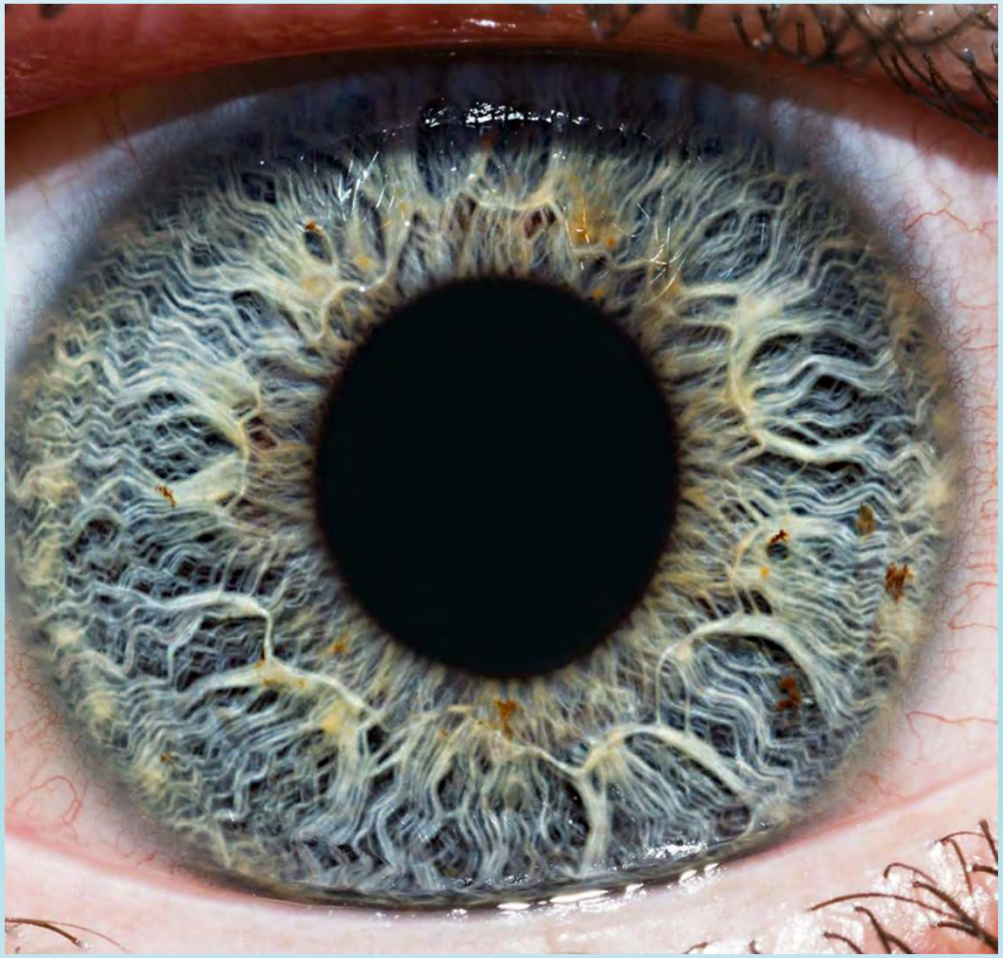
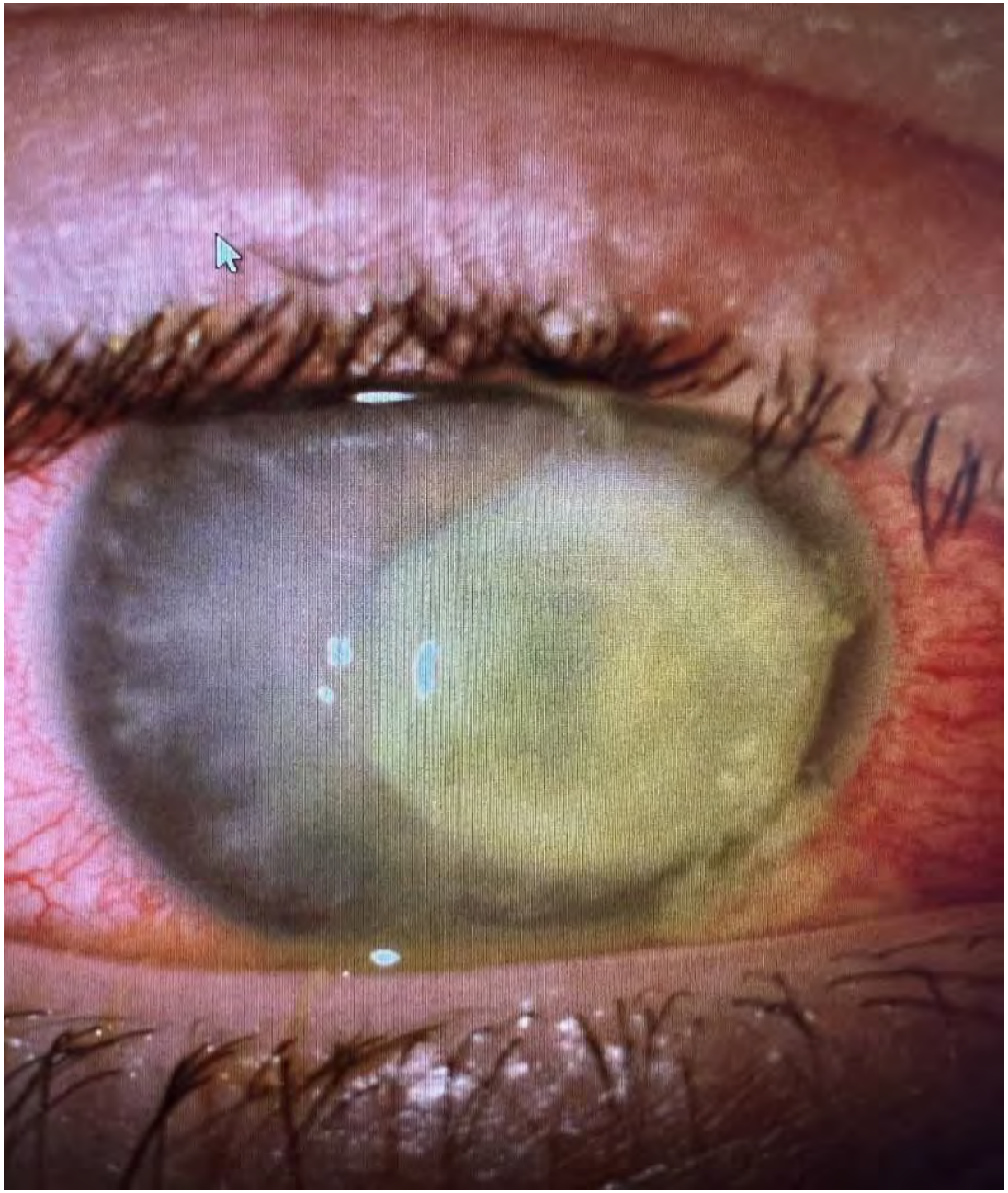
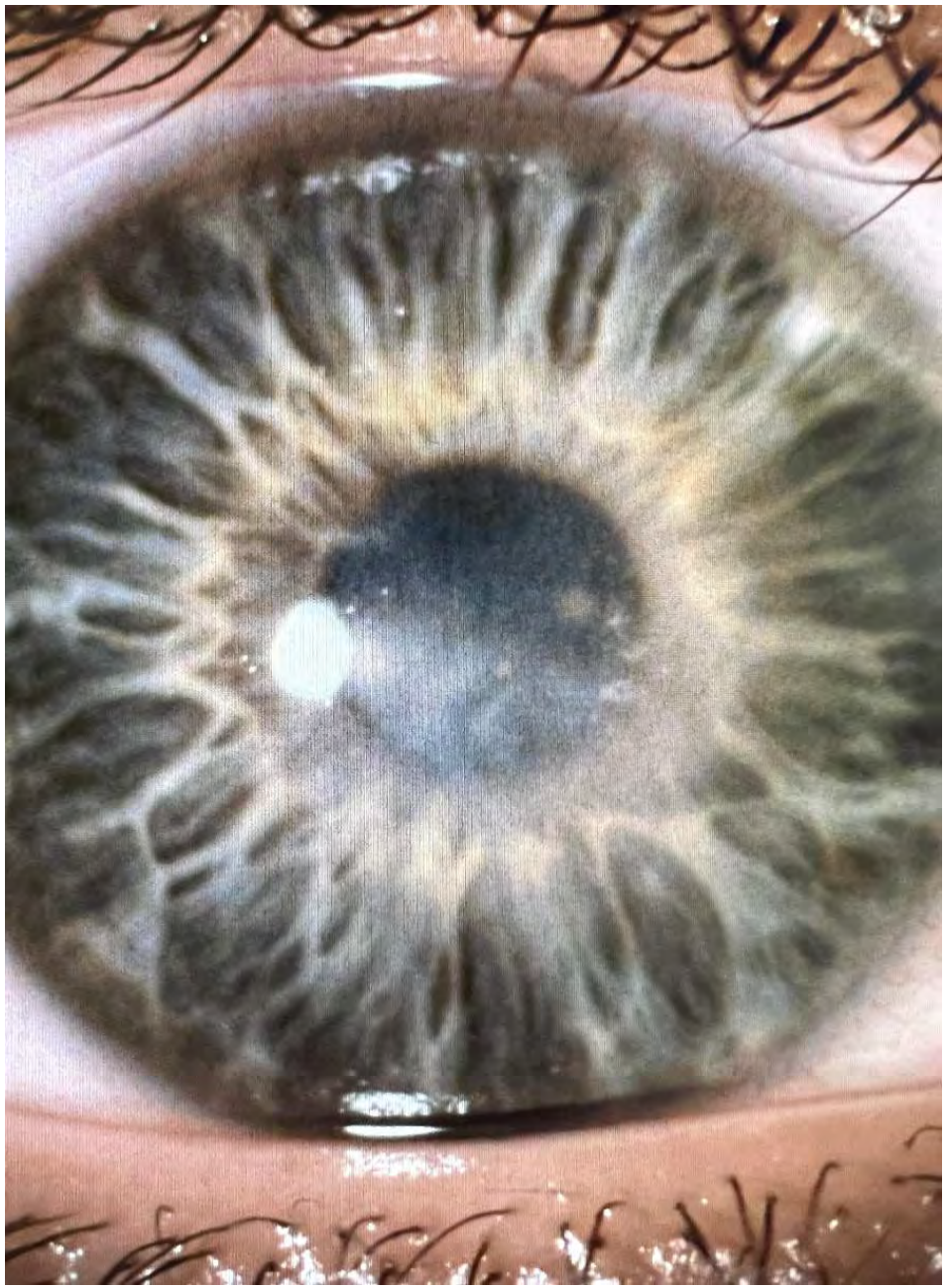
Procare March 2023
Daryl D. Kaswinkel,MD

