

New Therapeutics Update

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Eric E.
Schmidt, O.D.,
F.A.A.O.

- In the past 24 months, Dr Schmidt has received an honorarium or fees from the following:
- Allergan- Consultant, Advisory Board
- Topcon - Consultant
- Tarsus - Consultant
- Eyenovia – Consultant
- Thea Labs- Consultant
- Trukera - Consultant
- B&L – Consultant
- Harrow Pharmaceuticals
- Lumenis
- Sydnexis
- Sight Science
- Visus
- M&S Technology

But really, is there
anything new????



The Dry Eye Scene

Tell Me About Something New... Please!!



The newest thing in Dry Eye- Miebo

- Miebo (Perfluorohexyloctane) – B&L
- Indicated for treatment of evaporative Dry Eye Disease
- Mimics critical function of meibum
- QID (for how long)?

Miebo – Mechanism of Action



- Meibo is a perfluorocarbon
- A portion of the molecule anchors in the lipid layer
- The other portion rises away from the lipid layer
- Creates a low surface tension which allows for rapid spread across surface
- Forms an anti-evaporative layer
- Inhibits tear film evaporation for up to 6 hrs

Miebo – unique characteristics

- 100% drug (active ingredient)
- No vehicle
- No preservative
- No water
- Very small drop (11 mcl)
- Safe for long term usage
- Indicated for evaporative dry eye

- Reduces blink friction
- Improves tear film homeostasis
- Gets into glands and stays for 24 hrs
- Reduces evaporation by 28%
(even more w/ more meibum)

How do you diagnose evaporative dry eye?

So where does
Miebo fit into our
dry eye protocol?





The Next Newest Thing in Dry Eye





Vevye – Harrow Pharmaceuticals

- Cyclosporine 0.1%
- Just a super-charged Restasis?
- What's the difference?
- What's the Big Deal?



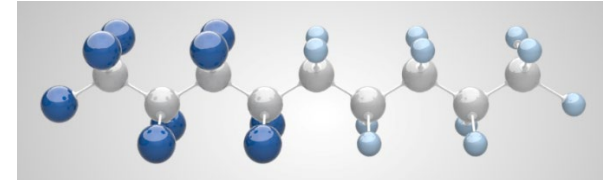
Vevye

- Released in January 2024
- Cyclosporine 0.1%
- BID dosing
- For chronic treatment of dry eye
- No pH, No water, No preservatives
- Vehicle – Perfluorobutylpentane (SFA)

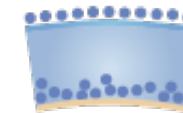
Water-free CsA 0.1% unfolds the full potential of cyclosporine

- Cyclosporine 0.1% dissolved in a semi-fluorinated alkane (Perfluorobutylpentane) solution for treatment of signs and symptoms of dry eye disease dosed BID
- free of oils, surfactants, or preservatives with superior spreading properties
- no pH, no osmolarity

**Perfluorobutyl-
pentane (SFA)
vehicle**



**Spreading and
API penetration**



~22x

Higher concentration that other cyclosporine emulsions approved for DED²

**Surface
residence time**



up to 8 hours

On the ocular surface^{1,2}

Comfort



10µl



Preservative
free

99.8%

of patients experienced either no or mild instillation site pain^{3,4}

Note: * development name of the water-free ophthalmic cyclosporine solution, 0.1 % in perfluorobutylpentane

¹⁾ ARVO 2018, Poster: Krösser S, et al.; ²⁾ Agarwal P, et al.. Int J Pharm. 2018 Mar; ³⁾ Sheppard JD, et al. Cornea. 2021 Oct; ⁴⁾ Akpek EK, et al. JAMA Ophthalmol. 2023 Apr

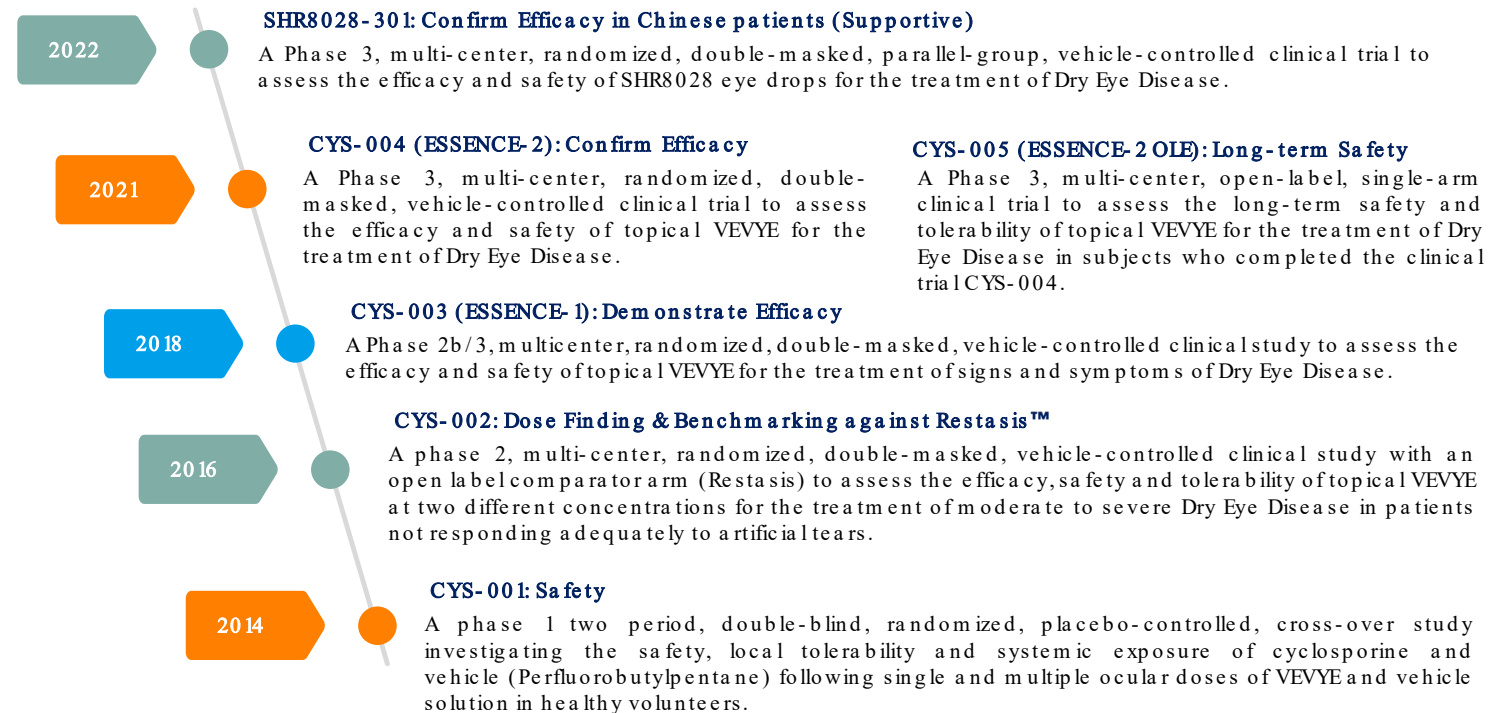
FDA-Approved Cyclosporine Formulations



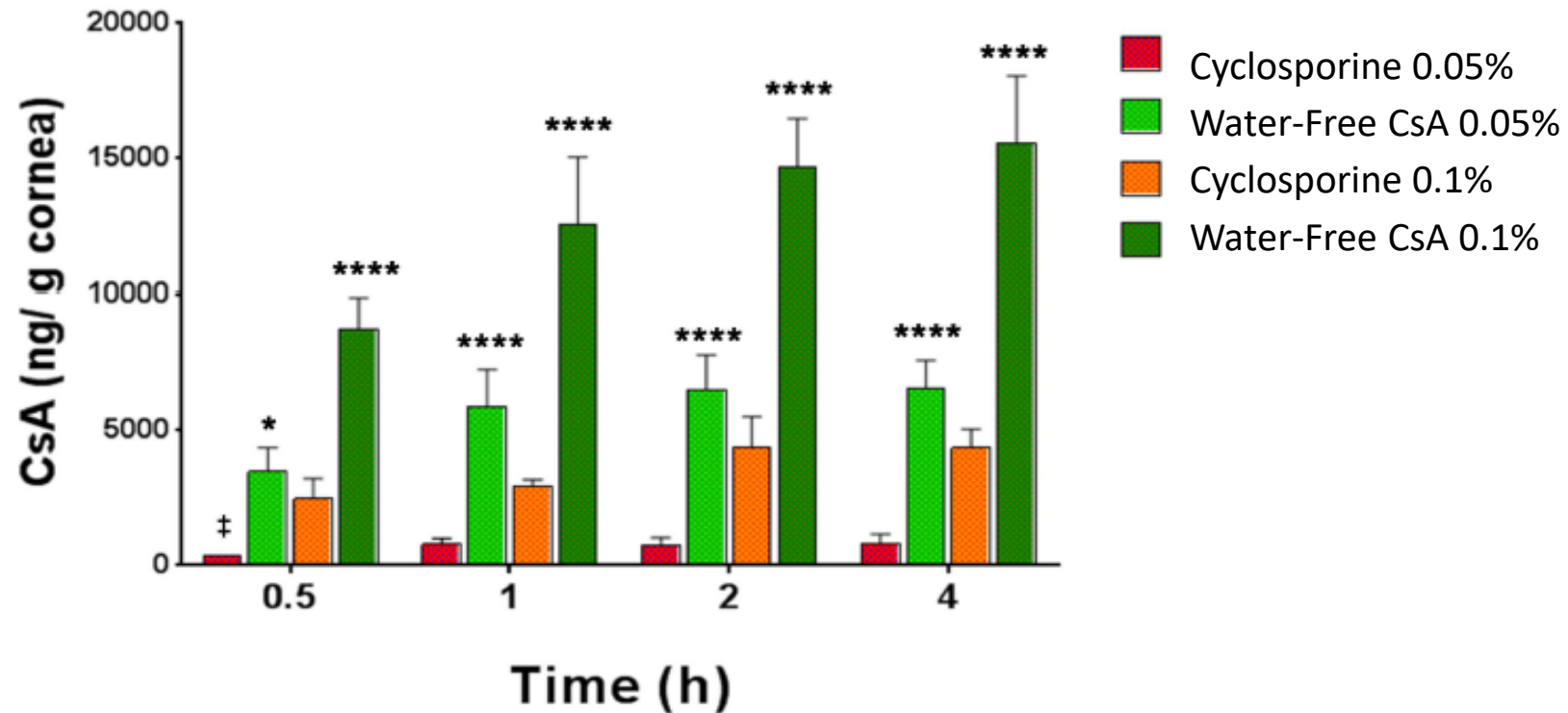
U.S. Launch Date	2023	2002	2019
Active Ingredient	Cyclosporine 0.1% Inactive: Perfluorobutylpentane	Cyclosporine .05%	Cyclosporine .09%
Indication	Signs and Symptoms of Dry Eye Disease	Increased Tear Production	Increased Tear Production
Primary Endpoint	29 Days	6 months	84 Days
pH Osmolality	None None	6.5 - 8.0 230 - 320 mOsmol/kg	6.5 - 7.2 160 - 190 mOsmol/kg
Tolerability Instillation Site Pain	8% (99.8% none or mild)	17%	22%

- Water-free CsA 0.1% was studied in >1,500 Patients with Moderate to Severe DED

In clinical studies worldwide

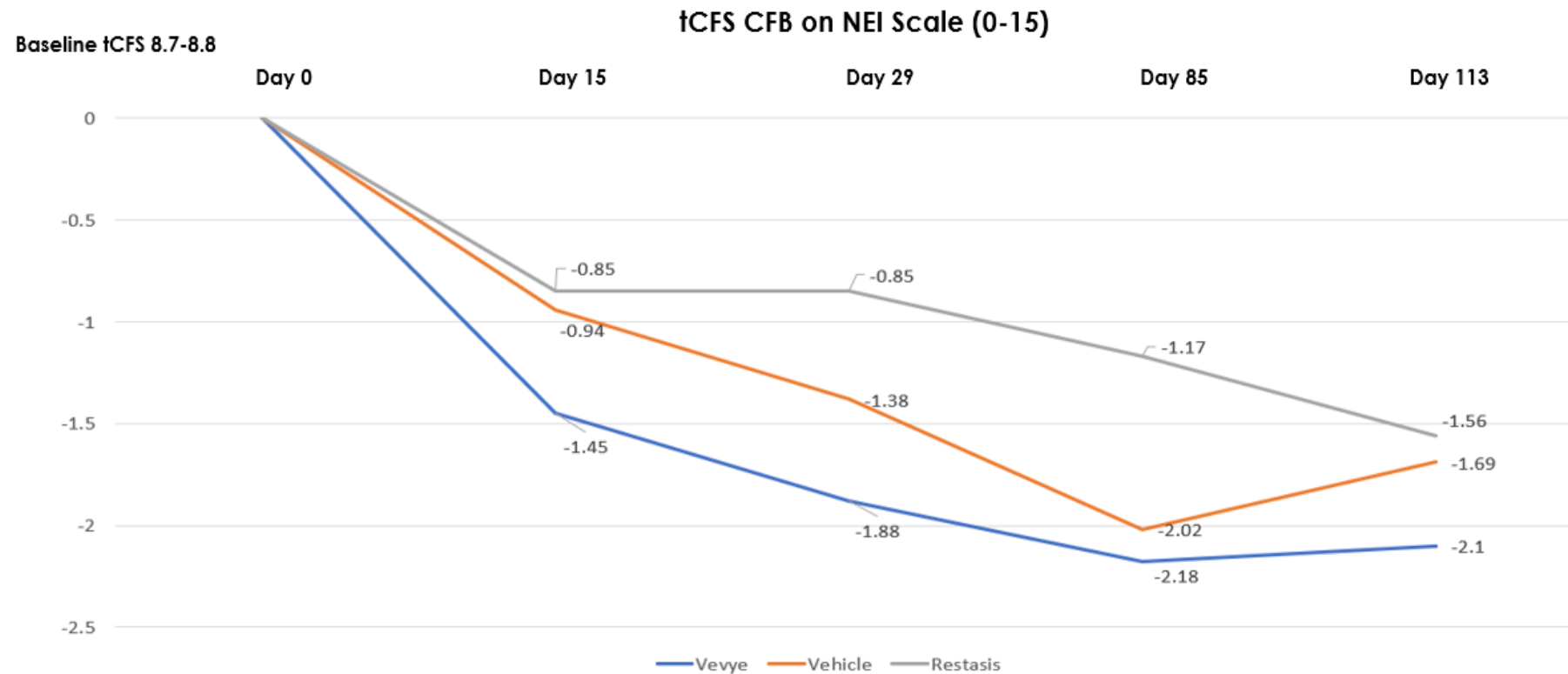


Ex-vivo Corneal Permeability of Cyclosporine in Porcine Eyes

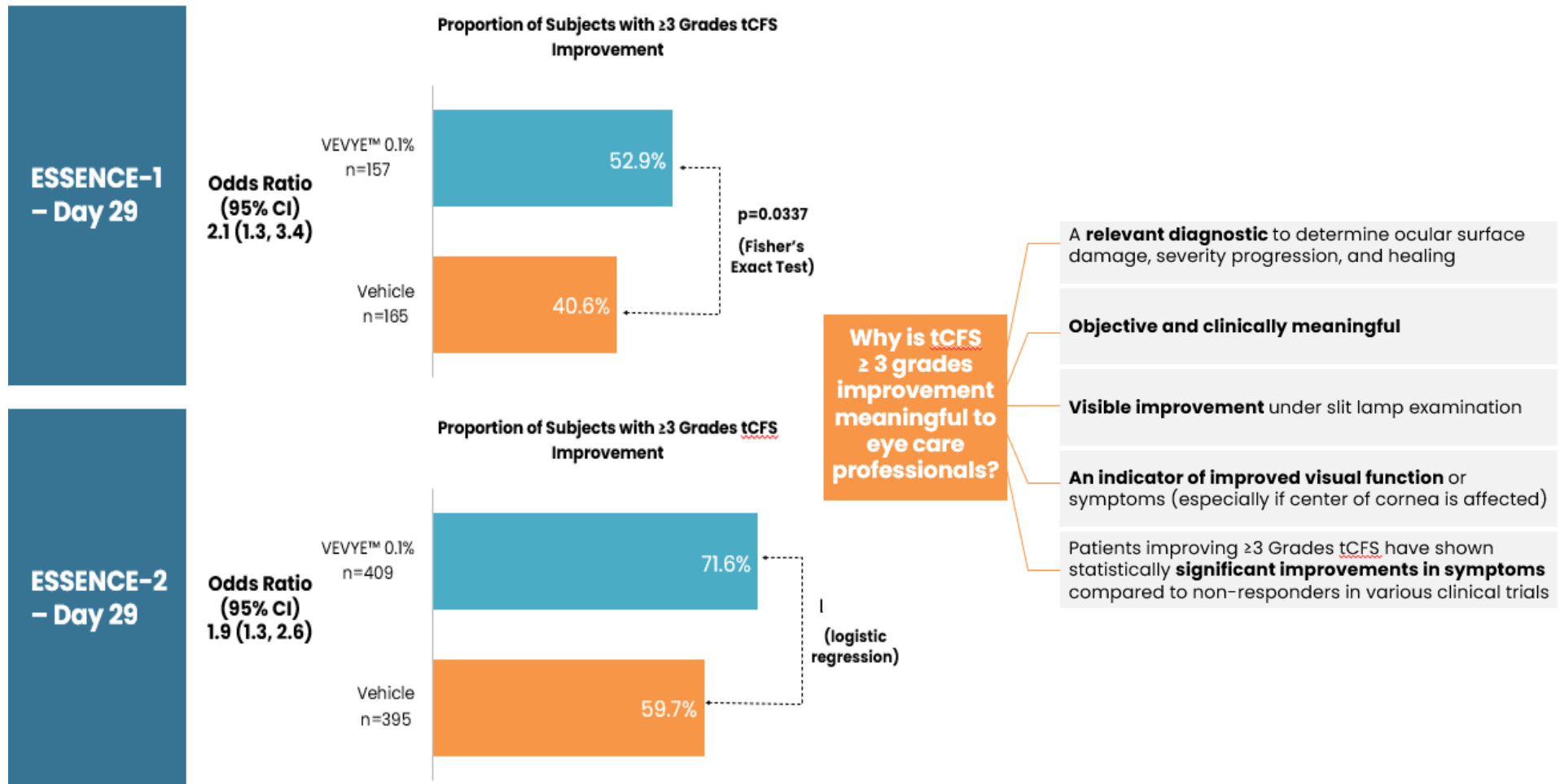


Water-Free Cyclosporine 0.1% Phase II Study

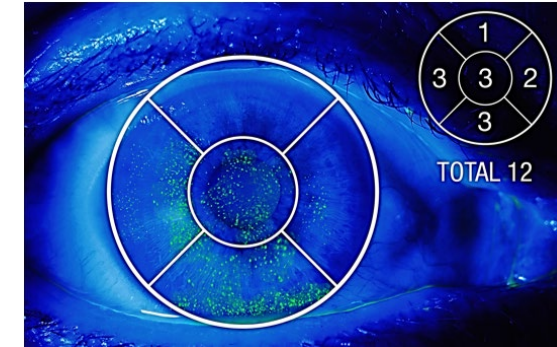
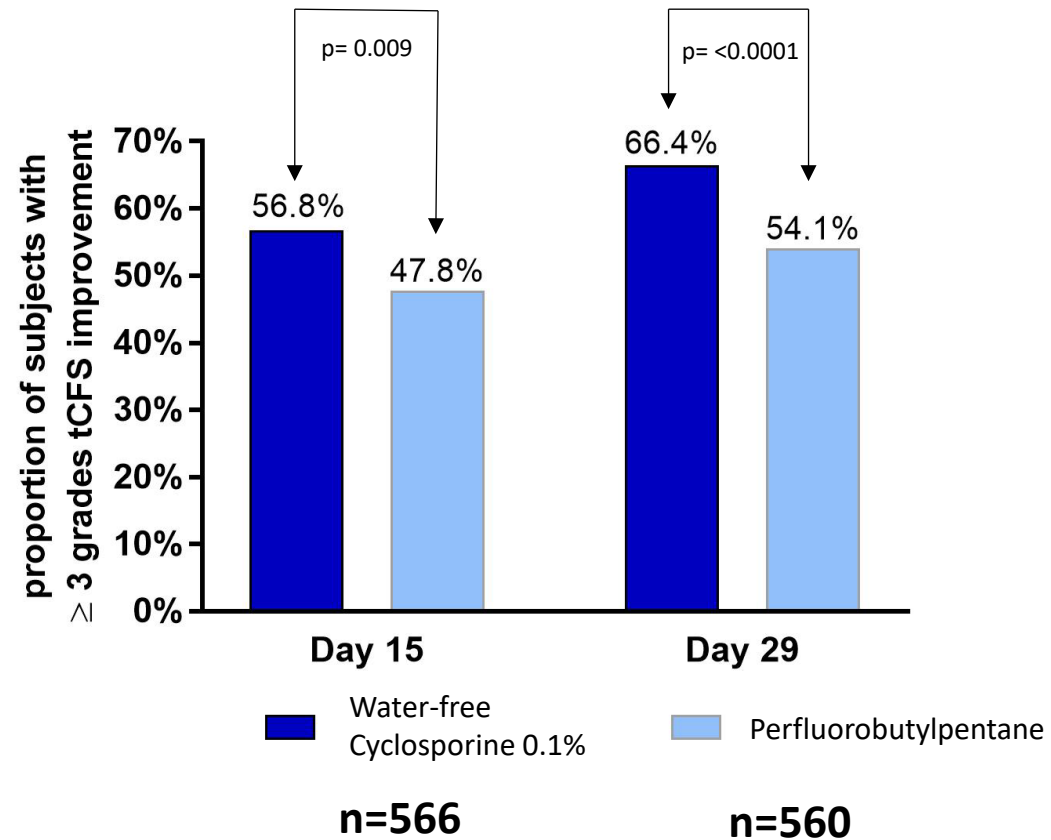
A Phase II Study to Assess Efficacy, Safety, and Tolerability of Vevye



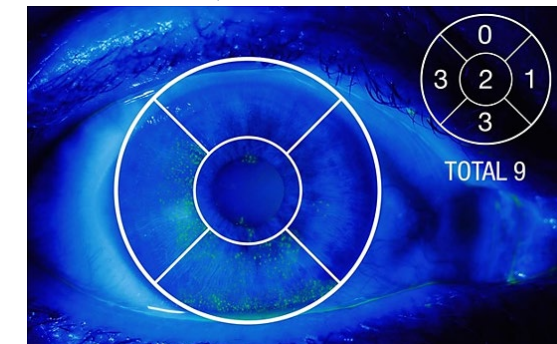
Water-Free CsA 0.1% demonstrated significantly meaningful tCFS improvement in ESSENCE-1 and ESSENCE-2



Majority of Patients Benefit from Water-free Cyclosporine 0.1% Therapy Within 2 Weeks



-3 grades



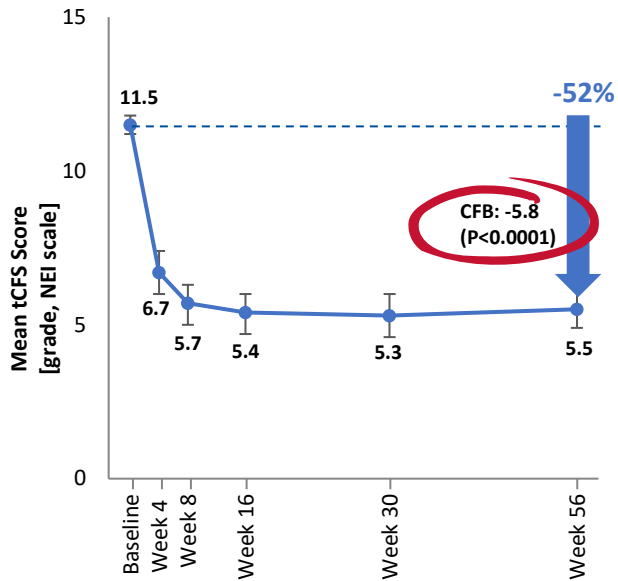
Note: tCFS: Total Corneal Fluorescein Staining, scale ranges from 0 – 3 (highest) per every of 5 regions
CFB: Change from baseline, NEI: National Eye Institute

ESSENCE 2-OLE: 12-Month Sign and Symptom Improvement

Water-free CsA 0.1% maintained clinical benefit over more than 12 months in both sign and symptom improvements for DED patients

