# Caring for Your Patient with Cancer

CECELIA KOETTING OD FAAO DIPABO
UNIVERSITY OF COLORADO SCHOOL OF MEDICINE

1

## 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

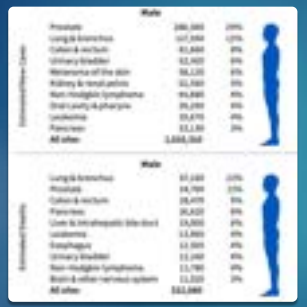
Intrepid

KOETTING CONSULTING, LLC

2

## Prevalence of Cancer 2023

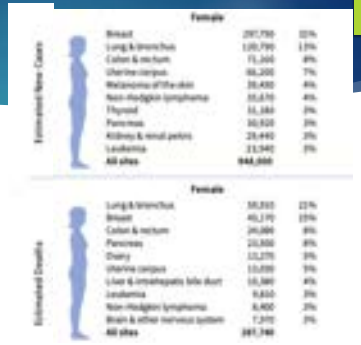
3



## 2023 Statistics: MALE

4

## 2023 Statistics: FEMALE



5

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

– American Cancer Society

6

## Understanding the Journey of Diagnosis

- Physical Exam
- Laboratory testing
- Imaging
- Biopsy

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

7

Often next step is port implantation

8

## 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.cancerstaging.org/references-tools/Pages/What-is-Cancer-Staging.aspx. Accessed September 9, 2020.

9

## 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.

10

## 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

11

## Treatments for Cancer

12


13

## 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.**

14


15

## 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

16

# Interferon treatment

17

## 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.

18

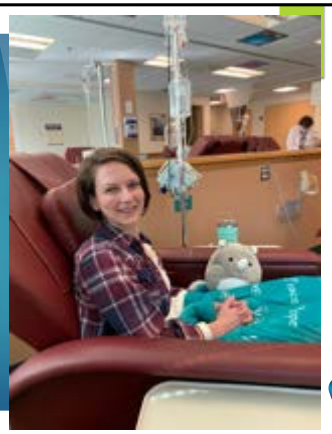
## Possible Ocular Side Effects

| Interferons | Cancer Type | Ocular Side Effects |
|---|---|---|
| **Interferon-alpha**<br>**Interferon-beta**<br>**Interferon-gamma** | Haematological malignancies<br>Chronic myeloid leukemia<br>Bladder cancer, melanoma, multiple myeloma, hairy cell leukemia, Kaposi sarcoma, follicular non-Hodgkins lymphoma, condyloma acuminate, kidney, carcinoid syndrome, islet cell | • Alopecia<br>• Trichiasis<br>• Corneal allograft rejection<br>• Retinopathy<br>• Retinal vein/artery occlusions<br>• Anterior ischemic optic neuropathy<br>• Myastnenia gravis<br>• Cranial nerve palsy |

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.

19

## Chemotherapy



20

## 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

21

**Chemotherapy Agents**

**Alkylating Agent**

| | Cancer Type | Ocular Side Effects |
|---|---|---|
| **Cisplatin** | Head and neck, lung, cervical, ovarian, testicular, upper gastrointestinal, osteogenic sarcoma, neuroblastoma, brain tumor in children, bladder cancer | • Optic Neuritis<br>• Papilledema<br>• Transient cortical blindness<br>• Homonymous hemianopsia<br>• Central scotoma<br>• Macular pigment changes<br>• CRAO |
| **Carboplatin** | Lung cancer, head and neck, ovarian, breast, gastro-intestinal, and osteogenic sarcoma | • Optic neuropathy<br>• Maculopathy<br>• Limitation of ocular motility |
| **Oxaliplatin** | Colon cancer, esophageal, pancreatic, epithelial ovarian, non-hodgkin's lymphoma, testicular cancer | • Blurred vision<br>• Eye pain<br>• Epiphora<br>• Conjunctivitis<br>• Visual field defects |
| **Chlorambucil** | Hodgkin's and non-hodgkin's disease, adult chronic lymphocytic leukemia | • Keratitis<br>• Diplopia<br>• Papilledema<br>• Retinal hemorrhages |
| **Cyclophosphamide** | Breast cancer, lymphomas, leukemias, retinoblastoma, small cell lung cancer, ovarian, sarcoma, multiple myeloma | • Blurred vision<br>• Keratoconjunctivis sicca<br>• Blepharoconjunctivitis<br>• Epiphora |
| **Ifosphamide** | Soft tissue sarcoma, osteosarcoma, non-hodgkin's lymphoma, small cell lung cancer, ovarian, testicular, cerivical | • Blurred vision<br>• Conjunctivitis |
| **Busulfan** | Chronic myeloid leukemia | • Posterior sub-capsular cataract<br>• Blurred vision<br>• Keratoconjunctivitis sicca |
| **Carmustine** | Brain neoplasms, multiple myeloma, hodgkin's and non hodgkin's lymphoma, cutaneous T-cell lymphoma, malignant melanoma | • Optic neuro-retinitis<br>• Optic neuritis<br>• Blurred vision<br>• Diplopia<br>• Optic Atrophy<br>• 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.