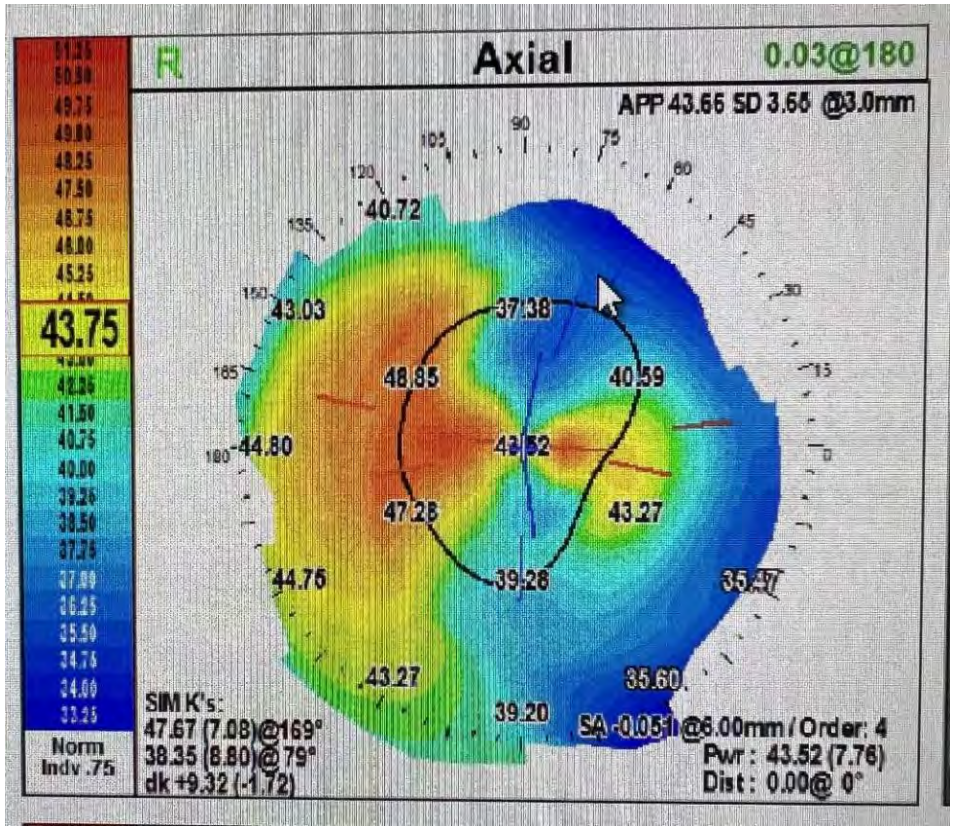


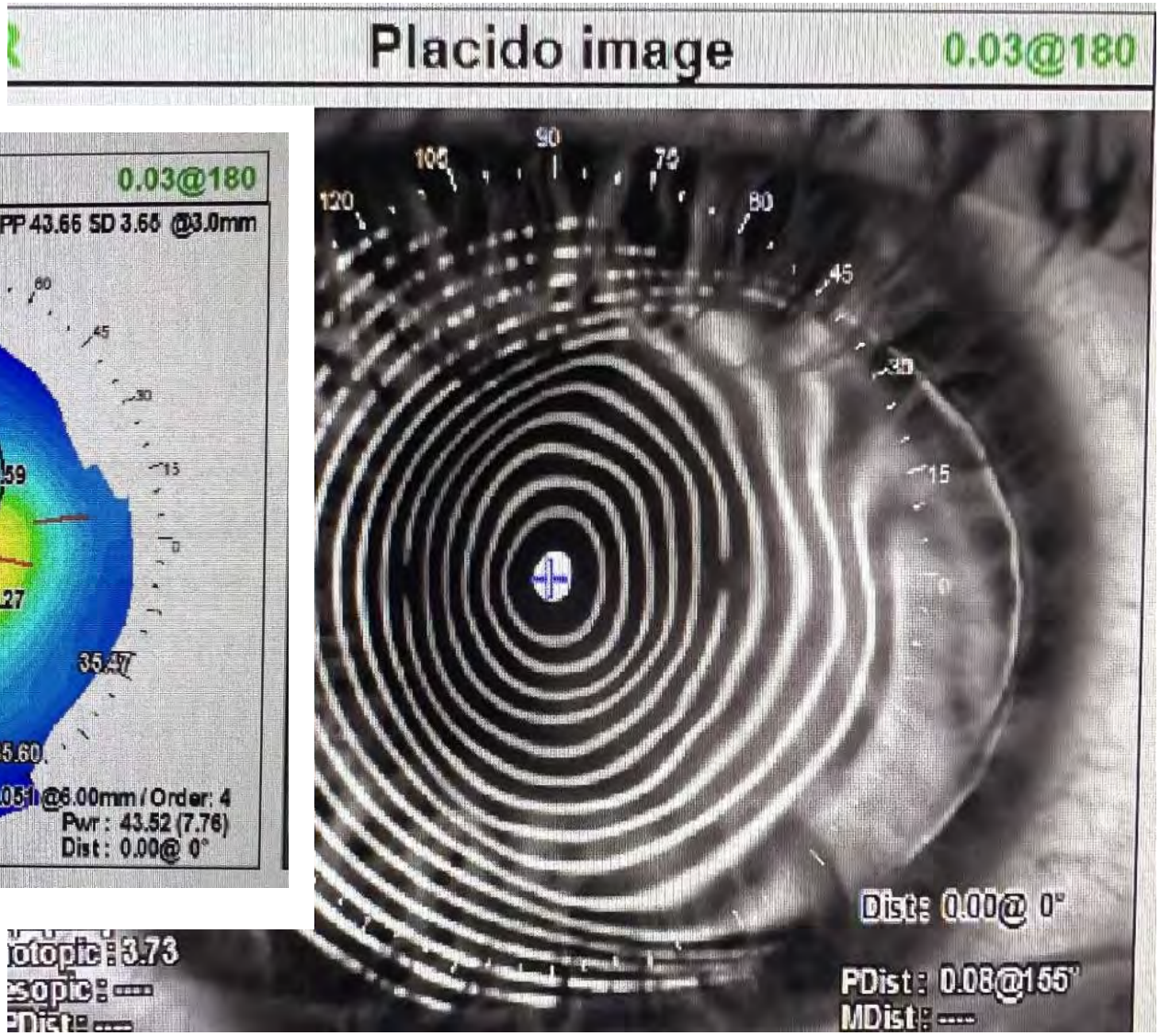


Pseudomonas Keratitis
Suppurative Infectious Keratitis

After 6 weeks Treatment

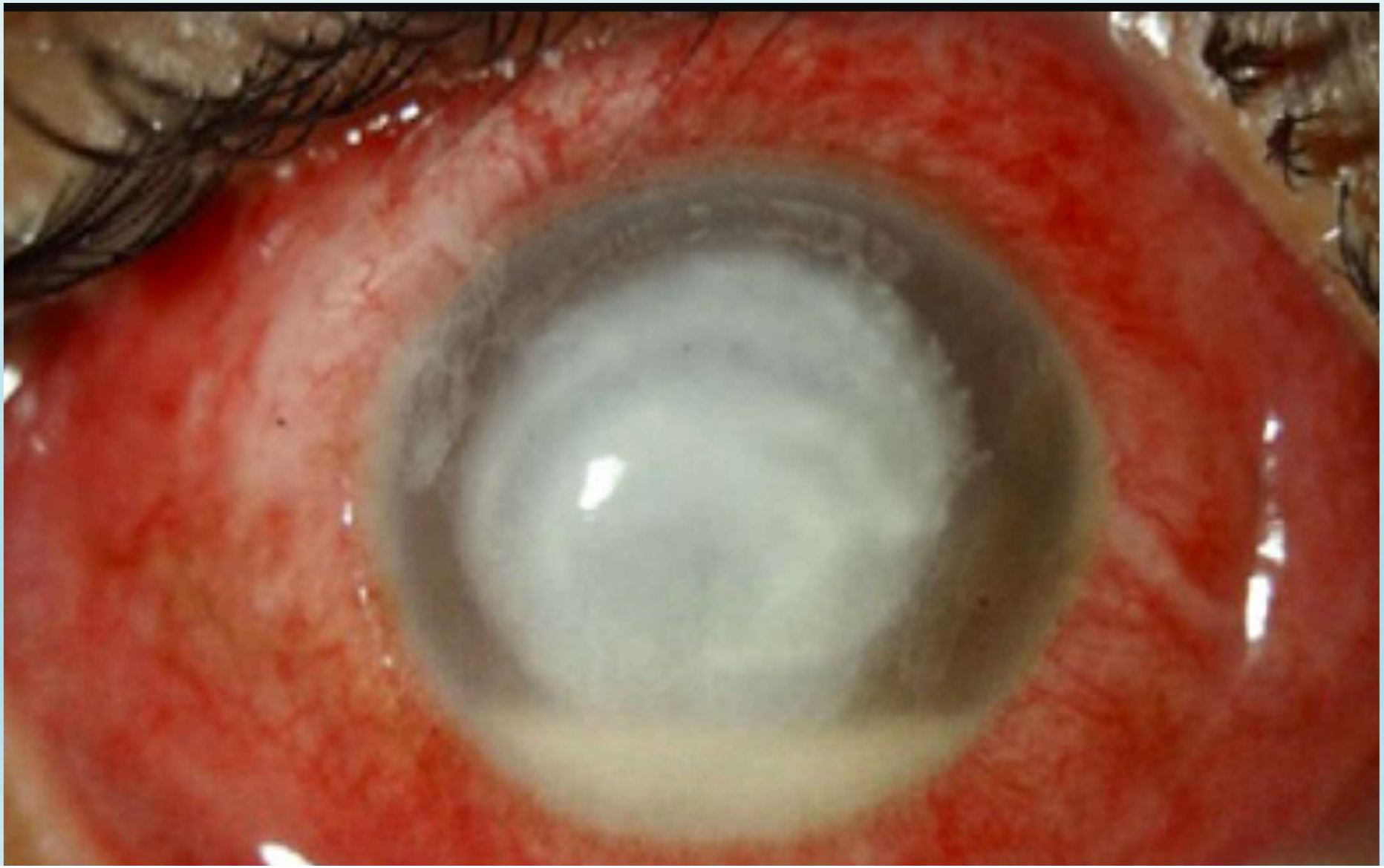






Topography with Pladico

Pseudomonas Keratitis
Suppurative Infectious Keratitis



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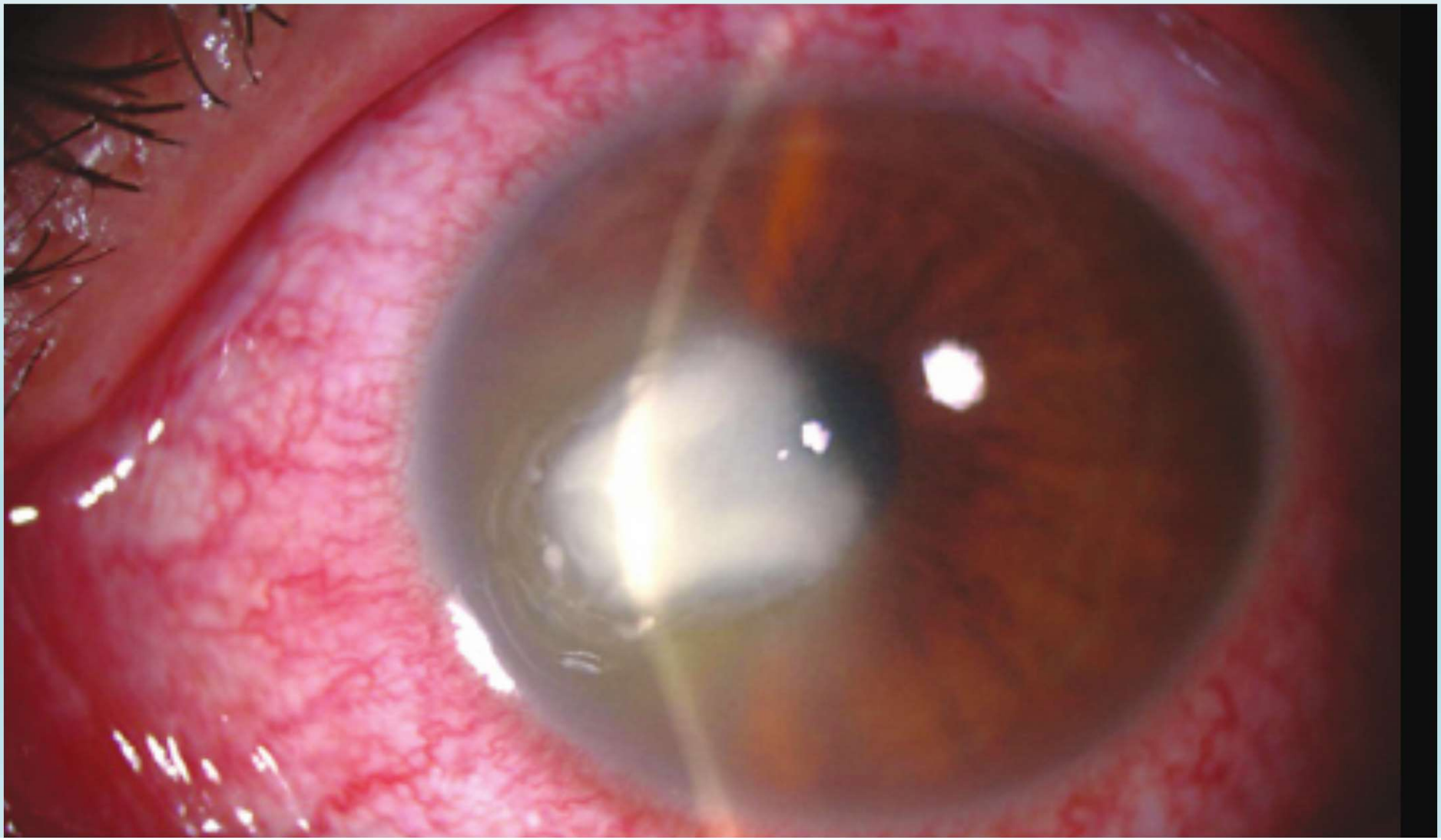
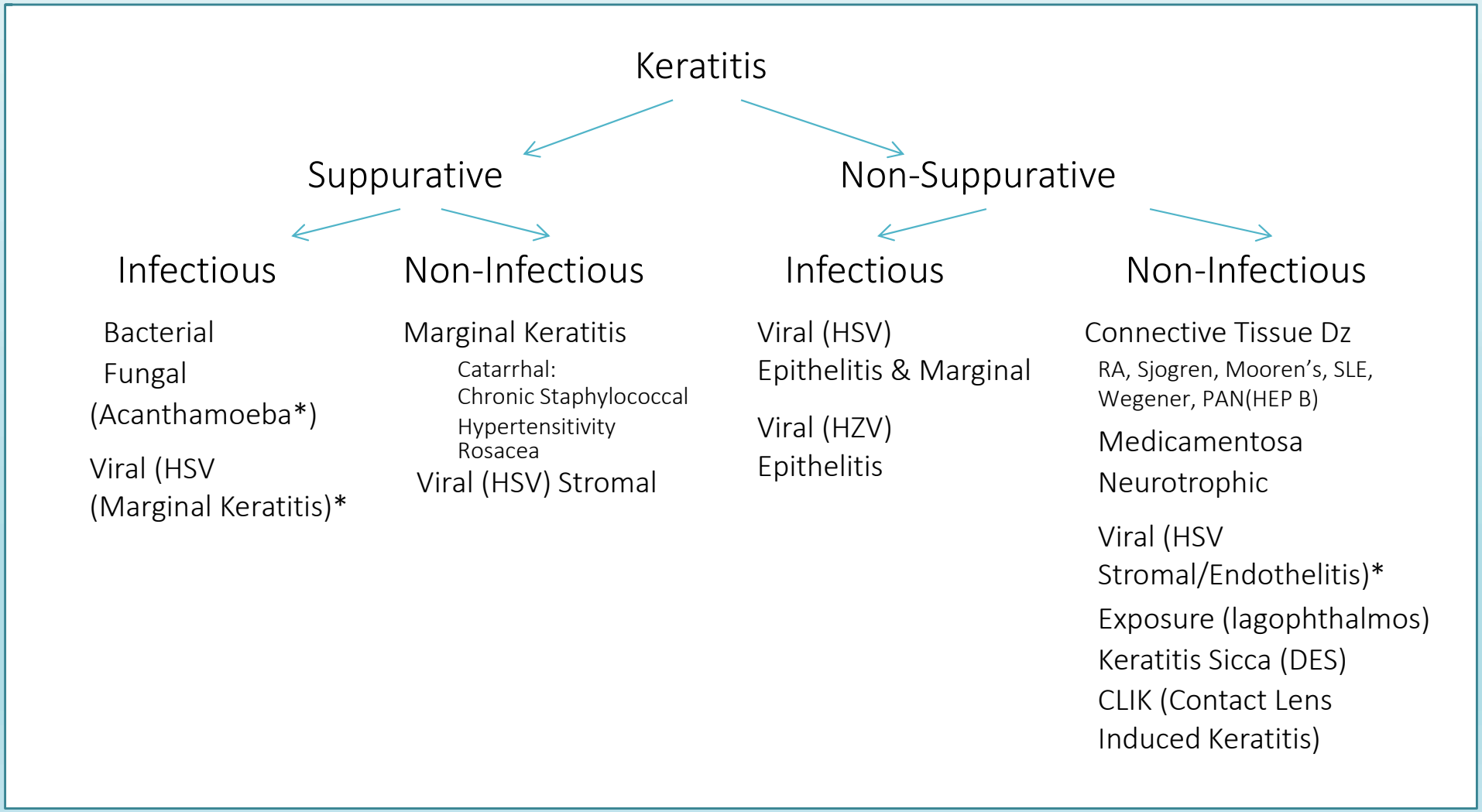


Pathophysiology

The most common groups of bacteria responsible for bacterial keratitis are as follows: *Streptococcus, Pseudomonas, Enterobacteriaceae* (including *Klebsiella, Enterobacter, Serratia,* and *Proteus*), nontuberculosis mycobacteria and *Staphylococcus* species including MRSA

Up to 20% of cases of fungal keratitis (particularly candidiasis) are complicated by bacterial co-infection.

Keratitis Diagnostic Classification



Laboratory Studies

Sight Threatening vs. Non-Sight Threatening

- Sight Threatening
  - *Location – Central, **Visual Axis***
  - *Size – Greater than **2 mm***
- Importance
  - Decision tree
    - *Sight Threatening - Culture and Sensitivity vs. Non Sight Threatening - Observation 24 hrs with Tx*
    - *Tx: Sight Threatening - Fortified Antibiotics vs. Non Sight Threatening - Mono-therapy*

Medical Treatment

If Sight Threatening Keratitis and no organisms are identified on the slide smear, initiate broad-spectrum antibiotics with the following:

fortified tobramycin (10-14 mg/mL) 1 drop every hour alternating with fortified cefazolin (50 mg/mL) or vancomycin (15 – 50 mg/mL) 1 drop every hour.

Subconjunctival/SubTenons injections of antibiotics based on sight threatening and other unusual circumstances.

Tobramycin (20mg), cefazolin (100mg), Vancomycin(25mg)

Intracameral/Intravitreal Cefazolin/Vancomycin corneal abscess/hypopon

Inracorneal injections of antibiotics

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Steroids for Corneal Ulcers Trial Results

3 months after enrollment, there was no significant difference between the corticosteroid and placebo groups in the study's primary outcome, best spectacle-corrected visual acuity (BSCVA). Nor were there any differences in the secondary outcomes of infiltrate/scar size, time to re-epithelialization, or corneal perforation.

BSCVA at 1 (400 patients) to 4 years(50 patients) was not significantly different between the two study groups.

There was, however, a significant improvement in BSCVA in the patients with the worst baseline vision and largest, most central and deepest ulcers. "Sight Threatening" – counter intuitive