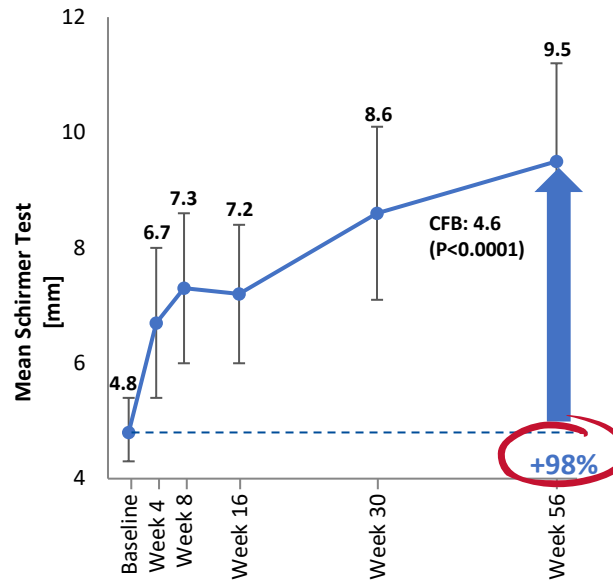
Signs

Corneal staining (tCFS)



n 98 98 93 92 85 85

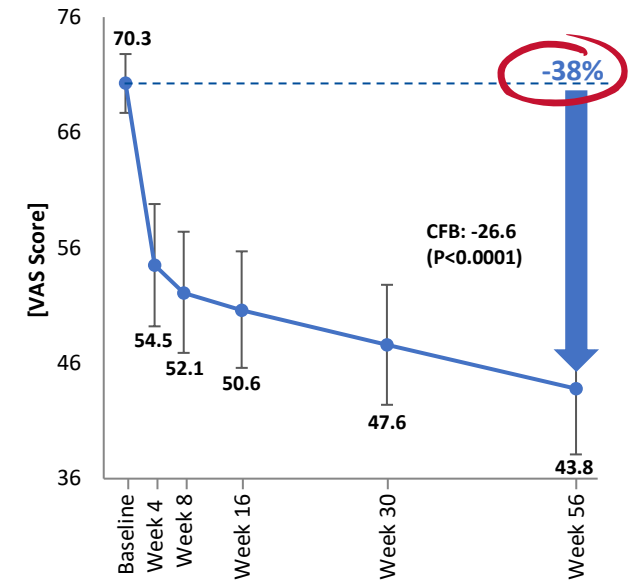
Tear production (Schirmer's test)



n 98 98 93 92 85 85

Symptoms

Discomfort (Dryness score)



n 98 98 93 92 85 85

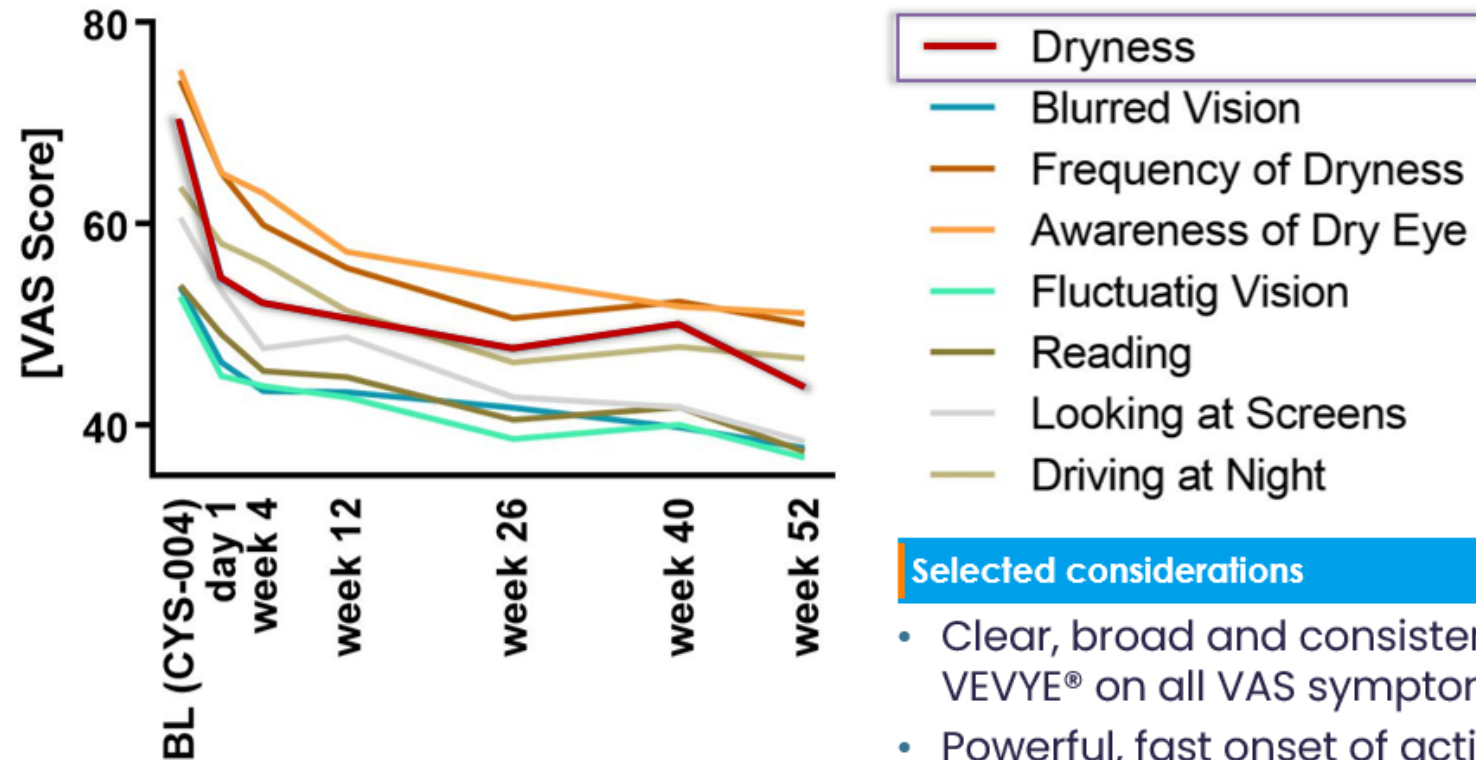
1 patient discontinued treatment due to an adverse event (mild stinging) in the 56-week study.

Note: Analysis shows mean change from baseline with p-value for the difference in least square means. tCFS: Total Corneal Fluorescein Staining, DED: Dry Eye Disease, CFB: Change From Baseline.

1) Akpek E, et al. Submitted to AJO.

Efficacy of All VAS Symptoms Over 12 Months

VAS symptoms (VEVYE® only)



Number of
enrolled
patients (n)

98	98	93	92	85	85	85
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Selected considerations

- Clear, broad and consistent effect of VEVYE® on all VAS symptom sub-criteria
- Powerful, fast onset of action followed by deepening efficacy over time up to 52 weeks

Water-free CsA 0.1% with its SFA vehicle (perfluorobutylpentane) was safe and well-tolerated with minimal reports of TEAEs between treatment groups

	ESSENCE-1		ESSENCE-2		OLE
All AEs	Vevye N= 162	Vehicle N= 166	Vevye N= 423	Vehicle N= 411	Vevye N= 200
Number of subjects with at least one TEAE	46 (28.4%)	44 (26.5%)	71 (16.8%)	73 (17.8%)	97 (48.5%)
Number of subjects with treatment-emergent SAEs	0 (0.0%)	3 (1.8%)	2 (0.5%)	3 (0.7%)	4 (2.0%)
Number of subjects discontinued treatment due to an AE	3 (1.9%)	0 (0.0%)	2 (0.5%)	3 (0.7%)	3 (1.5%)
Ocular AEs					
Number of subjects with at least one ocular TEAE	20 (12.3%)	14 (8.4%)	57 (13.5%)	62 (15.1%)	55 (27.5%)
Number of subjects with at least one treatment related ocular TEAE	9 (5.6%)	5 (3.0%)	46 (10.9%)	44 (10.7%)	20 (10%)
Ocular AEs occurring in more than 2% of patients					
Visual acuity reduced	5 (3.1%)	3 (1.8%)	7 (1.7%)	13 (3.2%)	6 (3.0%)
Instillation site pain/pruritus					
• Mild	4 (2.5%)	2 (1.2%)	42 (9.9%)	35 (8.5%)	13 (6.5%)
• Moderate	0	0	1 (0.2%)	1 (0.2%)	0
• Severe	0	0	0	0	0
Vision blurred	2 (1.2%)	4 (2.4%)	2 (0.5%)	2 (0.5%)	2 (1%)

Vevye – Clinical Info

BID chronically

2 ml bottle, very small drop size

Non-preserved

The vehicle is super important

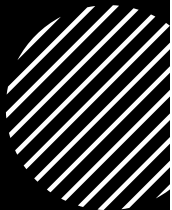
Works on both signs and symptoms (in as quick as 2 weeks????)

MOA- similar to cyclosporine and also to Xiidra as it works on ICAM1 as well.

Does the vehicle provide an additional MOA?



How Much Does It Cost?



Great News – There's A
Coupon!!!



Phil RX is the 3rd Party
Pharmacy



Harrow has stated a \$79 cap
on cost- Yeah Right...

Does It Really Work???



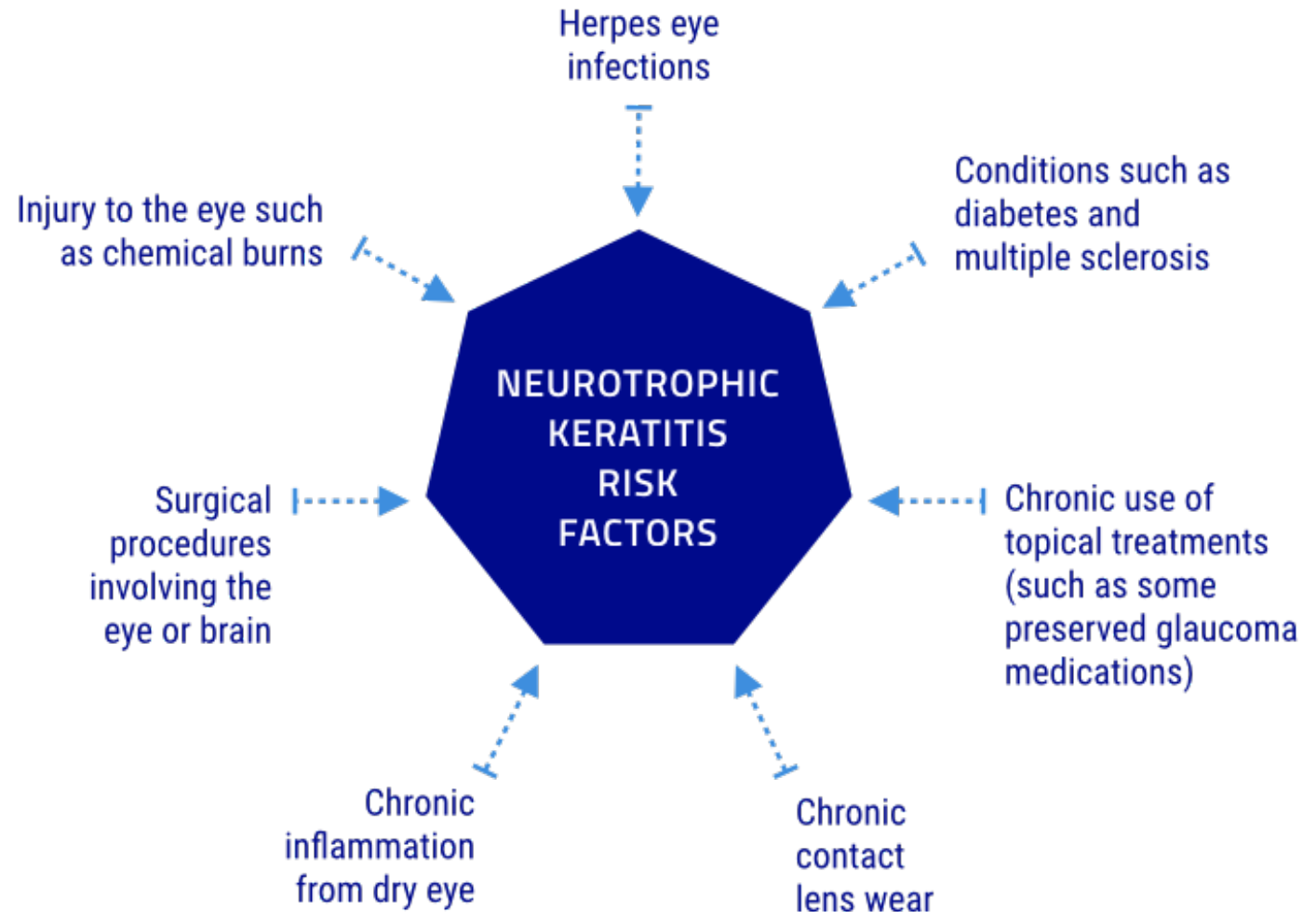
The New Dry Eye Hot Topic- Neurotrophic Keratitis!

- What is NK?
- How does it look clinically?
- What are the symptoms?
- How do you diagnose NK?
- How do you treat NK?

Neurotrophic keratitis

- Degenerative Corneal Disease Characterized by:
 - Impaired corneal healing
 - Decreased Corneal sensitivity
 - Spontaneous epithelial breakdown
- There is usually a predisposing cause, but impaired trigeminal nerve innervation is the root
- Symptoms may be absent- certainly underwhelming in comparison to their corneal appearance

Neurotrophic Keratitis





NK symptoms

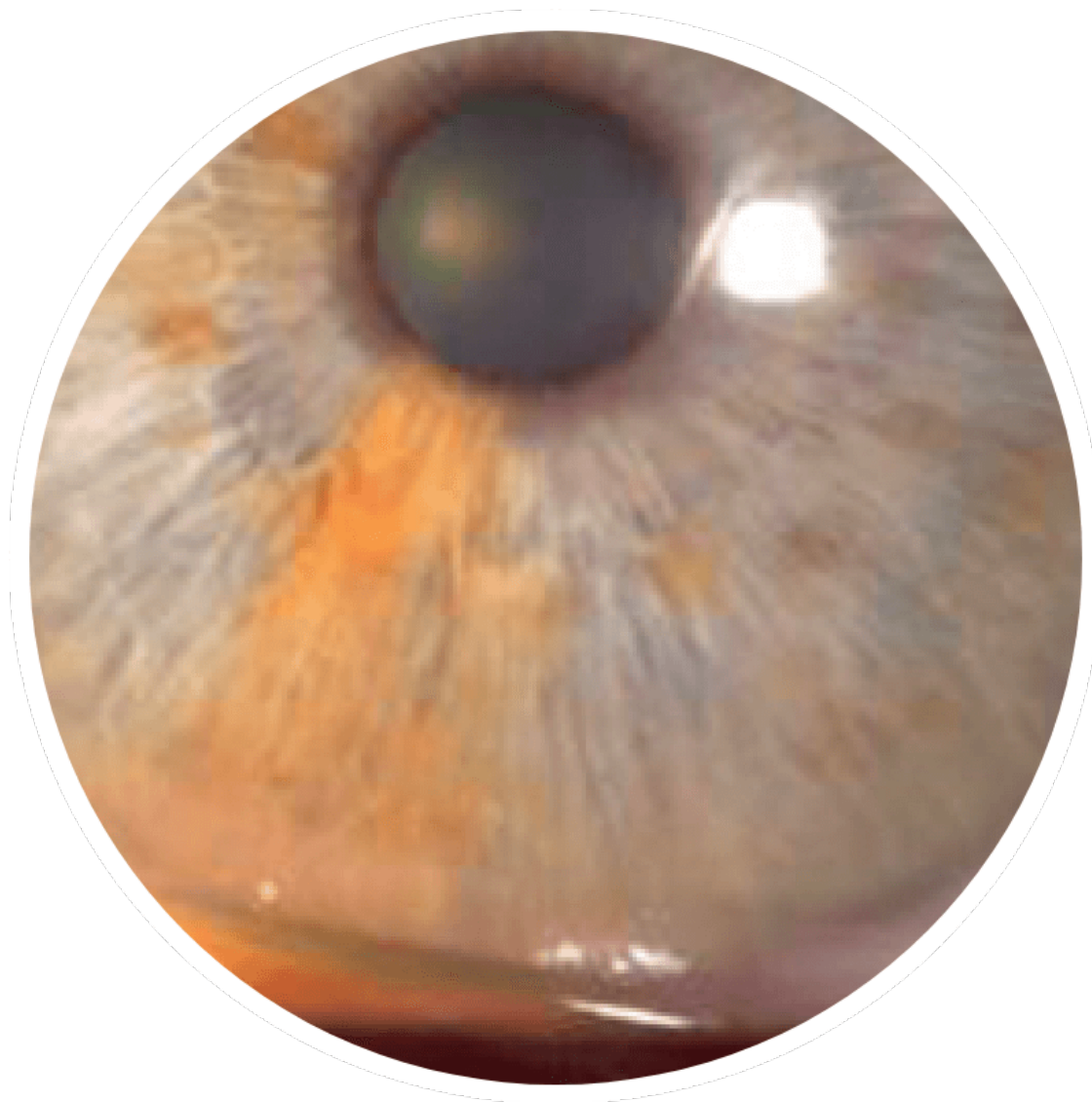
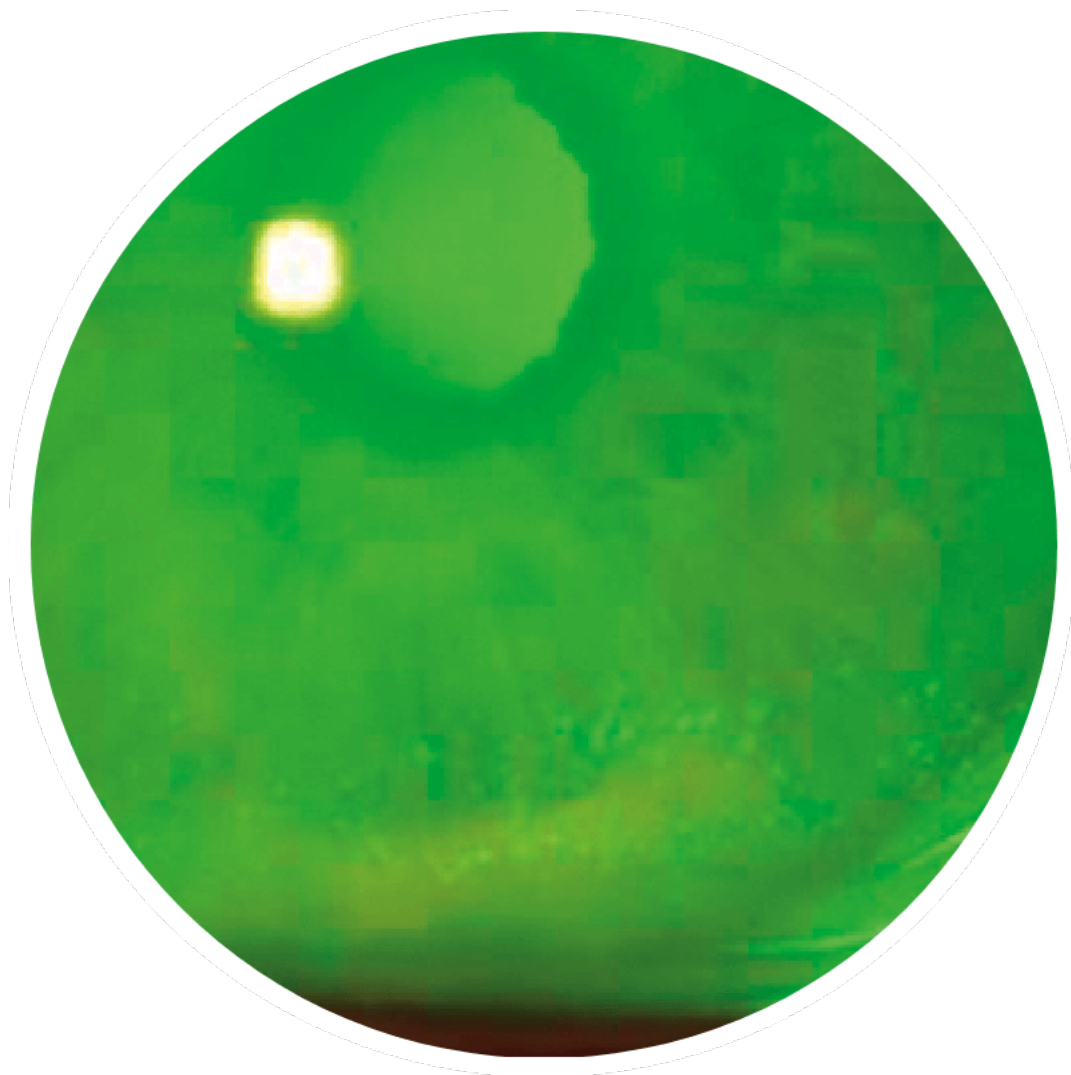
- Dryness
- Reduced Blink
- Blurred Vision
- Photophobia
- Px may be asymptomatic

NK- Diagnosis

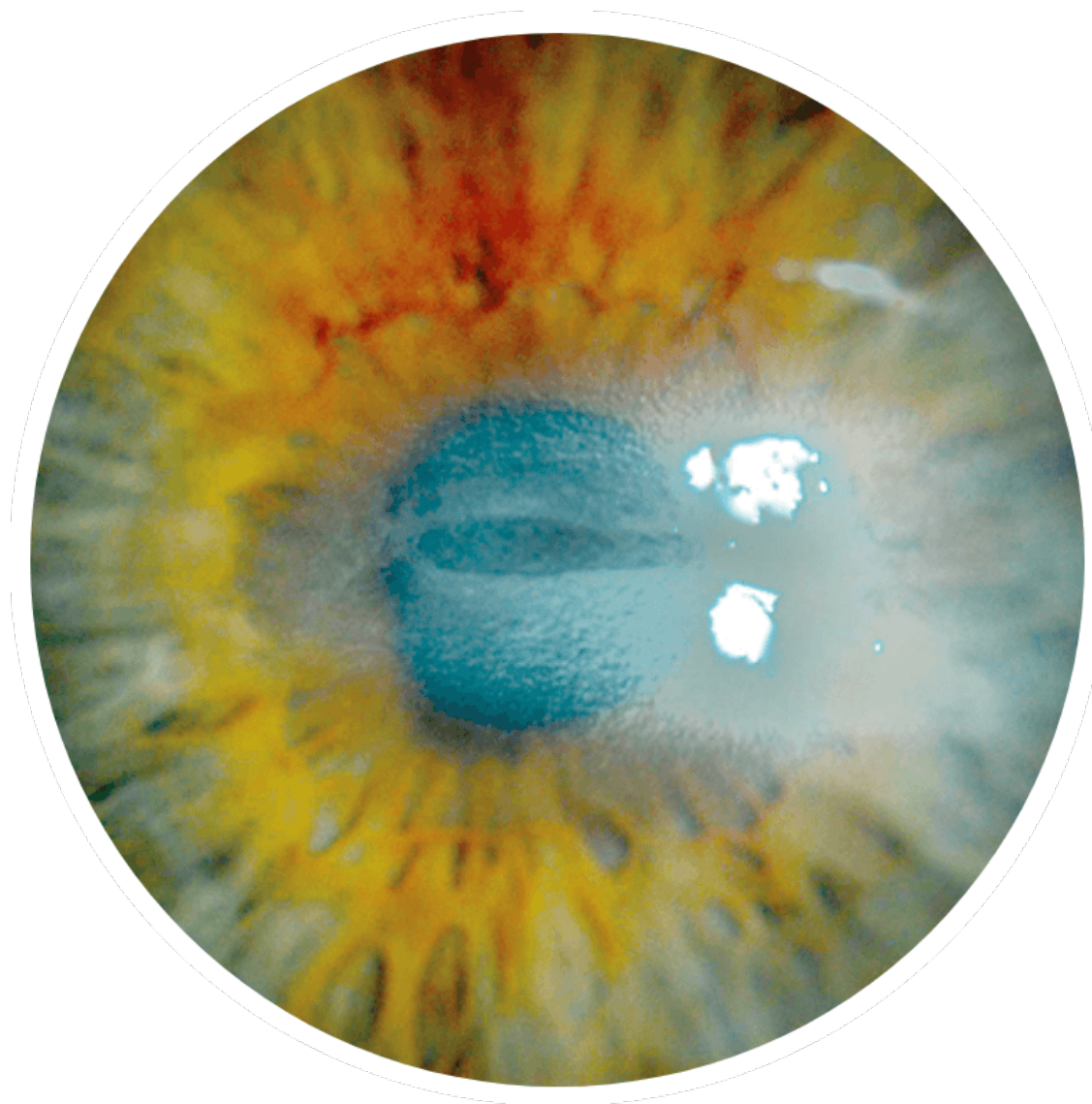
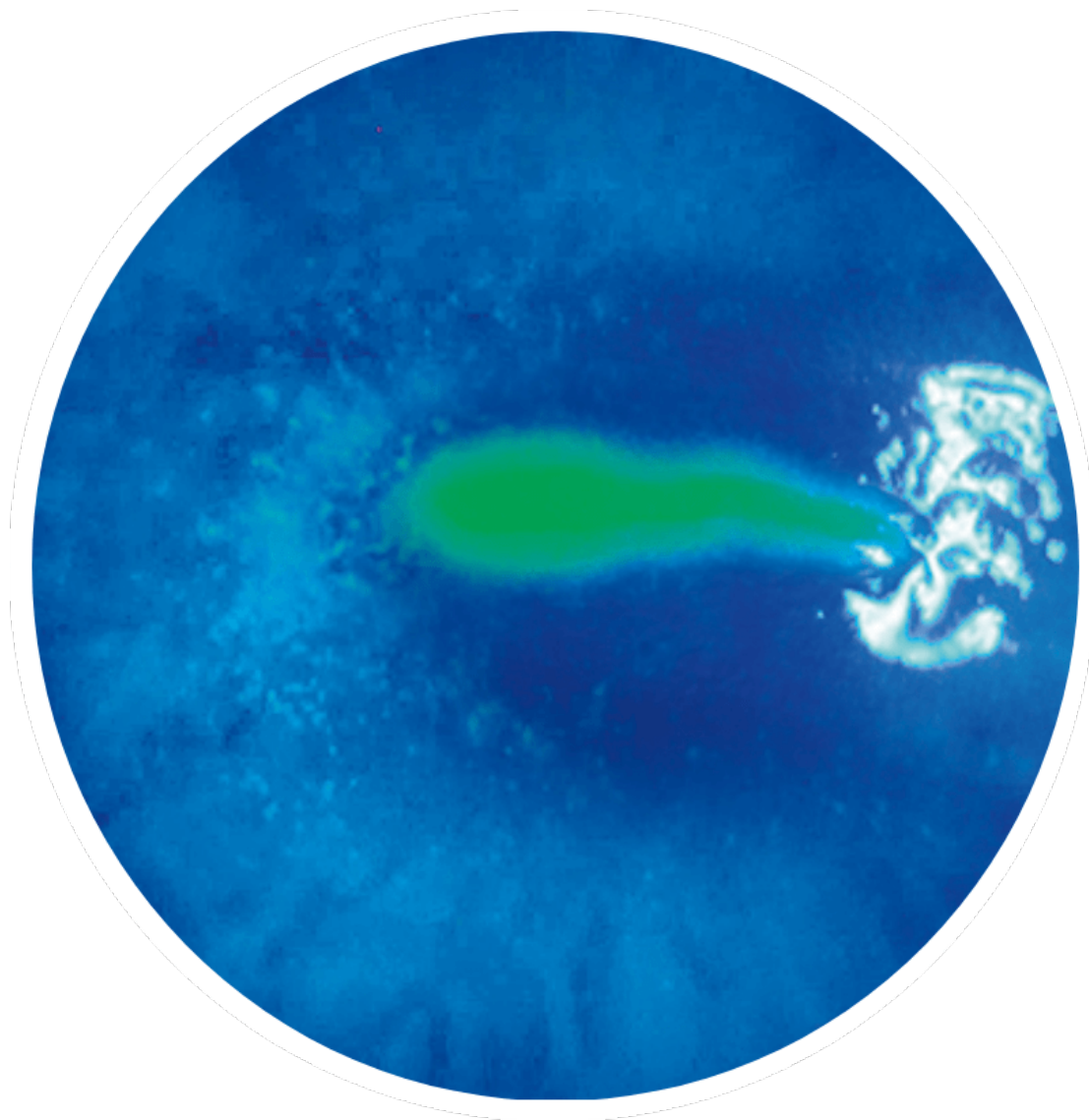
- History
- Slit lamp exam – corneal appearance
- Corneal sensitivity testing



