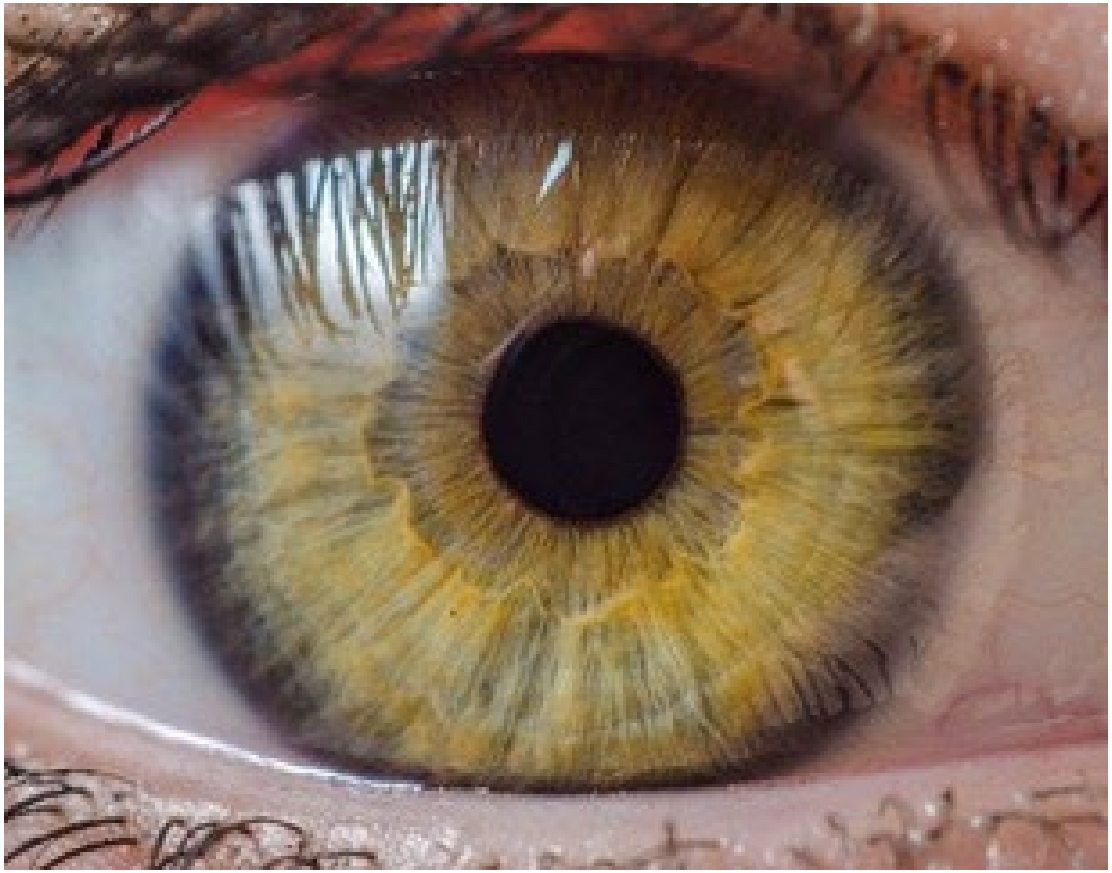
Daryl D. Kaswinkel, M.D.
Advancing Glaucoma and Cornea
March 2024



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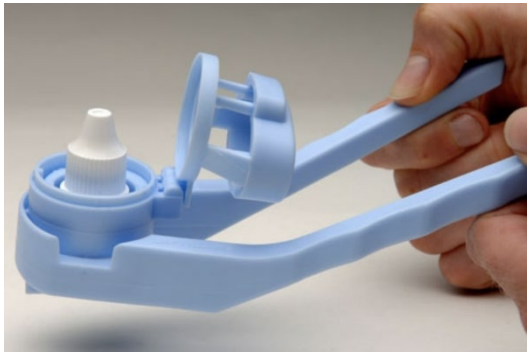
Sustained – Delivery Glaucoma Treatments

- Medical management challenges of glaucoma including compliance and reliability
- Compliance direct correlation between effective treatment and successful management
- non-compliance as high as 80%
- Reliability of medication delivery in typical elderly patient associated with dexterity from arthritis, tremors, memory impairment and low vision due to ocular comorbidities
- Sustained –delivery treatments offer best hope decreasing patient dependent factors in medical management of glaucoma

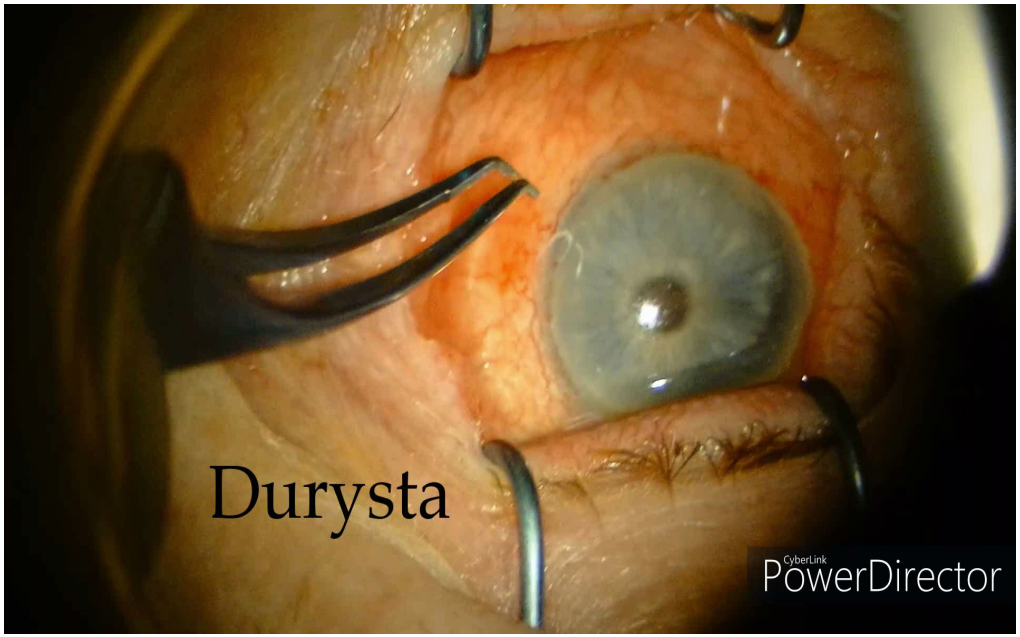
Eye Drop Dispensing Aids

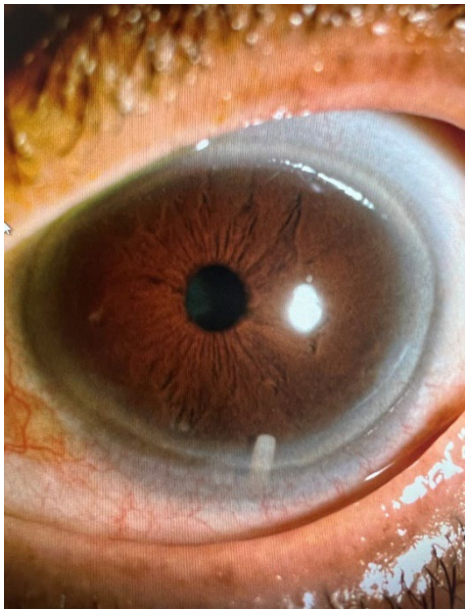


Durysta® Allergan

- First FDA (3-5-2020) – approved dissolvable ocular implant (Bimatoprost 10µg (10 units) to reduce intraocular pressure:
  - Ocular Hypertension (OHT) and Open-Angle Glaucoma (OAG)
- Prostaglandin IOP lowering expectations of 30 to 35%
- First sustained release therapy in long line of newer modalities
  - Conjunctival Fornix Inserts
  - Punctal Plugs
  - Contact Lens
  - Subconjunctival Injections
  - Iridocorneal Angle Injectables (Durysta, Ocular Therapeutix, iDose TR)

Durysta





What color irides are "most" affected by the increased number of melanosomes resulting from PGA (latanoprost) usage?