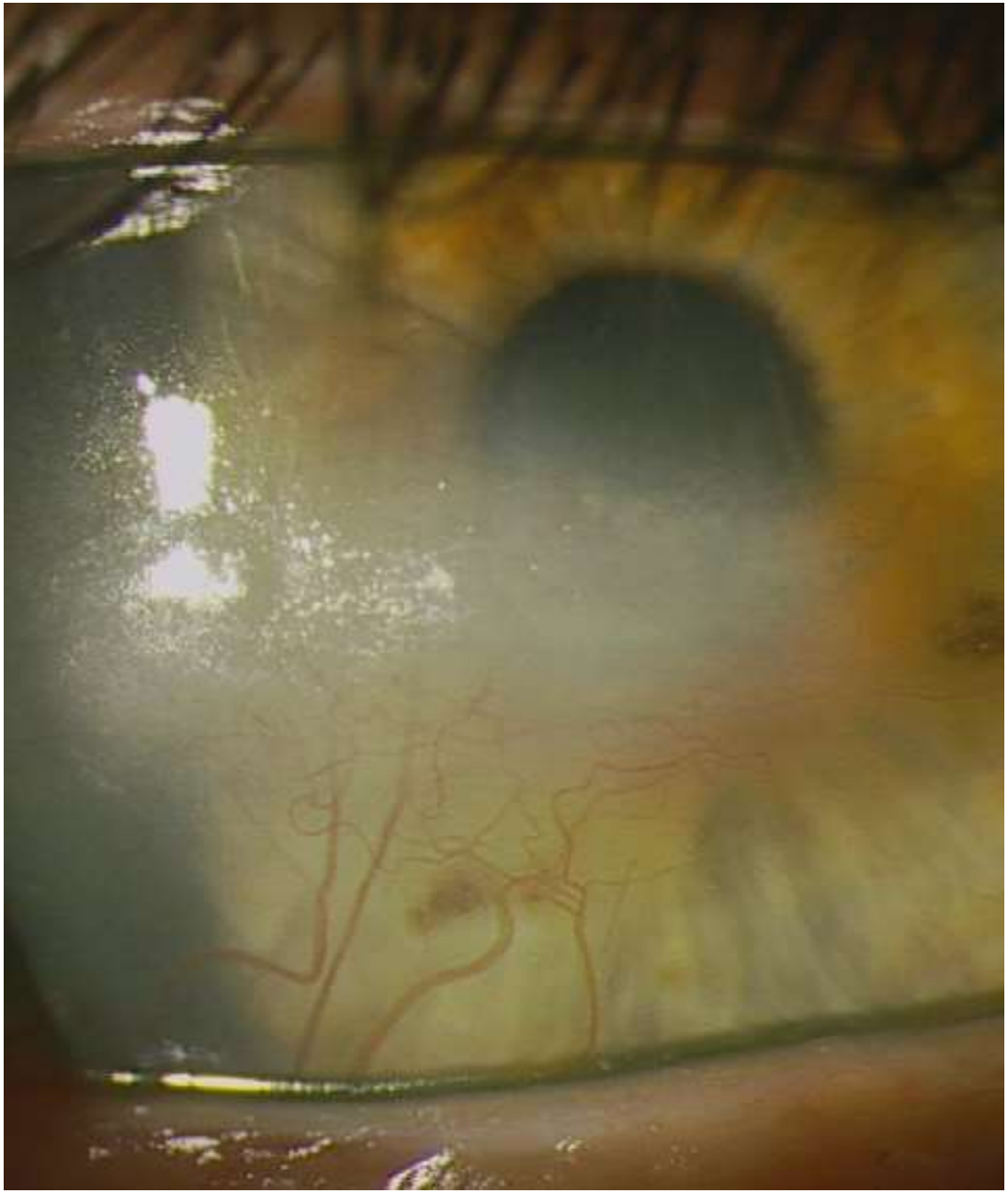
Steroids for Corneal Ulcers Trial Conclusions

Many cases in the study were non-central (Non Sight Threatening); these cases would be expected to have low visual morbidity and good visual recovery, either with or without steroid use.

Perceived message from this study may have been that “steroids don’t help bacterial keratitis,” encouraged by the fact that no harm came to those treated with steroids. It’s also reassuring to note that, in the most severe cases, there was indeed some long-term benefit to employing corticosteroids in bacterial keratitis especially if Sight Threatening.

Pseudomonas & Artificial Tears

- Global Pharma Healthcare recalling EzriCare and Delsam Pharma brands (drops and/or ointments)
- FDA: 55 adverse events: eye infections, permanent loss of vision and one death from sepsis
- Pseudomonas aeruginosa drug resistant strain
- California, Florida, New Mexico and Utah



Neurotropic Keratopathy Suppurative Non-infectious Keratitis

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 rare 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

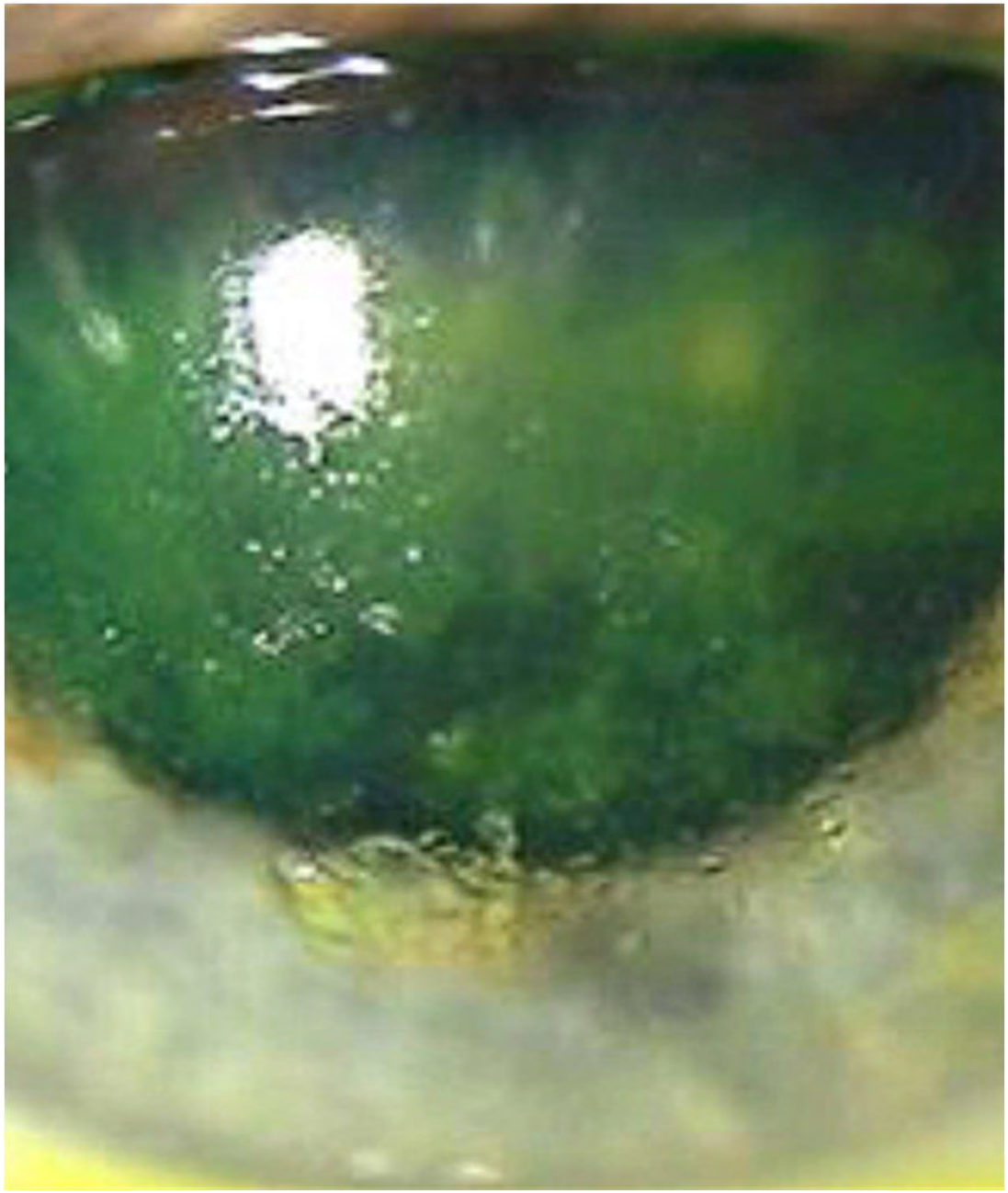
Nerves also produce nerve growth factor (NGF), supporting nerve themselves and corneal epithelium

NGF stimulates proliferation and differentiation of cornea epithelial cells and promotes tear production to lubricate and protect the eye

Oxervate – How it Works

NGF promotes corneal nerve growth lost in NK

Oxervate's active ingredient is recombinant form of human nerve growth factor (rhNGF), protein with identical structure to naturally occurring NGF

