Anterior Segment Challenges:

"You Used to Be So Sensitive-Now you are just a pain: Signs, Symptoms and Treatment for NK"

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Disclosure

- Presenter is on speaker's panel/consultant for:
  - Alcon, Allergan, Azura, B+L, J&J, Novartis, OcuSOFT, Olleyes, Reichert, Sight Sciences, Sun Pharma, Visus, Tarsus, Thea, Bruder, Dompe'
- Collaborative Corner Monthly Video Rant
- President of MRB Eye Consultants
- Past-President of the Optometric Council on Refractive Technology (OCRT)
- Presenter has NO financial interest in any products mentioned

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H47TDX

- H47TDX

- Peloton Referral Number!
  - Get one.

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Neurotrophic keratitis

"Some patients look great and feel awful.
Others look terrible and feel great."
John Sheppard

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Neurotrophic keratitis

"Stain without pain"

"A key differentiator is the reduction or total loss of corneal sensitivity…caused by damage to the corneal nerve, which leads to breakdown and poor healing of the epithelium."

Mastropasqua L, Massaro-Giordano G, Nubile M, Sacchetti M. Understanding the pathogenesis of neurotrophic keratitis: the role of corneal nerves. J Cell Physiol. 2017;232(4):717-724.

https://knownk.com/about-nk/#what-is-nk

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Nuerotrophic Keratitis

- Classified as a rare disease in the US
- A progressive disease
- Defined by impairment of the trigeminal innervation

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Corneal Nerves 101

- The cornea is the most powerful pain generator in the body
- 7000 nerve terminals per millimeter square
- Corneal nerves mainly originate
  - Ophthalmic division of the CN V (trigeminal nerve)
    - Branches of the nasaociliary branch
    - Branching into two long long ciliary nerves around the limbus
    - Enter radially mid-stromal
- Nociceptive Stimulus
  - Free nerve endings that respond to noxious stimuli
  - Skin, Organ motion, cornea and dental pulp

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Neuropathic Pain Perception

Itch	irritation	dryness	grittiness
burning	aching	light sensitivity	

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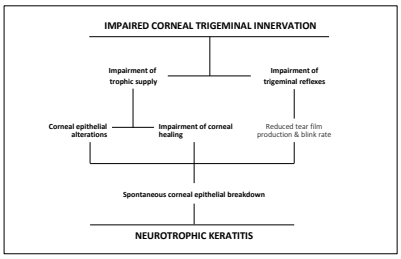
Nerve malfunction is the hallmark of NK[1,2]

Conditions that damage any level of the trigeminal nerve can **disrupt physiological processes** in the ocular surface and lead to NK

Impaired corneal sensitivity leads to diminished protective blink reflexes, abnormal epithelial cell metabolism, and failure to resist the effects of trauma, drying, and infection



1. Dua H, Said D, Messmer E, et al. Neurotrophic keratopathy. *Prog Retin Eye Res.* 2018;66:107-131.
2. Mastropasqua L, Massaro-Giordano G, Nubile M, Sacchetti M. Understanding the pathogenesis of neurotrophic keratitis: the role of corneal nerves. *J Cell Physiol.* 2017 232(4):717-24

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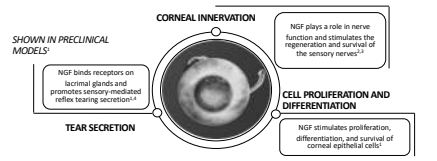
Endogenous NGF maintains corneal integrity by three mechanisms

Endogenous Nerve growth factor acts through specific high-affinity (i.e., TrkA) and low-affinity (i.e. p75NTR) nerve growth factor receptors in the anterior segment of the eye to support corneal innervation and integrity.[1]



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Conditions leading to NK

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Systemic

- Diabetes
- Multiple sclerosis
- Vitamin A deficiency
- Leprosy
- Amyloidosis

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Central nervous system

- Aneurysms
- Stroke
- Degenerative disorders of the CNS
- Post-neurosurgical procedures

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Genetic

- Riley-Day syndrome
- Goldenhar-Gorlin syndrome
- Mobius syndrome
- Familial corneal hypoesthesia

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Ocular Conditions for NK

- Post-herpes keratitis
- Chemical and physical burns
- Abuse of topical anesthetics
- Drug toxicity (eg, BAK)
- Chronic ocular surface injury
- Ocular surgery (eg, LASIK, cataract surgery)
- Contact lens wear
- Orbital neoplasia
- Corneal dystrophies
- Chronic DED

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My Vision is blurry…like a lot.