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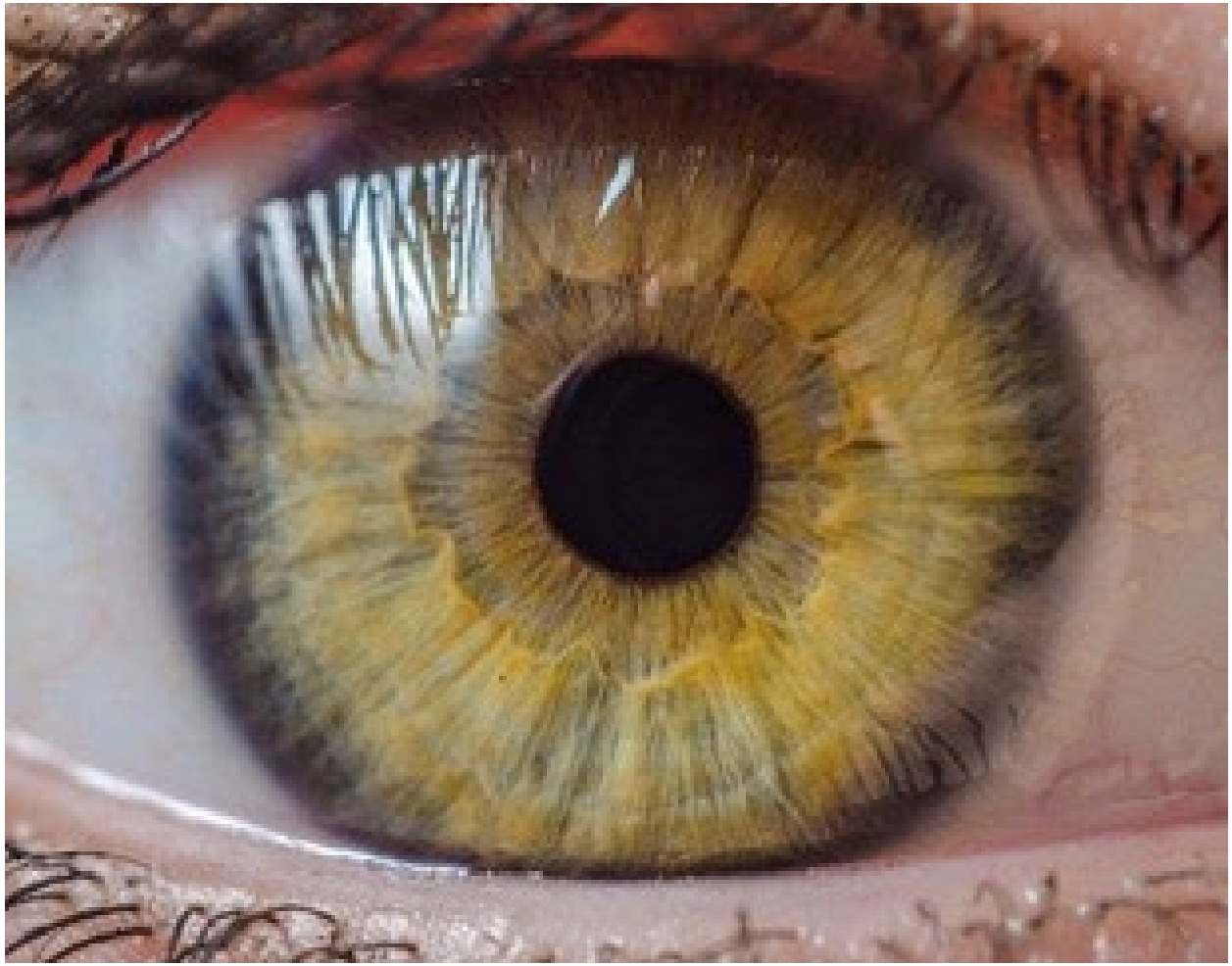

Delivery & Duration

Straight forward procedure: Slit Lamp or operating room (OR) microscope w/ patient lying down; logistically in OR more efficient.

Durysta prepackaged cartridge w/ release button one end and needle on other to inject the insert into the inferior anterior chamber angle.

Mechanism of action as that of topical bimatoprost; lowering IOP by increased outflow through TM and Uveoscleral routes

Designed to release medication up to 4 to 6 months w/ longer term effects on outflow.

Effective treatment in 40% to 12 months and 28% up to 2 years.

Durysta vs Eyedrops

- Improves Standard of Care
  - Continuous delivery 24/7 of brimatoprost
  - addressing non-compliance
  - Eliminates chronic side effects associated with topical glaucoma medications including medicamentosa (toxicity) and limbal stem deficiency
  - option in preparation for staged glaucoma surgeries, premium cataract surgery(LAL or RLE(refractive lensectomy)) & corneal transplants.

- Adverse effects:
  - mild temporary redness at injection site and from Betadine prep
  - Endothelial cell loss concerns
  - Phase 3 ARTEMIS 1 trials noted cell loss with 15µg vs FDA approved smaller 10 µg which in real world sudies no effects in cell loss up to 12 months.
  - ARTEMIS study noted cell loss with aggressive repeated injections at 4 and 8 months despite longer term IOP lower effects

Glaucoma Patients and Ocular Surface Disease (OSD)

- Typical Glaucoma Patient Elderly w/ decreased tear secretion
- On medications for life
- Frequently on multiple topical ophthalmic medications
- Abnormal tear film breakup time and OSD is associated with increasing number of eye drops with and without BAK
- May undergo further glaucoma surgeries (XEN/Trabeculectomy) with OSD directly affecting surgical healing.

Patient Selection

- One time uses: IOP control before other planned surgeries in staged approach of glaucoma control (prior XEN/Trabec) or short-term management of unexpected IOP “spike” surgical (Trimoxi) and nonsurgical care (topical steroid use, intravitreal retinal steroid injections)
- Broader inclusion Criteria: POAG and OHT patient cannot tolerate eyedrops for variety of reasons and alternative to SLT as first line tx or pre SLT
- Contraindications:
  - Primary/Secondary Angle Closure patients,
  - prior corneal transplants or risk for corneal decompensation(Fuchs’) due to direct mechanical injury to the endothelium
  - Active infection or inflammation.
  - PGA risks for macular edema.

Pseudophakic cystoid macular edema (CME) has been associated with what ocular medication?

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What glaucoma drops increase the risk of corneal decompensation in a patient with Fuchs' endothelial dystrophy?

