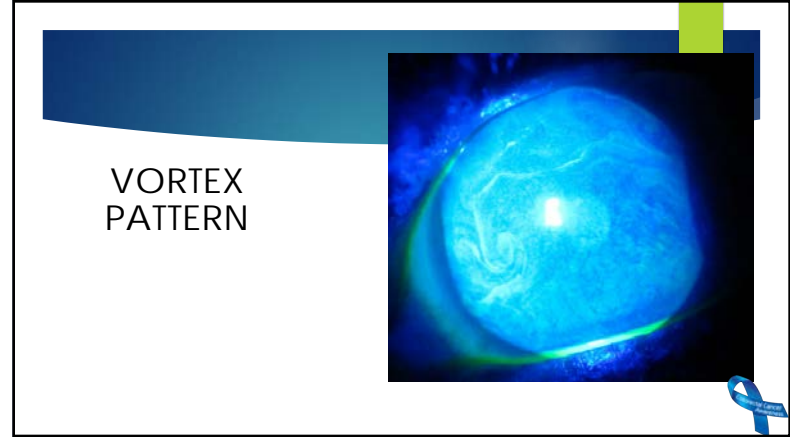
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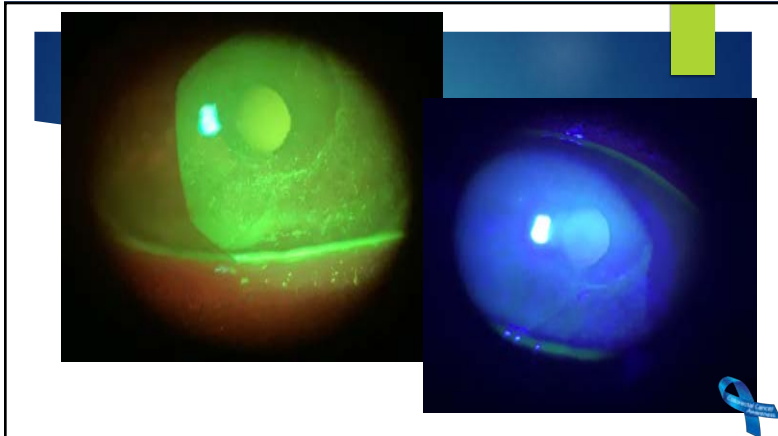
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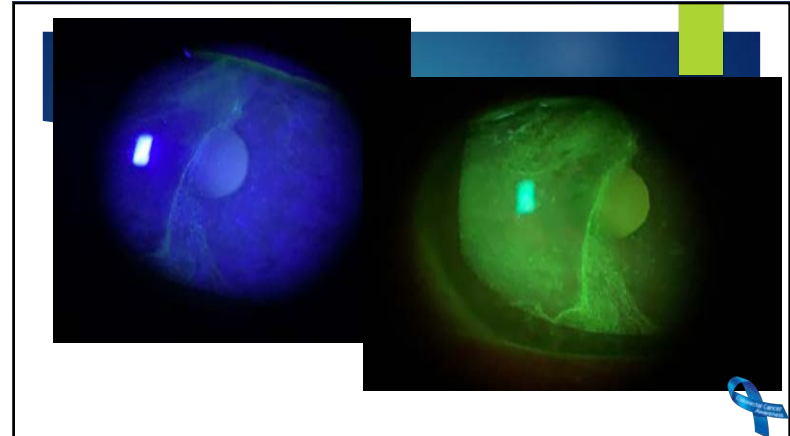
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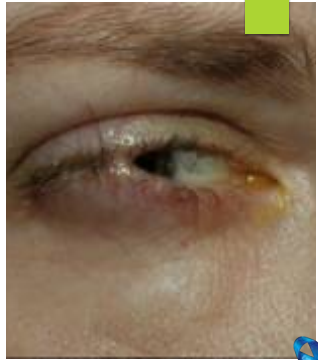
Non-Surgical Treatment

- ▶ Remove traumatic or toxic insults that may be the cause
 - ▶ Discontinue contact lens wear
 - ▶ Possible refit in scleral
 - ▶ Bandage CL?
 - ▶ Discontinue or switch topical medications
 - ▶ Glaucoma medications
 - ▶ Preservative sensitivity
 - ▶ BAK
- Treating underlying systemic causes
 - Autoimmune control
- Improve tear film and control inflammation
 - Vitamin A ointment QHS
 - Topical steroids
 - Compounded Preservative Free option
 - Topical cyclosporine
 - Preservative free AT
 - Punctal Plugs


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Next Step Treatments?