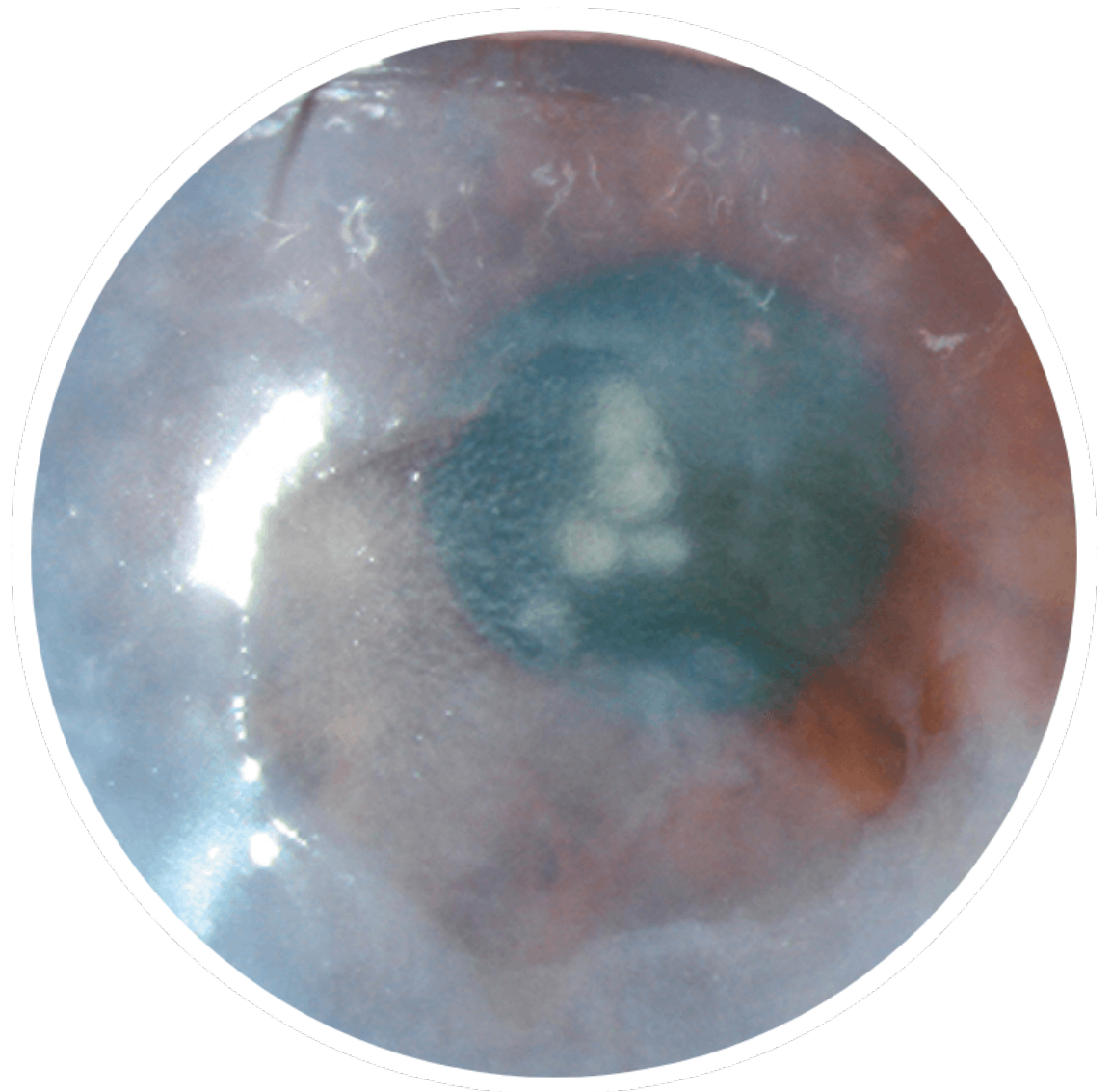
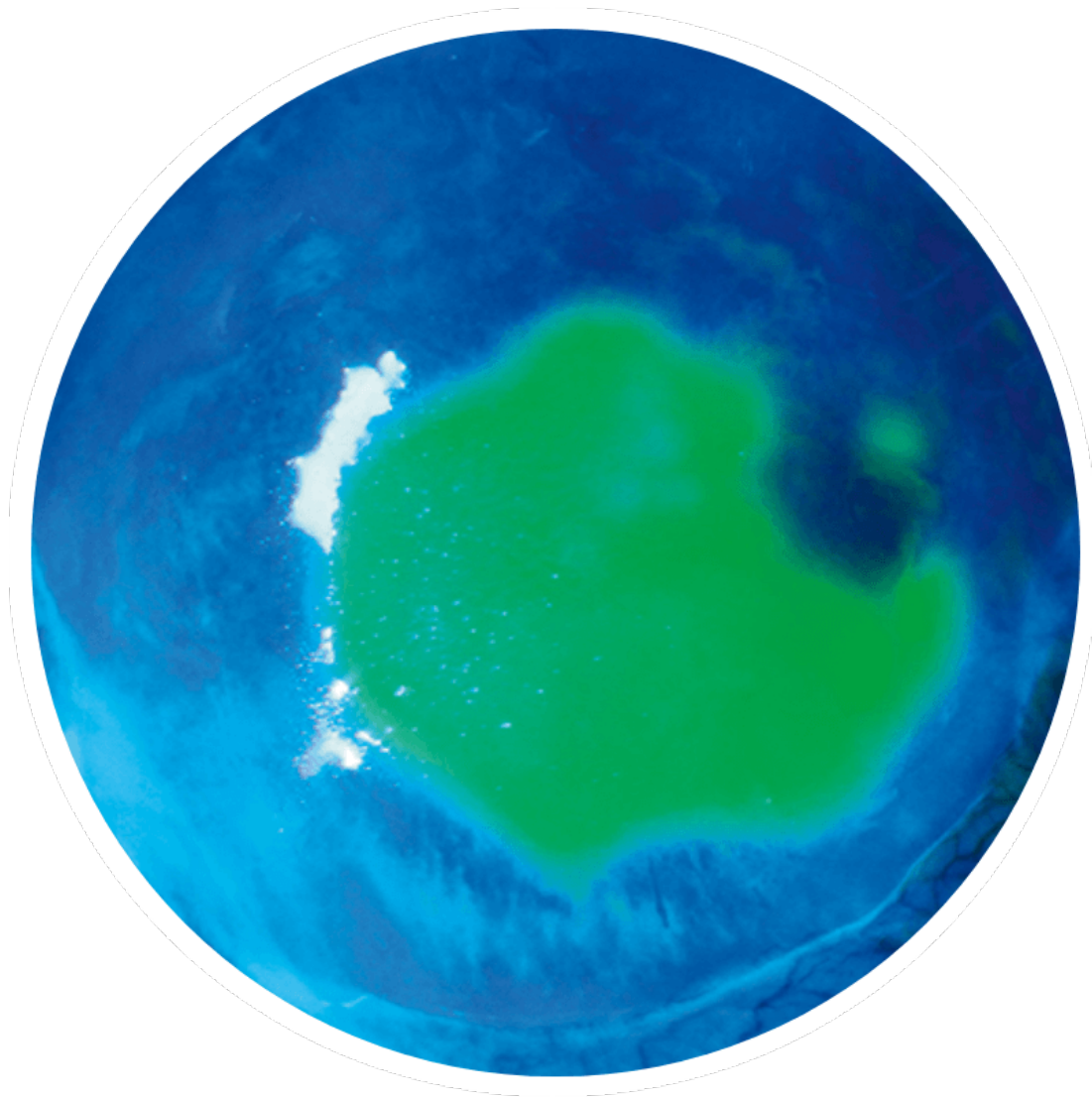
NK Stage 1



NK – Stage 2

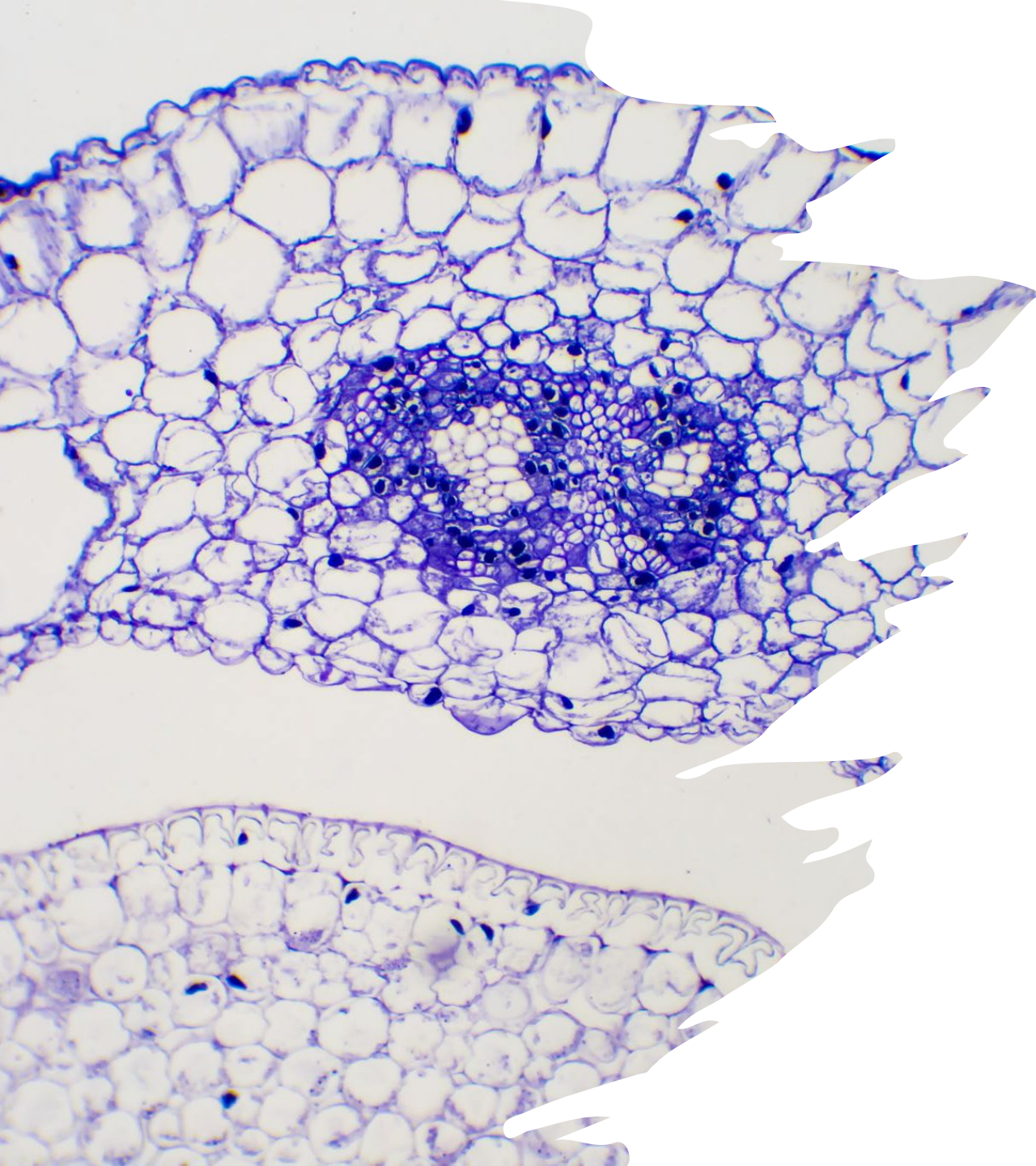


NK- Stage 3



NK Treatment

- BCL?
- Autologous serum
- Cryopreserved amniotic membrane
- Oxervate!!!



Oxervate- cenergemim (Dompe)

- Synthetic rhNGF
- Structurally identical to endogenous NGF
- Improves corneal nerve function (innervation)
- Promotes tear secretion
- Fosters epithelial cell growth

What exactly is Neurotrophic Growth Factor?

- NGF induces corneal healing and has the potential to restore sensitivity and may modulate inflammatory reactions in the eye
- NGF has the potential to increase tear production and conjunctival goblet cell density and promote nerve regeneration after mechanical corneal nerve injury
- NGF activates TrkA and p75 Neurotrophin receptor expressed on corneal epithelial cells and sensory neurons and may stimulate mucin release and goblet cell differentiation
- NGF is a naturally occurring neurotrophin is responsible for differentiation, growth and maintenance of neurons
- Neuromediators from corneal nerves provide trophic support to ocular surface tissues (particularly epithelial cells and keratocytes that: Stimulate wound healing and maintain anatomic integrity.
- Epithelial cells release neurotrophins, neuropeptides and growth factors (e.g. NGF) from epithelial cells and keratocytes that mediate nerve fiber survival, differentiation and maturation.
- Corneal nerves stimulate blinking and tear production.
- Tears contain growth factors and nutrients that stimulate epithelial cells

Oxervate



1 DROP 6X/DAY

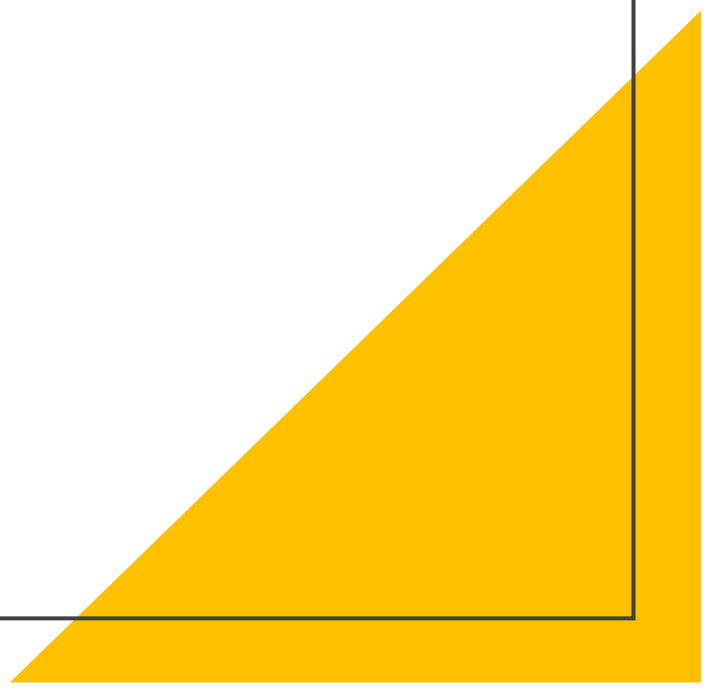


DELIVERED OVER A 12
HR PERIOD



8 WEEK TREATMENT
DURATION

Oxervate data

- 8 week study period- compared to placebo
 - 72% achieved complete K healing
 - Absence of NaFl stain at lesion site
 - No persistent staining on rest of corneal surface
 - 80% remained completely healed at 12 mths
 - Most common AE – Eye pain (12%)
- 
- A large yellow triangle is positioned in the bottom right corner of the slide, pointing towards the top right.

But Wait... There's More!

- Only 3 therapies effectively treat NK
 - Oxervate
 - Autologous Serum (Vital Tears)
 - Cryo preserved Amniotic Membranes
- So which works better?

Glaucoma Drugs – Tapping that Pipeline!!!

- Nothing New For A While, and then...
BOOOM!
- Rhopressa
- Rocklatan
- Vyzulta
- But those are so 2019!!
- Anything else??

But really... Is There Anything New??

Iyuzeh-
(latanoprost 0.005%)

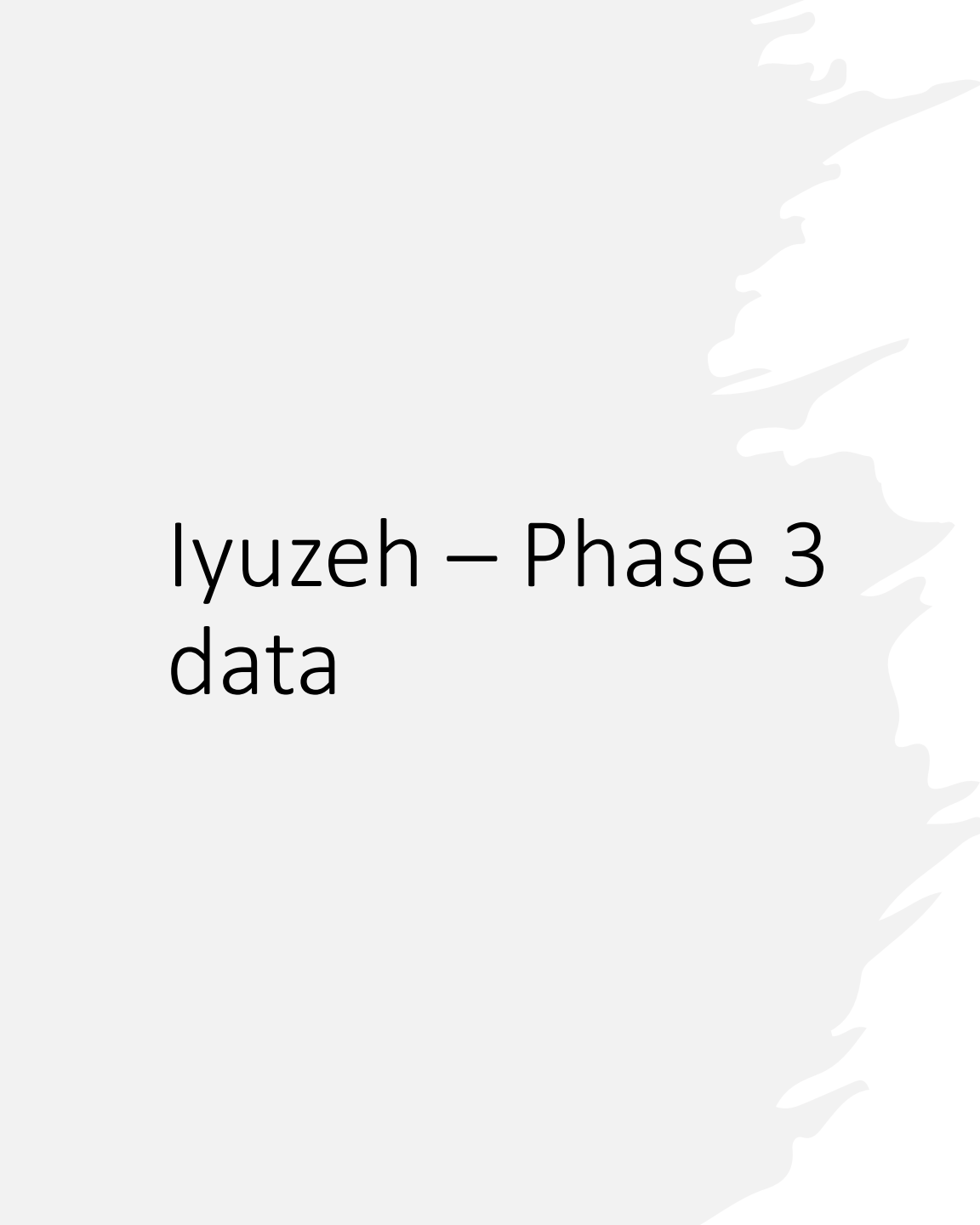
Thea Pharmaceuticals

Let's talk about this...



lyuzeh (latanoprost 0.005%)

- Does that sound familiar?
- Monoprost (in Europe) – the market leader in PGA in Europe
- This actually is PRESERVATIVE FREE latanoprost!!
- Single dose container
- But does it really work??



Iyuzeh – Phase 3 data

- Compared to Xalatan (Switch Study)
- Stable POAG pxs on Xalatan
- 8 day washout period
- 3 months on Iyuzeh
- IOP reduction was 4-8mm Hg on Xalatan
- IOP reduction was 3-8mm Hg on Iyuzeh
- Baseline IOP was 19mmHG!!

Iyuzeh – Phase 3 data- Adverse Effects

- Xalatan group
 - Hyperemia – 31%
 - Eye Irritation – 34%
- Iyuzeh Group
 - Hyperemia – 34%
 - Eye irritation – 19%
- ZERO reports of SPK

Subsequent Iyuzeh studies

- European data – Higher baseline IOP (24mm Hg)
 - IOP lowered to 15.5mm Hg
 - Same rate of adverse effects
- Bachrach data (2023 AGS)
 - 12 week trial comparing to Xalatan
 - Similar IOP reduction (as measured by ability to get IOP <18mm Hg)
 - 2% experienced redness or ocular irritation
 - 0% SPK

Fewer ocular side effects (13.9% vs 22.5%)
- PASSY study
 - 97% tolerated drop
 - AT usage decreased 24%



#What's The Big Deal??

- OSD is an epidemic in glaucoma
- Will this improve compliance?
- Will this cost \$1M??
- Is it better than what we have?



Rhopressa (netarsudil) – Aerie Pharmaceuticals

- New class of drugs – Rho-kinase inhibitor
- MOA – “Triple Action”
 - - relaxes trabecular meshwork similar to pilocarpine (enhances outflow)
 - - lowers episcleral venous pressure
 - - blocks fibrotic response at t.m.(increases perfusion)
- QD dosing
- Looks especially effective at IOP 25 mmHg or less

Rhopressa (netarsudil) -MOA



Works at the cellular level within the trabecular meshwork



ROCK inhibitors improve outflow by relaxing contraction and stress fibers at the t.m.

What Do We Know About Rhopessa (netarsudil 0.02%)

- Rhopessa QD is non-inferior to timolol 0.5% BID in lowering IOP
- Expected IOP reduction 3.7 -7.0mm Hg
- Rhopessa seems to better at lowering IOP (as compared to itself) in pressures < 25mm Hg
- IOP lowering effect is maintained over 12 months
- Was given a broad label by FDA

Rhopressa – Adverse Effects

Generally well tolerated

Conjunctival hyperemia – 53%

- Did not worsen with time
- Mild-36.8%, moderate – 10.5%, severe -0.6%
- D/C rate due to redness -~3%

Corneal verticillata – 18%

Conjunctival hemorrhage – 15%

- All are transient and considered mild

What's to like about Rhopressa?

New MOA so... it is absolutely different



It should be additive



Definitely works better at lower IOP



What about side effects?

Rhopressa- some thoughts

How are you positioning it in your practice??

What are our clinical experiences 2 years later?

Is it a first line drug?