22

## Adjunct Medications Commonly Used

23

**Antimetabolites**

| | Cancer Type | Ocular Side Effects |
|---|---|---|
| **Cytosine arabinoside** | Acute myeloid leukemia, lymphocytic leukemia, lyphomatous meningitis, chronic myeloid leukemia | • Ocular pain<br>• Epiphora<br>• Foreign body sensation<br>• Photophobia<br>• Blured vision<br>• Conjunctival hyperemia<br>• Corneal punctate opacities<br>• Optic neuropathy |
| **5-Flourouracil and Capecitabine** | Skin, head and neck, breast, gastrointestinal, colorectal, cervical cancer | • Blurred vision<br>• Ocular pain<br>• Photophobia<br>• Epiphora<br>• Conjunctivitis<br>• Periorbital edema<br>• Ectropion<br>• Keratitis |
| **Methotrexate** | Breast cancer, choriocarcinoma, osteogenic sarcoma, acute leukemia, cutaneous lymphoma, head and neck | • Peri-orbital edema<br>• Ocular pain<br>• Blured vision<br>• Photophobia<br>• Conjunctivitis<br>• Blepharitis<br>• Optic neuropathy<br>• INO<br>• Macular edema*<br>• RPE changes* |
| **Pemetrexed** | Pleural mesothelioma, small cell lung cancer | • Epiphora<br>• Conjunctivitis |
| **Fludarabine** | B cell chronic lymphocytic leukemia, non-hodgkins lymphoma, acute leukemias, mycosis fungoides | • Diplopia<br>• Photophobia<br>• Optic neuritis<br>• Blured vision |
| **Pentostatin** | Hairy cell leukemia, cutaneous T-cell lymphoma, chronic lymphocytic leukemia | • Blurred vision<br>• Conjunctivitis<br>• Epiphora<br>• Dry eye<br>• Photophobia<br>• 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.

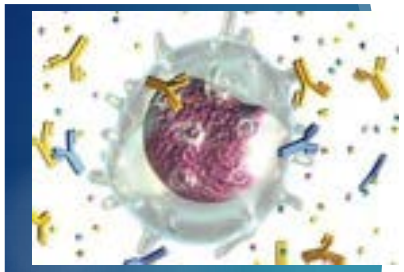
24

| Miotic Inhibitors | | |
|---|---|---|
| | Cancer Type | Ocular Side Effects |
| **Paclitaxel** | Breast cancer, ovarian cancer | • Scintillating scotoma<br>• Visual field impairment<br>• Photopsia<br>• Ischemic optic neuropathy |
| **Docetaxel** | Breast cancer, gastric, gastro-espophageal adenocarcinoma, head and neck, prostate cancer, non small cell lung carcinoma | • Erosive conjunctivitis<br>• Punctual stenosis<br>• Canalicular narrowing<br>• Naso-lacrimal duct obstruction |
| **Vincristine** | Lymphoblastic leukemia, ewing's sarcoma, hodgkin's disease, non-hodgkin's disease, lung, breast, soft tissue sarcomas | • Cranial nerve palsies (ptosis, lagophthalmos, INO, corneal hyperesthesia)<br>• Optic neuropathy<br>• Optic atrophy<br>• Cortical blindness<br>• Night blindness |
| **Topoisomerase Inhibitor II** | Retinoblastoma | • CRAO<br>• Retinal toxicity |

*in conjunction with cyclophosphamide when administered intra-carotid

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.