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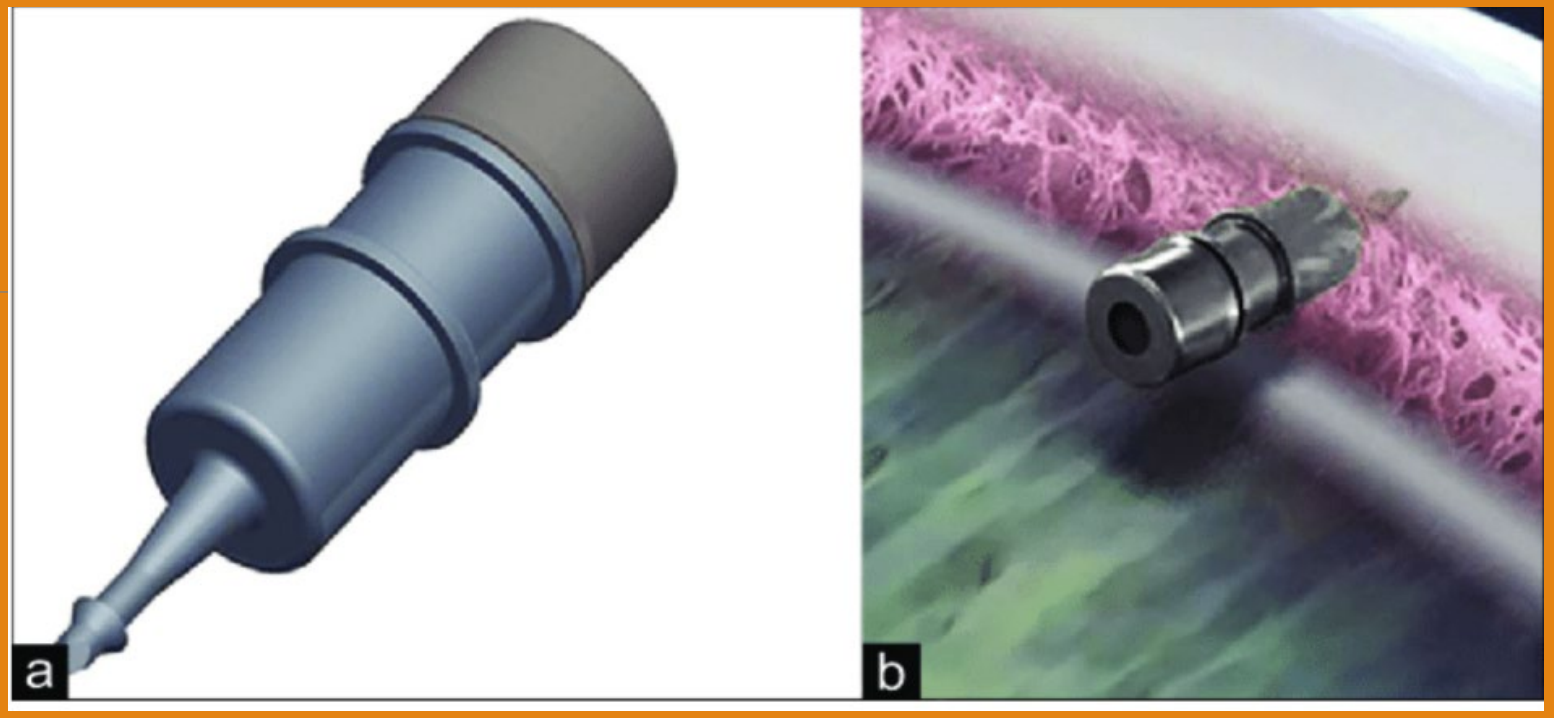
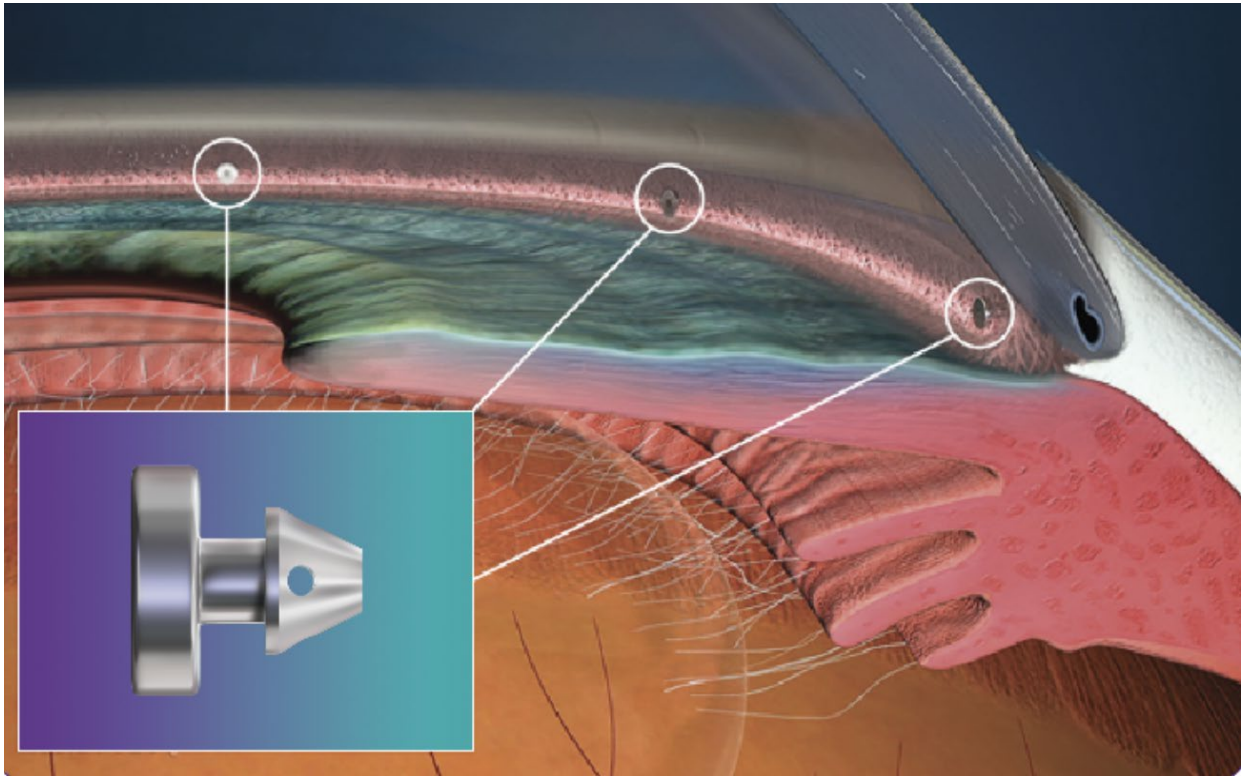


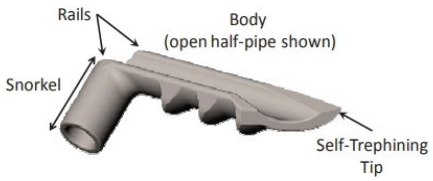
iDose TR

iDose TR Implant

- FDA New Drug Application (NDA) approval Glaukos Dec 2023
  - Commerical launch 2024 end of first quarter
- Delivery of travoprost intracameral implant 75µg
- Ocular Hypertension (OHT) and Open-Angle Glaucoma (OAG)
- Improves in Standard of Care
  - Continuous delivery 24/7 of travoprost
  - addressing non-compliance
  - Eliminates chronic side effects associated with topical glaucoma medications