What about insurance coverage?

What color top does it have??

Update on Rhopressa

- Relaxes Actin & Myosin fibers > Increases outflow at t.m.
- Yields 35% Improvement in tm outflow in glaucoma patients (vs 20% improvement in normal)
- Excellent response on episcleral venous pressure- netarsudil reduces EVP by 10% - no other drop achieves this
- No longer needs to be refrigerated after opening

M.O.S.T. Study

Real World Open Label Phase 4 Study

ASCRS 2020

To determine efficacy of Rhopressa as an adjunct med

Investigator's Choice – Rhopressa + any other agent

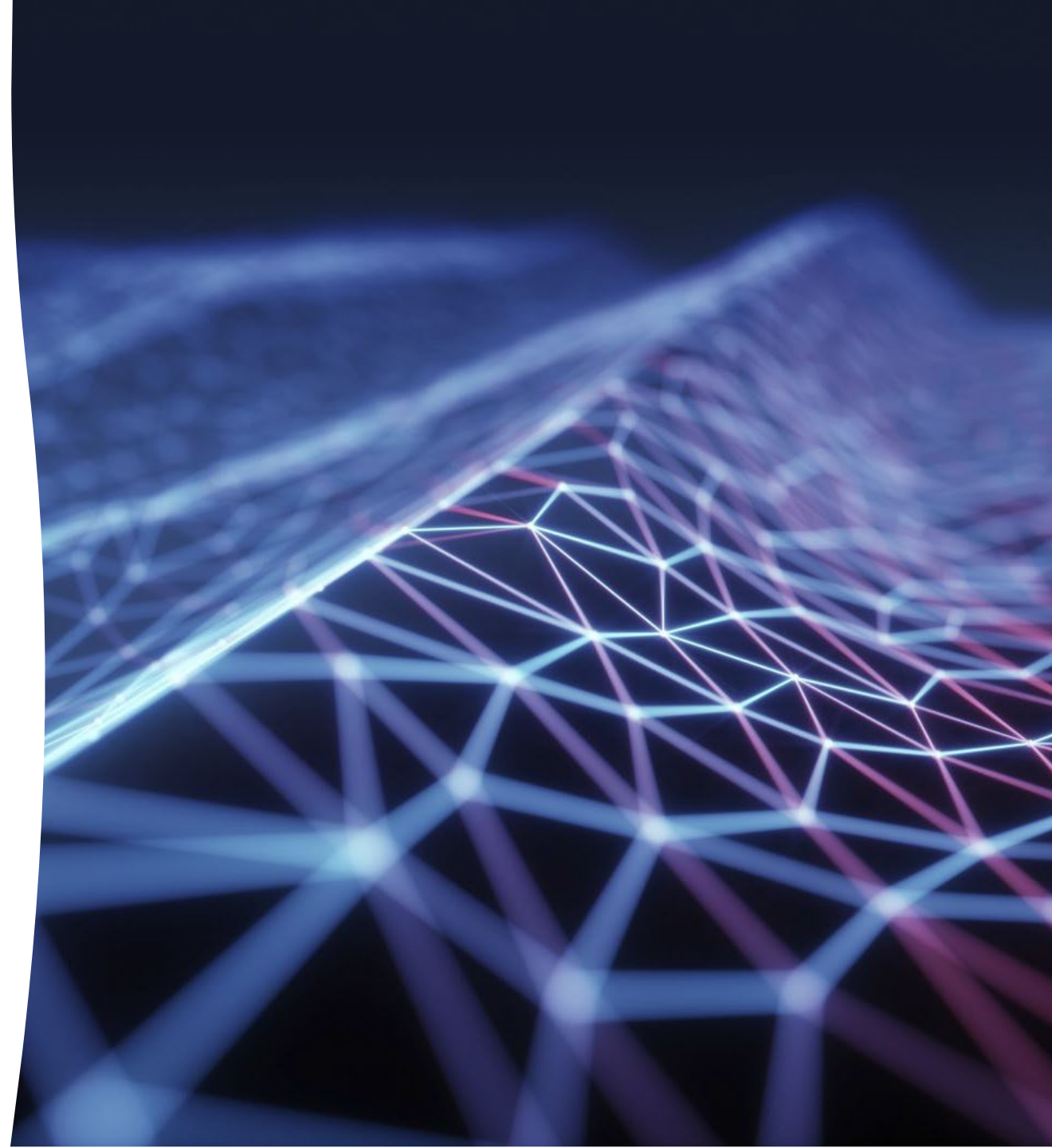
24.4% African-American participants

M.O.S.T. Results

Rhopressa + PGA - IOP 21.1 >
16.9 mmHg (20% reduction)

Rhopressa + 2 meds – 20.6 >
16.6 mmHg (20% reduction)

Notice the low baseline IOP



More M.O.S.T. Results

- % of pxs less than < 18mm Hg
 - <18mm -72.7 % (from 34.4%)
 - <17mm- 65% (from 25.2%)
 - <15mm -40.6% (from 15.9%)
 - <14mm- 30.1% (from 11.3%)
- 2/3 of all patients achieved IOP < 17mm Hg

M.O.S.T. Tolerability rates



Hyperemia – 20.* %



D/C rate – hyperemia 3.4%



Tolerability rating

67.8-73.1% good or decent
(physician response)

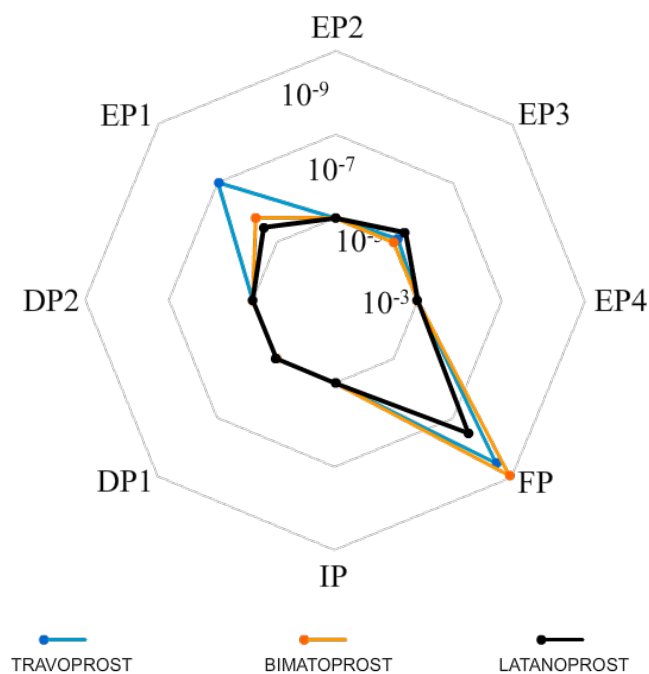
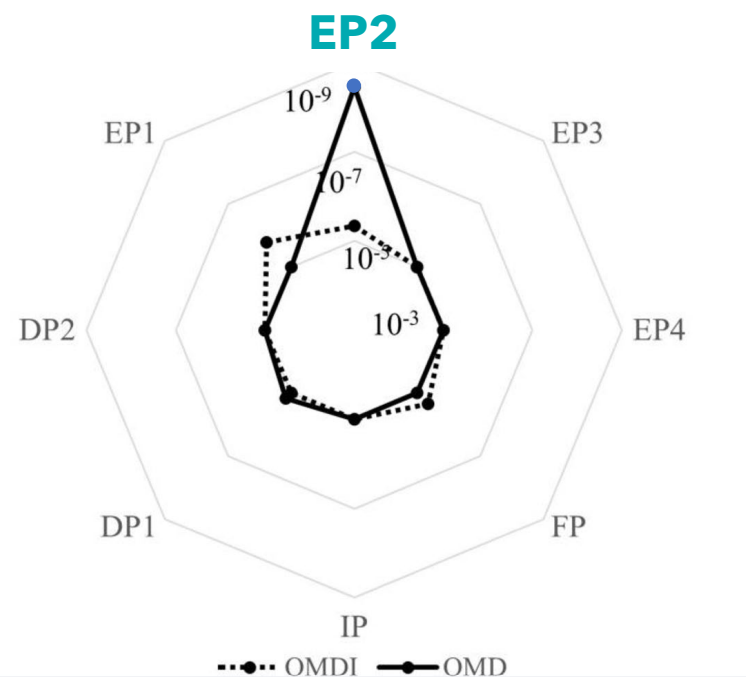
65-78% good or decent (Patient
response)

A Brand New Molecule to Discuss!!!

- Omlonti – omidenepag isopropyl
- MOA - EP2 Receptor
- Ocuvex/ Santen
- Approved for lowering IOP in Glaucoma and OHTN
- 1 drop QD



Receptor Affinity



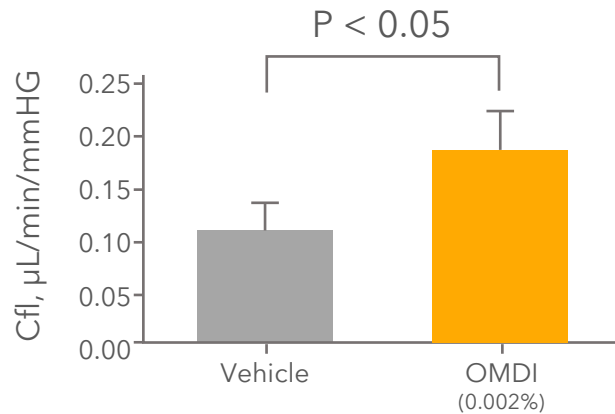
	EC ₅₀ , nM		
	EP1	EP2	FP
OMDI	>10,000	>10,000	>10,000
OMD (FREE ACID)	-	8.3	-

1. Kiriwara T, Taniguchi T, Yamamura K, Iwamura R, Yoneda K, Odani-Kawabata N, Shimazaki A, Matsugi T, Shams N, Zhang JZ. Pharmacologic Characterization of Omidenepeg Isopropyl, a Novel Selective EP2 Receptor Agonist, as an Ocular Hypotensive Agent. Invest Ophthalmol Vis Sci. 2018 Jan 1;59(1):145-153.
2. Matsuo M, Matsuoka Y, Tanito M. Efficacy and Patient Tolerability of Omidenepeg Isopropyl in the Treatment of Glaucoma and Ocular Hypertension. Clin Ophthalmol. 2022 Apr 26;16:1261-1279.
3. Kiriwara T, Taniguchi T, Yamamura K, Iwamura R, Yoneda K, Odani-Kawabata N, Shimazaki A, Matsugi T, Shams N, Zhang JZ. Pharmacologic Characterization of Omidenepeg Isopropyl, a Novel Selective EP2 Receptor Agonist, as an Ocular Hypotensive Agent. Invest Ophthalmol Vis Sci. 2018 Jan 1;59(1):145-153.
4. Stjernschantz JW. From PGF(2alpha)-isopropyl ester to latanoprost: a review of the development of xalatan: the Proctor Lecture. Invest Ophthalmol Vis Sci. 2001 May;42(6):1134-45. PMID: 11328719.

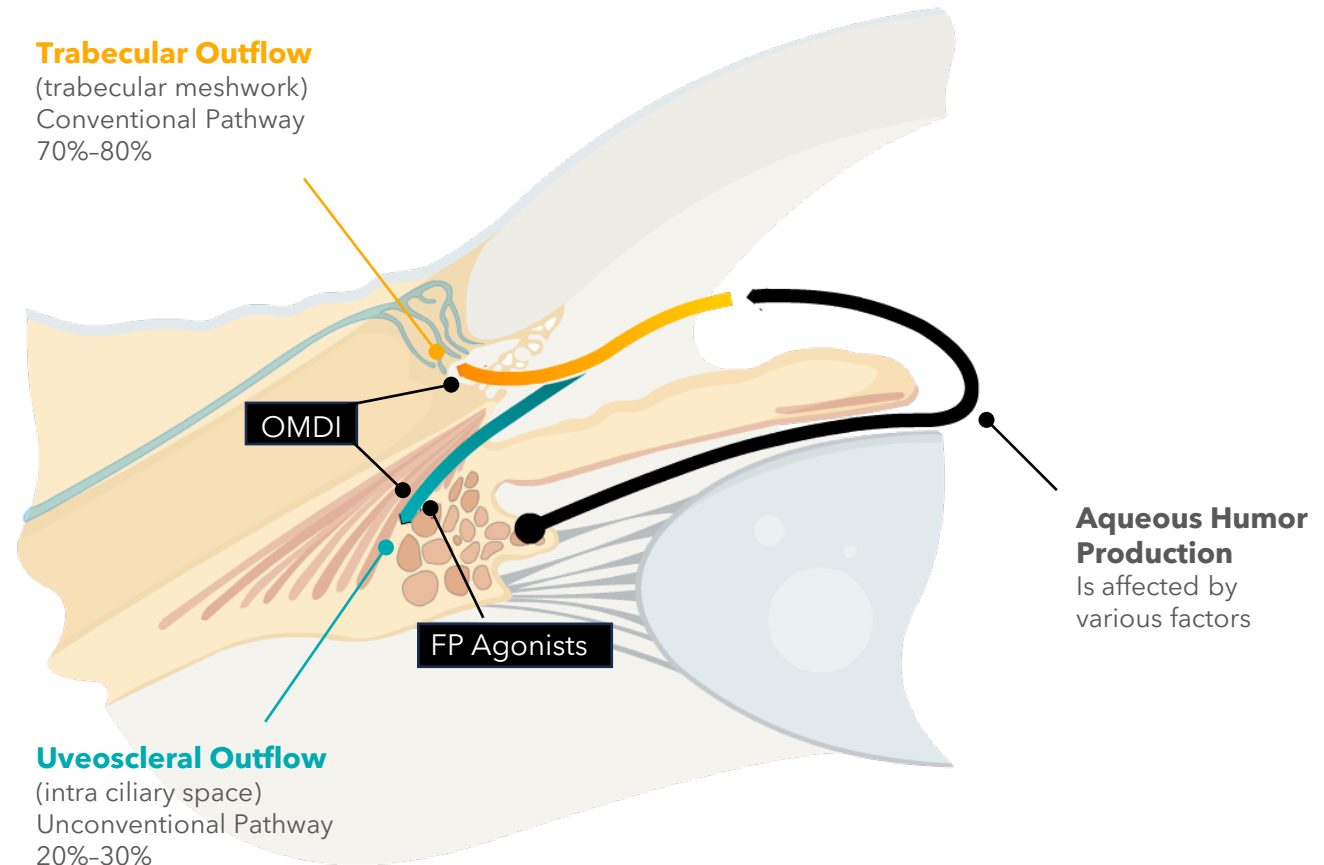
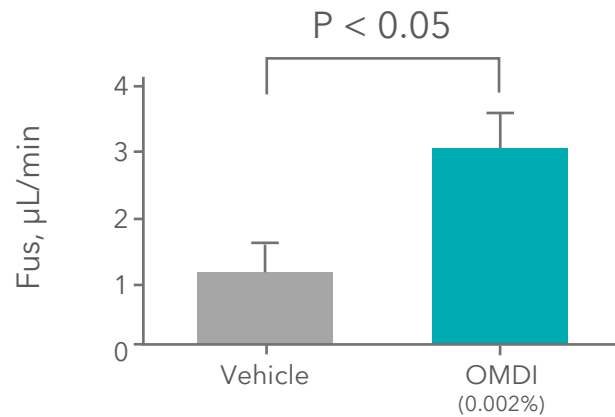
OMDI Affects Both Outflows

TRABECULAR OUTFLOW

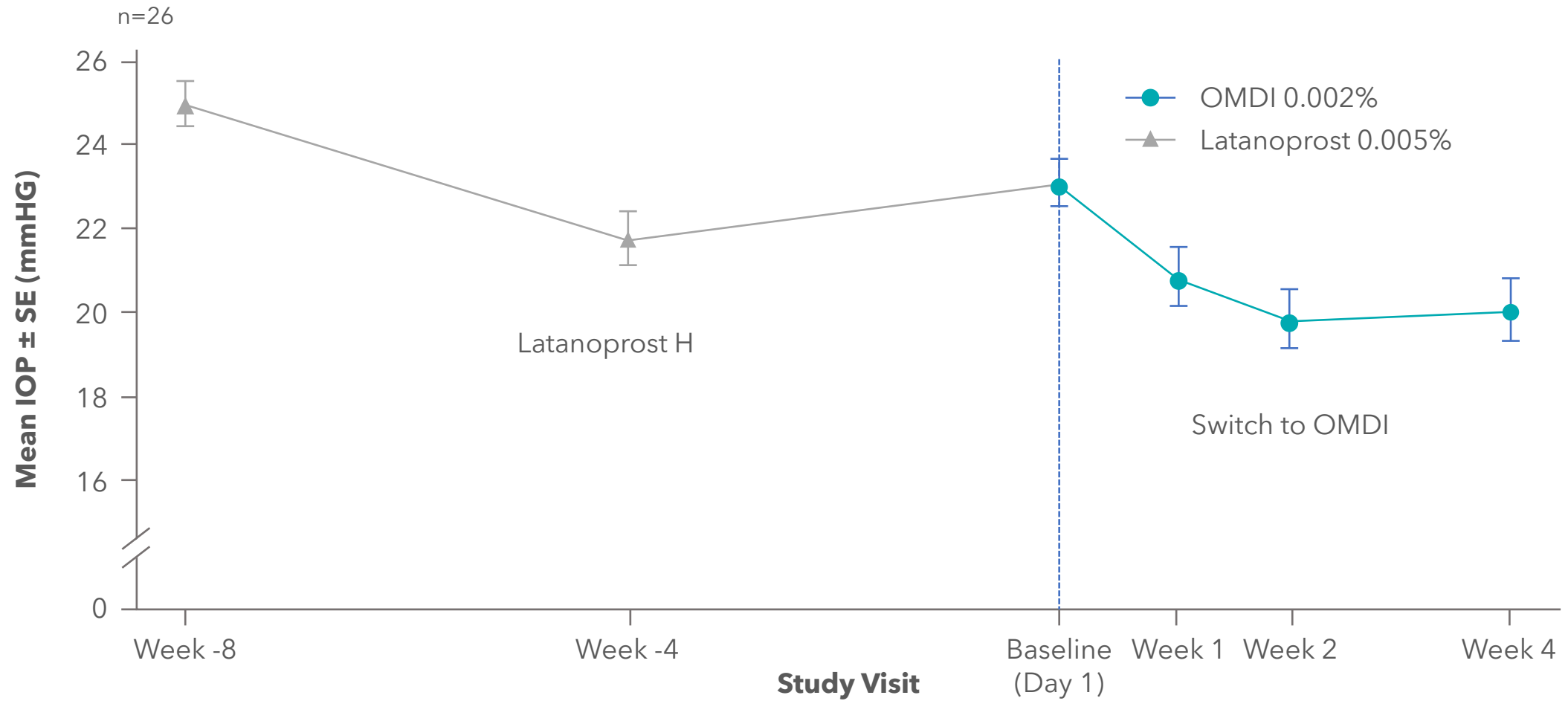
Fluorophotometric
outflow facility



UVEOSCLERAL OUTFLOW

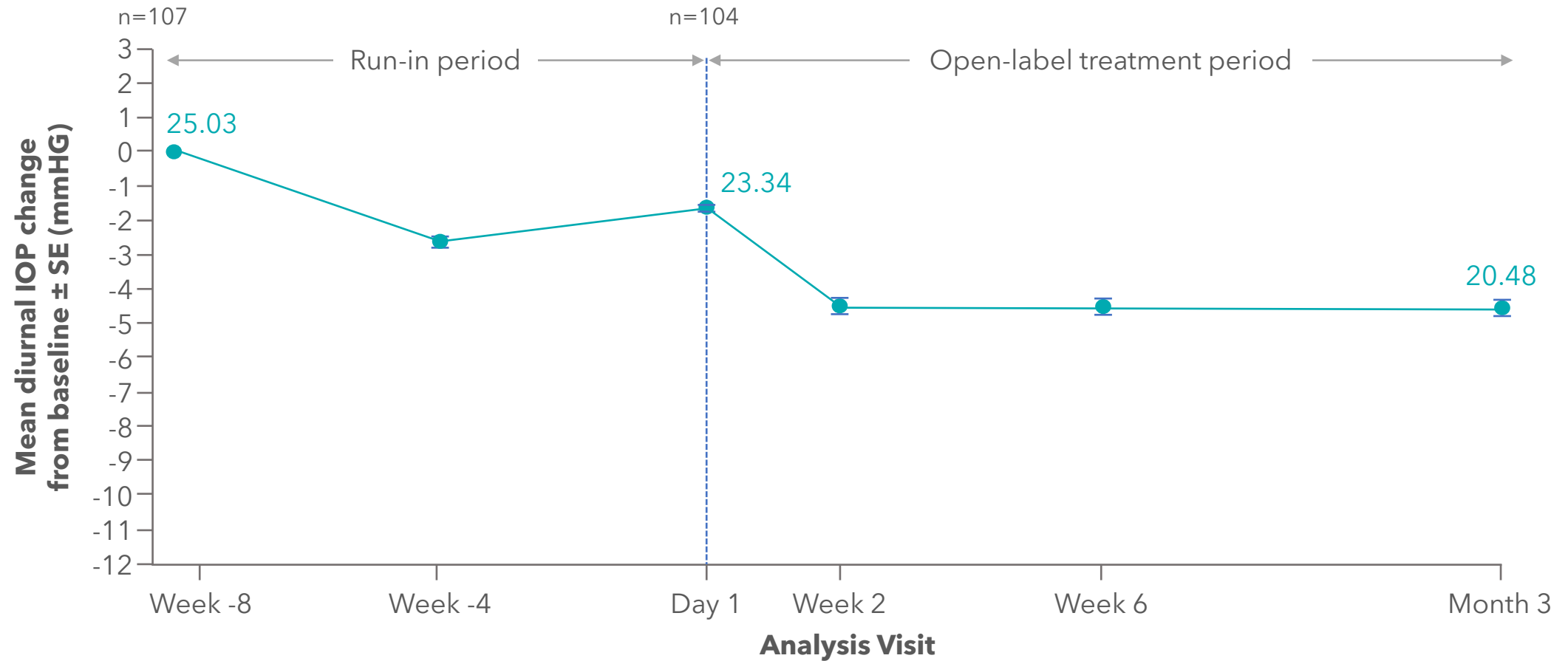


In Latanoprost Non-Responders



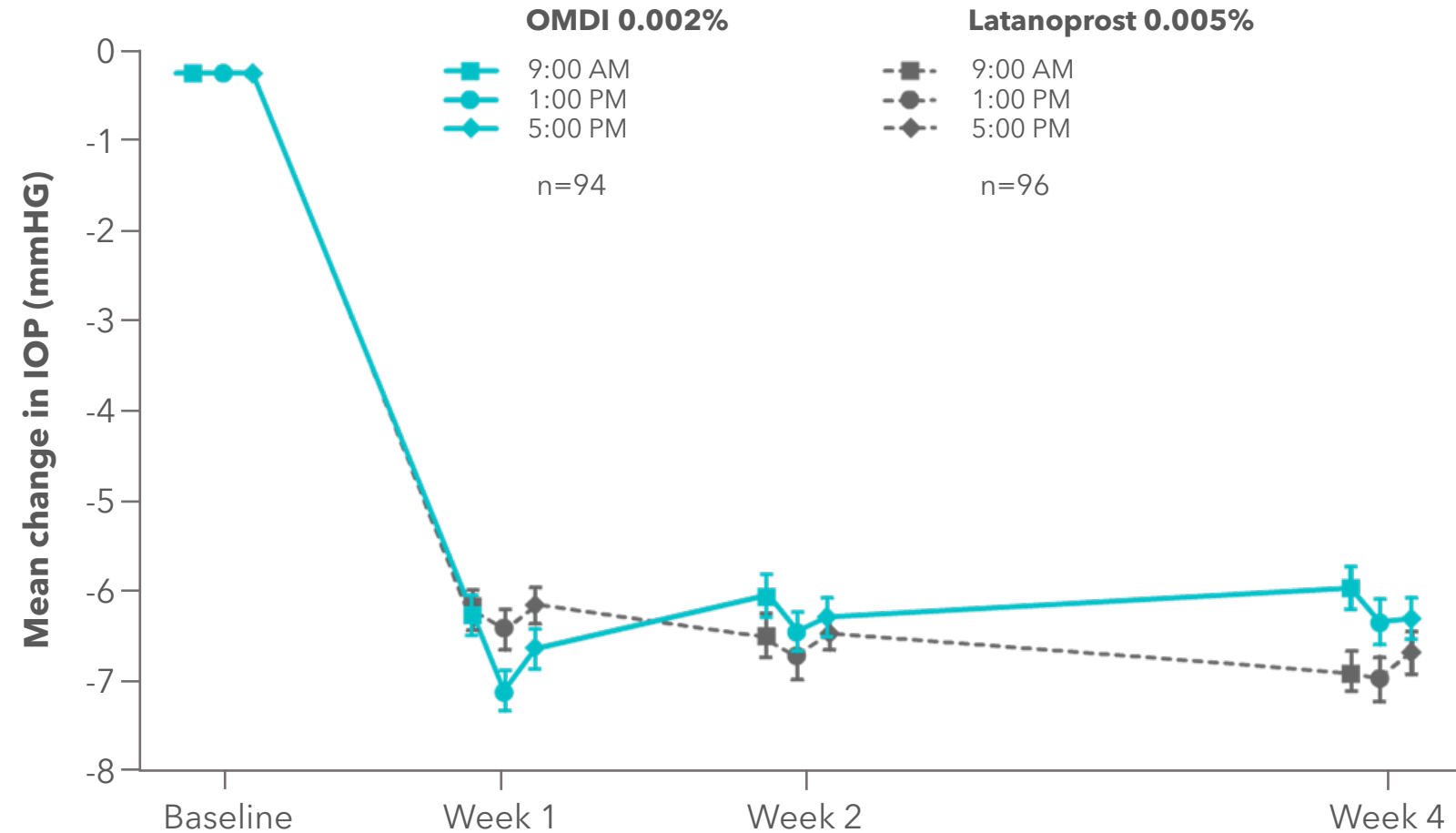
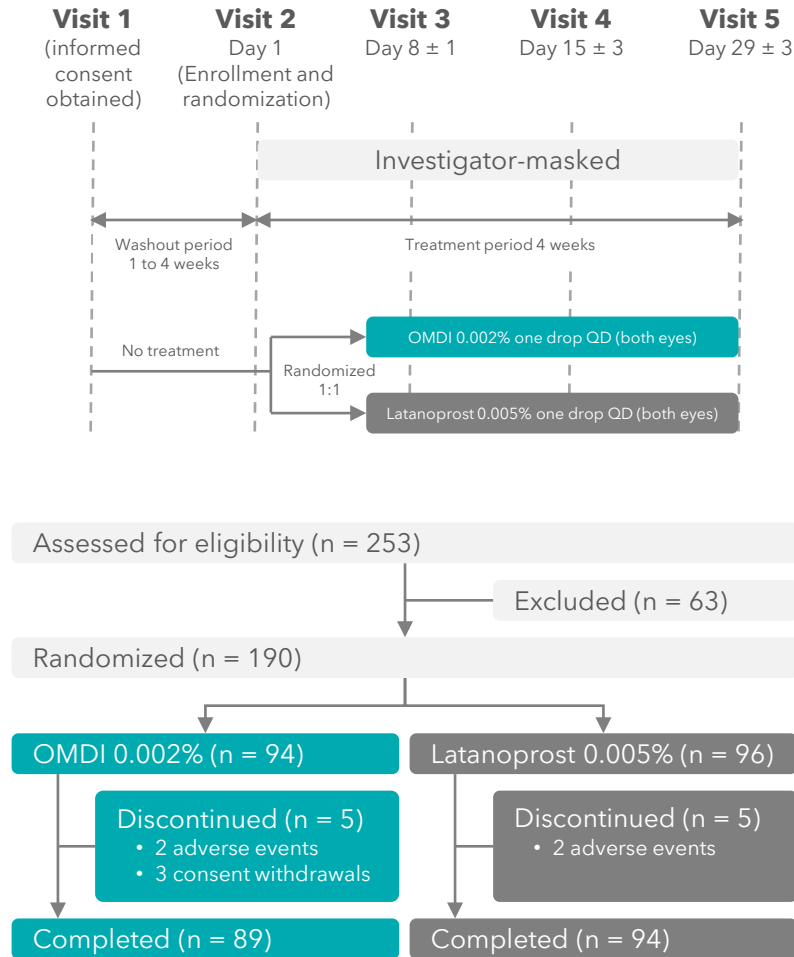
1. Aihara M, Ropo A, Lu F, Kawata H, Iwata A, Odani-Kawabata N, Shams N. Intraocular pressure-lowering effect of omidenepag isopropyl in latanoprost non-/low-responder patients with primary open-angle glaucoma or ocular hypertension: the FUJI study. Jpn J Ophthalmol. 2020 Jul;64(4):398-406. .