25



## 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
- Immunoconjugates
- Monoclonal antibodies
- Oncolytic virus therapy
- Targeted drug therapy

26

## Biologics for Cancer

*Biologicals* 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

27

| Biologic Agents<br>Inhibitor of Epidermal Growth Factor Receptor | | |
|---|---|---|
| | Cancer Type | Ocular Side Effects |
| **Gefitinib** | Non-small cell lung cancer | • Corneal erosion<br>• Corneal perforation<br>• Trichiasis<br>• Dry eye syndrome<br>• Blepharitis<br>• conjunctivitis |
| **Erlotinib** | Non-small cell lung cancer, pancreatic | • Corneal erosion<br>• Corneal perforation<br>• Infectious keratitis<br>• Trichiasis<br>• Periorbital rash<br>• Periorbital swelling<br>• Ectropion<br>• Conjunctivitis |
| **Cetuximab** | Colorectal, head and neck squamous cell carcinoma | • Corneal epithelium toxicity<br>• Corneal erosion<br>• Corneal perforation<br>• Trichiasis<br>• Dry eye syndrome<br>• Mebomian gland dysfunction<br>• Blepharitis<br>• conjunctivitis |
| **Panitumumab** | | • Corneal perforation<br>• Conjunctivitis<br>• Hyperemia<br>• Epiphora<br>• 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.

28

| Inhibitors of Vascular Endothelial Growth Factor Receptor | | |
|---|---|---|
| **Sunitinib** | Renal cell carcinoma, gastrointestinal stromal tumors | • Central visual field defect<br>• Cortical blindness<br>• Retinal detachment/tear |
| **Pazopanib** | Renal cancer | • Blurred vision<br>• Periocular edema<br>• Ptosis<br>• Corneal toxicity<br>• Retinal detachment/tear<br>• Retinal artery/vein occlusion<br>• Papilledema<br>• Optic neuropathy<br>• Uveitis<br>• Macular edema<br>• Conjunctival hemorrhage<br>• Retinal/vitreous hemorrhage |
| **Bevacizumab** | Colorectal, non small cell lung cancer, renal cell carcinoma, glioblastoma, cutaneous melanoma | • Cortical blindness<br>• Optic neuritis<br>• 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.

29

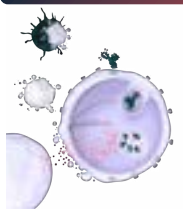
| Inhibitors of tumor specific proteins | | |
|---|---|---|
| **Crizotinib** | Non-small cell lung cancer | • Flashes<br>• Light trails<br>• Image persistence<br>• Light Dark adaptation abnormality |
| **Imatinib** | Chronic myeloid leukemia, Gastrointestinal stromal tumors | • Periorbital edema Subconjunctival hemorrhage<br>• Conjunctival chemosis<br>• Epiphora<br>• Ulcerative keratitis<br>• Dry eye syndrome<br>• Blurred vision<br>• Optic neuruis<br>• Optic disc edema<br>• Retinal edema<br>• Cystoid macular edema |
| **Vandetanib** | Melanoma | • Uveitis<br>• Iritis<br>• Retinal vein occlusion |
| **Ipilimumab** | Malignant melanoma | • Dry eye syndrome<br>• Proptosis<br>• Swelling of EOM<br>• Diplopia<br>• Iridocyclitis |
| **Ganglioside GD2** | Neuroblastoma | • Photophobia<br>• Accommodative deficiency<br>• 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.

30

## Mirvetuximab Soravtansine

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



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

AEs, adverse events; DM4, N2′-[4-[(3-carboxypropyl)dithio]-4-methyl-1-oxo-2-sulfopentyl]-N2′-deacetylmaytansine; FRα, folate receptor alpha.
[a]Antitumor activity with MIRV has been demonstrated with single-agent MIRV in FRα-high PROC (≥75% tumor cells FRα-positive by PS2+)[1] and in combination with other agents in FRα low-to-high PROC (≥25% tumor cells FRα-positive by PS2+).[4]
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: NCT04296890. Updated April 21, 2022. Accessed August 5, 2022. https://clinicaltrials.gov/ct2/show/NCT04296890. 4. Matulonis UA, et al. Presented at: 2018 European Society for Medical Oncology Congress; October 19-23, 2018; Munich, Germany. Abstract 949P.