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”Can I do my other eye first?”

- 72 yo Male
  - Cataracts in both eyes
    - Scheduled for surgery in left eye
    - Starting using drops pre-op
      - “I may have hit my eye with the tip of the drop?”
      - “My vision is way worse now”
    - VaSC
      - 20/200 ph 20/70 OD
      - 20/CF ph 20/200 OS
    - Slex:
      - OD-Corneal Clear, NSC/ASC
      - OS-

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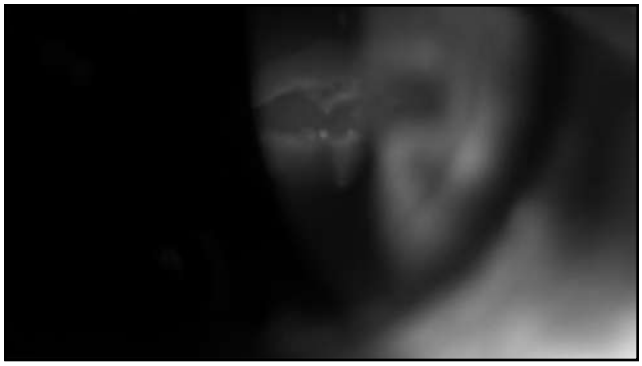

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Testing corneal sensitivity IS IMPORTANT TO DIAGNOSING NK

QUALITATIVE

COTTON THREAD
- When the cotton thread gently touches the cornea, normal subjects show a blink reaction and can describe the sensation of touch
- Patients with a loss of corneal sensitivity DO NOT react

QUANTITATIVE

COCHET-BONNET AESTHESIOMETER
- Commonly used
- Quantifies corneal sensitivity by a nylon filament of different lengths touching the cornea to elicit a blink or patient response
- Each quadrant of the cornea can be tested separately

Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. *Clin Ophthalmol*. 2014;8:571-579.

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"It is still blurry…"

- Used a BCL, AB
  - RTC 1wk
  - NO IMPROVEMENT
  - BCL-missing…however the patient stated "It feels fine!"
  - "Can I do surgery on the other eye?"
    - Cotton-tip sensation:
      - OD-5/10
      - OS- 0/10
- Prokera Slim inserted
- Rx'd Oxervate

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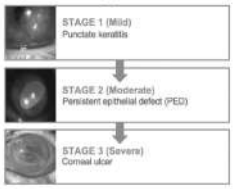
Mackie Classification

NK Is a Degenerative Disease[1]

The Mackie Classification Represents One Way to Assess NK Progression[2,3]



- Some vision loss can potentially be seen in all stages of NK[3]
- If untreated, moderate NK progresses to severe disease with associated risks of profound vision loss resulting from scarring and corneal perforation[3]

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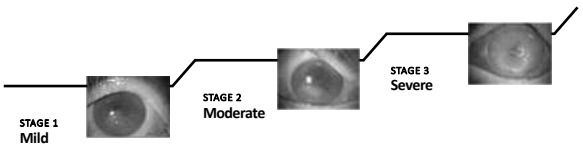
Mackie Classification



- Improve epithelial quality and transparency
- Avoid epithelial breakdown
- Prevent stromal involvement and corneal ulcer formation
- Promote corneal healing
- Stop stromal melting
- Prevent perforation that could lead to potential vision loss

1. Versura P, Giannaccare G, Pellegrini M, Sebastiani S, Campos EC. Neurotrophic keratitis: current challenges and future prospects. *Eye Brain*. 2018;10:37-45. 2. Dua HS, Said DG, Messmer EM, et al. Neurotrophic keratopathy. *Prog Retin Eye Res*. 2018;66:107-131.