Repeatable Results

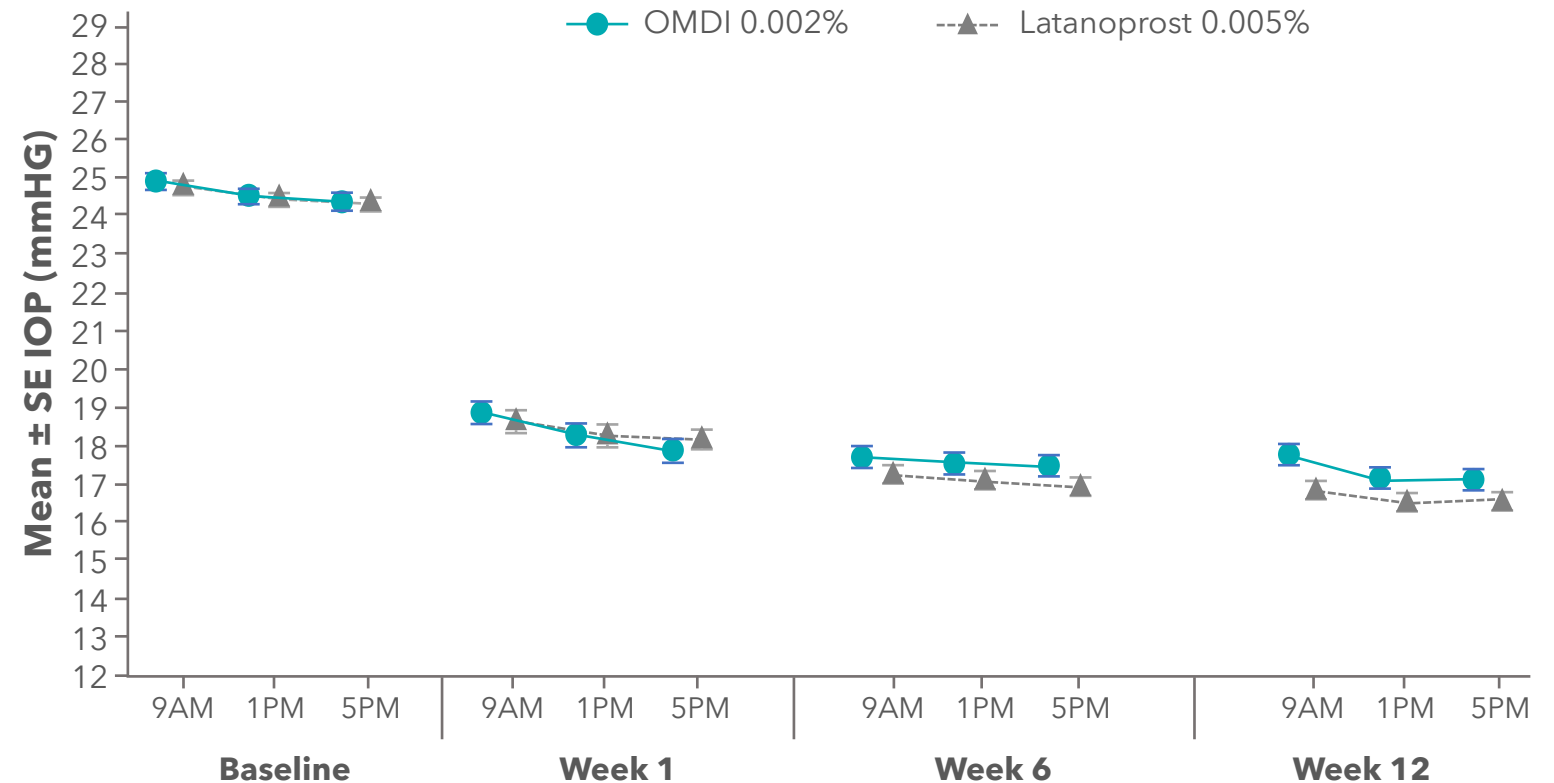
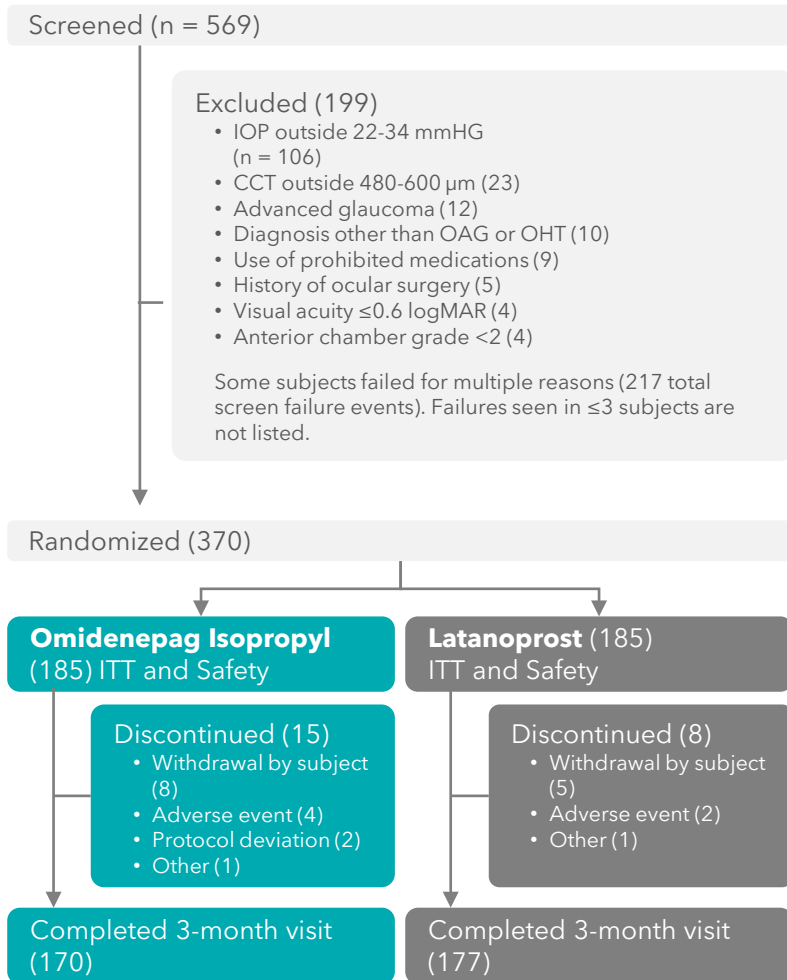


1. Panarelli JF, Bowden EC, Tepedino ME, Odani-Kawabata N, Pei Z, McLaurin EB, Ropo A. Omidenepeg Isopropyl in Latanoprost Low/Nonresponders With Primary Open Angle Glaucoma or Ocular Hypertension: A Phase 3, Nonrandomized, Two-Phase, Open-Label Study. J Glaucoma. 2023 Dec 1;32(12):999-1005.

Non-Inferiority — Latanoprost

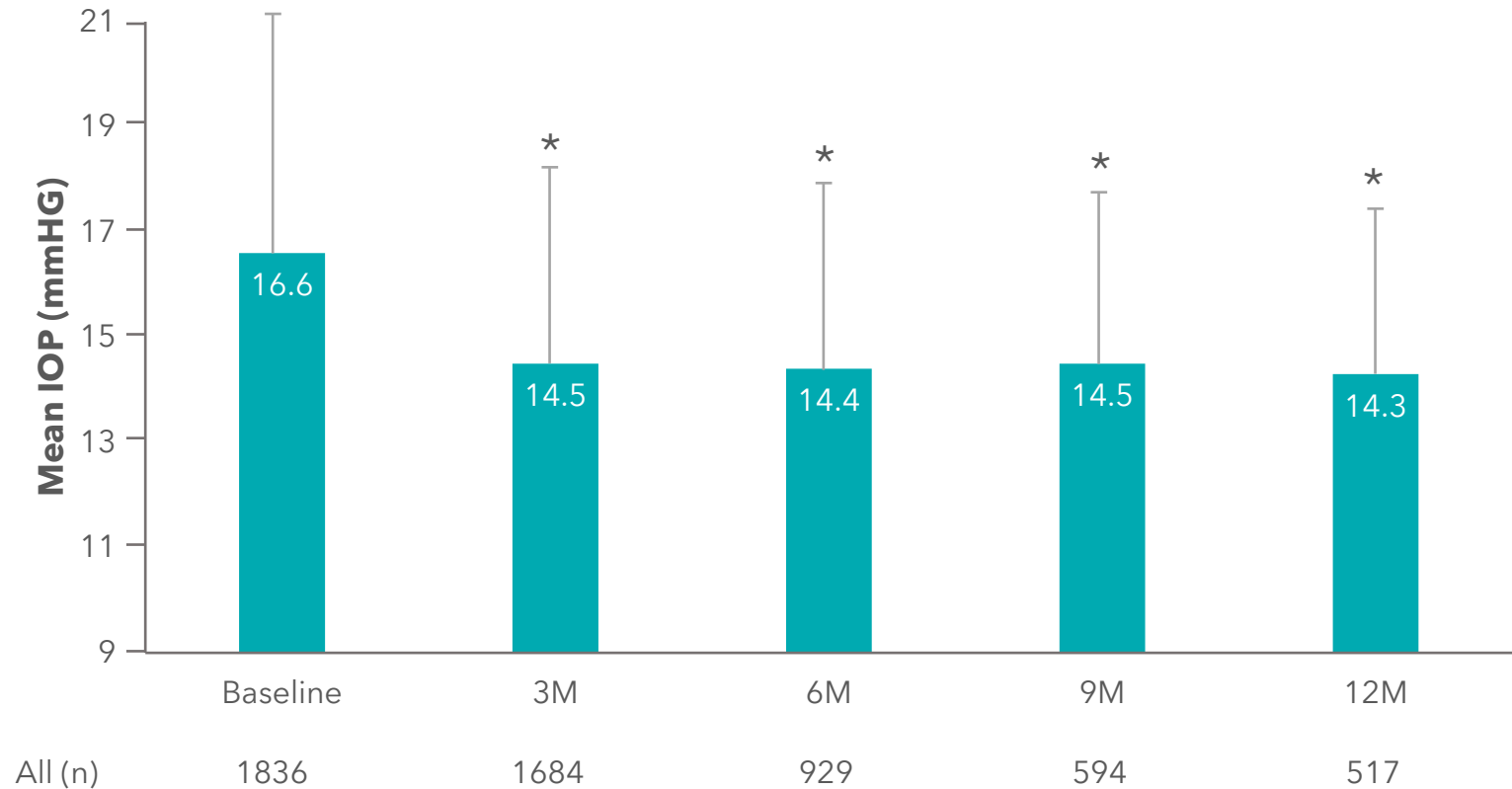
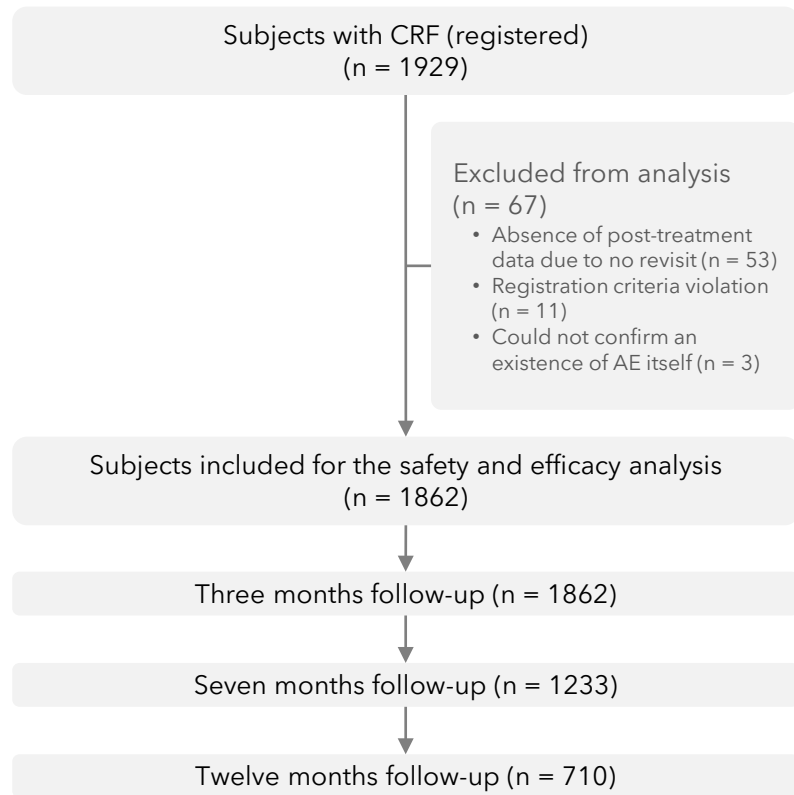


Non-Inferiority – 12 Weeks



1. Wang TH, Aung T, Lu DW, George R, Senthil S, Lu F, Odani-Kawabata N, Park KH. Omidenepag Isopropyl 0.002% versus Latanoprost 0.005% in Open-Angle Glaucoma/Ocular Hypertension: The Randomized Phase III PEONY Trial. Clin Ophthalmol. 2024 Jul 16;18:2093-2106.

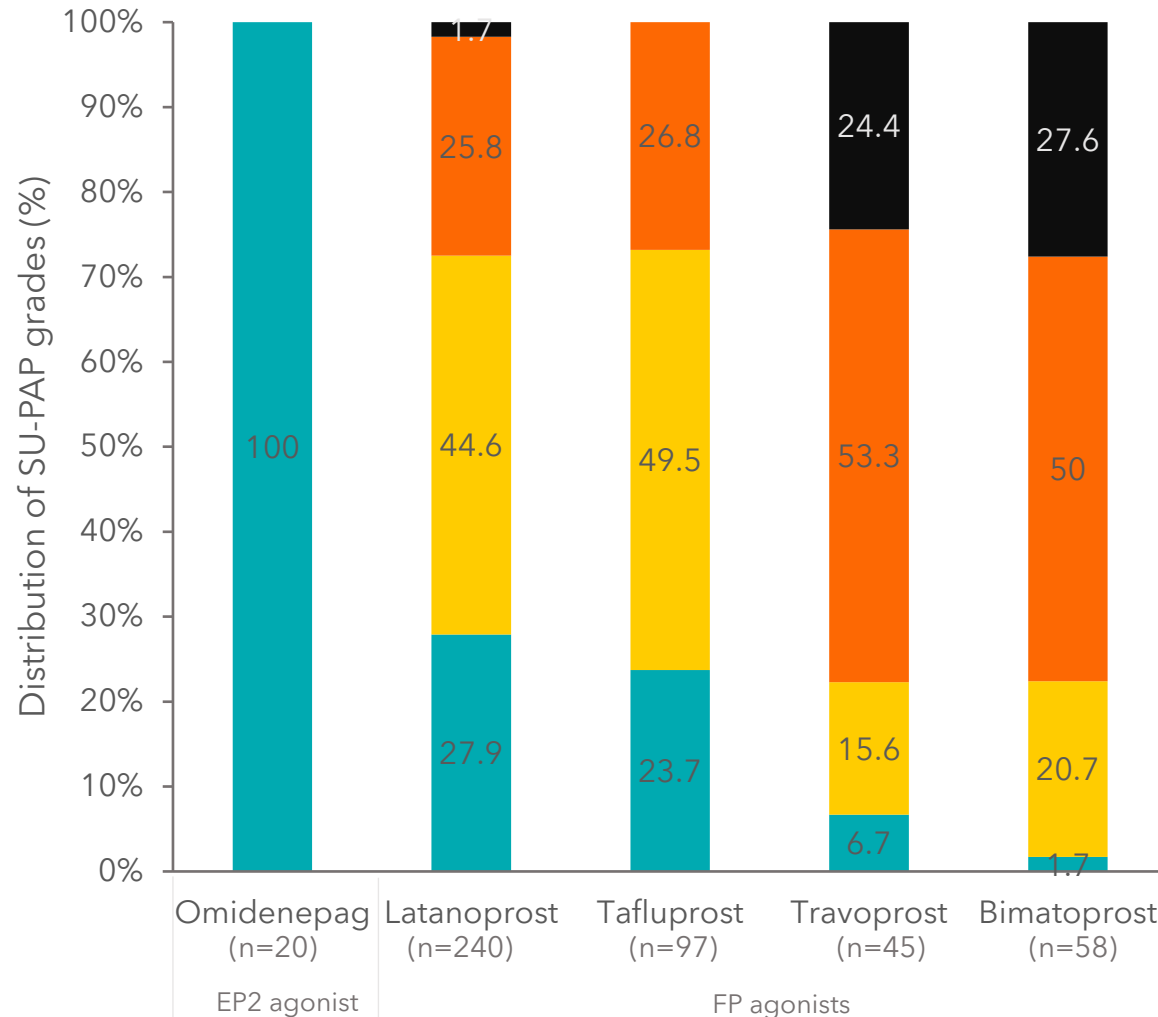
Long-Term Benefit





EP2 Agonist PAP | Side-effect profile

Prostaglandin-Associated Periorbitopathy



Grade 3

(Tonometric PAP, difficulty performing GAT and/or reduced reliability of GAT-measured IOP due to PAP-related DUES, hardening of eyelids, ptosis, or enophthalmos)

Grade 2

(Deep cosmetic PAP, cosmetic change(s) with at least one sign of PAP including DUES, blepharochalasis involution, periorbital fat loss, or enophthalmos)

Grade 1

(Superficial cosmetic PAP, cosmetic change(s) including eyelid pigmentation and/or eyelash growth)

Grade 0

(No PAP, no cosmetic change)

PAP may be improved at no risk to the patient.³

1. Matsuo M, Matsuoka Y, Tanito M. Efficacy and Patient Tolerability of Omidenepag Isopropyl in the Treatment of Glaucoma and Ocular Hypertension. Clin Ophthalmol. 2022 Apr 26;16:1261-1279.

2. Tanito M, Ishida A, Ichioka S, et al. Proposal of a simple grading system integrating cosmetic and tonometric aspects of prostaglandin-associated periorbitopathy. Medicine. 2021;100(34):e26874.

3. Nakakura S, Terao E, Fujisawa Y, Tabuchi H, Kiuchi Y. Changes in Prostaglandin-associated Periorbital Syndrome After Switch from Conventional Prostaglandin F2 α Treatment to Omidenepag Isopropyl in 11 Consecutive Patients. J Glaucoma. 2020 Apr;29(4):326-328.

A Predictable, Well-Tolerated Safety Profile

Appearance-altering AEs:

2.0% for OMLONTI (n = 4/204)¹

Hyperemia:

Most hyperemia events were mild in the trials.

Only **2%**
discontinuation
from Pivotal Phase 3
(n = 4/185)

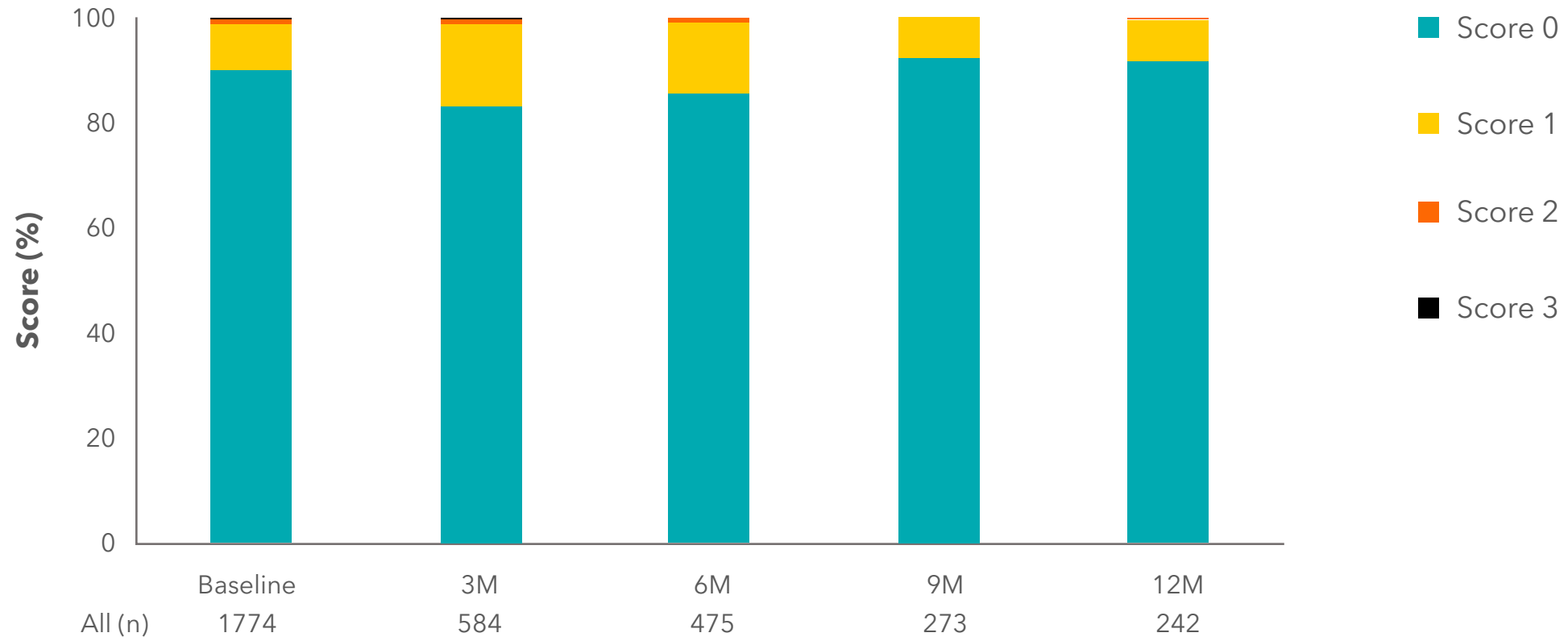
Most common AEs Pooled across all clinical trials.