31

## 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[b] | Best corrected visual acuity of 20/200 or worse in the affected eye |
| **Keratitis**[c] | Asymptomatic; clinical or diagnostic observations only; intervention not indicated | Symptomatic; moderate decrease in visual acuity | Symptomatic, with marked decrease in visual acuity; corneal ulcer; limiting self-care ADL[b] | Perforation; best corrected visual acuity of 20/200 or worse in the affected eye |
| **Dry eye**[d] | 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[b] | NA |
| **Photophobia**[e] | Symptomatic but not limiting ADL | Limiting instrumental ADL[a] | Limiting self-care ADL[b] | NA |

Best corrected visual acuity 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.
[a]Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc. [b]Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden. [c]Disorder characterized by inflammation to the cornea of the eye. [d]Disorder characterized by dryness of the cornea and conjunctiva. [e]Disorder characterized by fear and avoidance of light.
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_5x7.pdf



32

# Most common Anterior segment and Adnexal Side Effects

33

## 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

34

## 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 epithelium and to the barrier function of the limbus
- Once limbal stem cells are damaged the epithelium will be replaced by conjunctival goblet cells

35

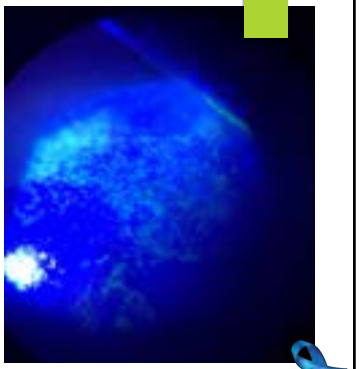
## Symptoms

- Decreased vision
- Photophobia
- Tearing
- Blepharospasm
- Recurrent pain

36

## Signs

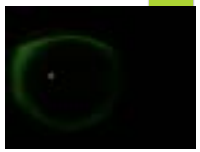
- Stippled superficial punctate late flourescein staining
  - Stained cells are more elongated and pill shaped than in SPK from DED
  - Early LSCD staining more concentrated peripheral near limbal area
  - More progressed LSCD staining spread central and becomes more diffuse
    - Natural migration of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



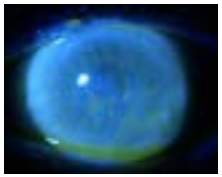
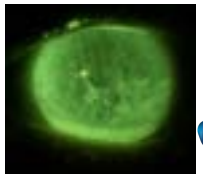
37

## NORMAL EYE



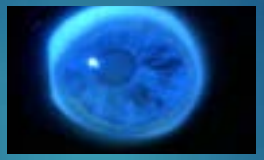
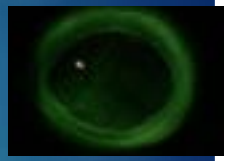
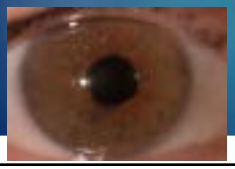
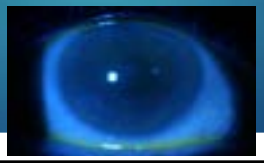
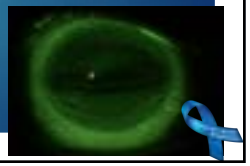