- ▶ Amniotic membrane
 - ▶ Dehydrated vs cryopreserved
- ▶ Amniotic membrane drops
 - ▶ Can be costly and not covered by insurance currently
- ▶ Serum Tears
 - ▶ Can be costly and inconvenient
- ▶ Oxervate
 - ▶ Neurotrophic keratitis
- ▶ Surgical
 - ▶ LS transplant
 - ▶ Tarsorrhaphy



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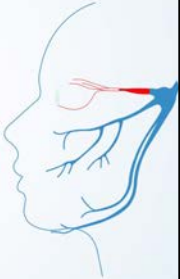
Neurotrophic Keratitis

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Neurotrophic Keratitis

IMPAIRED CORNEAL TRIGEMINAL INNERVATION

- ⊖ Impairment of trophic supply
- ⊖ Impairment of trigeminal reflexes
- ⊖ Corneal epithelial alterations
- ⊖ Impairment of corneal healing
- ⊖ Reduced tear film production & blink rate
- ⊖ Spontaneous corneal epithelial breakdown
- ⊖ **NEUTROTROPHIC KERATITIS**



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Mackie classification

STAGE 1
 Mild
 Punctate epithelial keratopathy (PEK)

STAGE 2
 Moderate
 Persistent epithelial defect (PED)

STAGE 3
 Severe
 Corneal ulcer

- Some vision loss can potentially be seen in all stages of NK²
- If untreated, moderate NK progresses to severe disease with associated risks of profound vision loss resulting from scarring and corneal perforation³

1. Dua N, Jha D, Maitra D, et al. Neurotrophic keratopathy. Prog Retin Eye Res. 2016;40:157-181. 2. Senjuntol T, et al. Neurotrophic keratopathy. Ophthalmologica. 2014;131:284-287. 3. Guzman M, Leshem A. Diagnosis and management of neurotrophic keratitis. Clin Ophthalmol. 2018;12:75-82. 4. Senjuntol T, Guzman M, Leshem A. Review of neurotrophic keratopathy. Curr Opin Ophthalmol. 2018;23:215-220. 5. Dua N, Jha D, Maitra D, et al. Neurotrophic keratopathy: A review. Clin Exp Ophthalmol. 2011;39:124-130.

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Corneal Sensitivity Testing: Esthesiometry

- Qualitative
 - Cotton tip applicator
 - Dental floss
- Quantitative
 - Cochet-Bonnet
 - Brill esthesiometer

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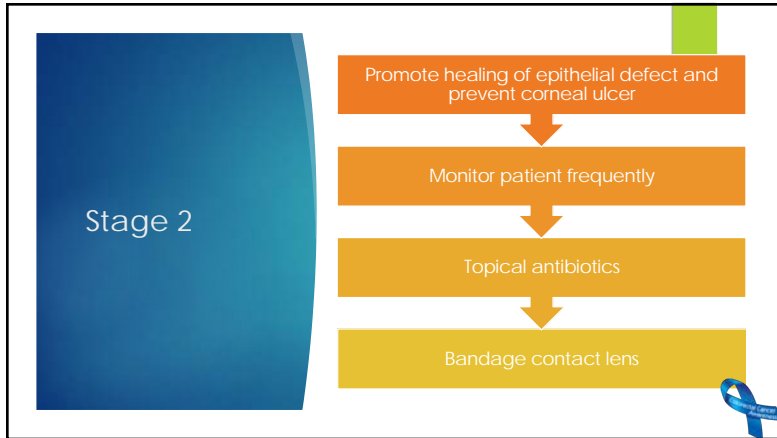
Persistent Epithelial Defect: Stage 2 NK Post Chemotherapy (finished 8 months prior)