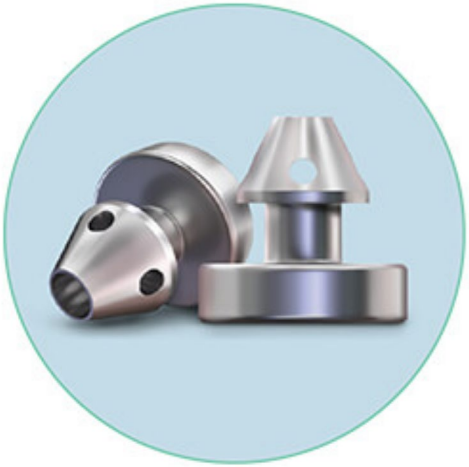


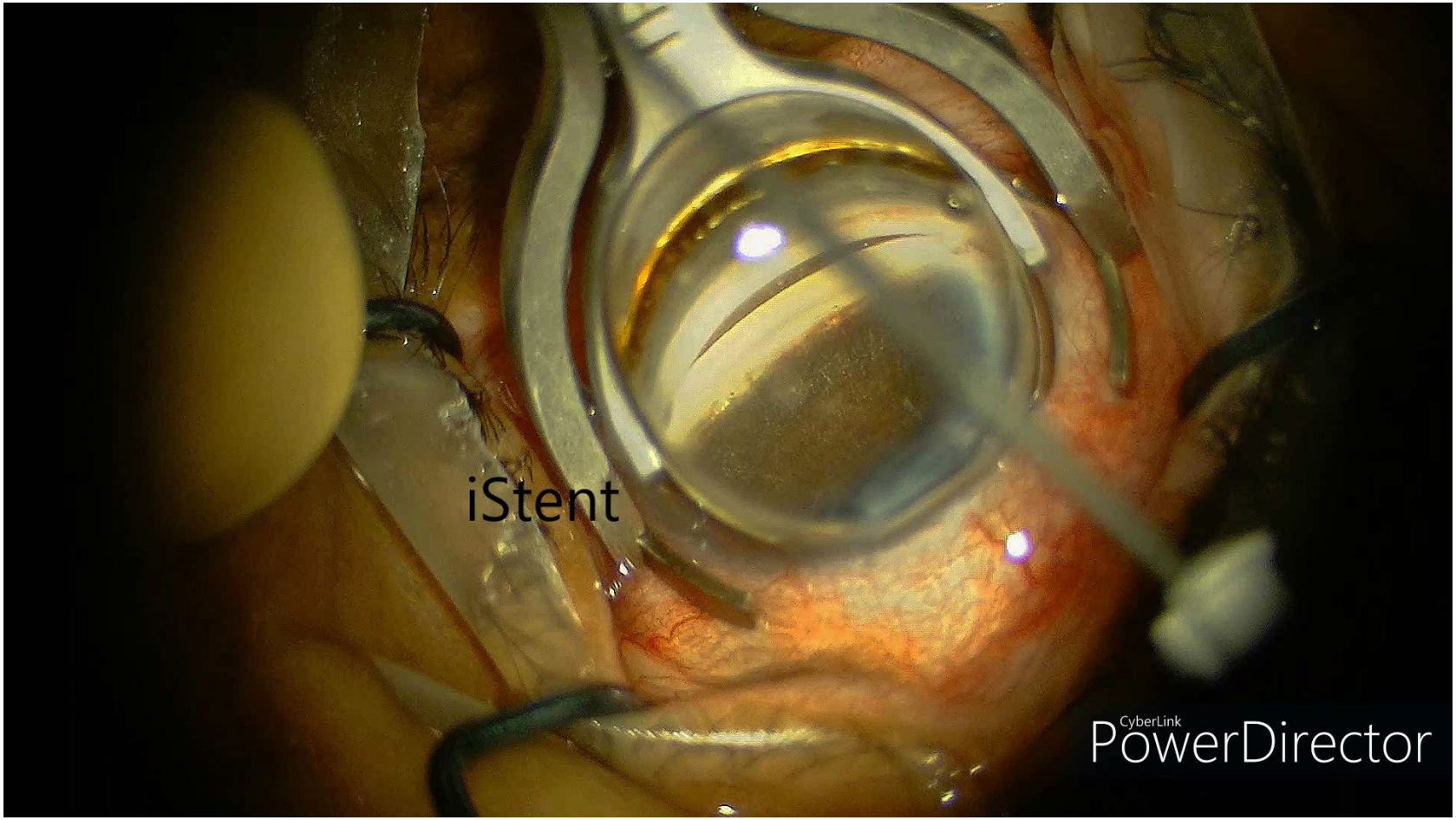
iStent Infinite® Glauckos



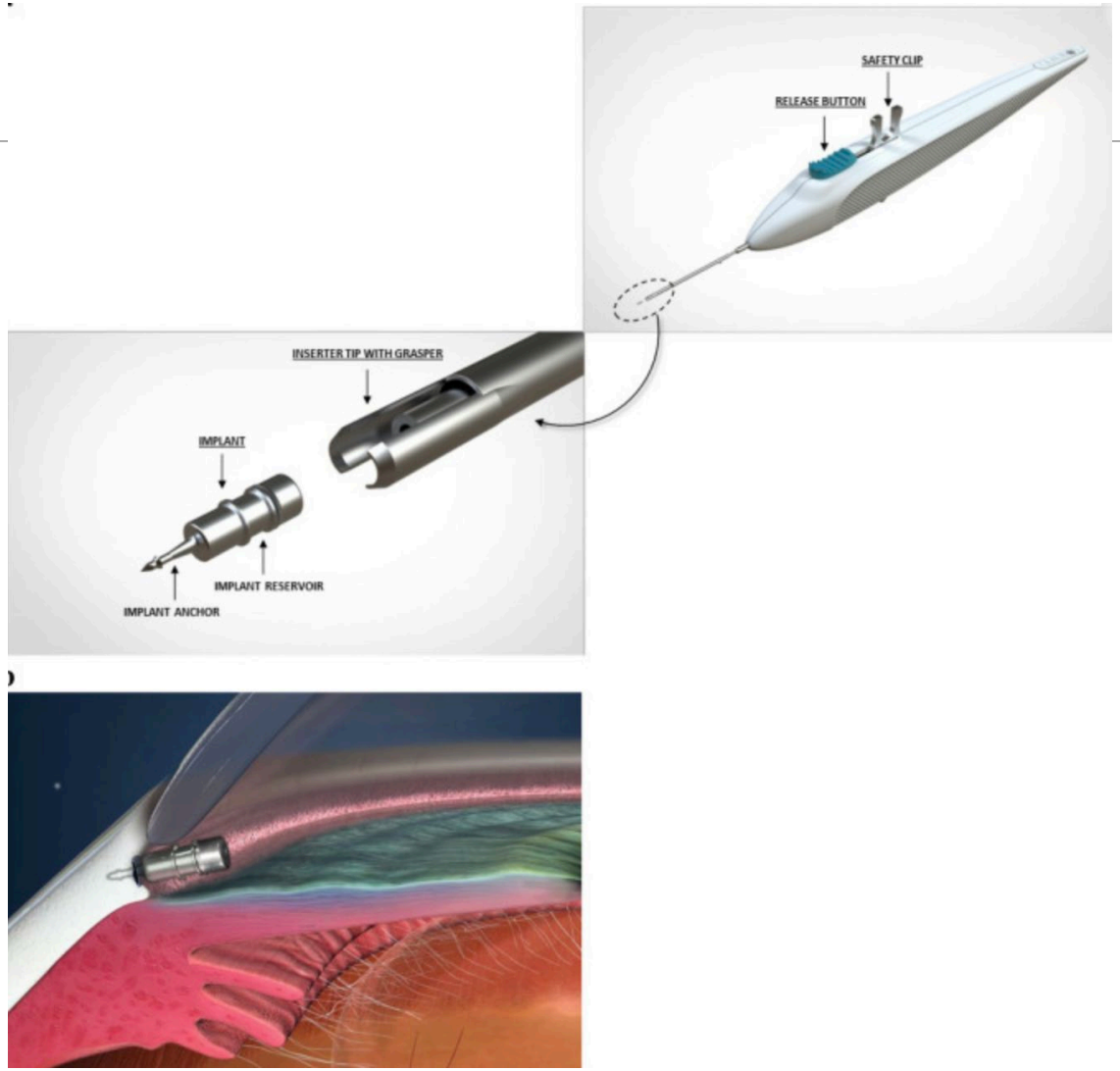
iStent infinite® Glauckos

- Patients Undergoing Cataract Surgery or Standalone Procedure
  - First micro-invasive standalone implantable alternative
- Micro-Bypass System Model iS3
  - First “snorkel” design approval in 6/2012