## TOTAL LSCD

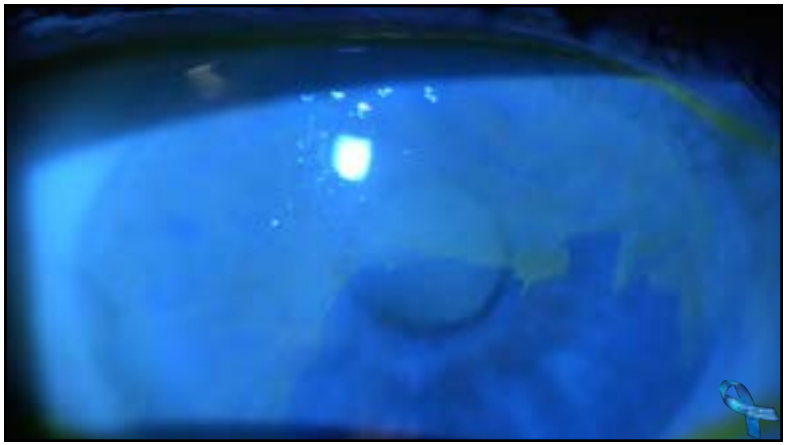




38

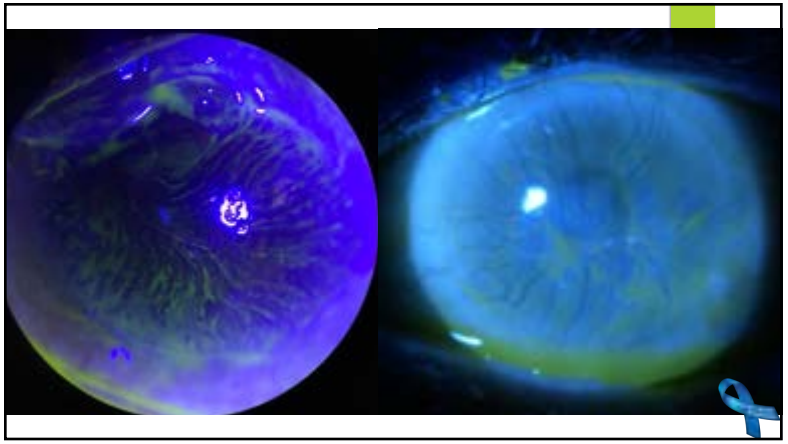
## LATE STAINING FLUORESCEIN PATTERN

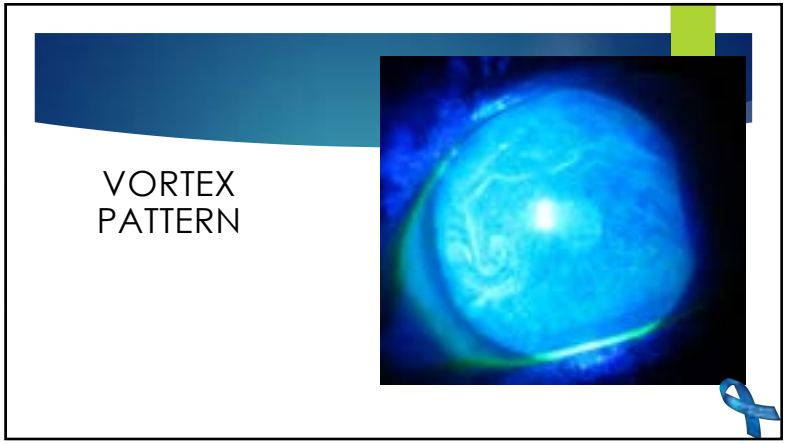
39



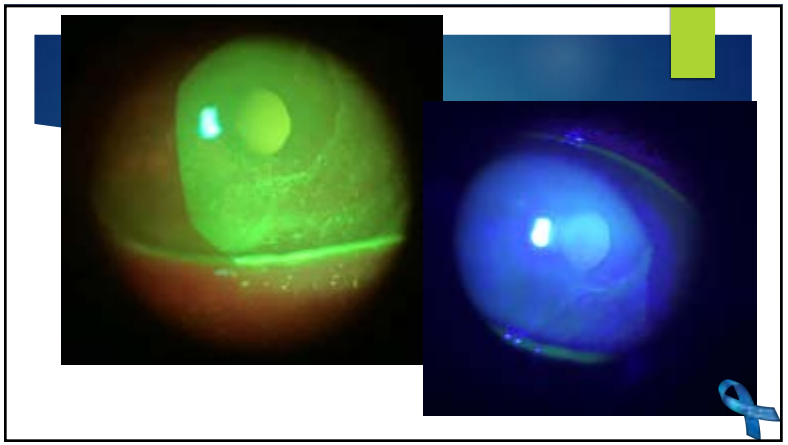
40



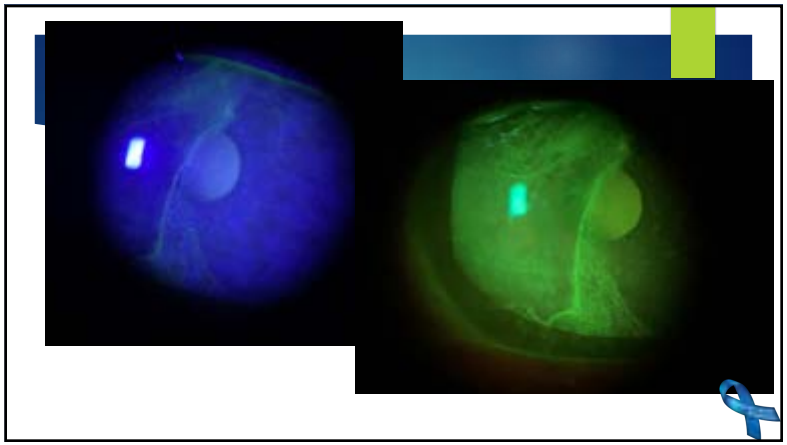
41




42



43



44

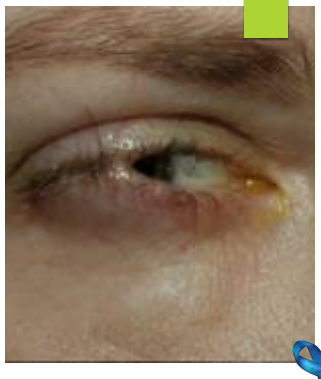
## Non-Surgical Treatment

- 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

45

## 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

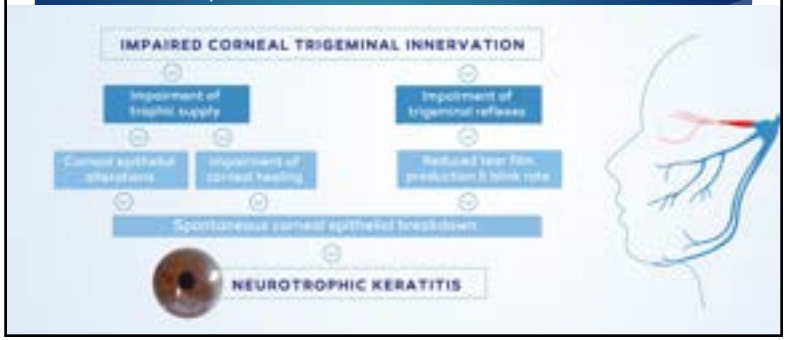


46

## Neurotrophic Keratitis

47

## Neurotrophic Keratitis




48

## Mackie classification

49

## Corneal Sensitivity Testing: Esthesiometry

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

50

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

51

## 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

52

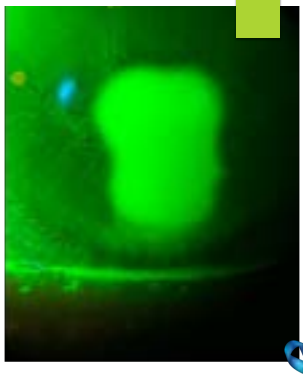
## Stage 2

- Promote healing of epithelial defect and prevent corneal ulcer
- Monitor patient frequently
- Topical antibiotics
- Bandage contact lens

53

## Stage 3

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



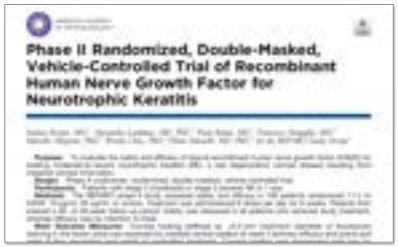
54

## 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

55

## 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

- 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

Bonini S, Lambiase A, Rama P *et al.* Phase II Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. *Ophthalmology* 2018;125:1332-1343.