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Stage 1 +2 +3 Treatment

- Remove any ocular medication that may be associated with toxicity
 - Preservative free options, tears and ointments
- Treat other associated ocular problems
 - LSCD
 - OSD/DED
 - Exposure keratitis
- Vitamin A ointment
- Amniotic membranes
- Autologous serum eye drops
 - Growth factors, neuromediators, cytokines, vitamins
 - Steroids

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Stage 3

- ▶ All the above
- ▶ Heavy antibiotics
 - ▶ Consider fortified
- ▶ Will need surgery if perforation

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Autologous Serum tears for NK

- ▶ Matsumoto et al 2004
- ▶ Complete healing of all the 14 eyes with NK treated with autologous serum drops and an increase in corneal sensitivity in 64.2% of cases
- ▶ The study demonstrated that serum harbors neurotrophins and growth factors to the ocular surface.
- ▶ More recent studies confirmed that autologous serum eye drops allowed high rates of corneal healing, and also the improvement of corneal nerve morphology with increased number, length, width, and density

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cenegermin-bkbj 20 mcg/ml was approved by FDA in August 2018

Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis

Yoshimura, MD,¹ Alvarado-Lanzetta, MD,² Pardo-Ramirez, MD,³ Fernandez-Solis, MD,⁴ Mencia-Alvarez, PhD,⁵ Trivedi-Chen, PhD,⁶ Evans-Marsali, MD, PhD,⁷ for the REPAIR Study Group⁸

Purpose: To evaluate the safety and efficacy of topical recombinant human nerve growth factor (rhNGF) for treating moderate-to-severe neurotrophic keratitis (NK), a rare degenerative corneal disease resulting from impaired corneal innervation.

Design: Phase II multicenter, randomized, double-masked, vehicle-controlled trial.

Participants: Patients with stage 2 moderate or stage 3 severe NK in 1 eye.

Methods: The REPAIR phase II study assessed safety and efficacy in 126 patients randomized 1:1:1 to rhNGF 10 µg/mL, 20 µg/mL, or vehicle. Treatment was administered 8 drops per day for 8 weeks. Patients then entered a 40-week follow-up period. Safety was assessed in all patients who received study treatment.

Main Results: Efficacy: Corneal healing (defined as $\geq 0.5\text{-mm}$ maximum diameter of fluorescein staining in the lesion area) was assessed by masked central readers at week 8 (primary efficacy and safety end point). 8-week corneal healing rates were 41.0%, 45.0%, and 38.0% for rhNGF 10, 20, and vehicle, respectively.

- ▶ Approved for the treatment of neurotrophic keratitis in adults and children age 2 and older
- ▶ Available for ordering since January 2019
- ▶ Developed by Dompé pharmaceuticals, available through specialty pharmacy

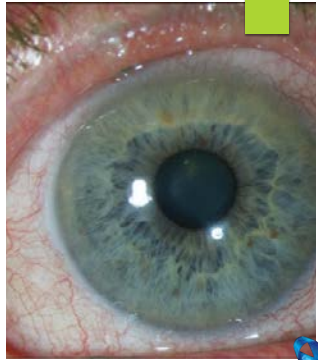
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Graft vs Host Disease

- ▶ Systemic disorder that occurs when the graft's immune cells recognize the host as foreign and attack the recipient's body cells.
- ▶ "Graft" = transplanted, or donated tissue
- ▶ "Host" = tissues of the recipient
- ▶ Common complication
 - Following allogeneic bone transplantation (most common)
 - Following transplantation of solid organs that are rich in lymphoid cells (eg. liver)
 - Following transfusion of un-irradiated blood

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1. Acute classic GVHD: Presents within 100 days of transplantation with classical clinical features of acute GVHD.
2. Persistent, recurrent, or late-onset acute GVHD: Manifests with clinical features of classic acute GvHD but after 100 days of transplantation.
3. Classic chronic GVHD: Presents after 100 days of transplant with classic clinical features of chronic GvHD.
4. Overlap syndrome: May present at any time post-transplant with features of both acute and chronic GVHD [\[1\]](#)