Adverse Event	Rate % (n = 600)
Conjunctival hyperemia	9%
Photophobia	5%
Blurred vision	4%
Dry eye	3%
Instillation site pain	3%
Eye pain	2%
Ocular hyperemia	2%
Punctate keratitis	2%
Headache	2%
Eye irritation	1%
Visual impairment	1%

1. OMLONTI [package insert]. Emeryville, CA: Santen Inc.; 2022.

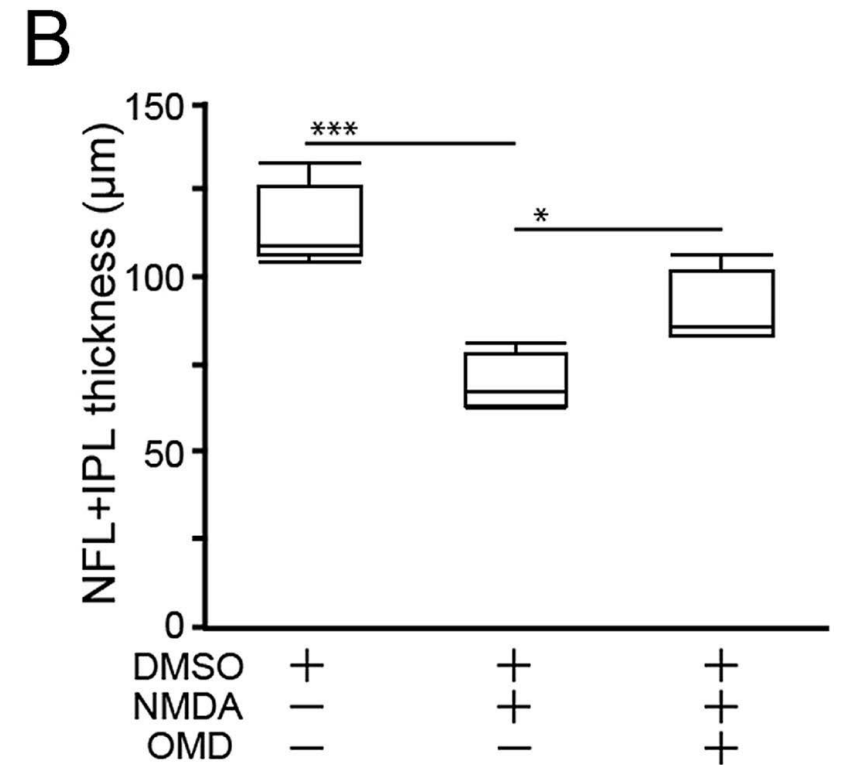
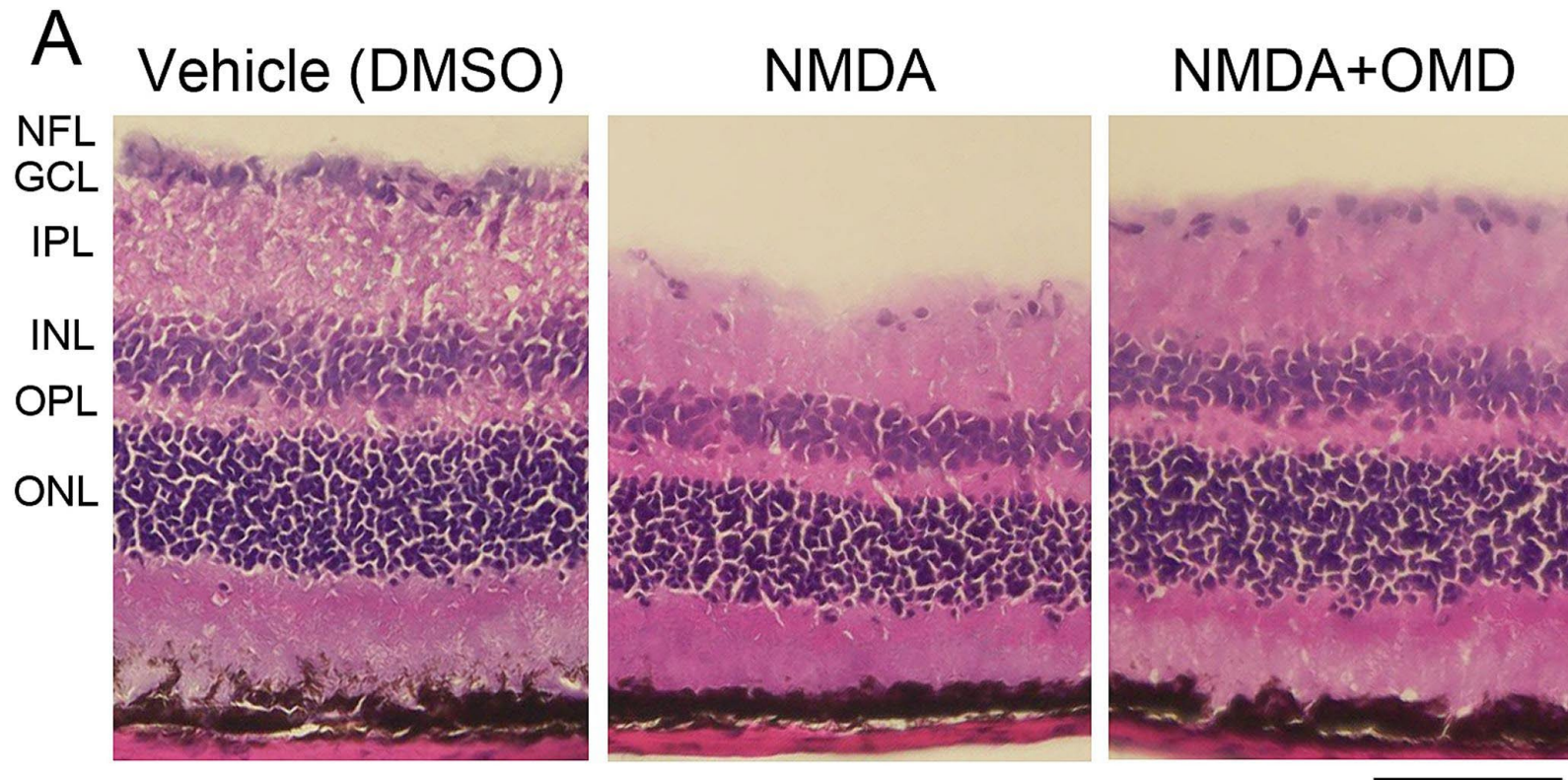
2. Wirta DL, Lu F, Odani-Kawabata N, Chabi A, Bacharach J. Omidenedapag isopropyl 0.002% QD vs timolol maleate BID for open-angle glaucoma/ocular hypertension: the SPECTRUM 4 Trial. Paper presented at: Annual Meeting of American Academy of Ophthalmology; November 12-15, 2021; New Orleans, LA. PO215.

Percentage of Patients for Each Hyperemia Score

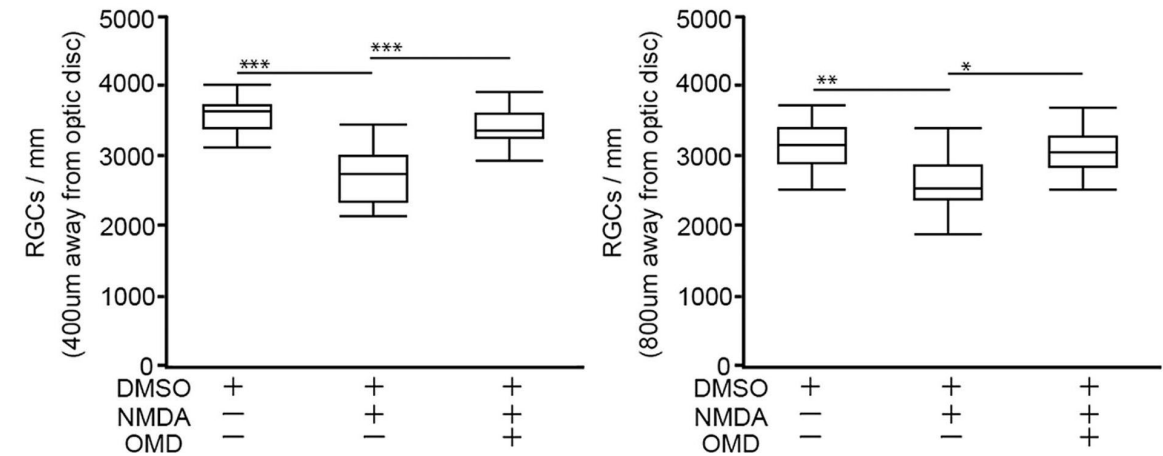
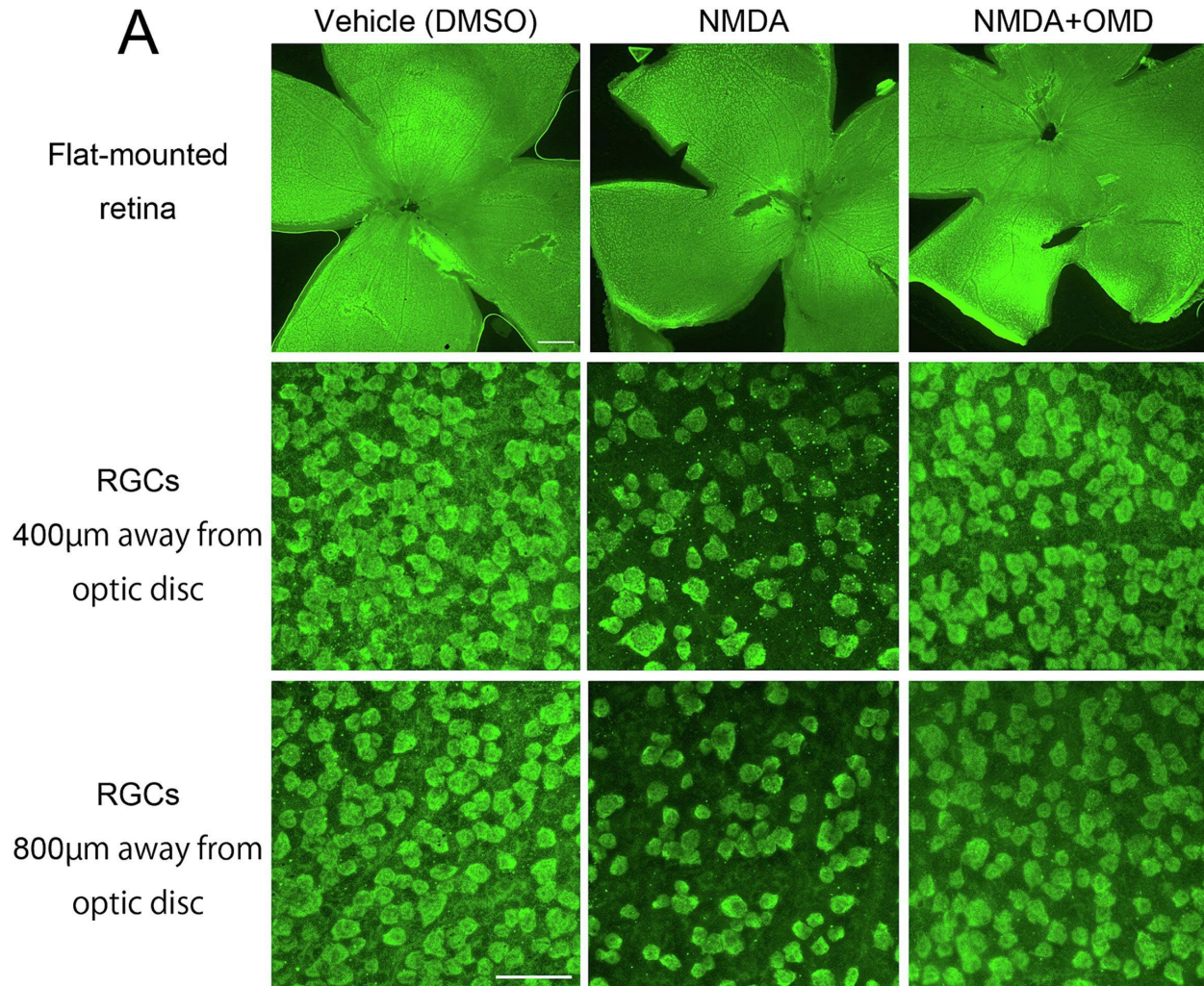


Neuroprotection with an EP2 Agonist

Omidenepag prevents retinal thinning



Omidenepag prevents RG cell loss



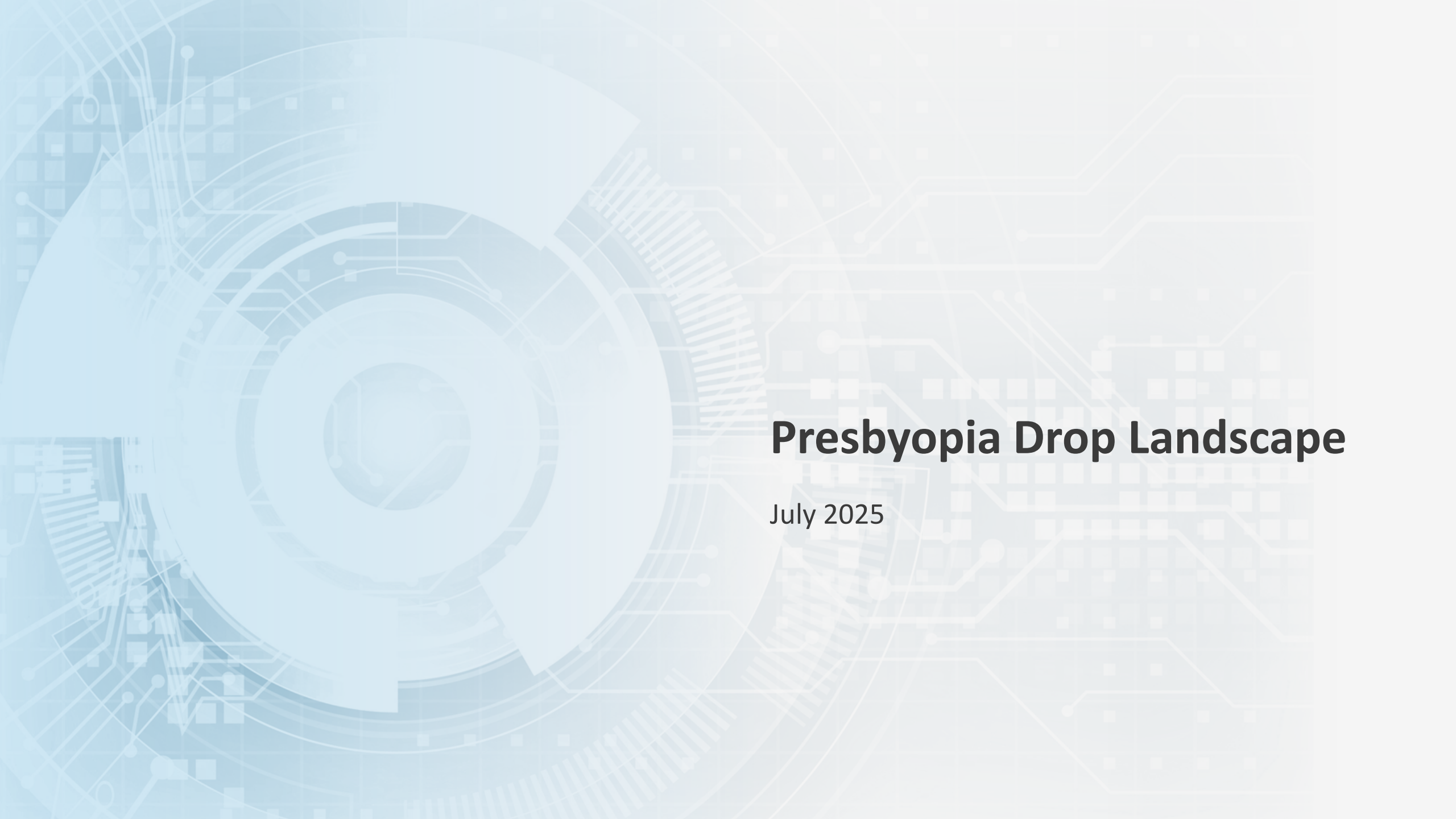
Omidenepag has shown to preserve RG cells and decrease the effects of excitotoxicity

What Does Neuroprotection Mean Clinically?

So, a patient
on
latanoprost
needs 4 more
mm of IOP
reduction- do
you...

- Add Rhopressa?
- Switch to Rocklatan??
- Add a combo drop??

- Switch to a combo drop??
- Switch to another PGA?
- SLT??



Presbyopia Drop Landscape

July 2025

PRESBYOPIA *by the numbers*

1.8 billion
affected globally¹
Affecting more people now
than ever before



128 million
American presbyopes^{2,3}

31 million
buy readers per year⁴
(often at drugstores or supermarkets)

100%
of adults at risk of
developing presbyopia
as they age⁵

1. Fricke TR, et al. *Ophthalmology*. 2018;125:1492-1499. 2. Chang DH. *Ophthalmology Times*. Accessed November 4, 2021. <https://www.opthalmologytimes.com/view/presbyopia-rethinking-approach-to-better-meet-patients-needs>. 3. Zebardast N, et al. *Am J Ophthalmol*. 2017;174:134-144. 4. Vision Council. Accessed October 20, 2021. https://www.thevisioncouncil.org/sites/default/files/research/VisionWatch_VisionCouncil_Member_Benefit_Report_September%202016_FINAL.pdf. 5. NIH. Accessed September 20, 2021. <https://www.nei.nih.gov/sites/default/files/health-pdfs/Presbyopia.pdf>.

- SMELLS LIKE OPPORTUNITY TO ME!!!!
 - But who is our target?
 - Do the drops really work?
 - Will they have a negative impact on m optical?
 - What about for CL wearers?
 - What about for Pseudophakes?
 - Are they safe?
- Do we have any new information?

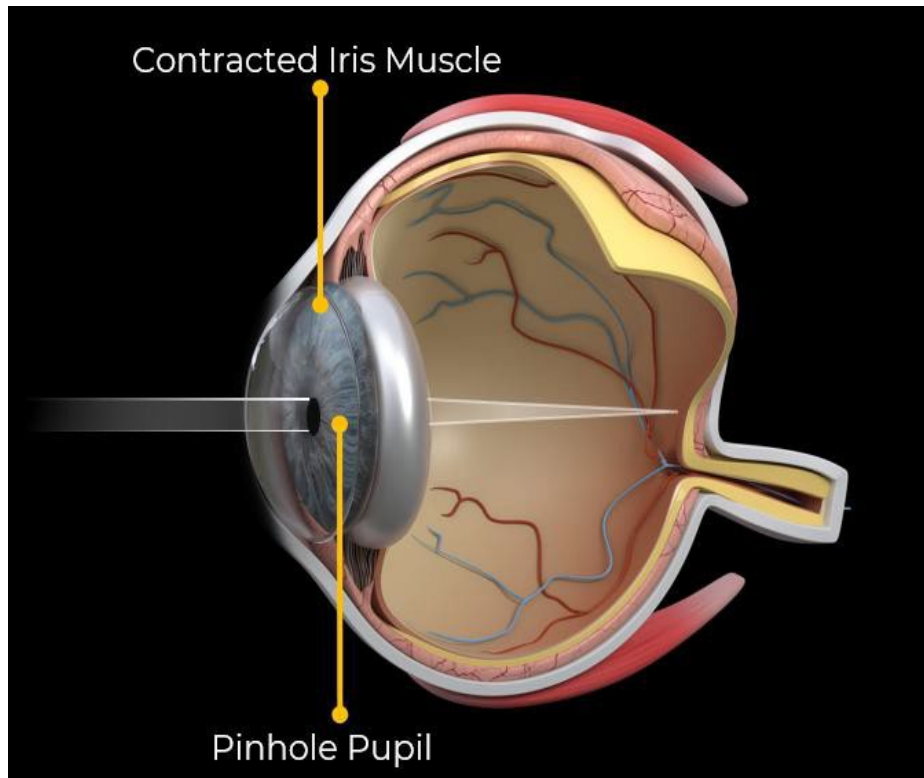


Presbyopia drop landscape

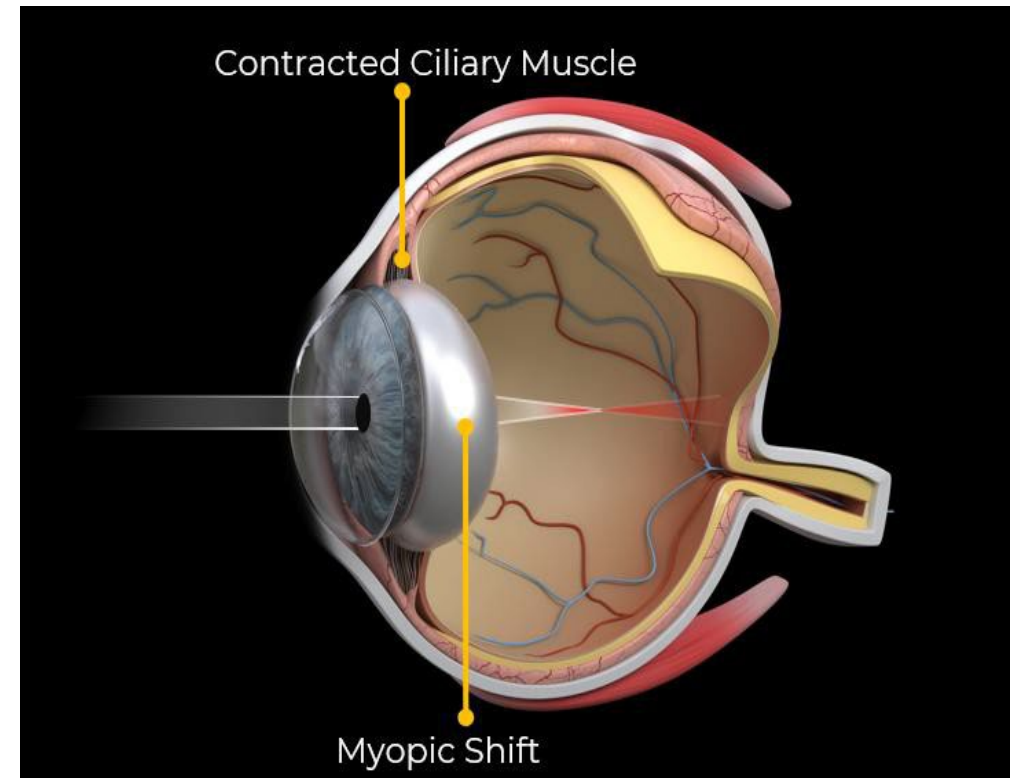
Drop	Company	Approval Status	Concentration of Active Ingredient
Brimochol PF	Visus Therapeutics	Phase 3 - ongoing, recruiting	Carbachol 2.75% + brimonidine 0.1%
LNZ100	Lenz Therapeutics	Phase 3 - ongoing, recruiting	Aceclidine 1.75% & Aceclidine 1.75% + brimonidine
Nyxol, Nyxol + Pilocarpine	Opus Genetics (partnering with Viatris)	Phase 3 - ongoing, recruiting	0.75% Phentolamine +/- pilocarpine 0.4%
Qlosi	Orasis Pharmaceuticals	FDA approved in October 2023	Pilocarpine 0.4%
Vuity	Allergan	FDA-approved for QD dosing in October 2021 and BID dosing in March 2023	Pilocarpine 1.25%

Ideal presbyopia eye drop creates a pinhole pupil while avoiding a myopic shift that impacts distance vision