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NK Study Group 7 Step Staging

Stage	Clinical Features	Imaging
0	Altered sensation without keratopathy	
1 (mild)	Epithelopathy without stromal haze	
2 (moderate)	Epithelopathy with stromal haze	
Stage 3 (severe)	Persistent or recurrent epithelial defects	

Stage	Clinical Features	Imaging
Stage 4 (severe)	Persistent or recurrent epithelial defect and stromal scarring without corneal ulceration	
Stage 5 (severe)	Persistent or recurrent epithelial defect with corneal ulceration	
Stage 6 (severe)	Corneal perforation	

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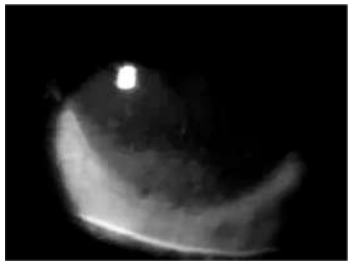
Neurotrophic keratitis



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Neurotrophic keratitis

	Early/less severe (e.g., Stage 1)	Moderate (e.g., Stage 2)	Later/more severe (e.g., Stage 3)
Discontinue all preservative-containing topical medications	+	+	+
Medical management			
Topical preservative-free drops	+	+	+
Topical preservative-free gel drops or ointments	+	+	+
Autologous serum drops, human umbilical cord serum, platelet rich plasma	+	+	+
Recombinant human nerve growth factor (cenegermin)	+	+	+
Prophylactic topical preservative-free antibiotics (excluding aminoglycosides)		+	+
Matrix metalloproteinase inhibitors	+	+	+
Non-surgical intervention (i.e., office procedures)			
Corneal therapeutic contact lenses	+	+	+
Fresh-frozen self-retained amniotic membrane		+	+
Punctal occlusion	+	+	+
Synthetic (cyanoacrylate) tissue adhesive			+
Surgical intervention (i.e., operating room procedures)			
Tarsorrhaphy		+	+
Amniotic membrane transplant		+	+
Corneal neurotization		+	+

[a]Treatments rated as potentially optimal, depending on the patient's individual circumstances
[b]Treatments rated as potentially appropriate, depending on the patient's individual circumstances (not noted in the manuscript)

Dana, R., Farid, M., Gupta, P.K. et al. Expert consensus on the identification, diagnosis, and treatment of neurotrophic keratopathy. BMC Ophthalmol 21, 327 (2021). https://doi.org/10.1186/s12886-021-02092-1

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Neurotrophic keratitis

The 20 most expensive pharmacy drugs in the U.S.

Amryt's Myalept takes the top spot while two newcomers enter the GoodRx rankings.

Drug	Company	Price per month (USD)
1. Myalept	Amryt Pharma	71306
2. Revcovi	Horizon Therapeutics	55341
3. Mepsevii	EMD Serono	53730
4. Actimmune	Horizon Therapeutics	52777
5. Cerezyme	Sanofi	49498
6. Takhzyro	Takeda	49464
7. Doxaprim	Vyera Pharmaceuticals	45800
8. Juxtapid	Amryt Pharma	44714
9. Cinryze	Takeda	44341
10. Cherdelvi	Retrophin	42570

https://www.fiercepharma.com/pharma/20-most-expensive-pharmacy-drugs-u-s-2020

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Monday Morning Patient
Scott Hauswirth, OD

- 71 yo Caucasian female
- 18-month history of dry eye, has seen 8 physicians
- Relatively sudden onset – shortly following uncomplicated cat sx, gradually worsening
- Primary symptoms: constant burning, moderate photophobia
- Treated with Restasis, Xiidra, ATs, Warm compresses, plugs, steroids, LipiFlow
- **"NOTHING HELPS!!"**

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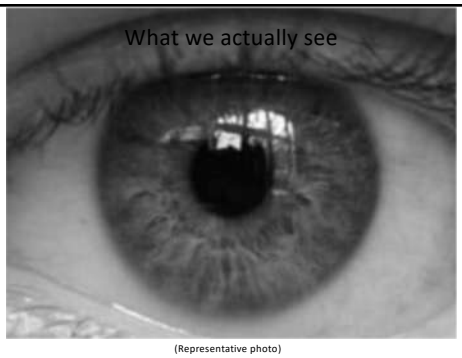

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Signs vs. Symptoms

- There is little correlation between signs and symptoms
- Symptoms may correlate with signs
- Most of us treat according to symptoms

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Treatment Options

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Neuropathic pain & dry eye

"Control / eliminate inflammation and then use your regenerative therapies. The inflammation is what hypersensitizes the nerves in the first place"

Scott Hauswirth, OD

https://www.youtube.com/watch?v=6VZAqNN_JoE

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Neuropathic pain & dry eye

"Don't prescribe stuff that continues to be an irritant to patients - if they don't tolerate Restasis/Cequa/Xiidra or whatever don't continue to push it, find an alternative"

Scott Hauswirth, OD

https://www.youtube.com/watch?v=6VZAqNN_JoE

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Treatment: What to Expect

- **Mild peripheral** cases difficult to differentiate from typical DE discomfort (continuum)
- **Moderate peripheral** cases respond well to combination of neuroregen + DE therapy
- **Centralized** cases (usually with photophobia) will take several months to respond
  - May require management with systemic medications
  - May require more intervention with pain management

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Neurostimulation

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varenicline solution.03mg Oyster Point

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There Is No Substitute for Natural Tear Film

Growth factors, such as nerve growth factor (NGF) and epidermal growth factor (EGF), found in natural human tears, are critical regulators for corneal wound healing.