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Ocular Presentation

- ▶ Lacrimal gland
 - ▶ Most affected and most severely affected
 - ▶ CD4 and CD8 T cell cause damage on preductal epithelial cells of lacrimal gland leading to permanent stenosis
 - ▶ Study found tear turnover rate in GVHD approx. same as Sjog
- ▶ Severe MGD
- ▶ Conjunctiva
 - ▶ Range from erythema to cicatrizing conjunctivitis 2/2 inflammation in approx. 11-12% of acute and chronic GVHD pt
- ▶ Cornea
 - ▶ LSCD, NK, K sicca, filaments, ulcers perforation
 - ▶ Cataract development (systemic steroid and radiation)
 - ▶ Post seg. rare more likely related to radiation or steroid as well



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NIH Ocular Scoring in Chronic GVHD [\[1\]](#)

Score	Definition
0	No dry eye symptoms.
1	Mild dry eye symptoms not affecting daily activities (requiring eye drops ≤3x/day) or asymptomatic signs of keratoconjunctivitis sicca.
2	Moderate dry eye symptoms partially affecting daily activities (requiring drops >3x/day or punctal plugs), without vision impairment.
3	Severe dry eye symptoms significantly affecting daily activities (special eyewear to relieve pain) or unable to work because of ocular symptoms or loss of vision caused by keratoconjunctivitis sicca.

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Treatment

- ▶ Cyclosporine
 - ▶ Systemic and topical
- ▶ Steroids
 - ▶ Systemic and topical
- ▶ Amniotic membrane
- ▶ PRP/autologous serum
- ▶ Frequent PF lubrication
- ▶ Vitamin A ointment

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Lid/Adnexal changes

- Ectropion
 - Treatment palliative vs surgical repair?
 - Trichiasis
 - Cause ?
 - Epilation, cauterization or surgical treatment
- Periorbital cutaneous hyperpigmentation
- Periorbital edema
 - Cold compresses
 - Topical or oral steroids possible treatment

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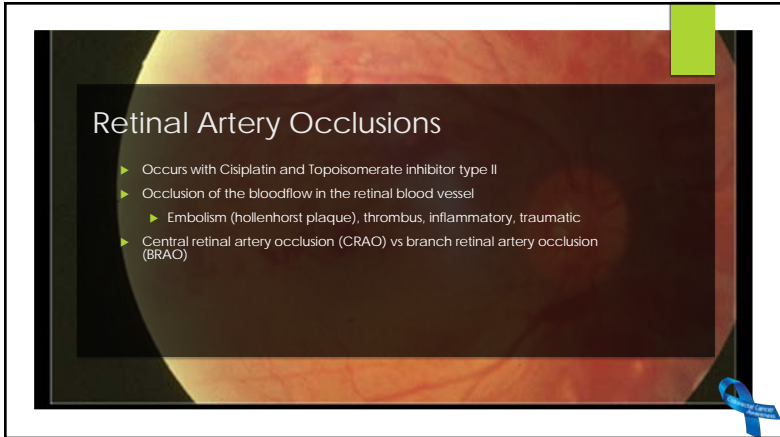
Cataract formation

- ▶ Remember high levels of steroids used in many protocols
- ▶ Can cause secondary development of PSC cataracts.
- ▶ Possible cataract surgery
 - ▶ Age, QOL considerations
 - ▶ Timing with treatment

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Most common Posterior Segment Side Effects