Create a pinhole pupil

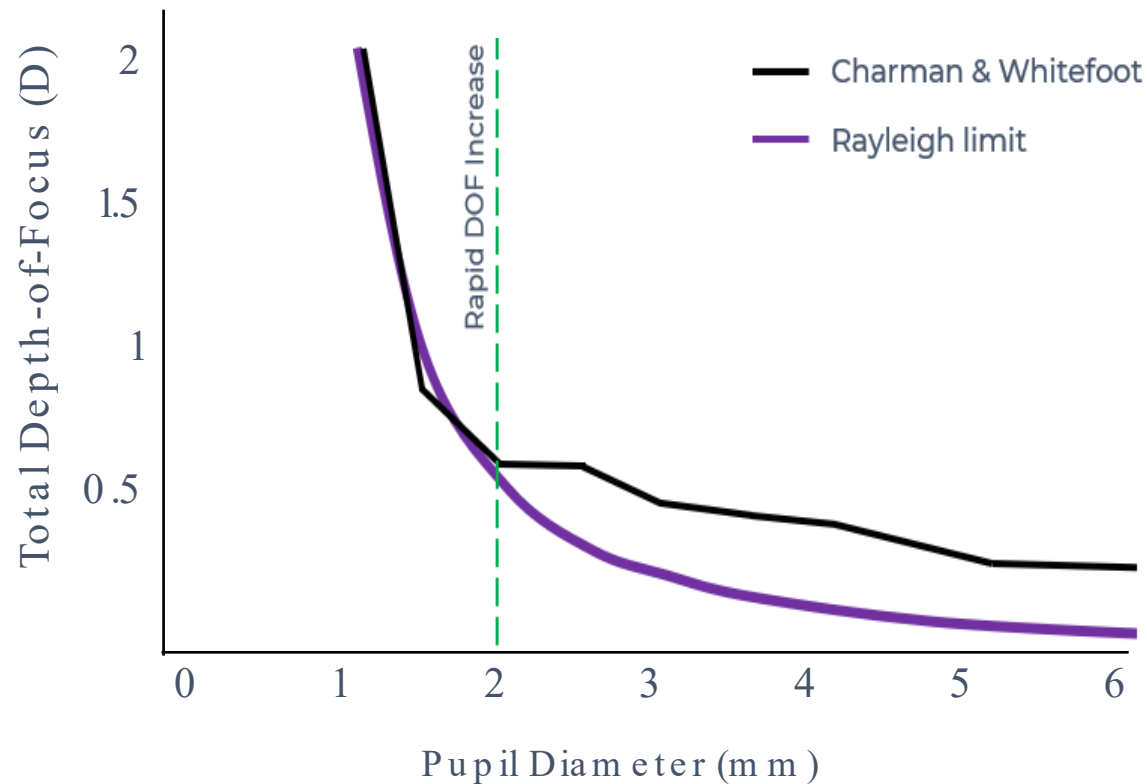


While avoiding a myopic shift

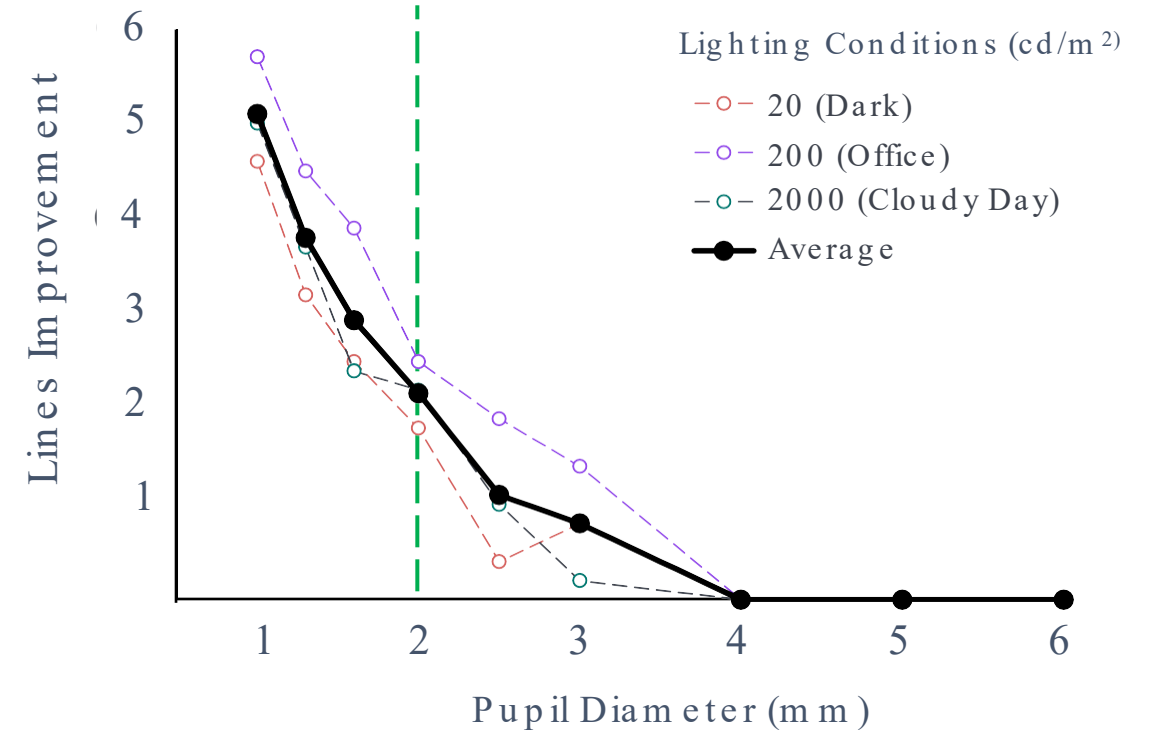


Pupil diameter correlates to depth of focus and near vision improvement

Total Depth-of-Focus

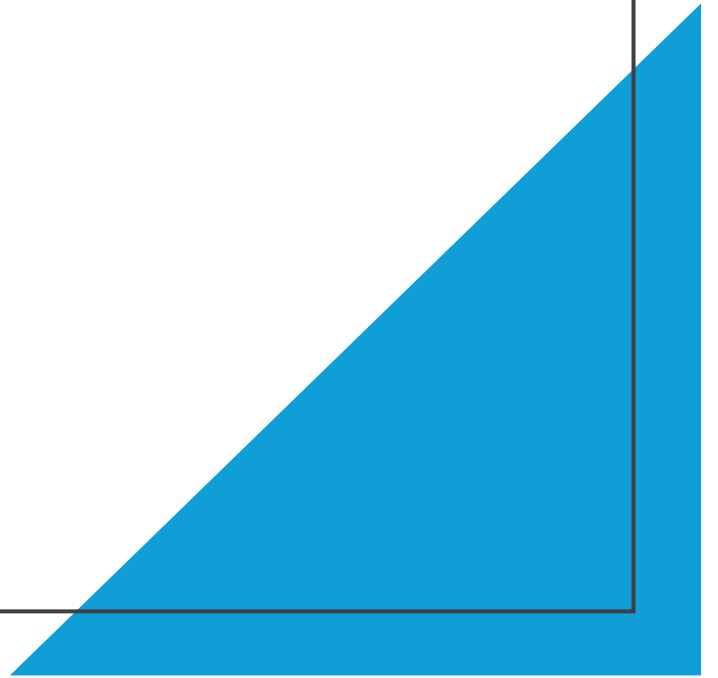


Near Vision Improvement



Qlosi - Orasis Pharmaceuticals

- Approved late 2024
- It is commercially available now
- Pilocarpine 0.4% BID
- Indicated for treatment of presbyopia in adults
- Doses should be applied 3-4 hours apart







Qlosi™

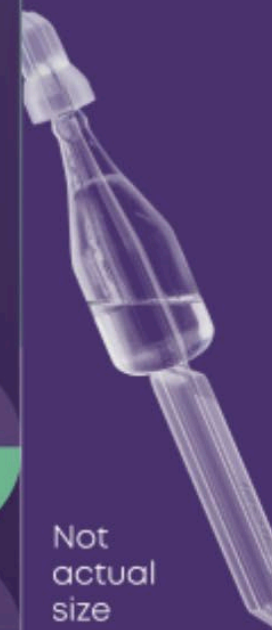
(pilocarpine HCl
ophthalmic
solution) 0.4%

Sterile / Rx only

For topical application in the eye

6 pouches containing 5 single-
patient-use vials (0.4 mL each)

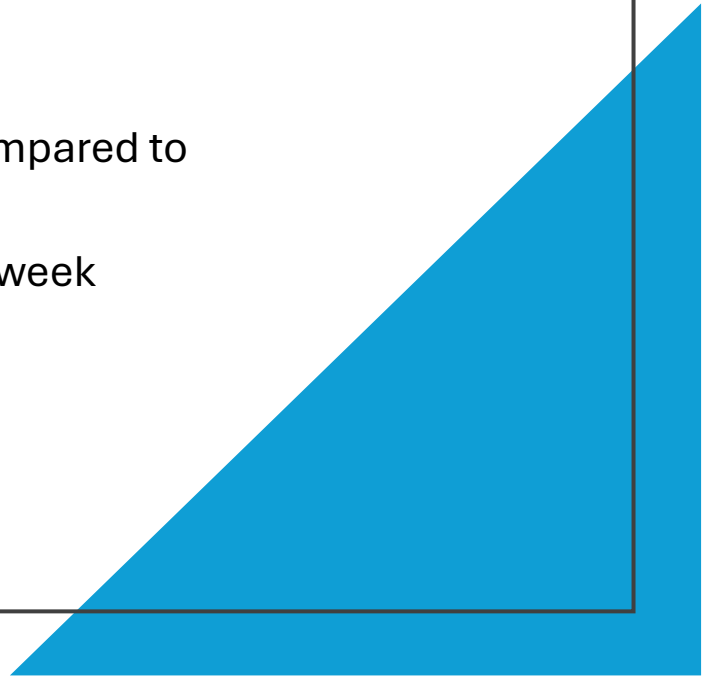
NDC 83661-018-30

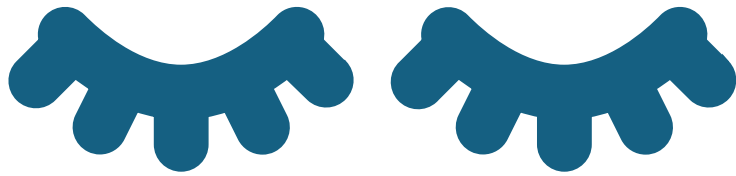


Not
actual
size

Qlosi – The Nitty Gritty

- Reduces pupil size to 2-3mm
- But does so in a dynamic fashion
- Preservative Free
- Near neutral pH
- Reduction in side effects (as compared to Vuity)
- Neuroadaptation takes about a week
- What about magnification??





Practical Strategies for Qlosi

- Prescribe through Blink Rx
 - \$79 per 1 month supply (30 vials)
 - \$99 per 60 day supply (60 vials)
 - Free shipping
- Thorough peripheral retinal exam is recommended
- What about CL wearers?
- Do we schedule for a “Qlosi exam”?

Qlosi vs Vuity

	QLOSI[®] 1.2 N=308	VUITY[®] 0.4 N=375
Concentration of Primary Active	0.4% Pilocarpine	1.25% Pilocarpine
pH	~6	3.5–5.5
Preservative-Free	Yes	No
Lubricating Agents	HA/HPMC	No
Common Adverse Reactions[†]		
Non-Ocular AEs		
Headache	21 (6.8%)	56 (14.9%)
Ocular AEs		
Instillation site pain	18 (5.8%)	16 (4.3%)
Visual impairment	3 (1.0%)	10 (2.7%)
Conjunctival hyperemia	5 (1.6%)	19 (5.1%)
Vision blurred	11 (3.6%)	17 (4.5%)

This chart does not reflect a head-to-head study of Qlosi and Vuity.

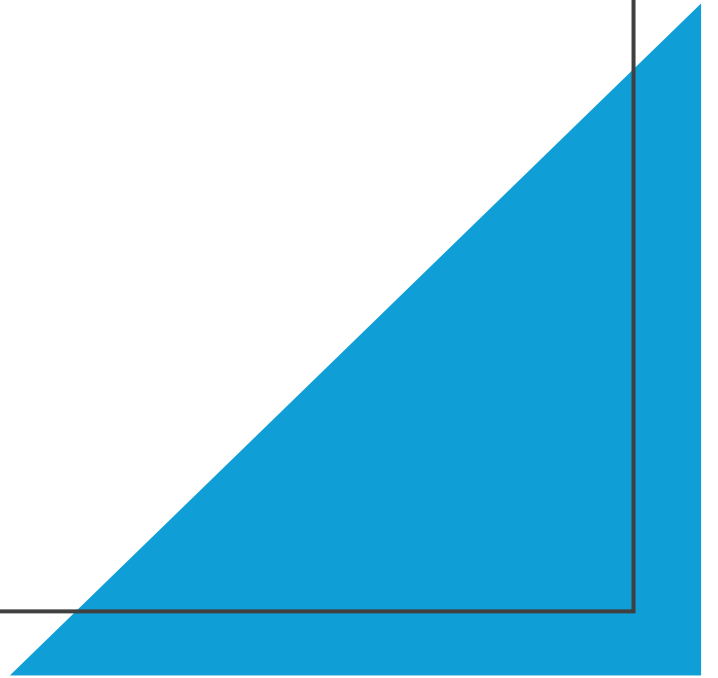


Important Safety Information - Qlosi

- Do not use Qlosi if you are allergic to any of the ingredients
 - Use caution when driving at night or performing hazardous activities in poor lighting. Qlosi may cause temporary dim or dark vision.
 - Temporary problems when changing focus between near objects and distant objects may occur. Do not drive or operate machinery if your vision is not clear
 - Seek immediate medical care if you experience sudden onset of flashes of light, floaters or vision loss
 - If you wear contact lenses, they should be removed before using Qlosi. Wait 10 minutes after dosing before reinserting your contact lenses.
 - Do not touch the tip of the vial to the eye or any other surface to prevent eye injury or contamination
 - If you use more than one eye medication, use each medication at least 5 minutes apart
 - The most common side effects reported with Qlosi in clinical trials are eye pain when administering Qlosi in your eye and headache. These are not all of the possible side effects with Qlosi.
-

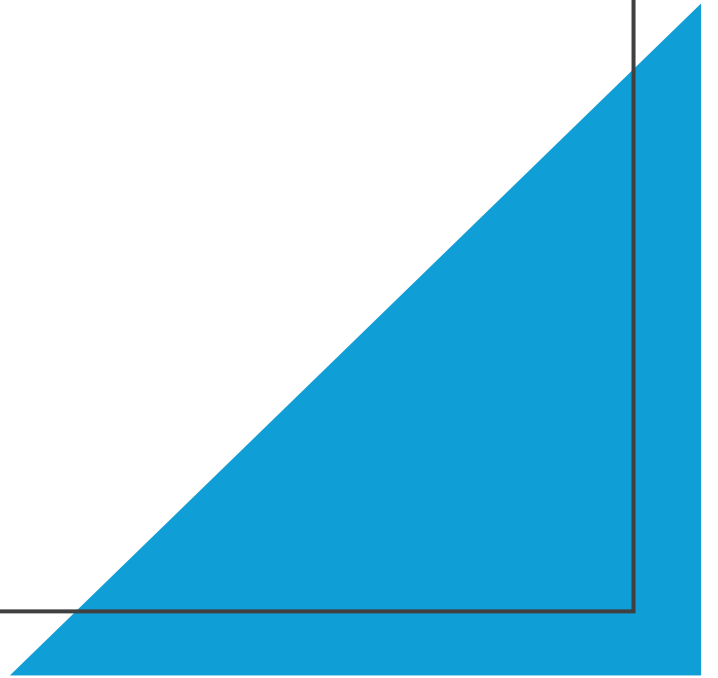
New Presbyopia drop #2

- LNZ 100 (Lenz Therapeutics)
- Aceclidine 1.75%
- QD dosing
- It is approved – not yet commercially available
- PDUFA date – August 8, 2025



LNZ 100 – What do we know?

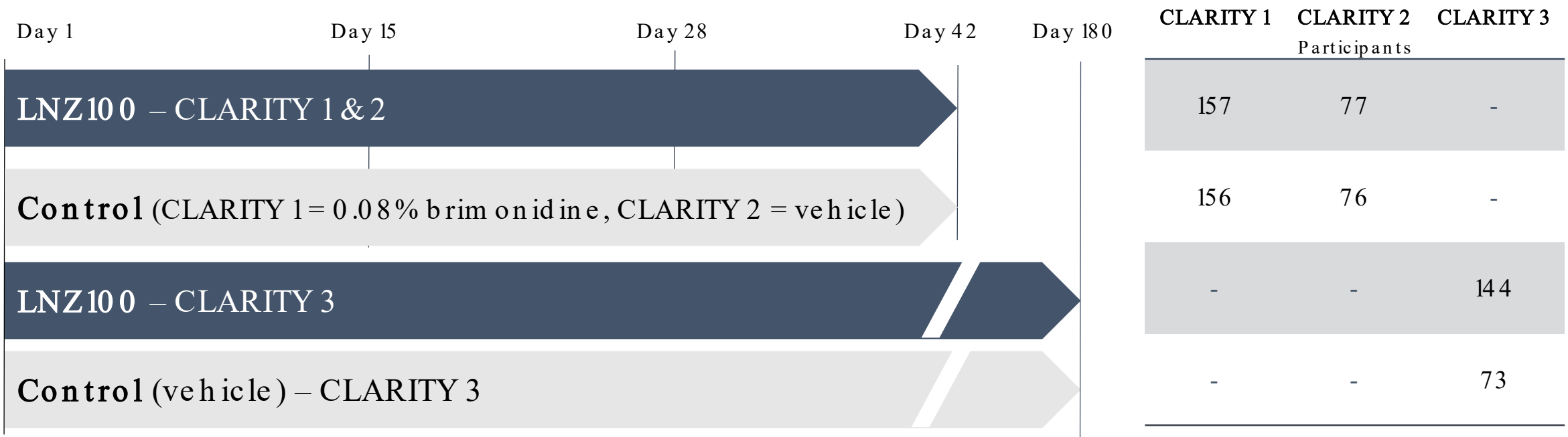
- Aceclidine 1.75%
- QD Dosing
- Has not been studied head -to -head vs Vuity or Qlosi
- Should be available in September



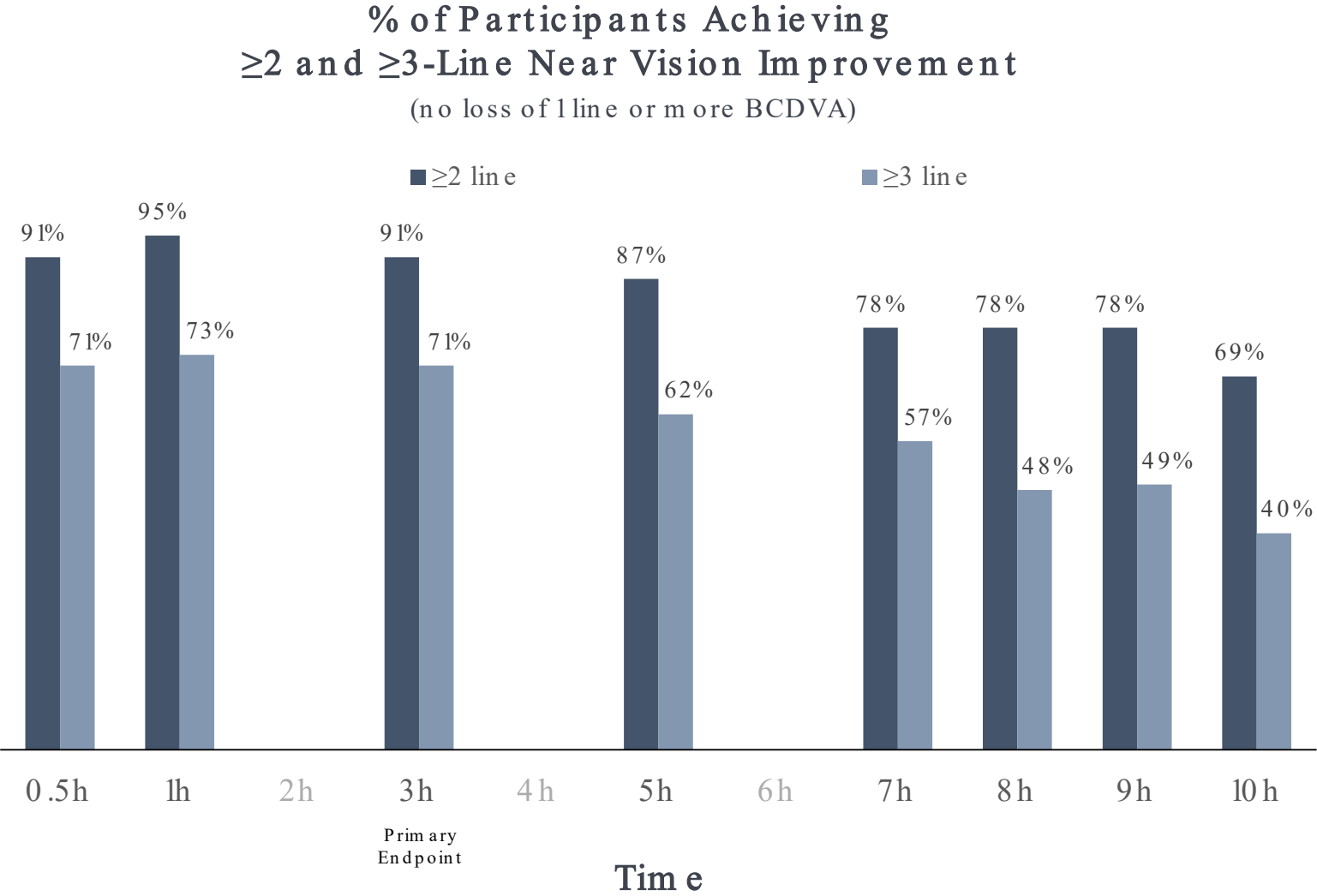
CLARITY LNZ100 Phase 3 Study Design

Randomized, double masked, controlled, Phase 3 trials (NCT05656027, NCT05728944, NCT05753189)

Ages 45 – 75, Mean 55 years ¹	Refractive range -4D SE to +1D SE	Inclusive of post-LASIK presbyopes and pseudophakes	Baseline near visual acuity 20/50 or worse ¹
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Clarity Phase 3 Results



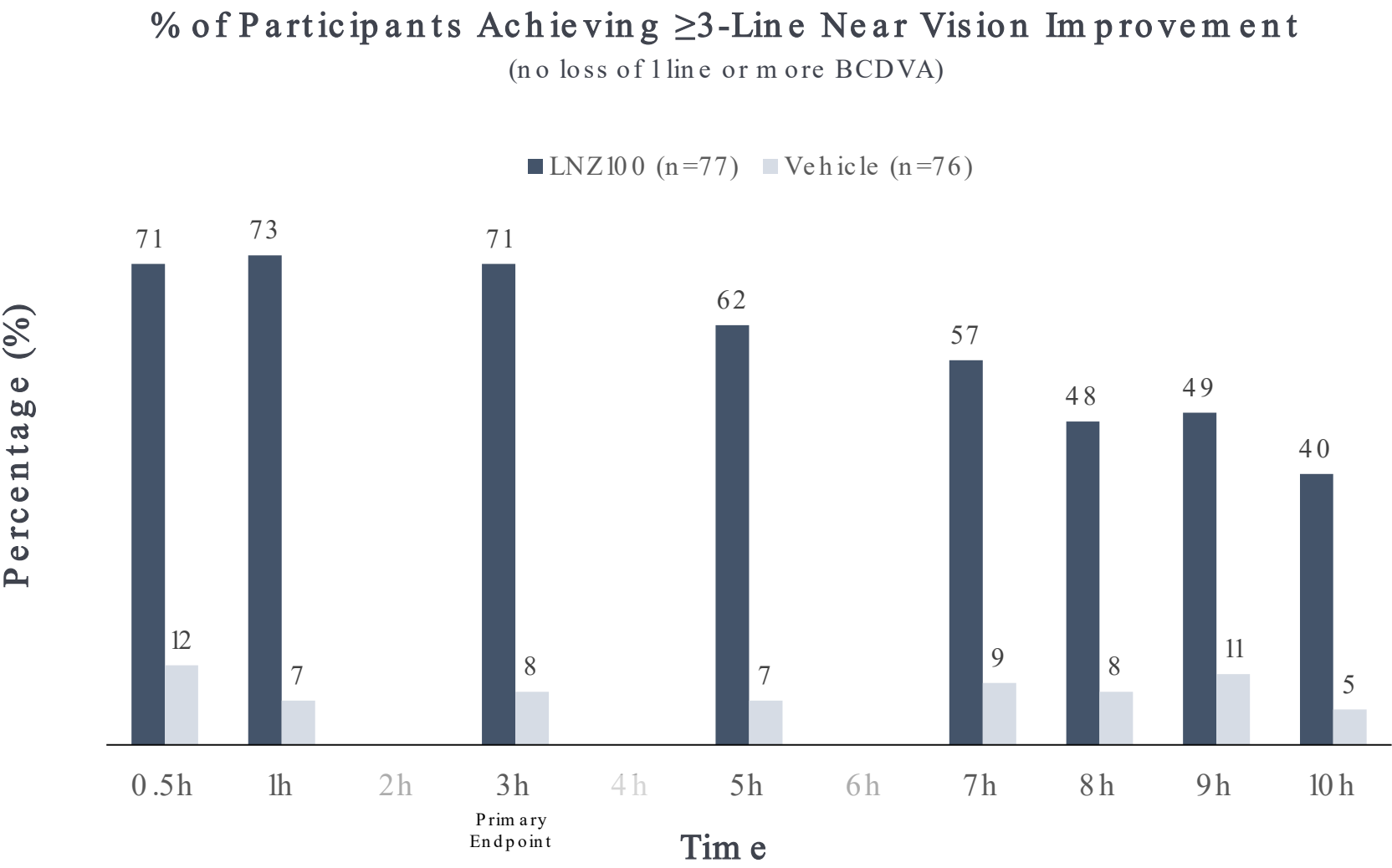
Once daily, rapid onset, long duration for vast majority of presbyopes makes LNZ100 the ideal presbyopia eye drop

3 lines FDA endpoint and 71% achieved at 3hr (primary)