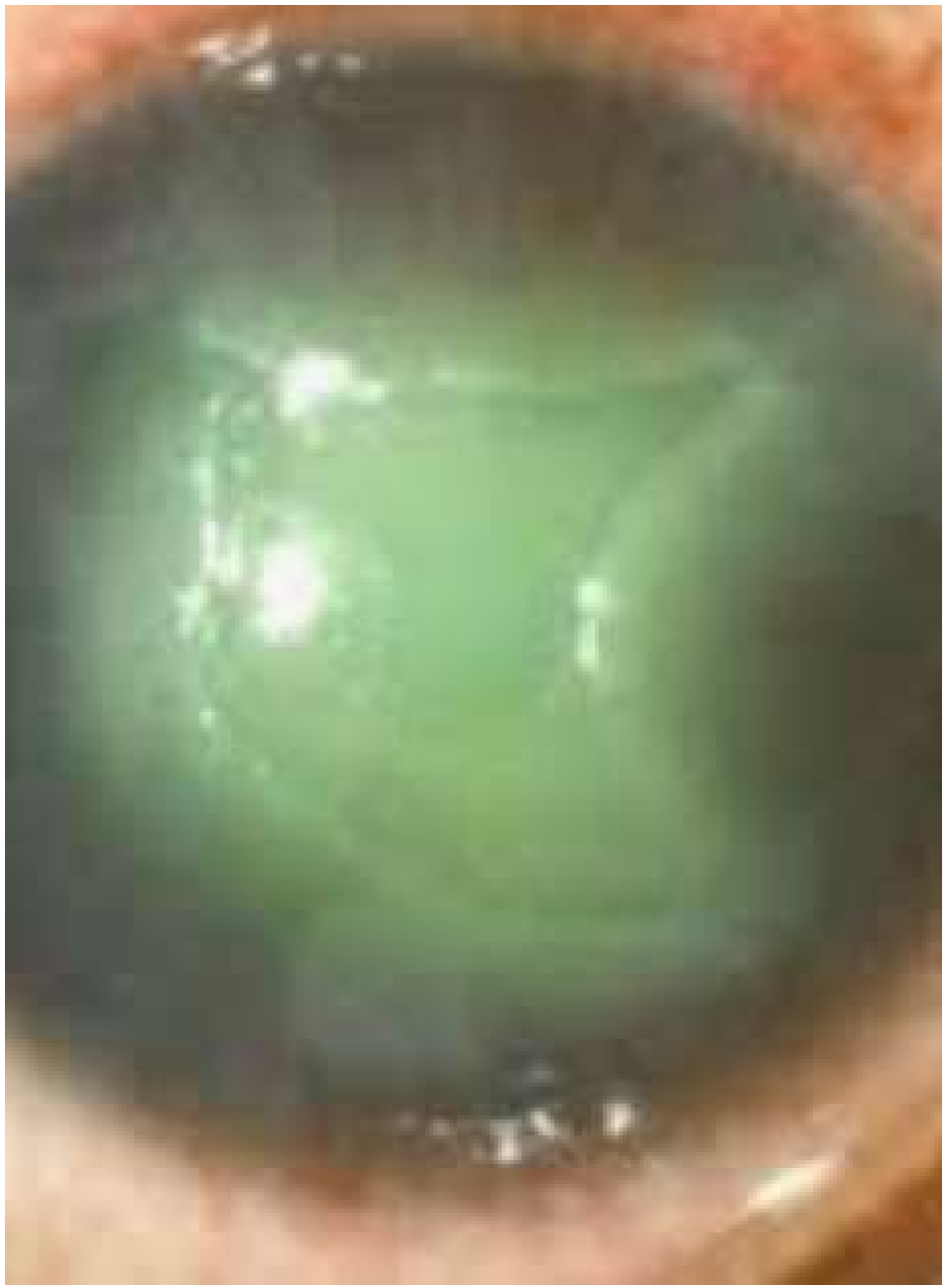


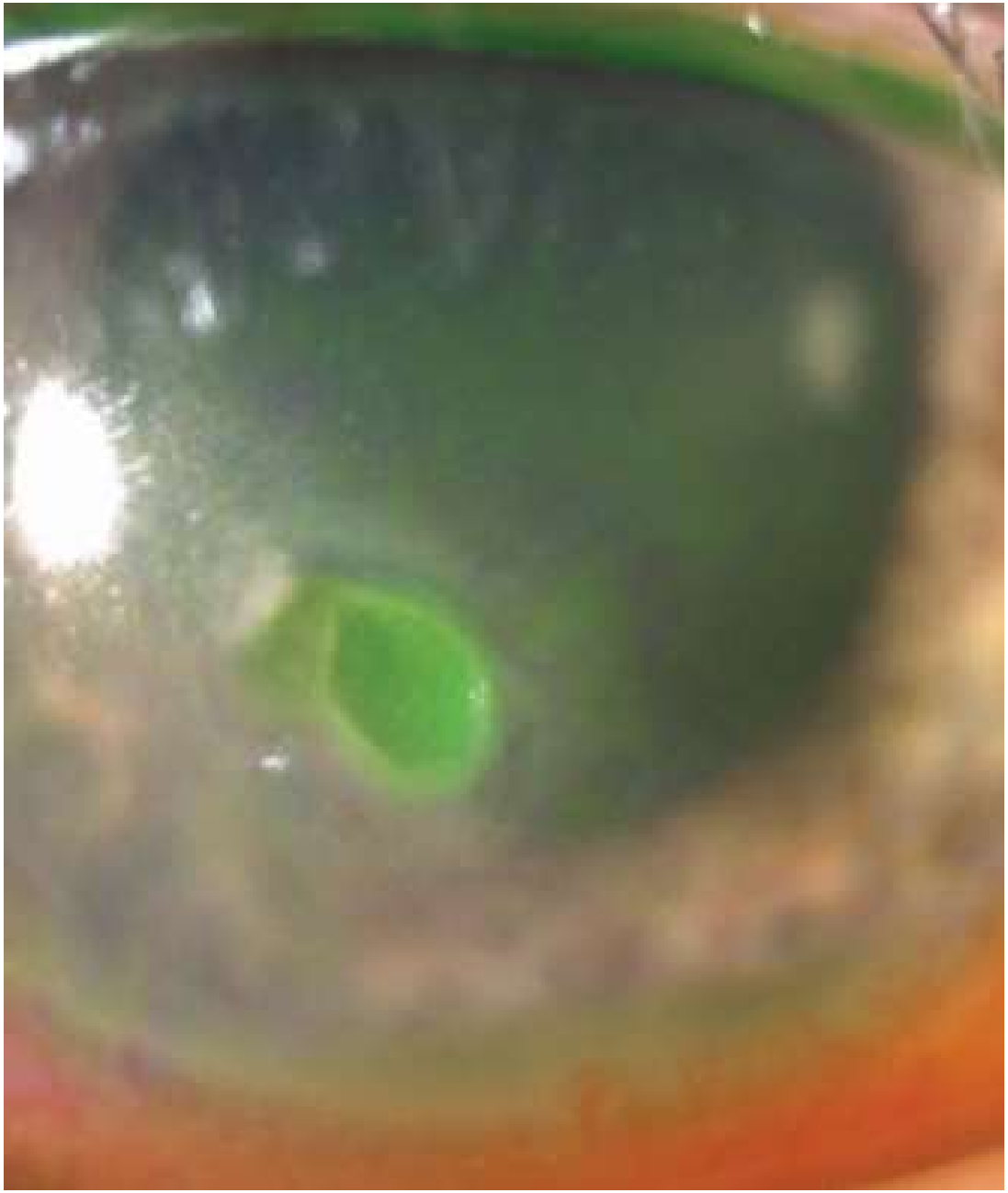
Stages of NK-Mild

Stage 1: Ocular Surface Irregularity and reduced vision

Stages of NK - Moderate

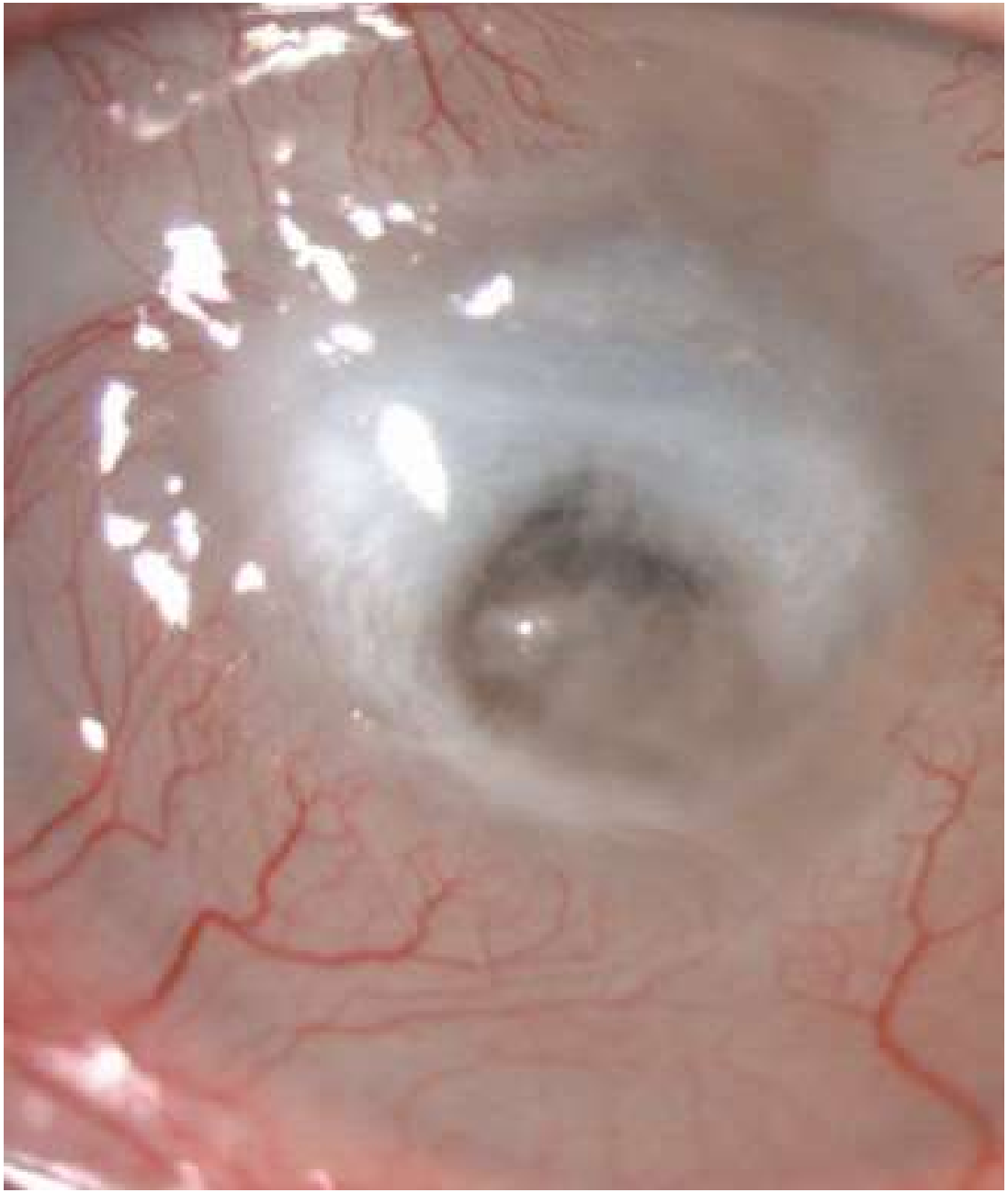
Stage 2: nonhealing persistent eptihelial defect (PED)