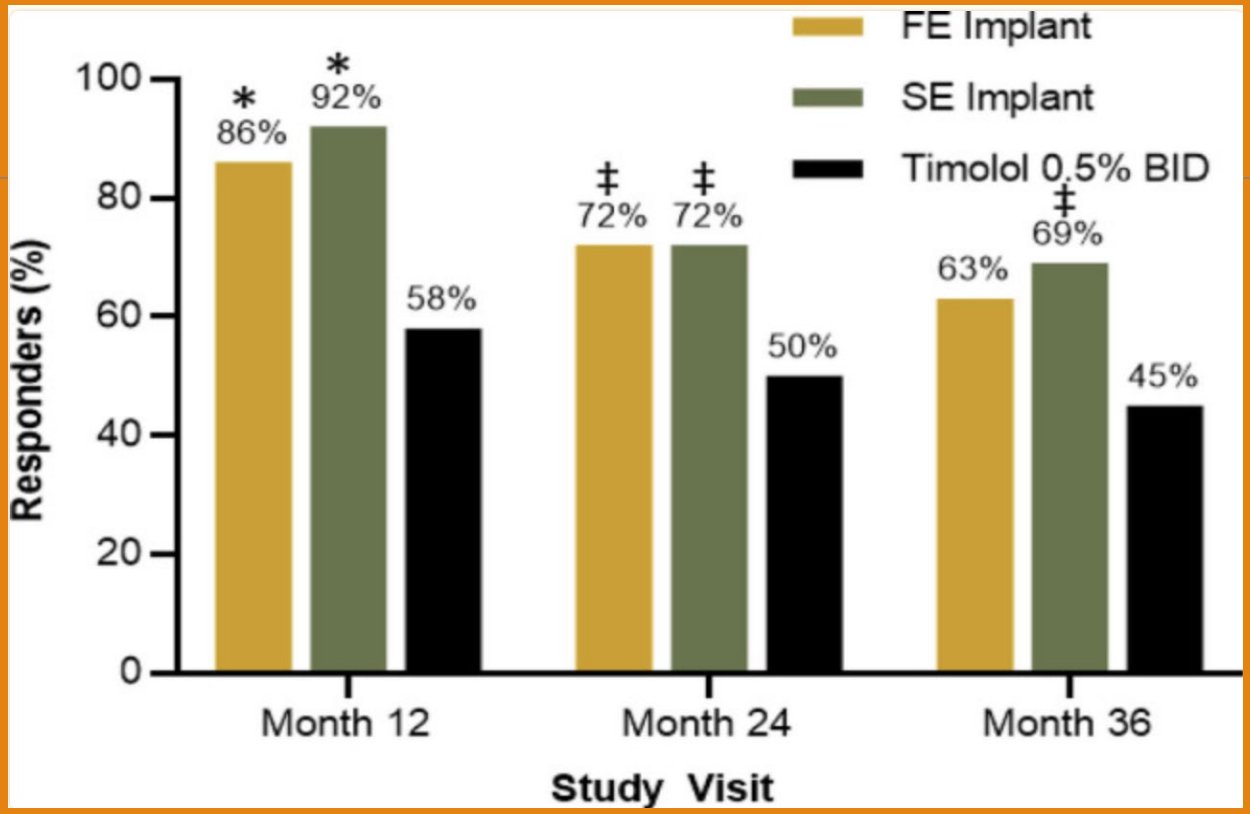

iStent
CyberLink
PowerDirector

iDOSE TR Implant

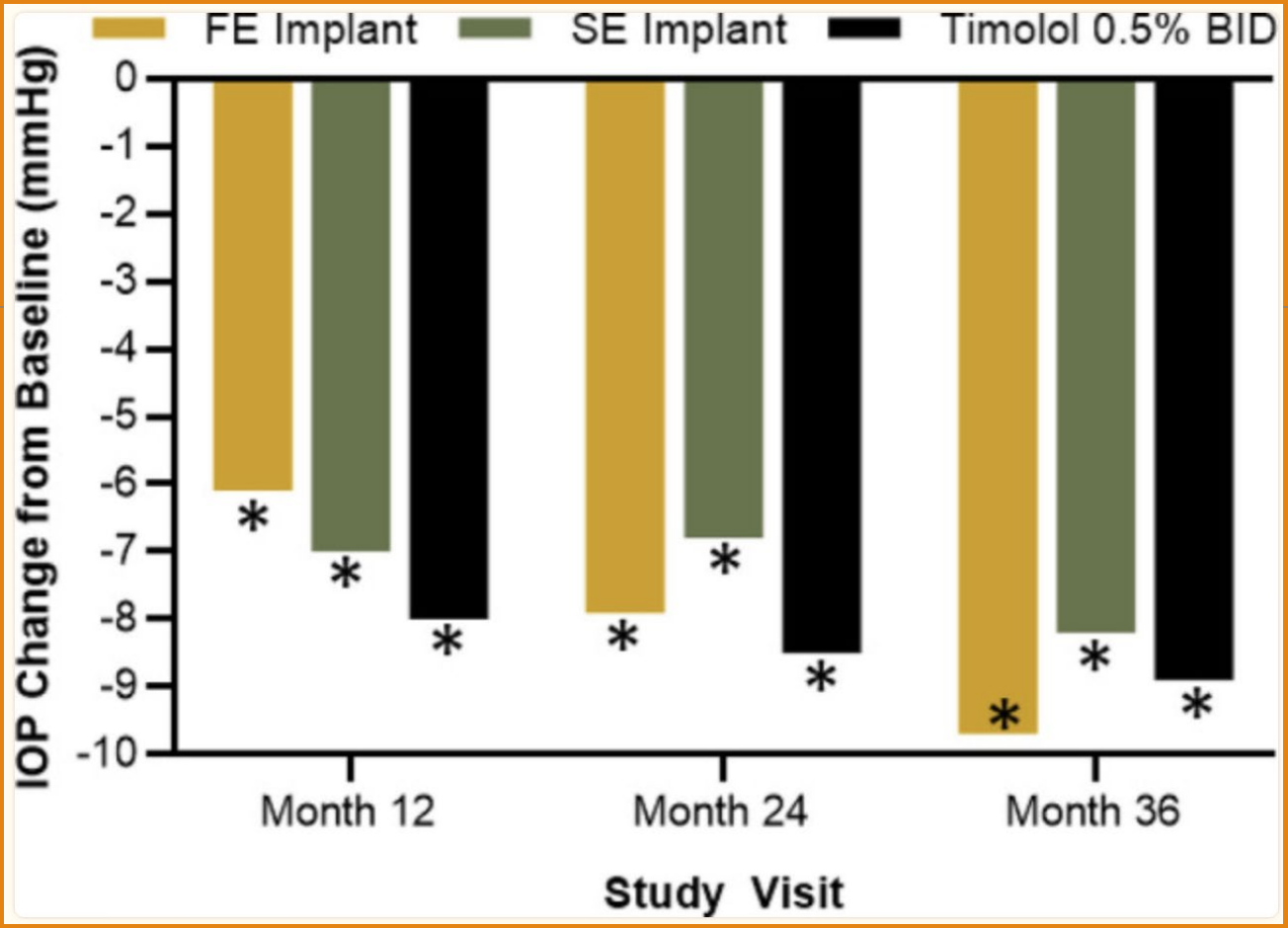


Clinical Trials

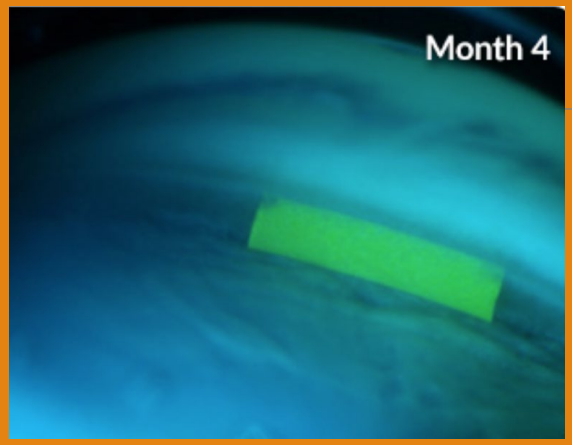
- Approval of two Phase 3 trials
- Achieved efficiacy through three months and favorable profile through 36 months
  - 81% were free of topical mediations at 12 months
  - Adverse Events
    - No corneal endothelial cell loss
    - No serious corneal effects
  - "Cannot market" Single Use due to FDA's conservatism on readministration of intracameral implants; less restrictive than Durysta's label and allow physician discretion

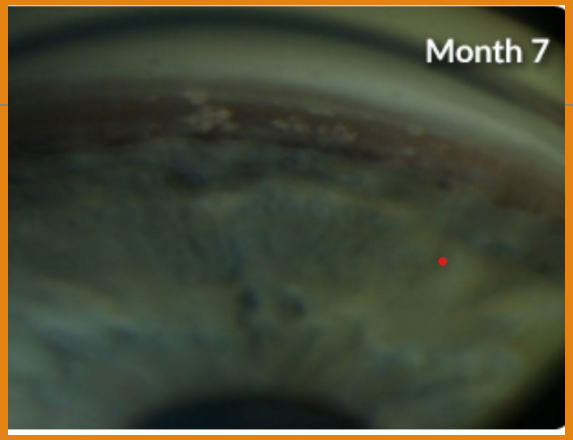


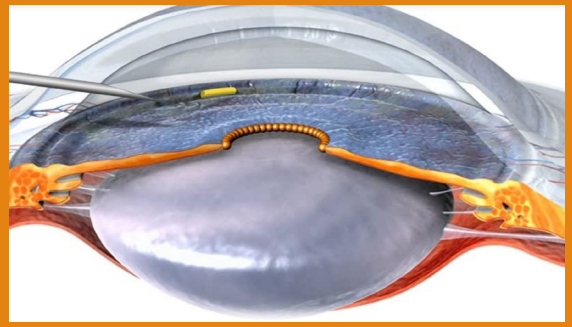
Percentage of study eyes “not” requiring additional IOP lowering Medications per protocol
Diurnal IOP(mmHg) 21-36 baseline w/ IOP not to exceed 18



Mean IOP reduction in subgroups while on the same or lesser number of topical medications at screening, reduced burden of topical medications in iDose grougs







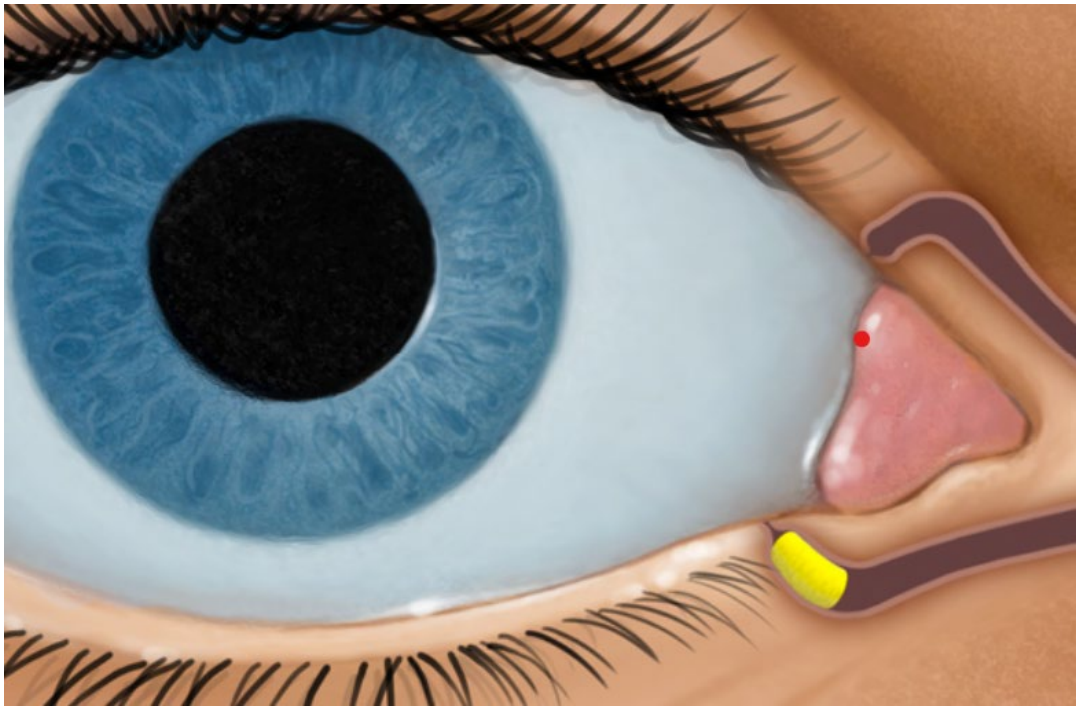
Ocular Therapeutix Travoprost intracameral