A healthy tear film lubricates and protects the eyes from injury and infection, washes away foreign particles, and contributes refractive power for clear vision.

TFOS DEWS II tear film report

Natural tears contain a complex mixture of lipids, proteins, mucins, and electrolytes[1,2]

- Over 1,500 proteins
- 5+ lipid classes
- 20+ mucins
- Contains growth factors and has anti-inflammatory and antimicrobial properties

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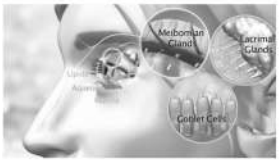
Parasympathetic Nervous System Controls Tear Film Homeostasis

The trigeminal nerve is **accessible within the nasal cavity**, and is activated by OC-01 (varenicline) by stimulating **cholinergic receptors**.

The trigeminal nerve provides the pathway for **parasympathetic stimulation** of the lacrimal functional unit (LFU) to activate **complete natural tear film**.



34% of basal tear production is due to inhaling air through the nose[1]

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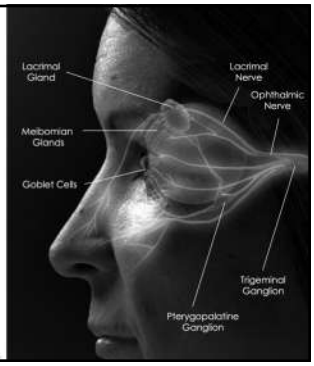
Lacrimal Gland Postganlionic Innervation

- The LFU is innervated by the trigeminal nerve
- Loss of parasympathetic stimuli results in chronic reduction of tear secretion and morphologic destruction of the lacrimal gland



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Anti-Inflammatory

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New Players and Old Friends

Lotemax SM
- (loteprednol etabonate ophthalmic gel) 0.38%
- tid

Inveltys
- (loteprednol etabonate ophthalmic suspension 1%)
- bid

Flarex
- (fluorometholone acetate ophthalmic suspension) 0.1%

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DEXTENZA (Ocular Therapeutix

- Dextenza (dexamethasone ophthalmic insert 0.4% mg)
  - Indicated to treat inflammation and pain following cataract surgery
  - Statistically significant level of patients were pain-free on post-op day 8

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Autologous serum tears

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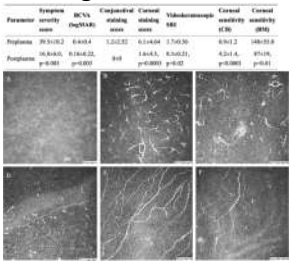
Autologous plasma & nerve regeneration

- Rao (Houston) et al. BJO May 2010
- 11 eyes, 6 pts
- Neurotrophic corneas without active disease
  - Punctate keratopathy / persistent epithelial defects included
- Improvements in aesthesiometry
- Increase in mean CND, CNL, CNW, mean # via confocal
- Complete alleviation in 7, significant improvement in 4



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https://www.youtube.com/shorts/pfAblYPaWHk

:36

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Vital Tears™

https://vitaltears.org

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1:33

https://www.youtube.com/watch?v=3kmTTfGFQgQ

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Amniotic Membrane

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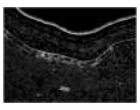
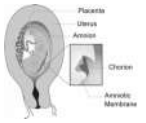
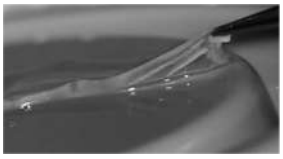
The Amniotic Membrane

- The amniotic membrane is the innermost lining of the placenta (amnion)
- Amniotic membrane shares the same cell origin as the fetus
  - Stem cell behavior
- Structural similarity to all human tissue







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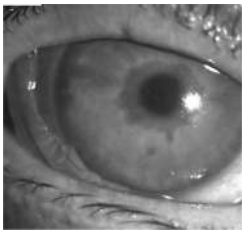
Clinical Study