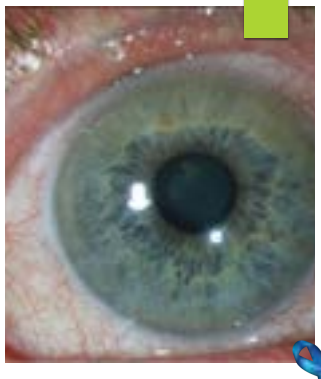
56

## 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

57

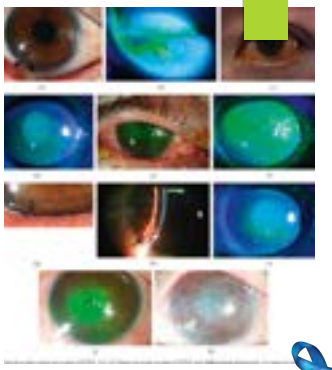
1. Acute classic GVHD: Presents within 100 days of transplantation with classical clinical features of acute GVHD.
2. Persistent, recurrent, or late-onset acute GVHD: Manifests with clinical features of classic acute GvHD but after 100 days of transplantation.
3. Classic chronic GVHD: Presents after 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 [11].



58

## Ocular Presentation

- Lacrimal gland
  - Most affected and most severly affected
  - CD4 and CD8 T cell cause damage on periductal epithelial cells of lacrimal gland leading to permanent stenosis
  - Study found tear turnover rate in GVHD approx. same as Sjo
- 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