Stages of NK - Severe

Stage 3: Corneal ulceration involving the subepithelial (stromal) tissue



Stages of NK

Stage 4:
Ultimately
Corneal melting,
perforation, then
Descemetocele

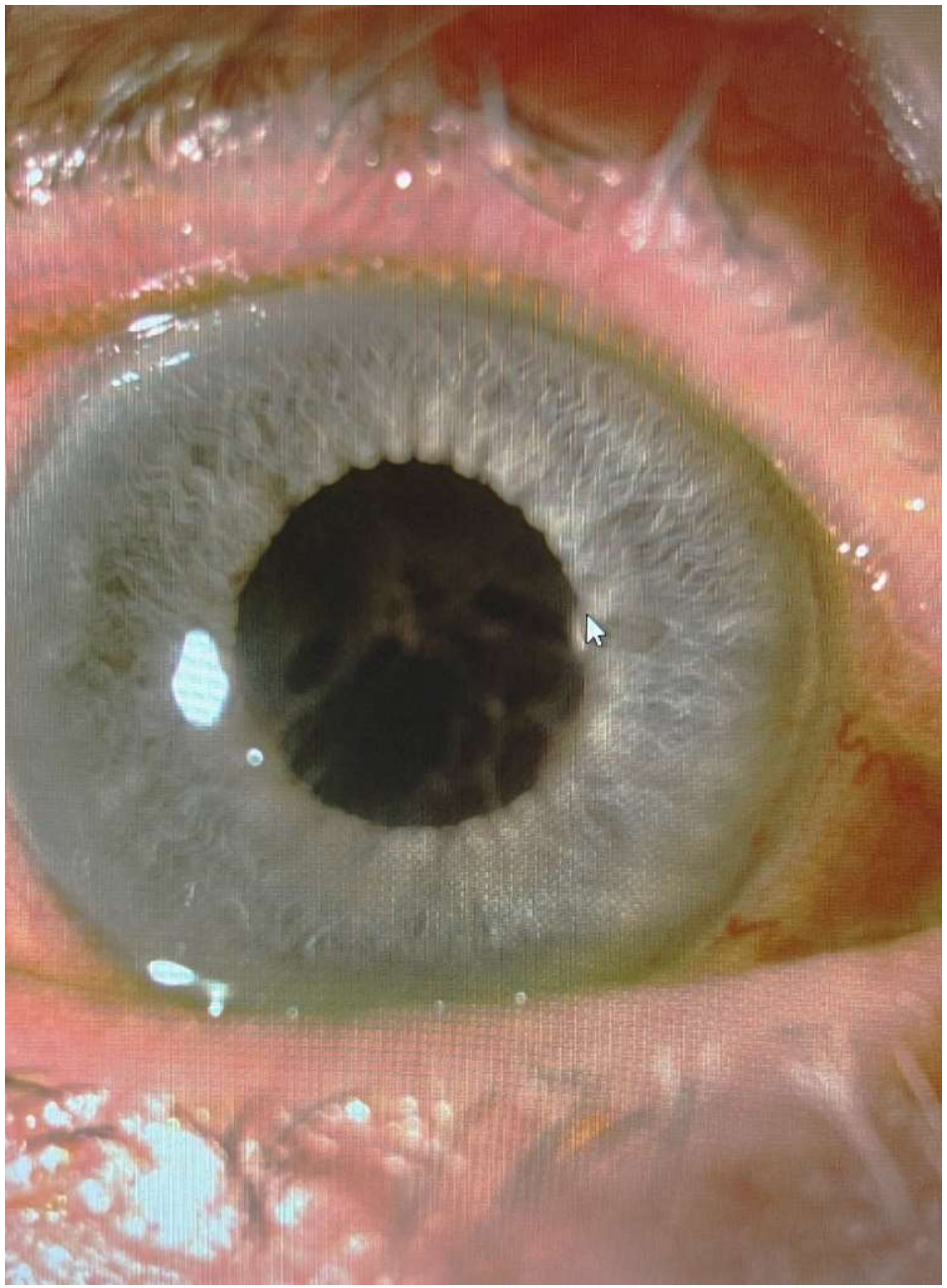
Key Findings

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

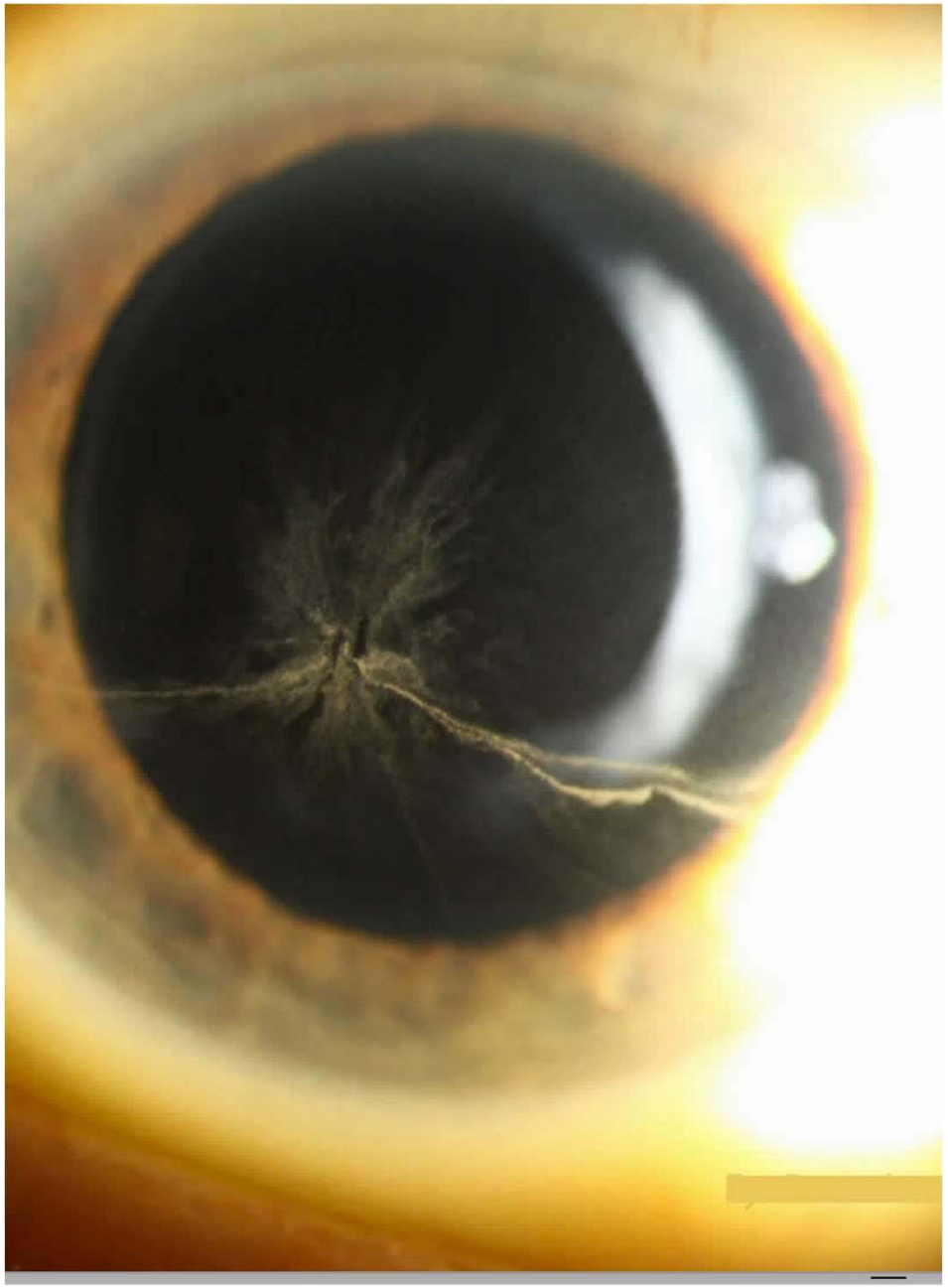
2+6=8

- 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

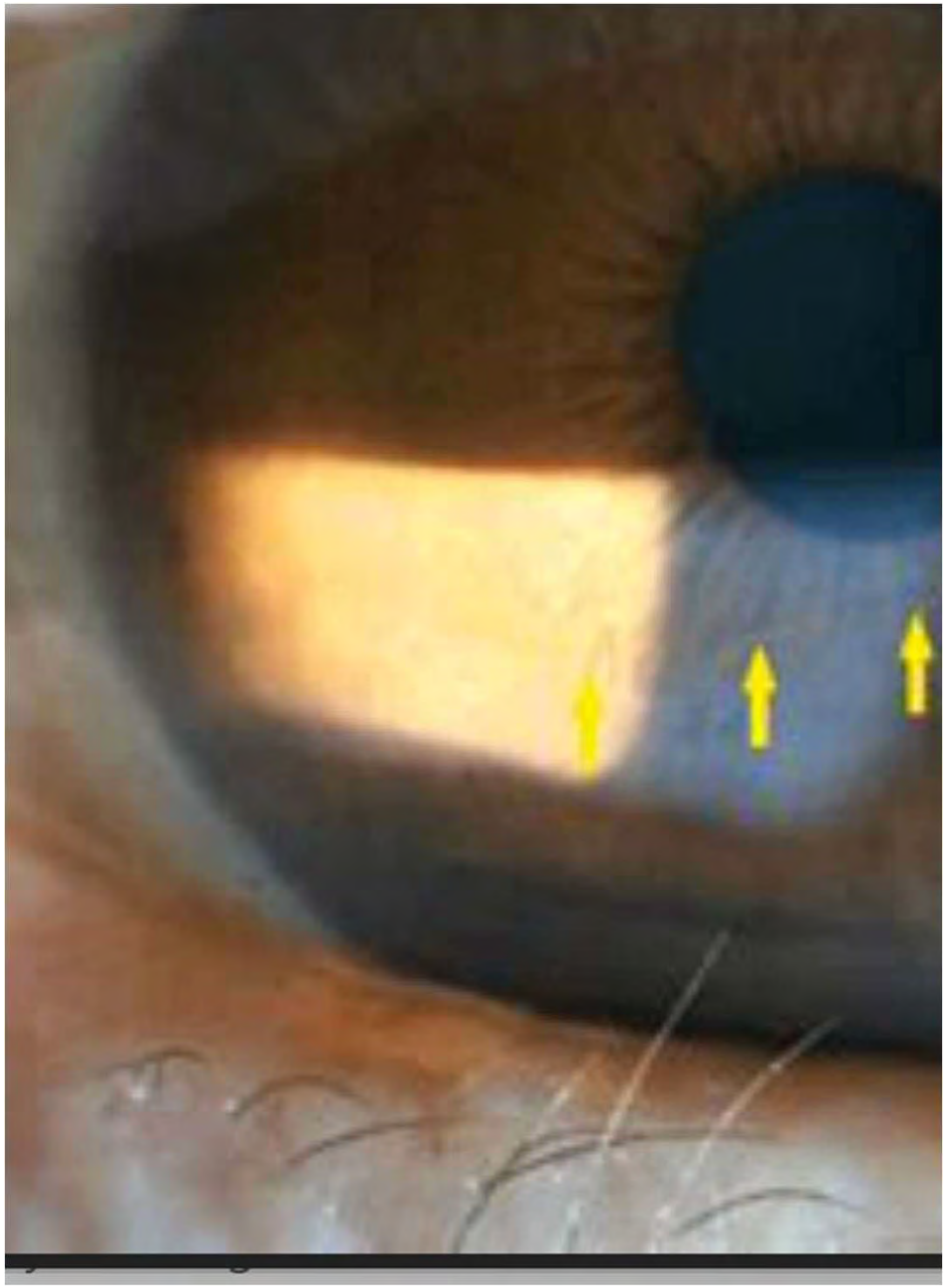
“Rhopressa Verticillata” Non-Suppurative Non-Infectious Keratitis



Corneal Verticillata Amiodarone

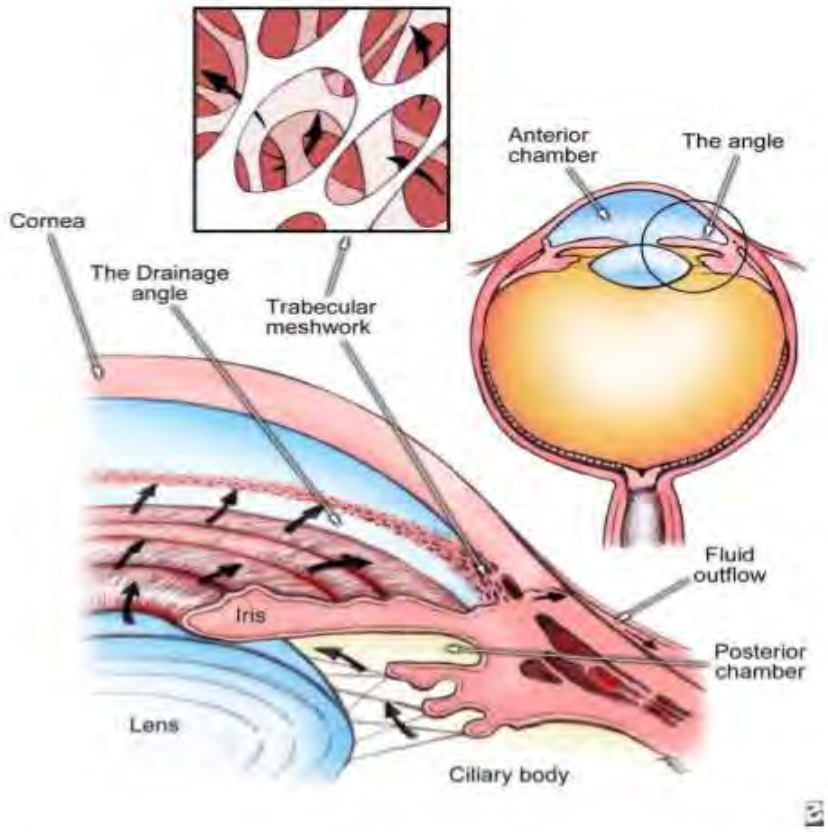


Hudson-Stälhi Line



Value of Rhopressa™ ++

- Directed at site of pathology
  - The trabecular meshwork
- Enhanced compliance
  - Once-a-day dosing
- Efficacy
  - Achieves noninferiority to timolol where AA's (Brimonidine) and CAI's failed
  - Consistent IOP lowering across broad baseline range
  - Additive to prostaglandins
- Safety
  - Lack of serious and systemic adverse events