Corneal Nerve Regeneration after Self-Retained Cryopreserved Amniotic Membrane in Dry Eye Disease

CAM vs. conventional DE Tx	
Reduction in VAS	• 7.1 to 2.2
Reduction in SPEED	• 21.8 to 5.9
Increase in CND/CNL	• Baseline: 12,241 +/- 5083 um/mm^2 • 3 mo: 18,827 +/- 5453 um/mm^2
Improvement in TBUT	• 8.3 +/- 2.5 to 13.9 +/- 2.2
Control group showed no change in all parameters	



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The CRYOTEK™ Method

- Patented and proprietary cryopreservation
- Ensures key active components of the Extracellular Matrix (ECM) are retained
- The **only** method that retains both:
  - The integrity of the tissue structure
  - The key active (ECM) components
- Safe and effective
  - Supported by over **300** peer-reviewed articles
  - Over **100,000** implanted
- Bio-Tissue Cryopreserved Amniotic Membrane is the **ONLY** AM granted wound healing indication by the FDA.

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PROKERA®: BIOLOGIC CORNEAL BANDAGE

PROKERA® utilizes the proprietary CryoTek™ cryopreservation process that maintains the active extracellular matrix of the amniotic membrane which uniquely allows for regenerative healing.

PROKERA® is the only FDA-cleared therapeutic device that both reduces inflammation and promotes scar less healing.

PROKERA® can be used for a wide number of ocular surface diseases with severity ranging from mild, moderate, to severe

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Acellular Amniotic Membrane

ACELLFX
- HCT/P (human cells, tissue, and cellular-based product)
- Nutrient rich
  - Collagen III, IV, and V
  - Fibronectin
  - Lamin
  - Proteoglycans
- Thea Pharmaceuticals

Human amniotic membrane sourced from Cesarean donors

Processed without chemicals, cross-linking agents, germicides or antibiotics

Air dried

Sterilized

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Acellular Amniotic Membrane

- Ready to use immediately
  - No thawing
  - No rinsing
- No up/Down orientation
- Flexible membrane with no ring
- Allows for multiple applications
- Convenient storage at room temperature for 5 eyars
- WOO-WOO

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Only FDA Approved for NK

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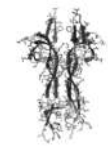
Active ingredient structurally identical to human nerve growth factor produced in ocular tissues



- Naturally occurring neurotrophin is responsible for differentiation, growth, and maintenance of neurons[1]
- The regenerative potential of nerve growth factor (NGF) was discovered by Nobel-prize winning scientists in the early 1950s[1]
- Cenegermin-bkbj, a novel recombinant human nerve growth factor (rhNGF), is **STRUCTURALLY IDENTICAL** to the NGF protein[2]

1. Lambiase A, Rama P, Bonini S, Caprioglio G, Aloe L. Topical treatment with nerve growth factor for corneal neurotrophic ulcers. *N Engl J Med* 1998;338:1174-80. 2. Voelker R. New Drug Treats Rare, Debilitating Neurotrophic Keratitis. JAMA. 2018;320(13):1309.

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FDA APPROVAL WAS BASED ON COMPLETE CORNEAL HEALING DEFINED AS ABSENCE OF STAINING OF THE CORNEAL LESION AND NO PERSISTENT STAINING IN THE REST OF THE CORNEA AFTER 8 WEEKS OF TREATMENT.

CENEGERMIN CLINICAL TRIALS: Study overview

	NGF0212 (REPARO) (n=156)	NGF0214 (n=48)
Geography	Europe 6 Countries (Italy, Germany, UK, France, Spain, Poland) 32 Clinical Centers	USA 11 Clinical Centers
Design	3 treatment arms: (vehicle, cenegermin 10 mcg/mL, cenegermin 20 mcg/mL)	2 treatment arms: (vehicle, cenegermin 20 mcg/mL)
Vehicle & cenegermin composition	Without antioxidant	With antioxidant (methionine)
Duration of follow up	48 weeks	24 weeks
Uni/bilateral disease	Unilateral	Unilateral and bilateral
Endpoints	Week 8 (based on a post-hoc analysis) Complete corneal healing (defined as 0.0 mm maximum diameter of fluorescein staining in the lesion area) *Primary analysis was <0.5 mm maximum diameter of fluorescein staining in the lesion area at Week 4	Week 8 Complete corneal healing (defined as 0.0 mm maximum diameter of fluorescein staining in the lesion area)

1. 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. 2. Pflugfelder SC, Massaro-Giordano M, Perez VL, et al. Topical recombinant human nerve growth factor (cenegermin) for neurotrophic keratopathy: a multicenter randomized vehicle-controlled pivotal trial.