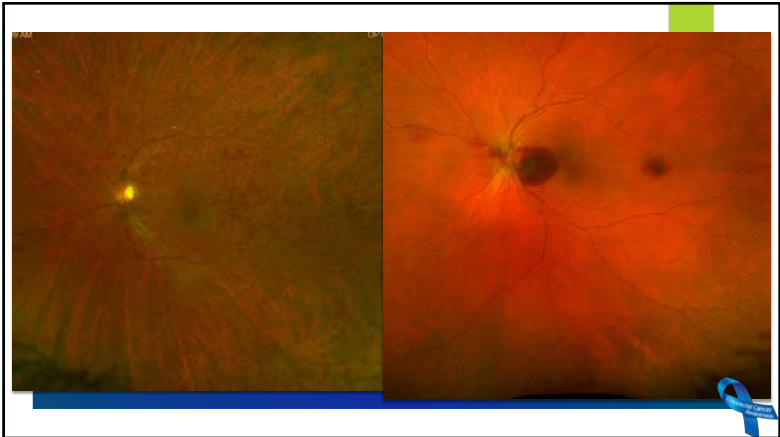
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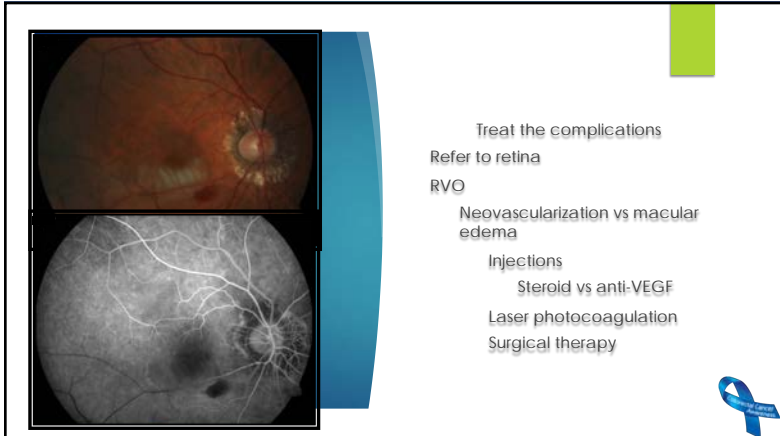
Retinal Artery Occlusions

- ▶ Occurs with Cisplatin and Topoisomerase inhibitor type II
- ▶ Occlusion of the bloodflow in the retinal blood vessel
 - ▶ Embolism (hollenhorst plaque), thrombus, inflammatory, traumatic
- ▶ Central retinal artery occlusion (CRAO) vs branch retinal artery occlusion (BRAO)

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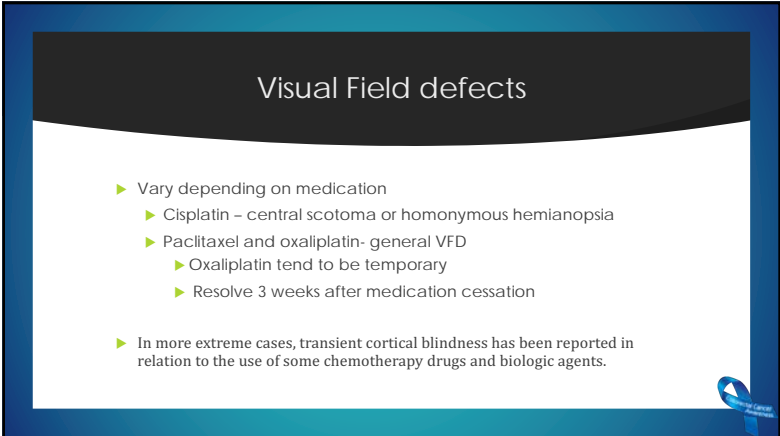
Treat the complications

Refer to retina

RVO

- Neovascularization vs macular edema
- Injections
 - Steroid vs anti-VEGF
- Laser photocoagulation
- Surgical therapy

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Visual Field defects

- ▶ Vary depending on medication
 - ▶ Cisplatin – central scotoma or homonymous hemianopsia
 - ▶ Paclitaxel and oxaliplatin- general VFD
 - ▶ Oxaliplatin tend to be temporary
 - ▶ Resolve 3 weeks after medication cessation
- ▶ In more extreme cases, transient cortical blindness has been reported in relation to the use of some chemotherapy drugs and biologic agents.

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Treatment?


- ▶ Let the oncology team know
- ▶ Monitor consistently
- ▶ Discussion with patients regarding adaptation to visual changes and prognosis for improvement is important
- ▶ Temporary prisms and other low vision devices may be helpful in improving these patients' quality of life.