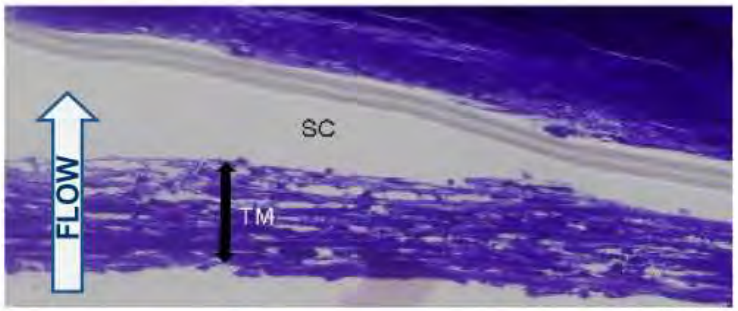


++Data on file from Aerie Phase 3 clinical trials, Rocket 1, Rocket 2 and Mercury 1.

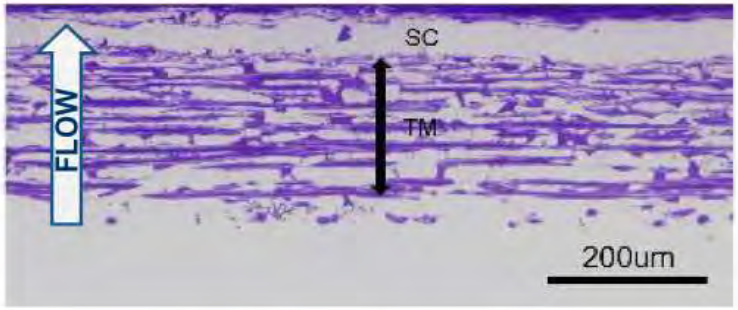
Rhopressa Causes Expansion of TM Tissue,
Opening Spaces for Increased Outflow

Dan Stamer (Duke), Haiyan Gong (Boston University)

Control



+ Netarsudil



TM: Trabecular Meshwork
SC: Schlemm's Canal
Control = buffered saline solution

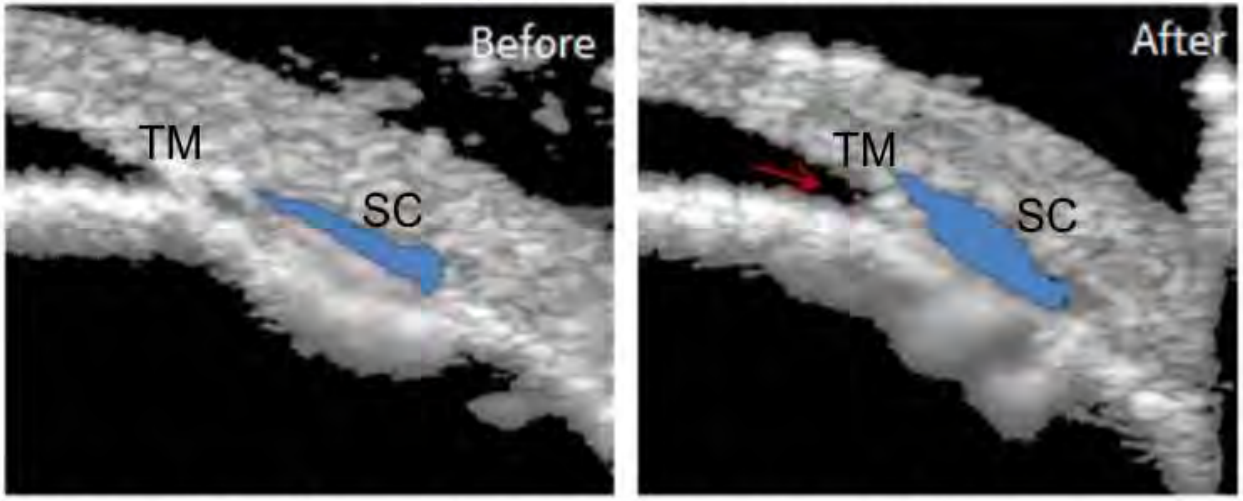
Increasing Trabecular Outflow, Reducing Fibrosis Could Stop Degeneration of Outflow Tissues in Glaucoma

*Active ingredient of Rhopressa™

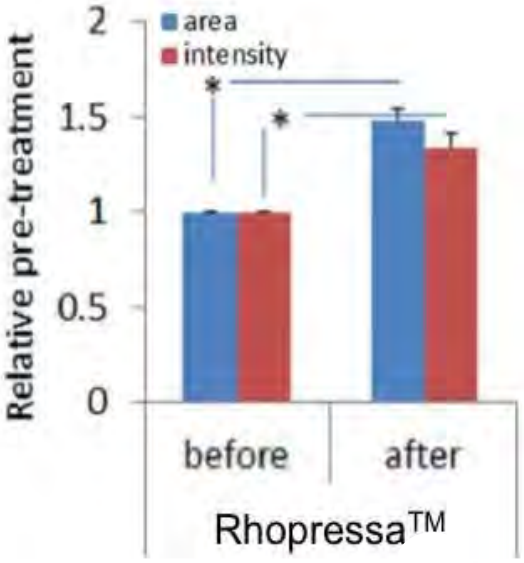
Live Imaging of Rhopressa™-induced Increase in Trabecular Meshwork Outflow

- Rhopressa™-induced increase in trabecular outflow of aqueous humor visualized in real time using live-animal OCT imaging in mice
  - First study to show glaucoma drug affecting target tissue in real time

Rhopressa™ Treatment



Blue shading shows Schlemm's Canal expanding due to enhanced fluid flow through TM



Li G. et al. Visualization of conventional outflow tissue responses to netarsudil in living mouse eyes.
Eur J Pharmacol. 2016 Apr 13. pii: S0014-2999(16)30206-0

Rhopressa™ Adverse Events Summary

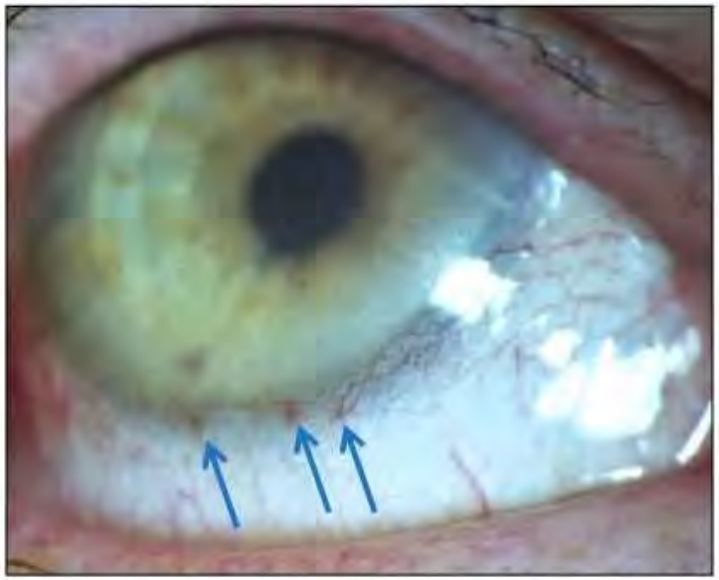
- Hyperemia – absent or sporadic for 90% of patients
  - only 10% of patients had hyperemia AE at all 6 study visits
- Conjunctival Hemorrhage – sporadic subconjunctival petechiae
  - none noted at month 12 visit
- Corneal Deposits (verticillata*) – asymptomatic non-toxic lipid deposits
  - high resolution rate
- Visual Acuity Reduced – sporadic, mostly single visit, only one eye
  - incidence reduced over time
- Vision Blurred – sporadic and significantly reduced over 12 months

When Present, 80% of Rhopressa™ QD Hyperemia Graded as Mild

Grade	Image	Description
0		None/Normal
1		Mild
2		Moderate
3		Severe

+Lumify – Brimonidine 0.025%

Conjunctival Hemorrhage Using Biomicroscopy Evaluation



- Subconjunctival petechiae seen sporadically in Rhopressa™ Rocket studies
  - MedDRA coded to conjunctival hemorrhage
- No conjunctival hemorrhages noted at month 12 visit

Perspective on Rhopressa™ Advantages*

Clinical:

Mechanism of action at site of pathological site - TM

- Triple mechanism of action
- Potential PGA synergy
- More consistent IOP-lowering across baselines than PGAs and timolol
- No systemic side effects

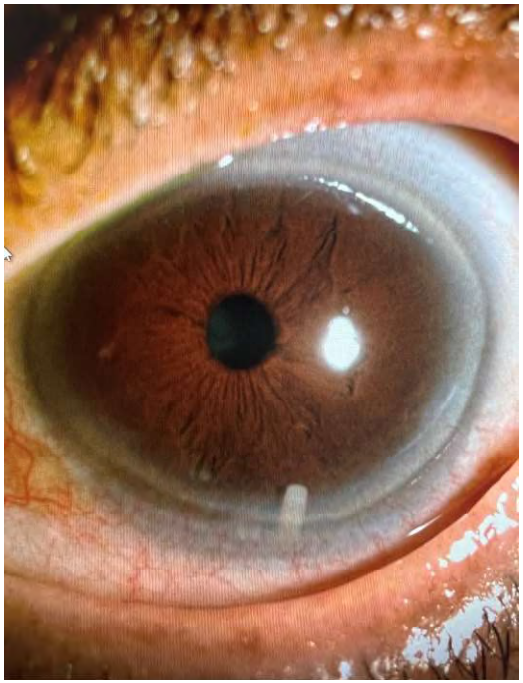
Research:

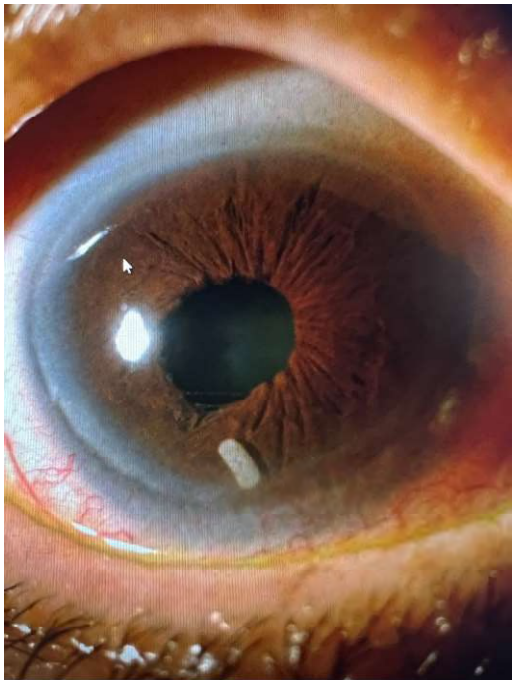
- Targets diseased trabecular meshwork in glaucoma
- Potential to preserve health of trabecular outflow pathway**
- Potential to promote retinal ganglion cell survival and axon regeneration**

Roclatan™ Summary

aerie Pharmaceuticals Inc.