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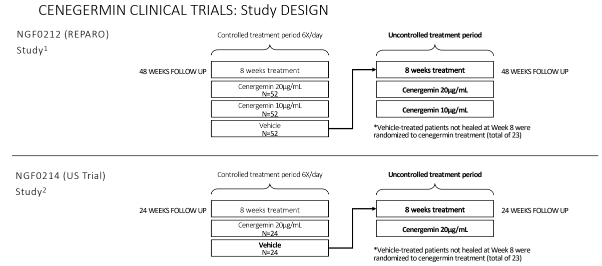
CENEGERMIN CLINICAL TRIALS: Study DESIGN



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CENEGERMIN CLINICAL TRIALS: INCLUSION AND EXCLUSION CRITERIA

MAIN INCLUSION CRITERIA

- Adult NK patients with stage 2 or 3 NK
  - Unilateral NK only in NGF0212/REPARO
  - Unilateral or bilateral NK permitted in NGF0214
- Evidence of decreased corneal sensitivity (<40mm by Cochet-Bonnet aesthesiometer) within the area of the PED or corneal ulcer and outside of the area of the defect, in at least 1 corneal quadrant
- Refractory to ≥1 nonsurgical treatment
- No improvement in in 2 weeks prior to enrollment

MAIN EXCLUSION CRITERIA

- Infection, inflammation, other ocular disease requiring topical treatment
  - Glaucoma patients were switched to systemic meds during the study
- Severe blepharitis or MGD
- Prior surgical treatment for NK
  - Exception for AMT performed >6 weeks prior or membrane disappeared >2 weeks prior
- Stromal involvement in posterior third, corneal melting, or perforation in study eye

1. 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 . 2. Pflugfelder SC, Massaro-Giordano M, Perez VL, et al. Topical recombinant human nerve growth factor (cenegermin) for neurotrophic keratopathy: a multicenter randomized vehicle-controlled pivotal trial. *Ophthalmology*. 2020;127(1):14-26.

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CENEGERMIN CLINICAL TRIALS: BASELINE DEMOGRAPHICS

	NGF0212/REPARO Study[1,3]		NGF0214 (US Trial) Study 2,3	
PRIMARY NK DIAGNOSIS, NO. (%)	OXERVATE® (N=52)	VEHICLE (N=52)	OXERVATE® (N=24)	VEHICLE (N=24)
Stage 2 (moderate)	27 (51.9)	28 (53.8)	15 (62.5)	18 (75.0)
Stage 3 (severe)	25 (48.1)	24 (46.2)	9 (37.5)	6 (25.0)
Underlying cause, no. (%)				
Herpetic eye disease	11 (21.2)	18 (34.6)	9 (37.5)	8 (33.3)
Neurosurgical procedure	8 (15.3)	7 (13.4)	1 (4.2)	5 (20.8)
Ocular surgery or procedure	5 (9.6)	7 (13.4)	3 (12.5)	4 (16.7)
Dry eye disease	6 (11.5)	5 (9.6)	3 (12.5)	3 (12.5)
Ocular surface injury/inflammation	5 (9.6)	5 (9.6)	2 (8.3)	1 (4.2)
Other	5 (9.6)	3 (5.8)	2 (8.3)	1 (4.2)
Topical medication (glaucoma)	1 (1.9)	1 (1/9)	1 (4.2)	1 (4.2)
Stroke	2 (3.8)	0	0	1 (4.2)
Unknown origin	1 (1.9)	0	2 (8.3)	0
Systemic medication	0	0	1 (4.2)	0

The formulation that was tested in REPARO (Study NGF0212) did not include the antioxidant methionine and is not the final formulation that is marketed as OXERVATE®. Methionine is an excipient added to the commercial formulation to improve its stability. More than one study was conducted with the final commercial formulation. No difference in safety was seen in either of the trials.

1. 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. 2. Pflugfelder SC, Massaro-Giordano M, Perez VL, et al. Topical recombinant human nerve growth factor (cenegermin) for neurotrophic keratopathy: a multicenter randomized vehicle-controlled pivotal trial. *Ophthalmology*. 2020;127(1):14-26.
3. Accessdata.fda.gov. Drug approval package: OXERVATE (Cenegermin-bkbj). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/761094Orig1s000SumR.pdf.