OTX-TIC

- travoprost intracameral implant
- early clinical trials, OTX-TIC exhibited an acceptable safety profile, maintenance of drug levels in the aqueous humor, and a sustained lowering of intraocular pressure.
- Administered with 27G or 26G needle
- Resides in the iridocorneal angle
- Fully biodegradable

Dry Eye Syndrome - **OTX-CSI**

- ***cyclosporine*** intracanalicular insert
- Designed to deliver therapy up to ***12 weeks*** with a single insert
- Occludes the punctum

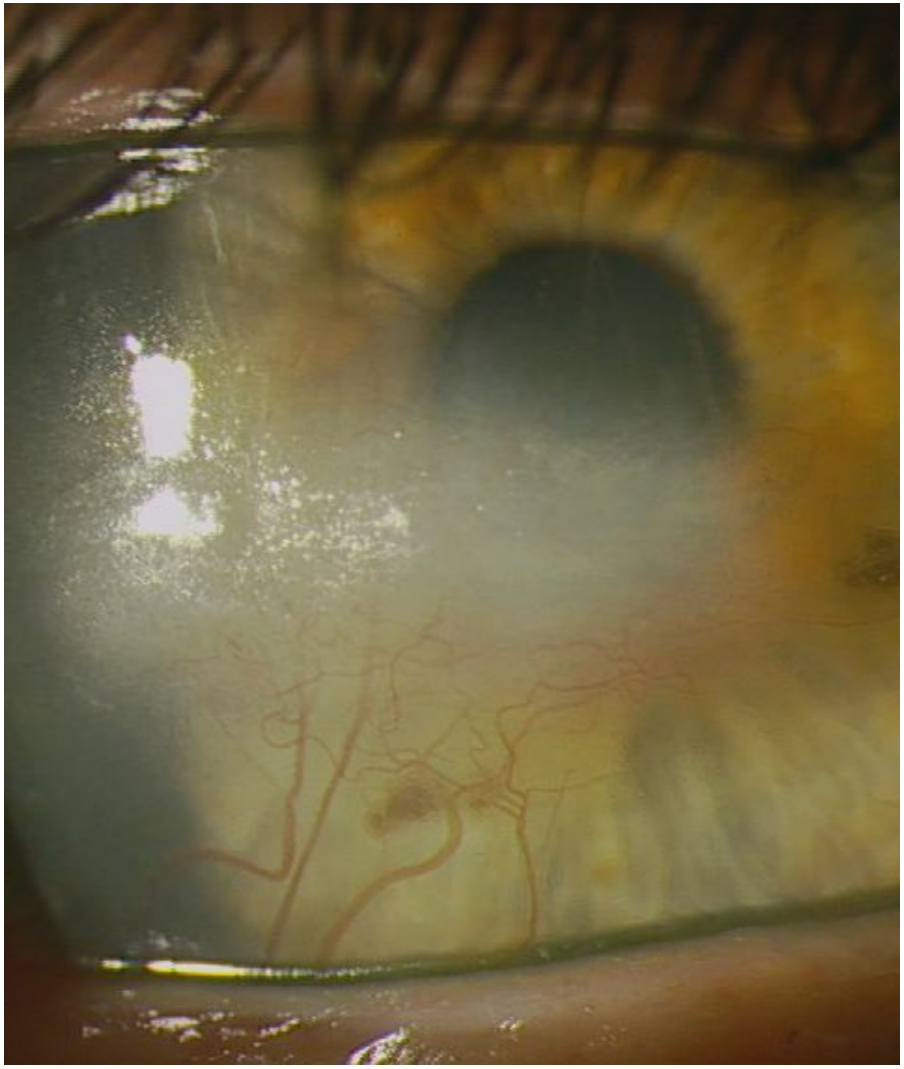


Dry Eye Syndrome - OTX-DED

- ***dexamethasone*** intracanalicular insert
- low dose, intracanalicular insert of dexamethasone for the treatment of patients with episodic dry eye disease.
- release dexamethasone over a period of ***two - three*** weeks for the short-term
- Occludes the punctum
- < 0.4 mg, lower dose and smaller insert size.

Dextenza
OCULAR THERAPEUTIX™

- 0.4 mg of intracanalicular use
- replace the need for patients to administer ~70 steroid eye drops
- designed to deliver a tapered dose of steroid (dexamethasone) to the ocular surface for up to 30 days
- **Itching Associated with Allergic Conjunctivitis**
- **Postoperative Ocular Surgery ocular inflammation and pain**



Neurotropic Keratopathy Suppurative Non-infectious Keratitis

What risk is lower in deep anterior lamellar keratoplasty (DALK) than in penetrating keratoplasty (PK)?

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DALK

- Since no penetration into the anterior chamber, DALK has lower risks
- Cystoid Macular Edema
- Glaucoma
- Cataracts
- Expulsive Hemorrhage
- Retinal Detachment (RD)
- Endohphthalmitis
- No endothelial Rejection (PKP all layers at risk)
- “Large Diameter” DALK with less astigmatism

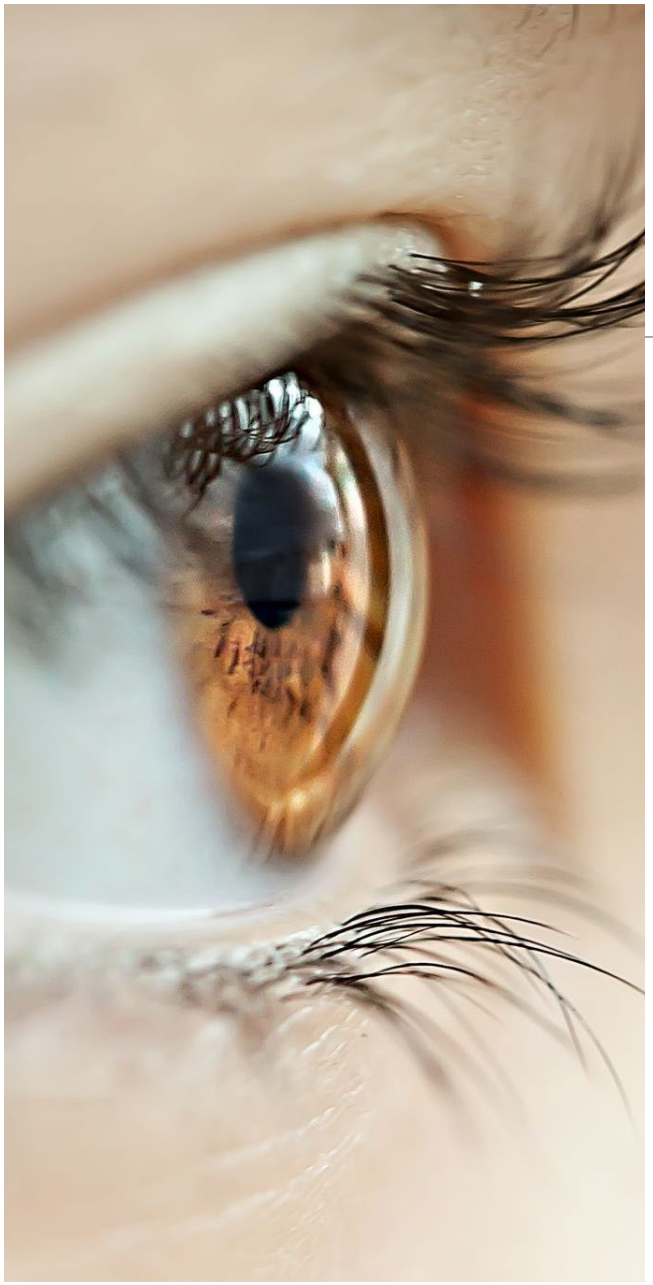
Neurotrophic Keratopathy(NK) Cornea

Oxeravate 0.002%(20mcg/ml)