59

**NIH Ocular Scoring in Chronic GVHD**

| 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. |

60

## Treatment

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

61

## 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

62

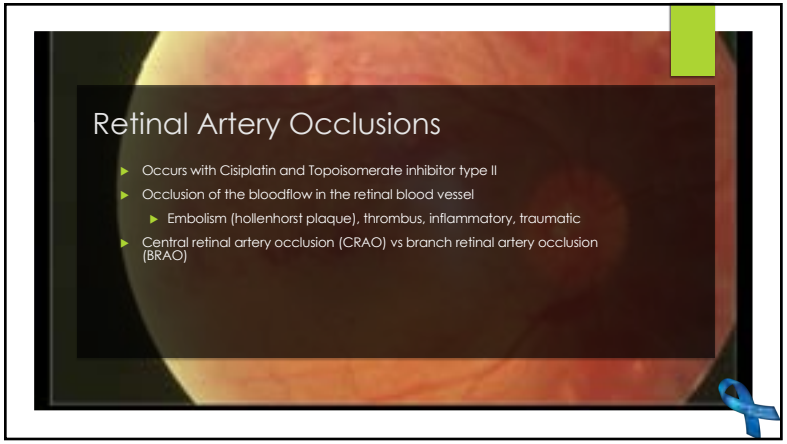
## Cataract formation

- 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

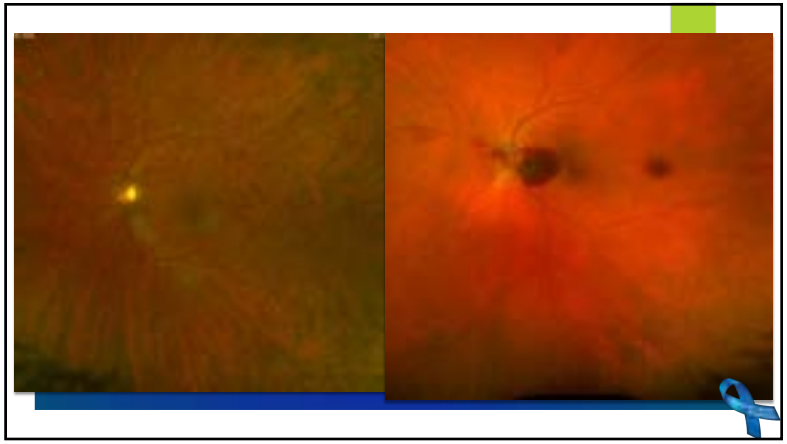
63

## Most common Posterior Segment Side Effects

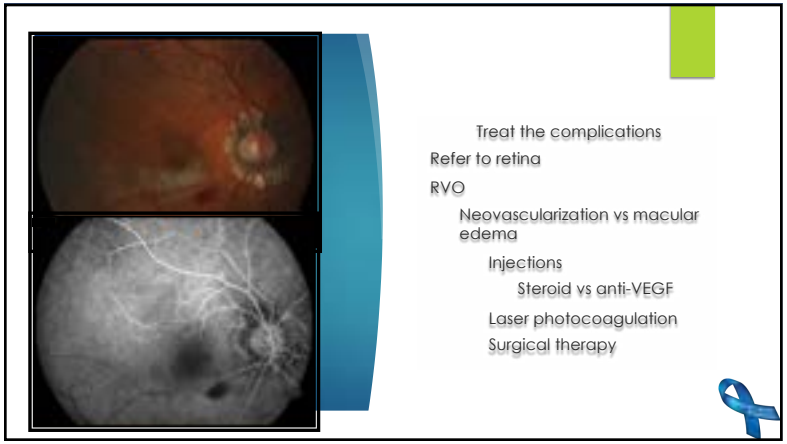
64


Retinal Artery Occlusions
Occurs with Cisiplatin and Topoisomerate 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)

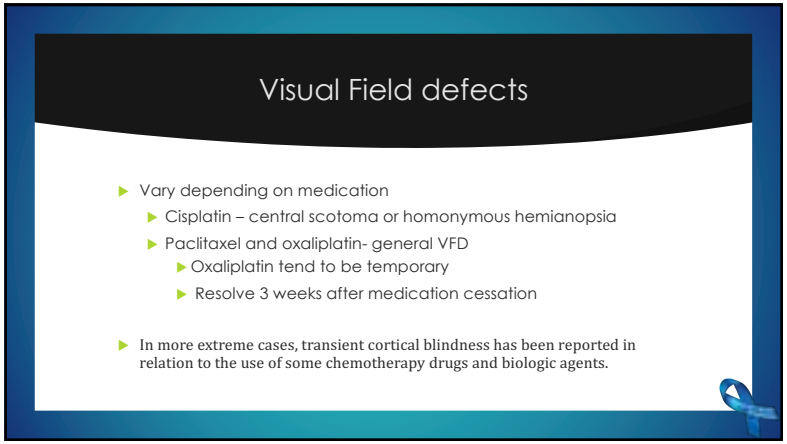
65



66


Treat the complications
Refer to retina
RVO
Neovascularization vs macular edema
Injections
Steroid vs anti-VEGF
Laser photocoagulation
Surgical therapy

67


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.

68

## 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.

69

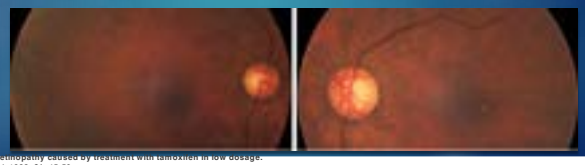
## Hormone Modulation

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

70

## 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



Heier JS, Dragoo 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

72

## Neuro-Ophthalmic Side Effects/ Neurotoxicity

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

73

## 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

74

## Take Away

01 Be kind and considerate

02 Remember, we CAN help

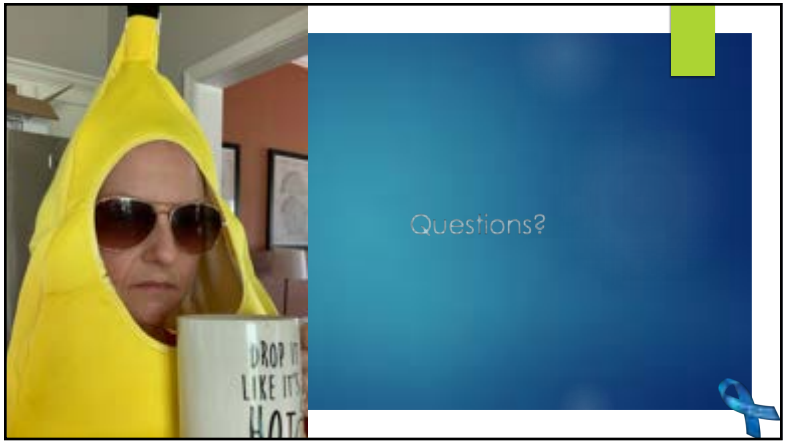
03 Work together as a team

75

## 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

76


Questions?

77


Thank you!
Dr.CeceliaKoetting@gmail.com
UNDER-
ESTIMATE ME.
That'll be fun

78