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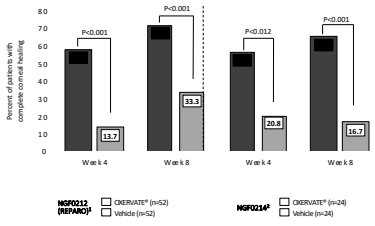
CENEGERMIN CLINICAL TRIALS: RESULTS



Safety: The most common adverse reaction was eye pain following instillation which was reported in approximately 16% of patients. Other adverse reactions occurring in 1-10% of OXERVATE® patients and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation and tearing[3]

Complete corneal healing defined as 0-mm staining in the lesion area and no other persistent staining in the rest of the cornea after 8 weeks of treatment(last post-baseline observation carried forward; chi-squared test).

The formulation that was tested in REPARO (Study NGF0212) did not include the antioxidant methionine and is not the final formulation that is marketed as OXERVATE®. Methionine is an excipient added to the commercial formulation to improve its stability. More than one study was conducted with the final commercial formulation. No difference in safety was seen in either of the trials.

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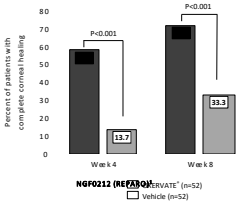
CENEGERMIN CLINICAL TRIALS: ngf0212 1-year follow-up data



80% of patients who achieved complete corneal healing* in Study NGF0212 (REPARO) were still healed 48 weeks after completing one 8-week OXERVATE® treatment cycle[1,2]

*Complete corneal healing defined as 0-mm staining in the lesion area and no other persistent staining in the rest of the cornea after 8 weeks of treatment

The formulation that was tested in REPARO (Study NGF0212) did not include the antioxidant methionine and is not the final formulation that is marketed as OXERVATE®. Methionine is an excipient added to the commercial formulation to improve its stability. More than one study was conducted with the final commercial formulation. No difference in safety was seen in either of the trials.

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1. 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. 2. Data on file. Clinical study report. Study NGF0212. Boston, MA: Dompé U.S. Inc.; 2016.. 3. OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/ml) [US package insert]. Boston, MA: Dompe U.S. Inc.; 2019.

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CENEGERMIN CLINICAL TRIALS: safety results

- No serious adverse reaction related to the treatment occurred in any clinical trials[1,2]
- The majority of adverse reactions were mild and transient ocular reactions that did not require treatment discontinuation or any corrective treatment[1,2]

The most common adverse reaction was eye pain (16%) following instillation, which was reported in approximately 16% of patients.[3]

12/75 = 16%
7/21 = 30.4% (LIS Trial)
5/52 = 9.6% (REPARO)

Other adverse reactions occurring in 1%-10% of patients taking OXERVATE® and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation, and tearing.[3]

1. 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. 2. Pflugfelder SC, Massaro-Giordano M, Perez VL, et al. Topical recombinant human nerve growth factor (cenegermin) for neurotrophic keratopathy: a multicenter randomized vehicle-controlled pivotal trial. *Ophthalmology*. 2020;127(1):14-26 3. OXERVATE® (cenegermin-bkbj) ophthalmic

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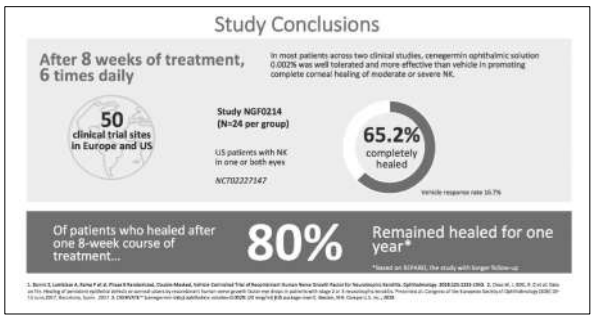

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Recombinant NGF

- Multiple studies support use of NGF to repair damaged nerves
- Oxcervate (Dompe, Italy)
  - FDA approval December 2018 for neurotrophic keratitis
  - 85,000 x 6 weeks
- NGF also important for epithelial cell turnover & migration[1], LSCN maintenance[2]
- Could it be used to mitigate pain response?

1) Blanco-Mezquita T, et al. IOVS, 2013 Jun 6;54(6):3880-90.
2) Kalil S, et al. Stem Cells. 2019 Jan;37(1):139-143.