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Hormone Modulation

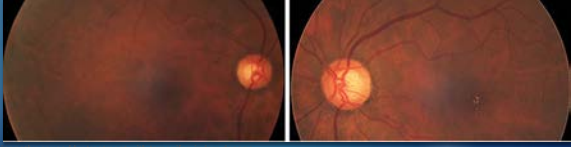
- ▶ Tamoxifen
 - ▶ Selective Estrogen receptor modulator
 - ▶ Used for 5 years after hormone receptor-positive breast cancer to reduce risk of re-occurrence
 - ▶ Some instances of use as preventative




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Tamoxifen Retinopathy

- ▶ Characterized by crystalline deposits and pseudocystic foveal cavitations
- ▶ Occurs 1.5 to 11.8%
- ▶ Monitor patients: (frequency not defined)
 - ▶ OCT macula
 - ▶ VF 10-2
- ▶ In some patients refractile crystalline deposits appear to fade
- ▶ Can also occur with Mitotane and interferon treatment




▶ Tamoxifen retinopathy: Retinopathy caused by treatment with tamoxifen in low dosage. Acta Ophthalmol (Copenh). 1983; 61: 45-50
Heier JS, Drago R.A., Enzenauer R.W. Screening for ocular toxicity in asymptomatic patients treated with tamoxifen. Am J Ophthalmol. 1994; 117: 772-775



71

Kim et al. 2020


- ▶ Retrospective analysis identified 30 of 251 patients with tamoxifen retinopathy, all of which were on a 20mg per day dose for ≥ 2 years.
- ▶ Found that patients with a higher BMI and hyperlipidemia may be at increased risk
- ▶ Suggests that patients on a low dose of tamoxifen are still at risk for toxicity
 - ▶ may be more likely if they possess these risk factor



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Neuro-Ophthalmic Side Effects/ Neurotoxicity

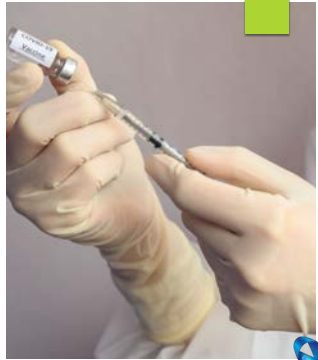
- ▶ Can manifest as papilledema, retinal edema and optic neuritis
 - ▶ Both unilateral and bilateral
- ▶ High doses or high cumulative doses of chemo
 - ▶ Possible retrobulbar optic neuritis



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Other culprits

- ▶ Patients receiving chemotherapy via intracarotid injection have presented with more severe ocular and orbital toxicity including ipsilateral retrobulbar neuritis
- ▶ Tamoxifen (again)
 - ▶ Can cause bilateral optic neuritis leading to optic atrophy and vision loss in high doses



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Take Away

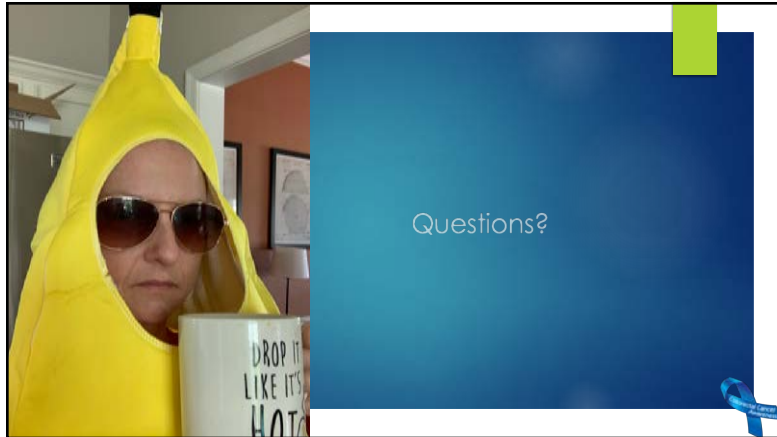
01 Be kind and considerate	02 Remember, we CAN help	03 Work together as a team
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Get yo' self checked

- ▶ Diagnosing cancer at its earliest stages often provides the best chance for a cure.
- ▶ With this in mind, talk with your doctor about what types of cancer screening
- ▶ Advocate for your PATIENTS and YOURSELF

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