- Demonstrated superiority over both latanoprost and Rhopressa™ for the primary efficacy analysis at all 9 time points ($p<0.0001$)
- IOP-lowering effect was greater (1-3 mmHg) than monotherapy with either latanoprost or Rhopressa™ throughout the duration of the study
- There were no drug-related serious adverse events and no evidence of treatment-related systemic effects
- The main adverse event was conjunctival hyperemia, ~50% of patients and was scored as mild for ~80% of these patients





Durysta

Glaucoma Patients & Ocular Surface Disease (OSD)

Glaucoma Patients:

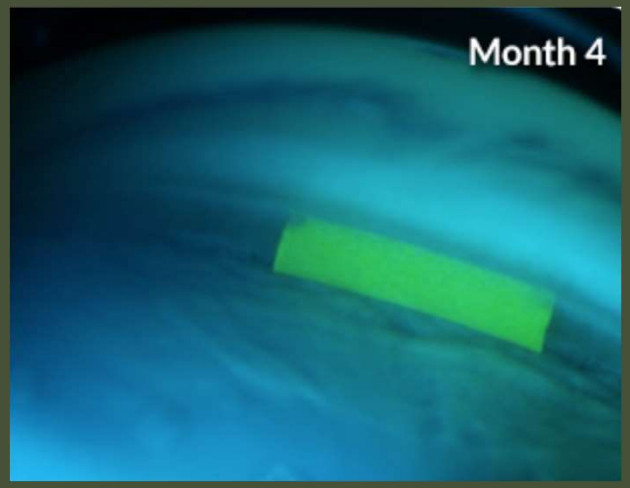
- Elderly (decreased tear secretion)
- On medications for life
- Frequently on multiple topical ophthalmic medications[1]
- Abnormal tear film breakup time is associated with increasing number of eye drops and drops with and without BAK[2]
- May undergo filtering surgery (impact on healing)

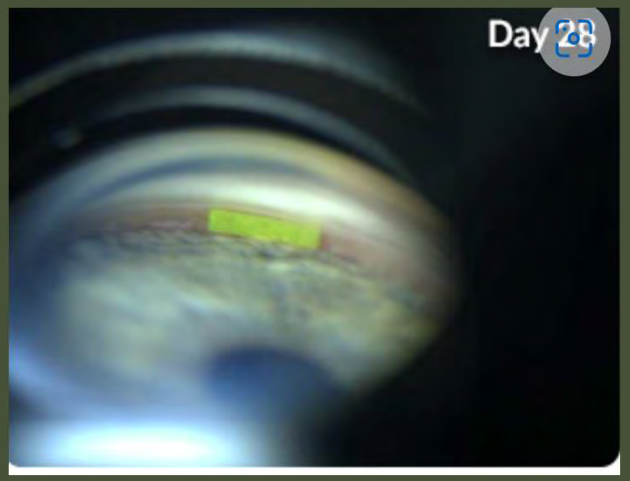
GLAUKOS

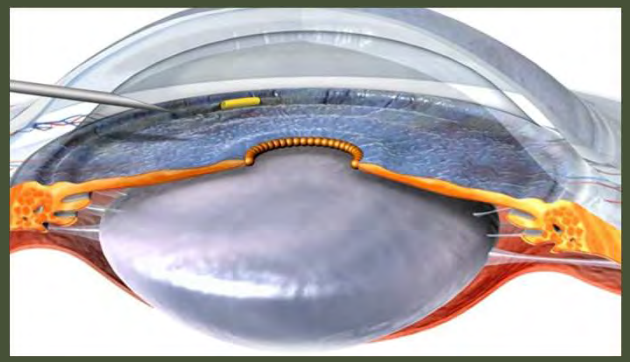
Durysta® Allergan

- First and presently only FDA (3-5-2020) – approved dissolvable ocular implant (Bimatoprost 10mcg) to reduce intraocular pressure:
  - Chronic Open Angle Glaucoma
  - Ocular Hypertension

- 30% reduction from baseline at 3 months with 40% control at 12 months and 28% control at 24 months.
  - FDA Phase IV 18 month studies pending June 2023



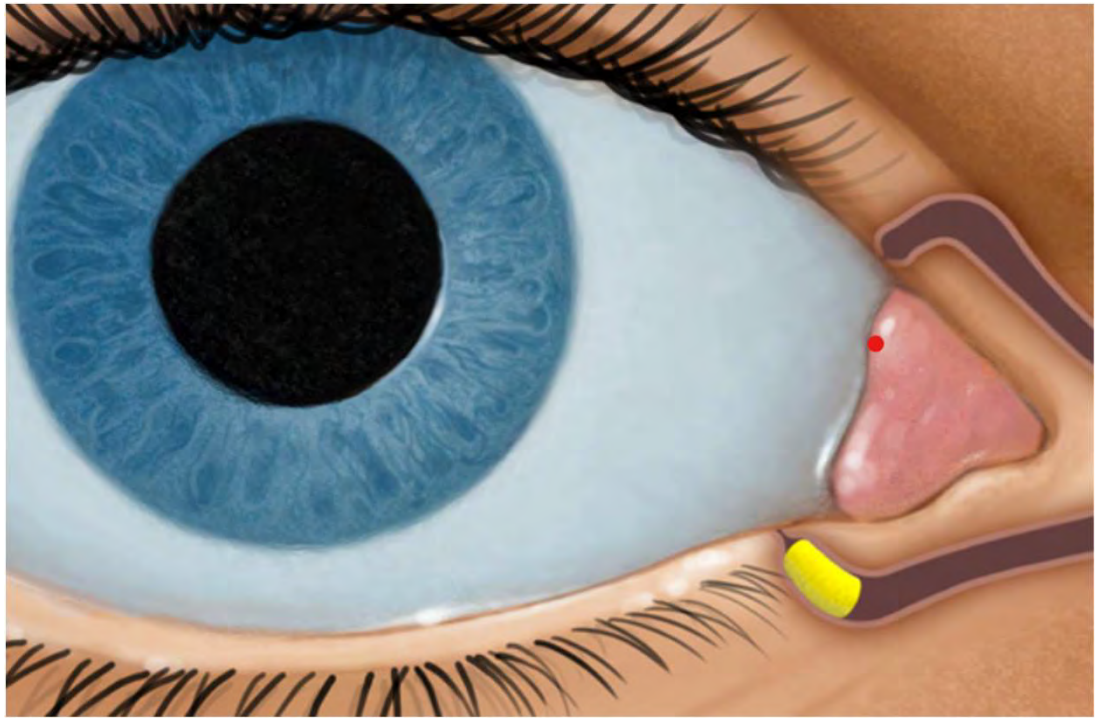




Ocular Therapeutix
Travoprost intracameral

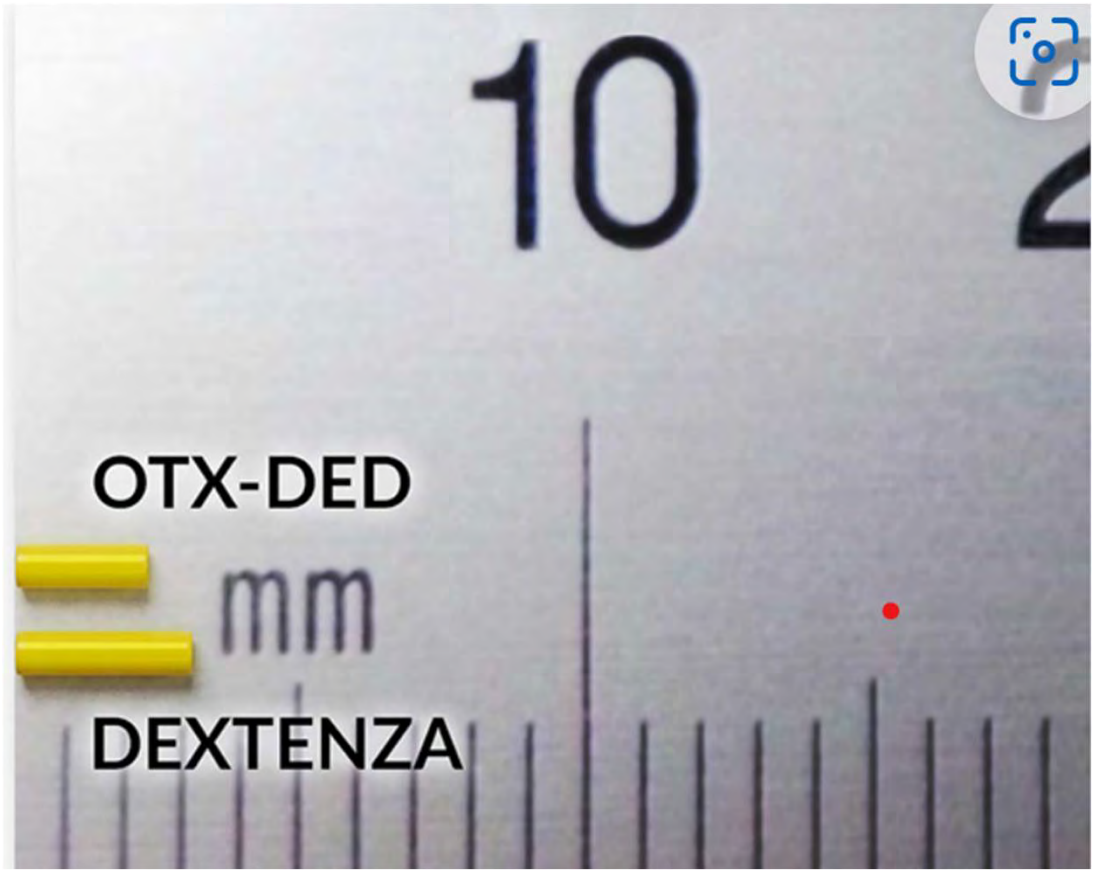
OTX-TIC

- 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**