- Cenegermin ophthalmic solution

First topical biologic, recombinant human growth factor (rhNGF)

Potential to completely heal NK



NK

NK underdiagnosised and progressive eye disease lead to scarring and vision loss

- ~65,000 patients in USA affected

Conditions leading to NK:

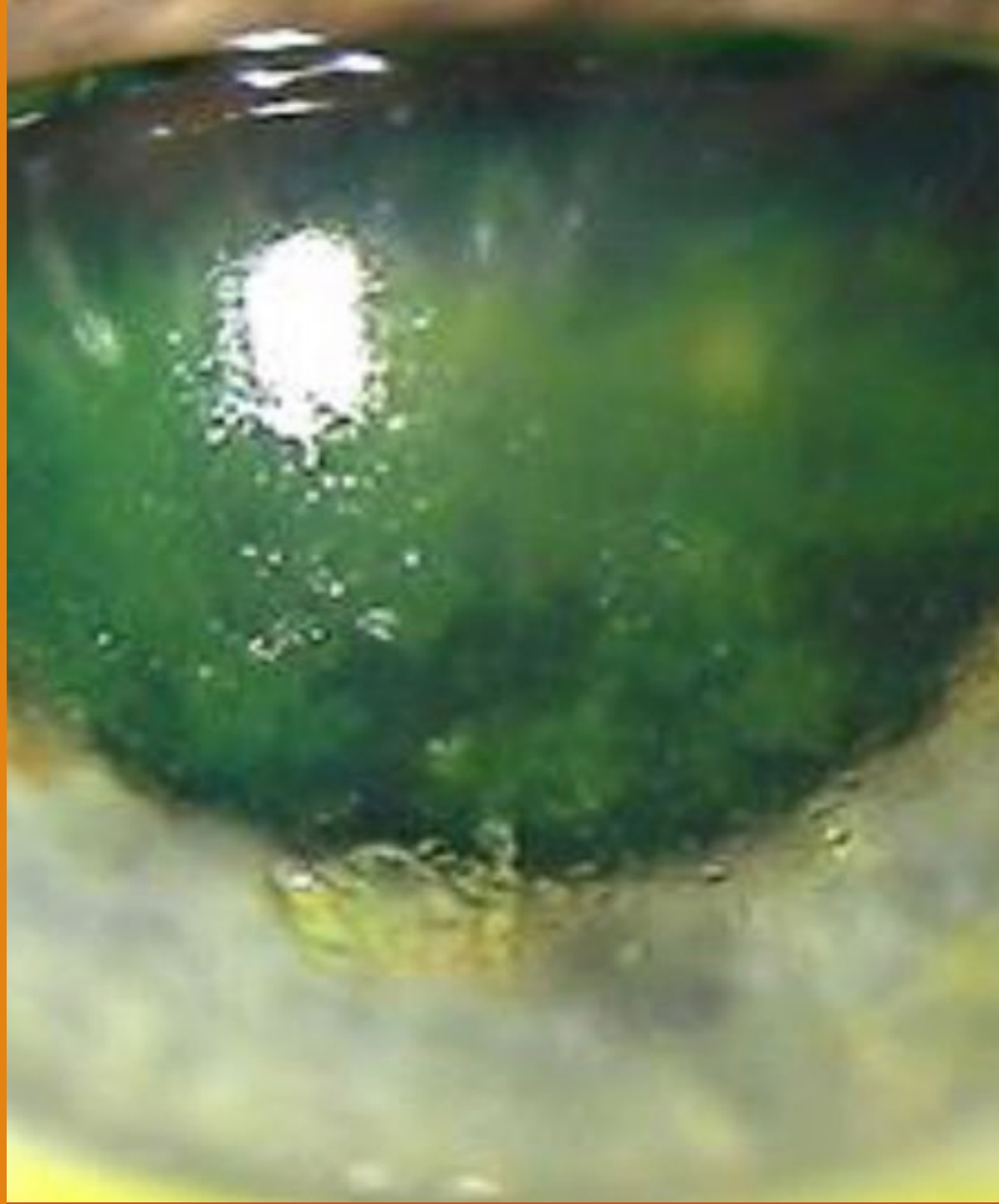
- Herpetic infections
- Dry Eye Disease
- Ocular or Neurosurgical Procedure
- Systemic Conditions impairing corneal Sensation (CVD – Primary or Secondary Söjgrens Syndrome)

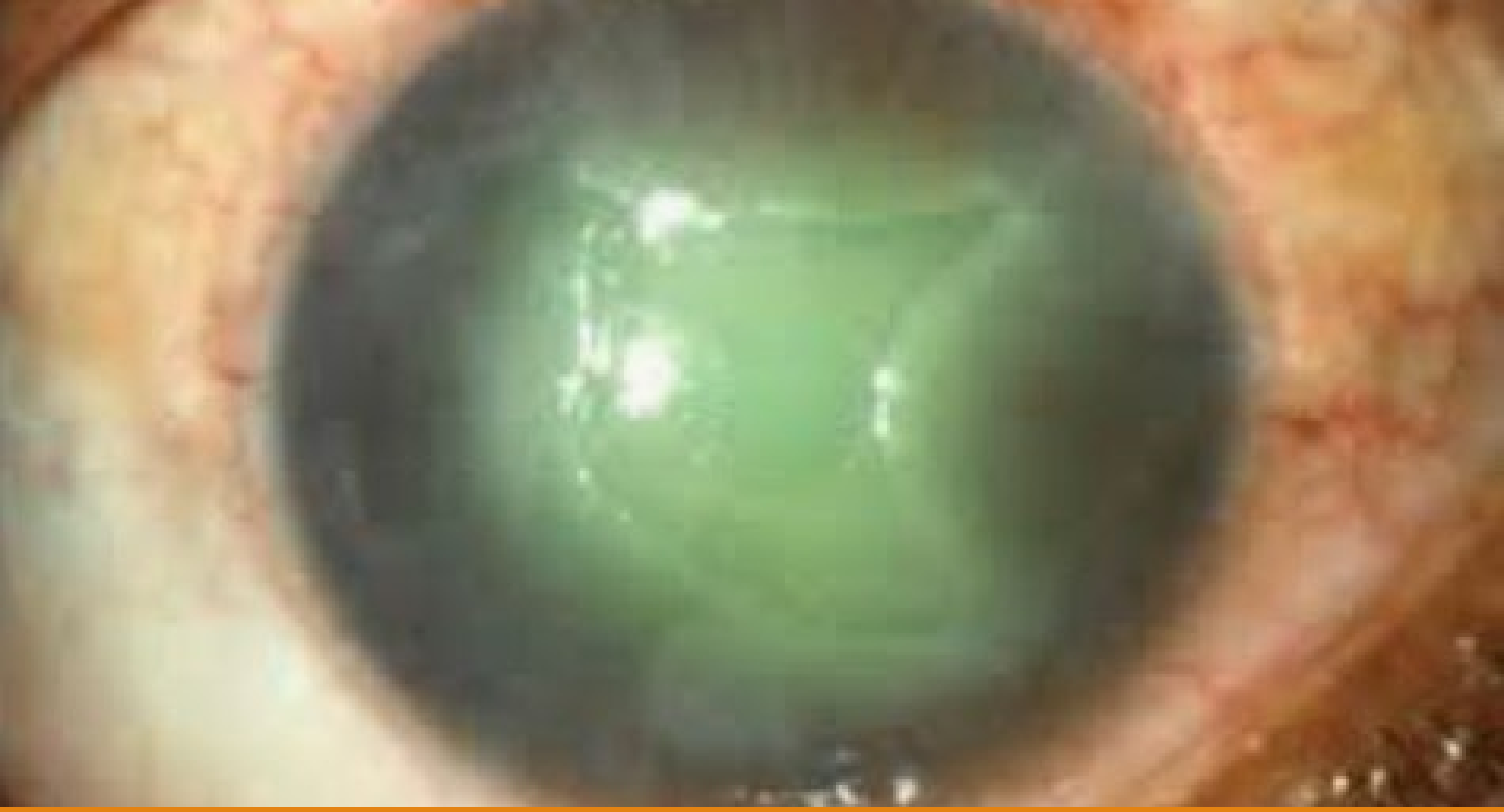
Oxervate – How it Works

- Cornea ~7,000 nerve endings/mm^2
- Nerves mediate blinking/tearing reflexes vital in maintaining corneal health
- Nerves also produce nerve growth factor (NGF), supporting nerve themselves and corneal epithelium
- NGF stimulates proliferation and differentiation of cornea epithelial cells and promotes tear production to lubricate and protect the eye