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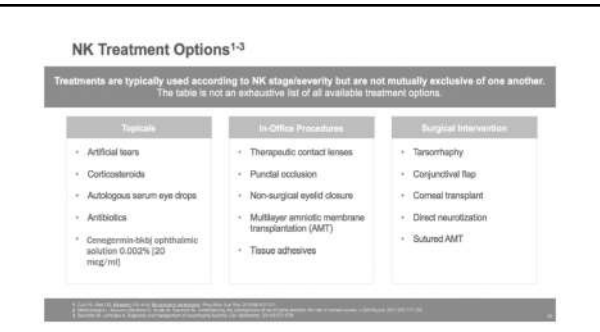

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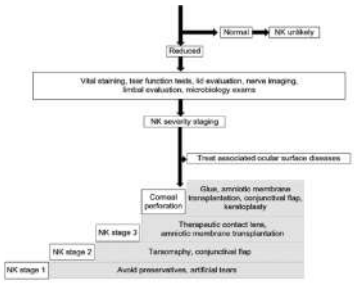
Treatment Algorithms



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Cases

70

Stage 1 NK

- 45 yo Female
- Medical Hx
  - Diabetic
    - Neuropathy
    - Retinopathy
      - PPPV
      - Severe dry eyes
        - Punctal plugs
      - CC: "my eyes ae really irritated, tearing, itching, light sensitive and my vison is blurry"
        - "I can't drive comfortably and reading is difficult"

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Current Therapy

- Has tried the following and found no symptom relief:
  - cyclosporine ophthalmic emulsion 0.05%
  - lifitegrast ophthalmic solution 5%
  - topical steroids
  - topical antibiotic ointment and drops
- Using warm compresses and lid scrubs
- Taking 4000 IU omega-3 fatty acids
- Plugs did not help: OD is gone, OS present but states OS is worse
- Has used and is using OCT PF AT without relief

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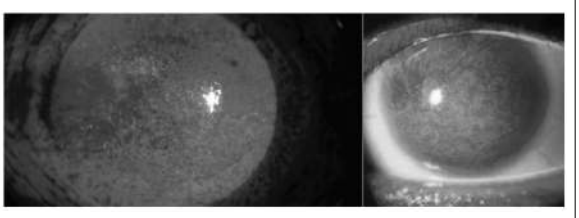

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What would you do next?

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Stage 1 NK

- Swirl like staining to cornea
- Hx of topical treatment with out success
- Question between sever dry eye and early NK
  - It is a fine line between the two

75

Treatment

- Started
  - AcellFx AM
  - Ivizia q1h
  - Ordered Oxervate
- Two weeks of being on Oxervate
  - VA improved
  - Pateint felt happy
- After using 8 week course the eye has remained stable for over a year

76

Case 2

77

- 78 yo Female
- "Constant feeling of a contact in my left eye"
- Seeing local OD for contact lens treatment in left eye
- Medical History
  - Diabetes

78

Ocular History

2/2018 phaco with IOL
2/28/2018 emergent CPC for increased IOP
CME OS: S/P multiple IV VEGF injections OS
Meds:

- Bimatoprost 0.01% OU QHS
- Brinzolamide/brimonidine 1%/0.2% TID OD
- Prednisolone acetate 1% TID OS
- Moxifloxacin TID OS
- Acyclovir 400 mg PO BID
- Artificial tears PF AT PRN

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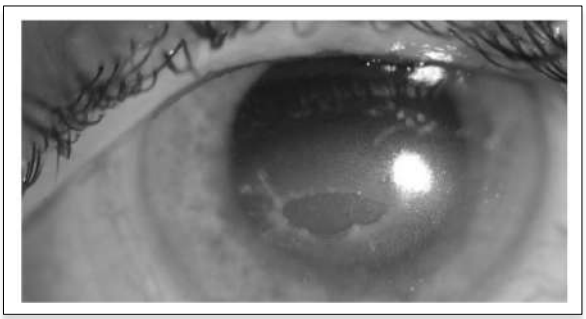
Case 2

- Ocular Findings
  - Vasc
    - OD CF @5ft and OS 20/20
  - IOP
    - 19 mmHg OU
  - Slit lamp exam OS:

80



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Case 2

- Cotton-Tip Wisp
  - OD-7/10
  - OS-2/10
- Diagnosed Stage 2 NK
  - Prokera AM inserted
  - Oxervate Ordered

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Thank you

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