Stages of NK-Mild

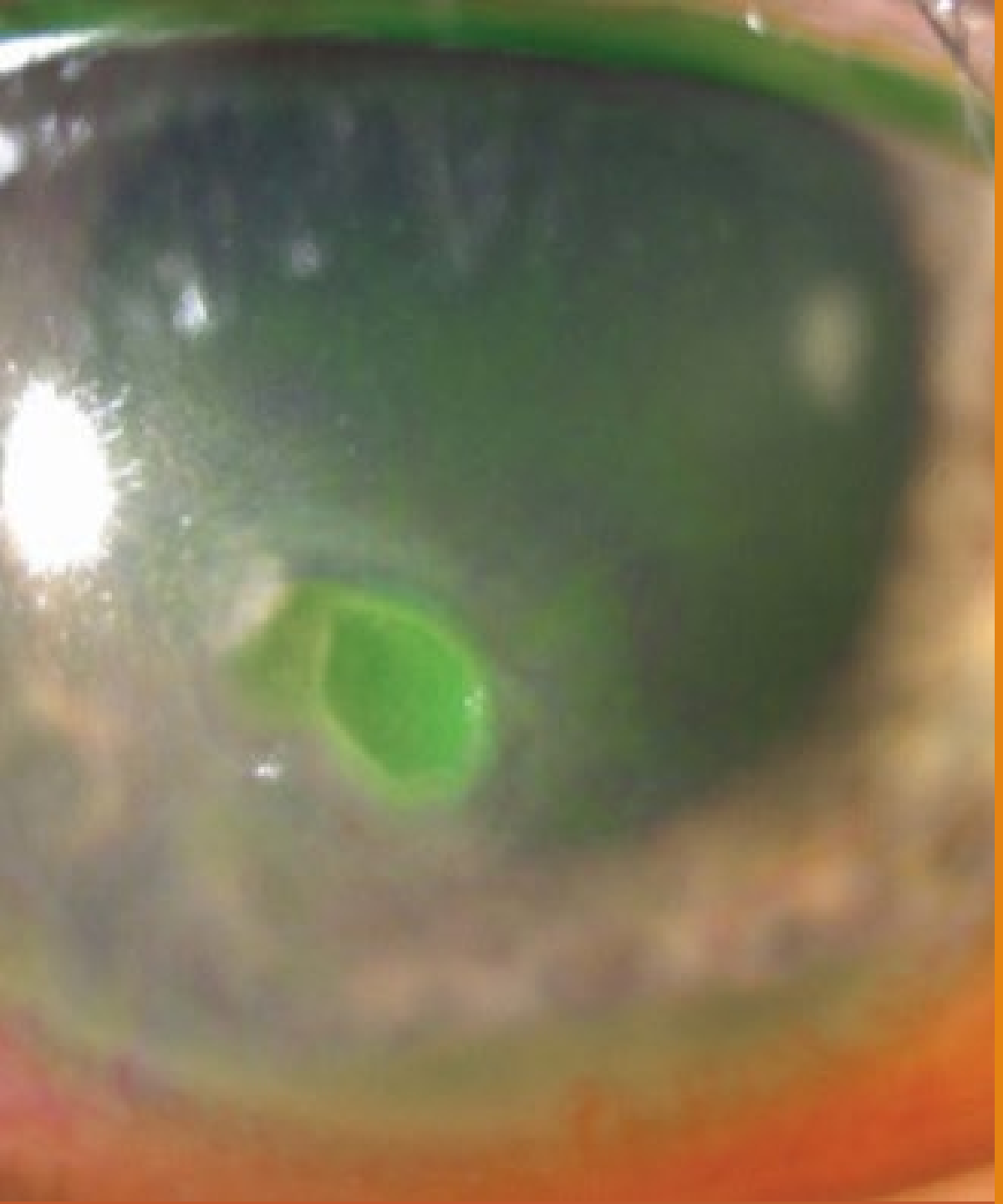
STAGE 1: OCULAR SURFACE IRREGULARITY AND REDUCED VISION





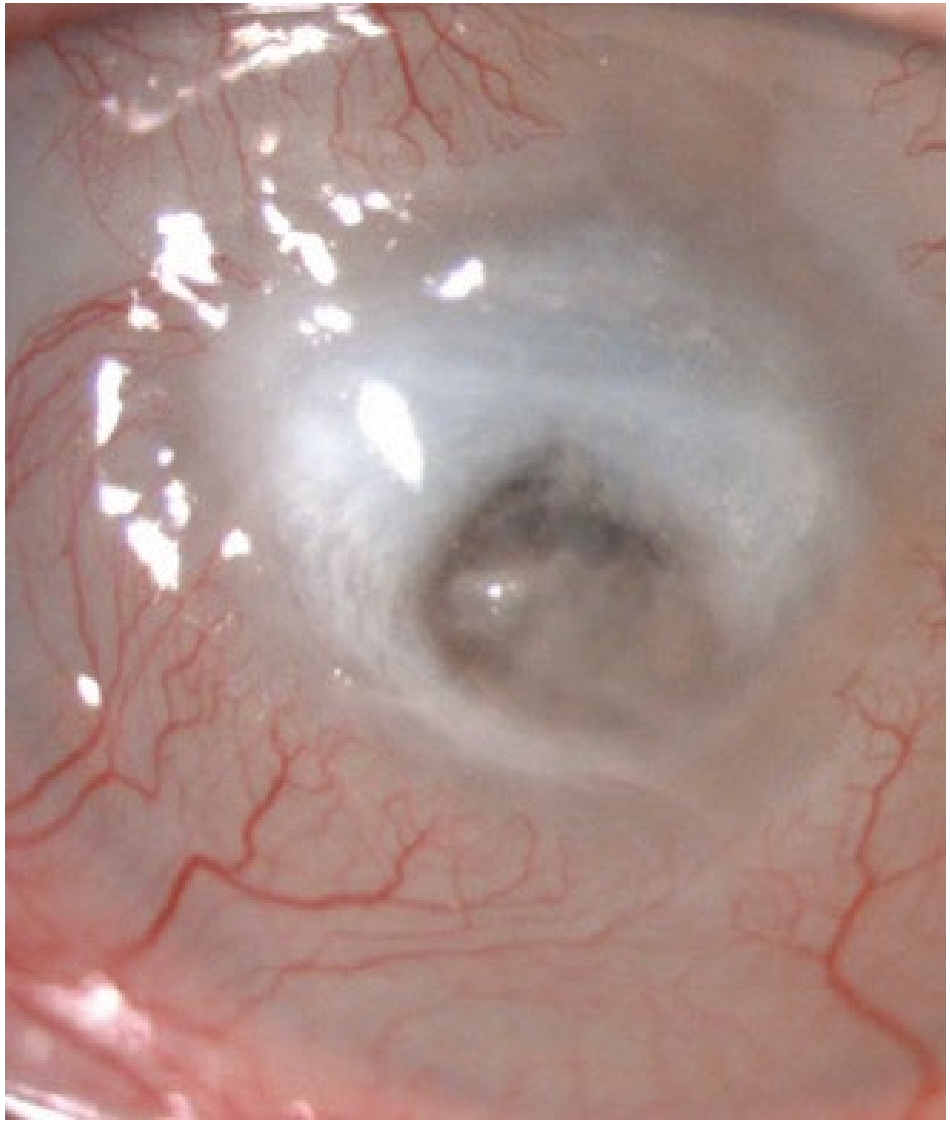
Stages of NK - Moderate

STAGE 2: NONHEALING PERSISTENT EPTIHELIAL DEFECT (PED)



Stages of NK - Severe

STAGE 3: CORNEAL ULCERATION INVOLVING THE SUBEPITHELIAL (STROMAL) TISSUE



Stages of NK

Stage 4: Ultimately Corneal melting, perforation, then Descemetocele

What is contraindication to crosslinking in keratoconus?

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What is a common clinical finding in persistent corneal epithelial defects?

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Key Findings

Majority of patients in clinical studies with topical oxverate well tolerated and more effective in promoting complete corneal healing of moderate or severe NK

2+6=8

- Every 2 hrs w/a at least 6 times a day for 8 weeks
- 65 to 72 % completely healed
- 80% remained healed for one year

Questions and Answers