2 lines clinically meaningful and 95% achieved at 1hr

p<0.0001 for all time points

Dose Response Time



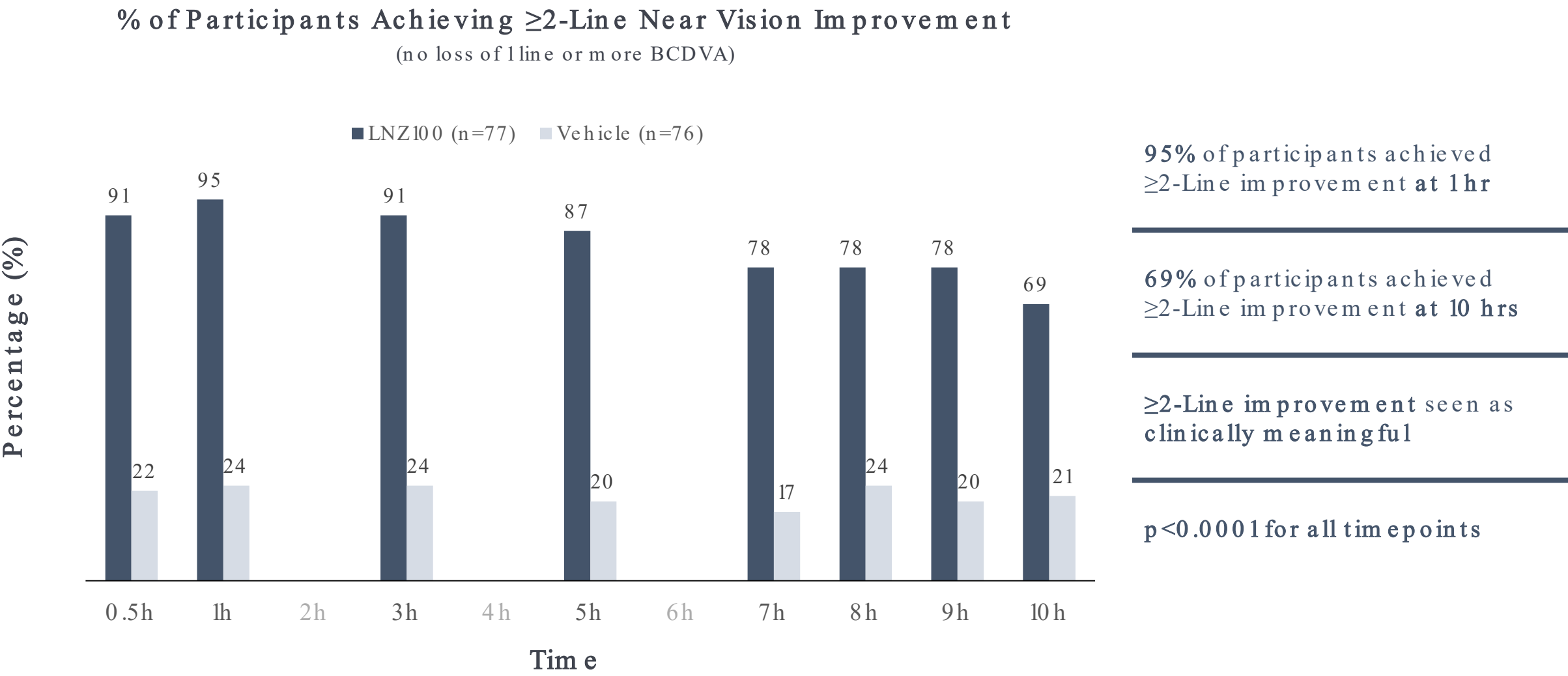
Rapid onset with 71% of participants achieving ≥ 3 -Line improvement at 30 min

Achieved Primary Endpoint with 71% participants achieving ≥ 3 -Line improvement at 3 hr

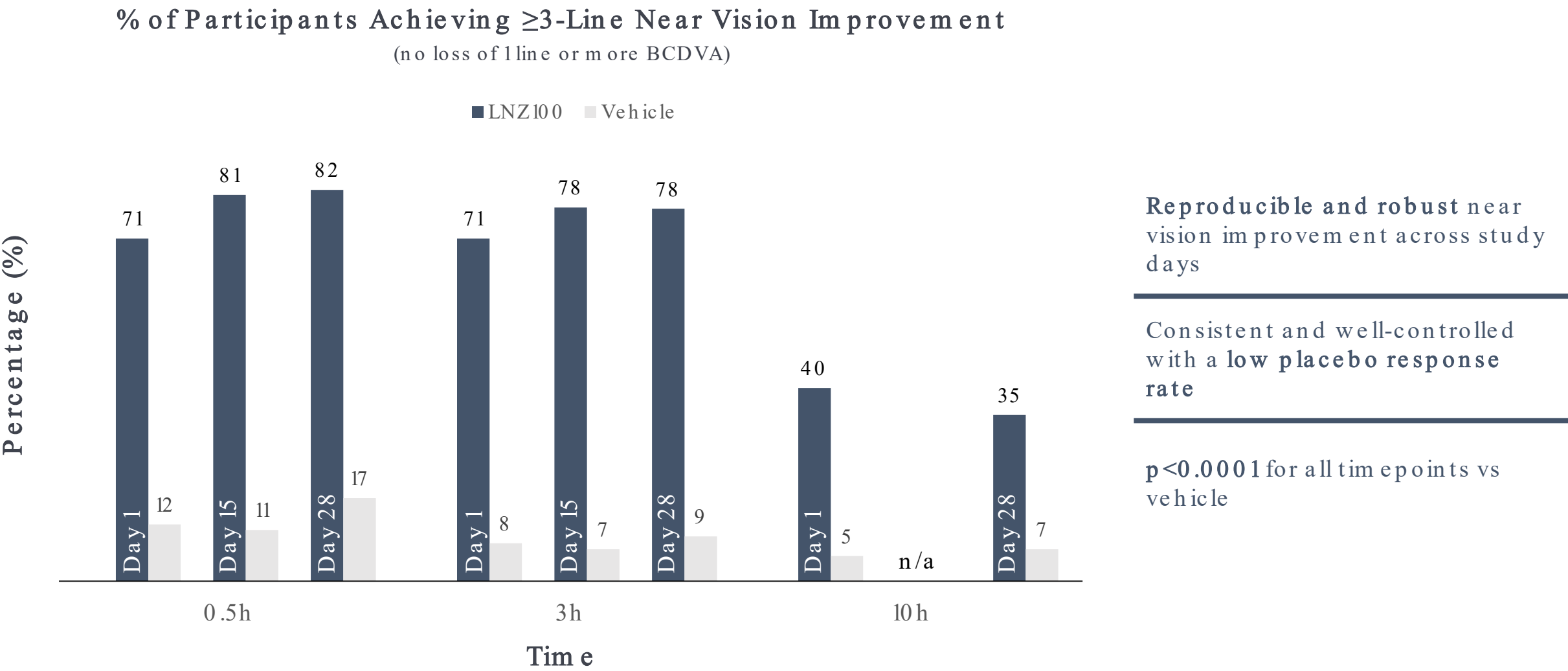
Long Duration with 40% response at 10 hours

$p < 0.0001$ for all time points

Nearly all participants (95%) achieved a ≥ 2 -Line improvement

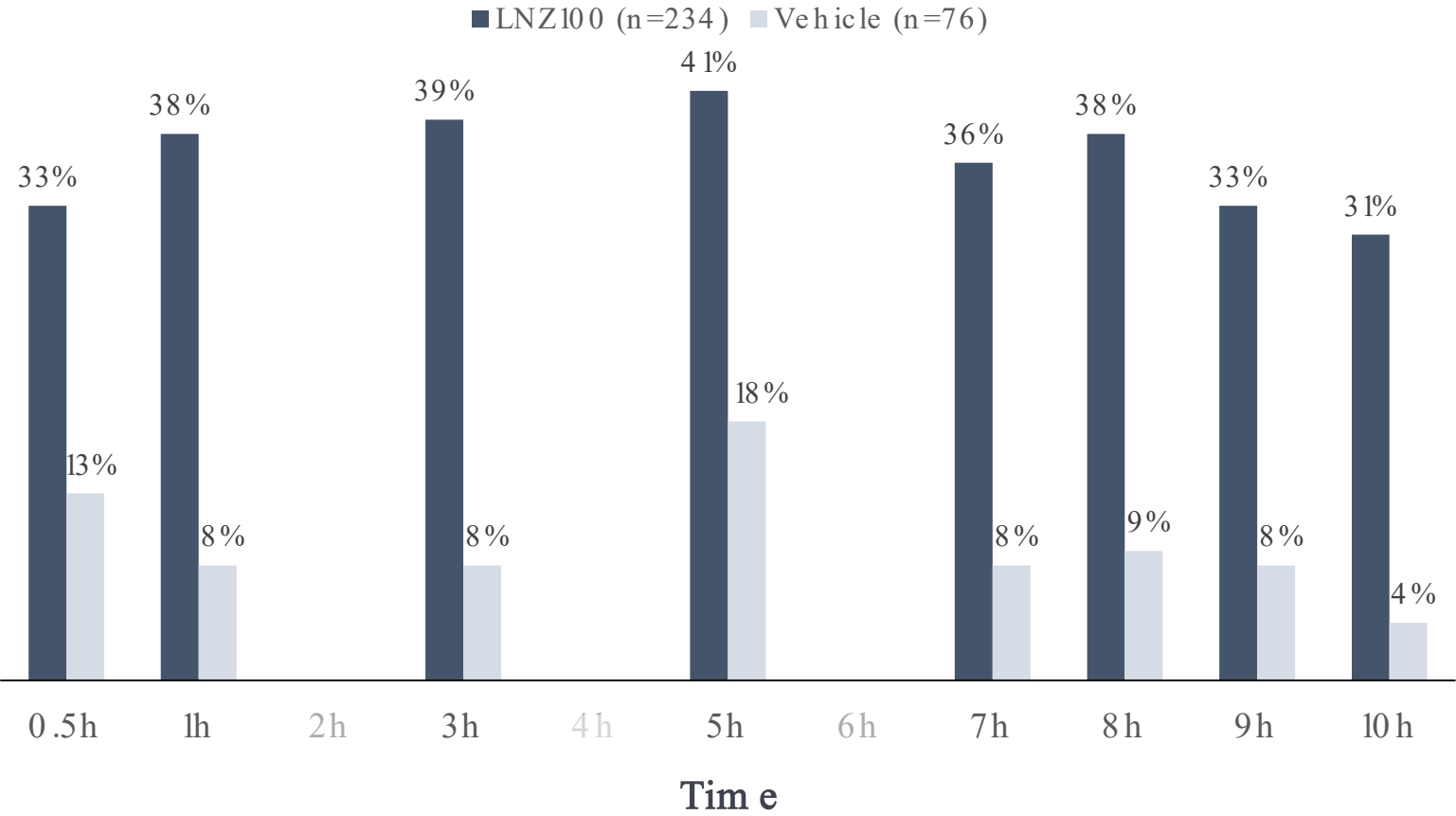


Consistent near vision improvement over 28 days



Statistically significant improvement in distance vision

% of Participants Achieving ≥ 1 -Line Distance Vision Improvement
Best Corrected Distance Visual Acuity



41% of participants achieved at least 1 Line of distance vision improvement

Testing was done while participants were wearing their normal distance vision correction

No negative impact to distance vision in low light

Reported side effect profile

Pooled analysis of CLARITY 1 & 2

	LNZ100 N=234 n (%)		Vehicle N=76 n (%)
Ocular AEs			
Instillation site irritation <i>(mild stinging upon instillation)¹</i>	47 (20.1%)	100% mild	8 (10.5%)
Visual impairment <i>(mild dimness)¹</i>	31 (13.2%)	100% mild	1 (1.3%)
Hyperemia <i>(mild eye redness)</i>	21 (9.0%)	100% mild	2 (2.6%)
Non-Ocular AEs			
Headache	27 (11.5%)	89% mild 7% moderate	3 (3.9%)

33% no longer experienced such transient response to installation after day 2 of product use, 44% after day 7 and 70% after day 28²

No serious treatment related adverse events

Ocular AEs classified by participants and investigators as 100% mild

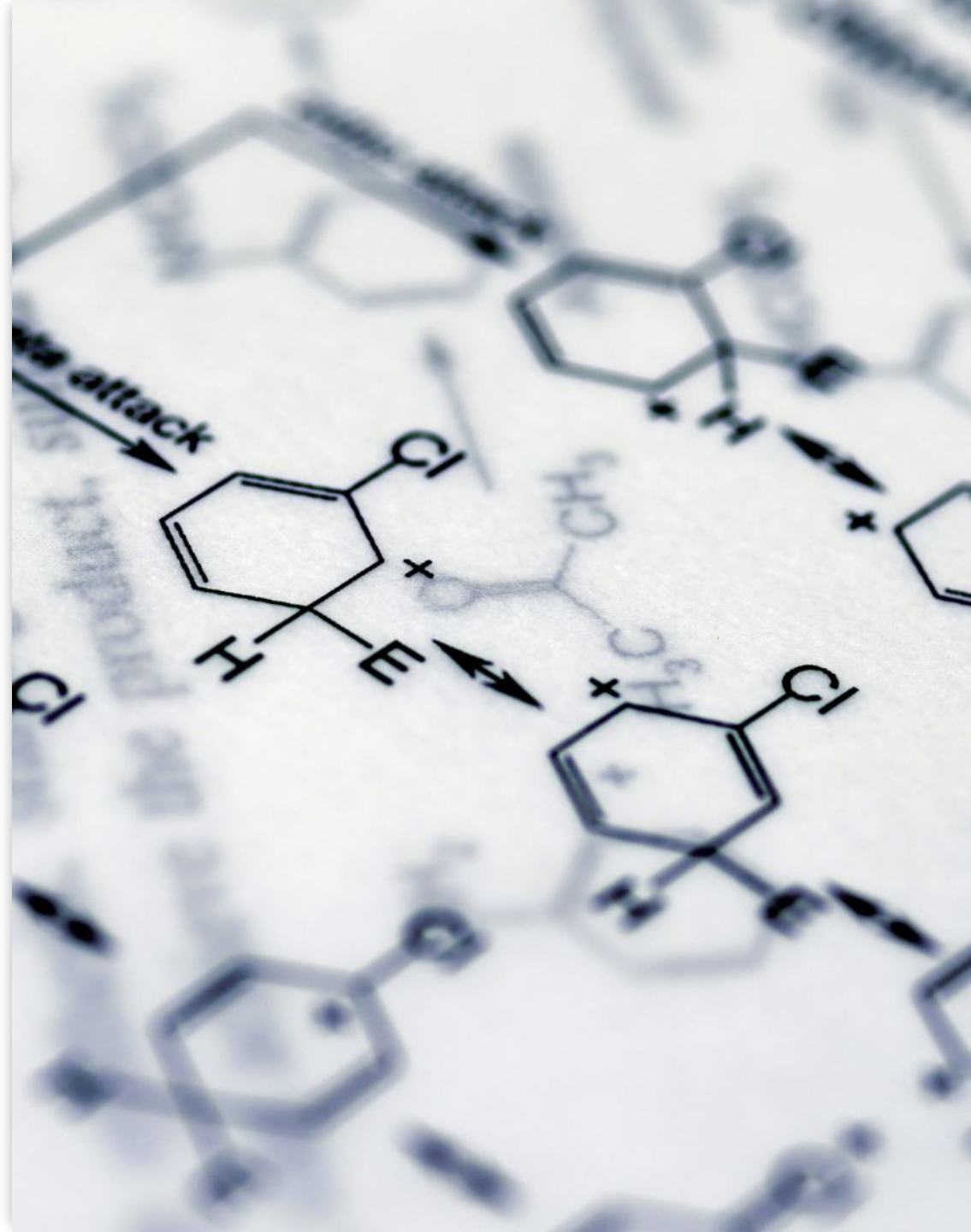
Placebo corrected headache incidence of 7.6% and mostly reported as mild

Less than 4% discontinue-rate due to treatment related AEs

Across all CLARITY trials 378 participants for a combined 30,000+ days on LNZ100 without treatment related serious AEs

LNZ 100 – So What???

- A different molecule
 - Constricts the pupil
 - Creates a pinhole effect
- A different dosing schedule
- It was studied on CL wearers
- It was studied on higher myopes (up to -4)
- It is preservative free
- Is it better?



Brimochol PF – Tenpoint Therapeutics

Combination drug preservative-free (PF) combination ophthalmic solution of carbachol 2.75%, a miotic agent for pupil constriction, and brimonidine tartrate 0.1%, which inhibits iris dilator muscle contraction.⁶

Brimonidine is also believed to possibly inhibit ciliary muscle contraction, thereby assisting to decrease associated side effects, as well as act as a vasoconstrictor leading to increased bioavailability and duration of action of the carbachol molecule.⁶

- Phase 3 pivotal BRIO-I trial met its primary endpoint, without a loss of ≥ 5 letters at distance, starting at Hour 1 and maintaining across all time points through Hour 6.⁶ The drug was well-tolerated by trial subjects, with no significant adverse events.⁶

Brimochol PF – Tenpoint Therapeutics

- Combination drop
 - Carbachol 2.75% - (miotic)
 - Brimonide tartrate 0.1% - (inhibits iris dilator muscle and inhibits ciliary muscle contraction)
- So What?!?!?!?
- How is this different?



Brimochol PF



Preservative free



Increased bioavailability (because of brimonidine)



Thus longer duration of action



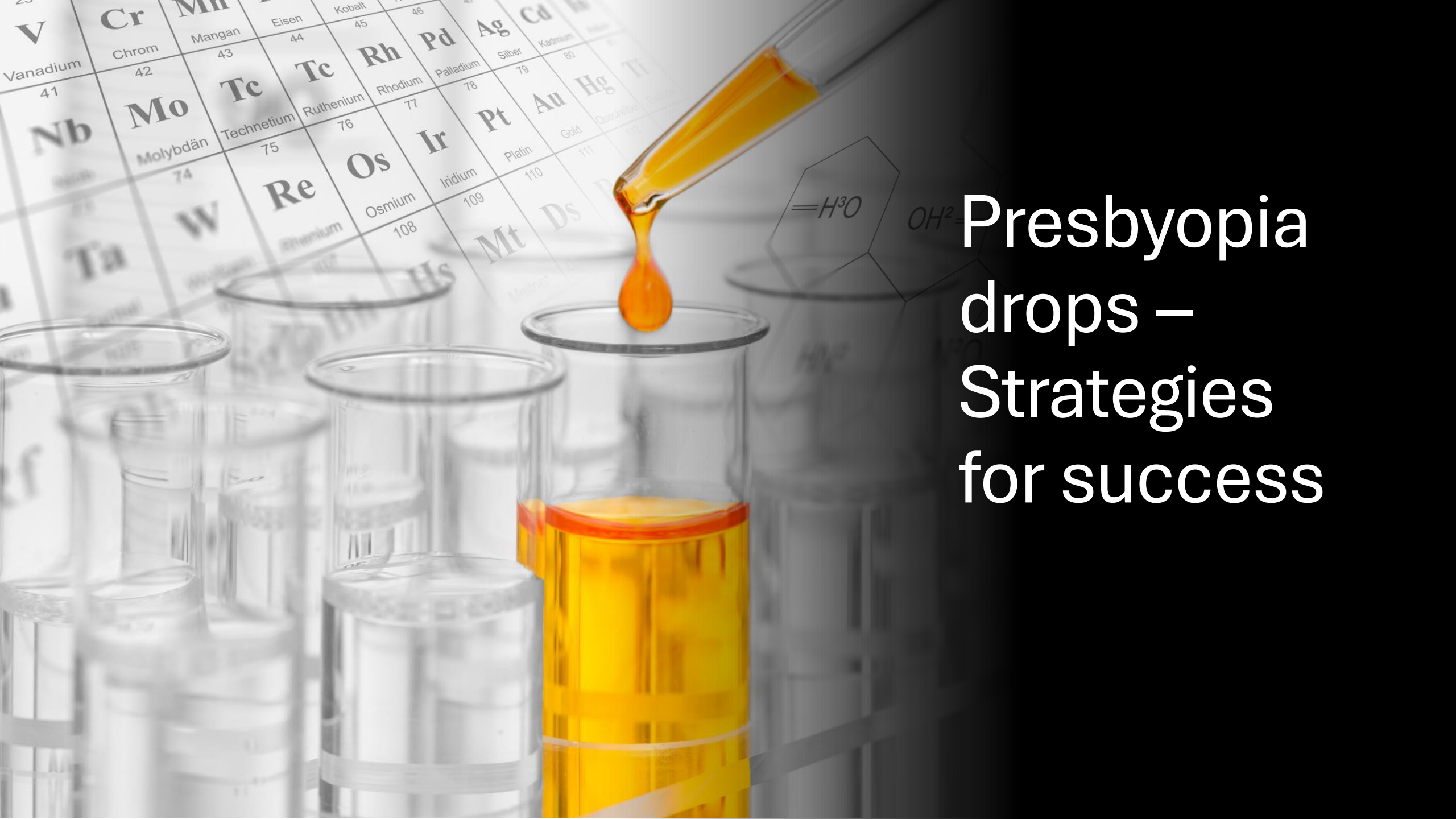
Dosage- QD



Lasts up to 10 hrs, but does have a reduced effect after hour 8

Brimochol PF Study results – Phase 3

- 12 month study
- Emmetropes or pseudophakes
- Compared to placebo
- >15 letters at near improvement
- > Works as quickly as 20 minutes



Presbyopia drops – Strategies for success

Have a well thought out process

- Start with easy targets
 - Low myopes/ emmetropes
- Pseudophakes
- Schedule for a dedicated exam- including a detailed peripheral retinal exam!!!
- Adjust dosing schedule as needed
- Avoid hyperopes (to begin with)
- Have them back for a follow up at 3 months



One final word about glaucoma therapies

A lot of money is being spent on delivery systems

These may be cheaper alternatives

Optometry cannot sleep on this

Automated Direct SLT (Belkin)



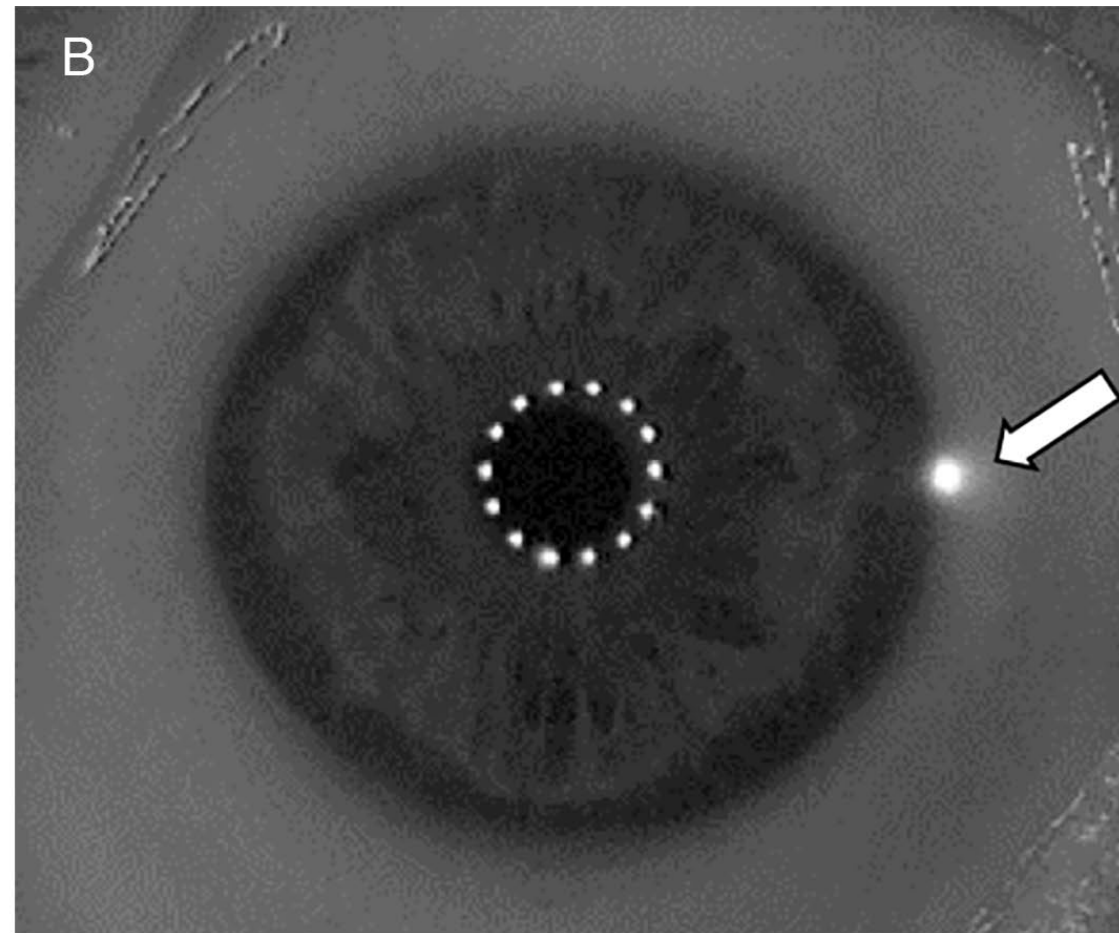
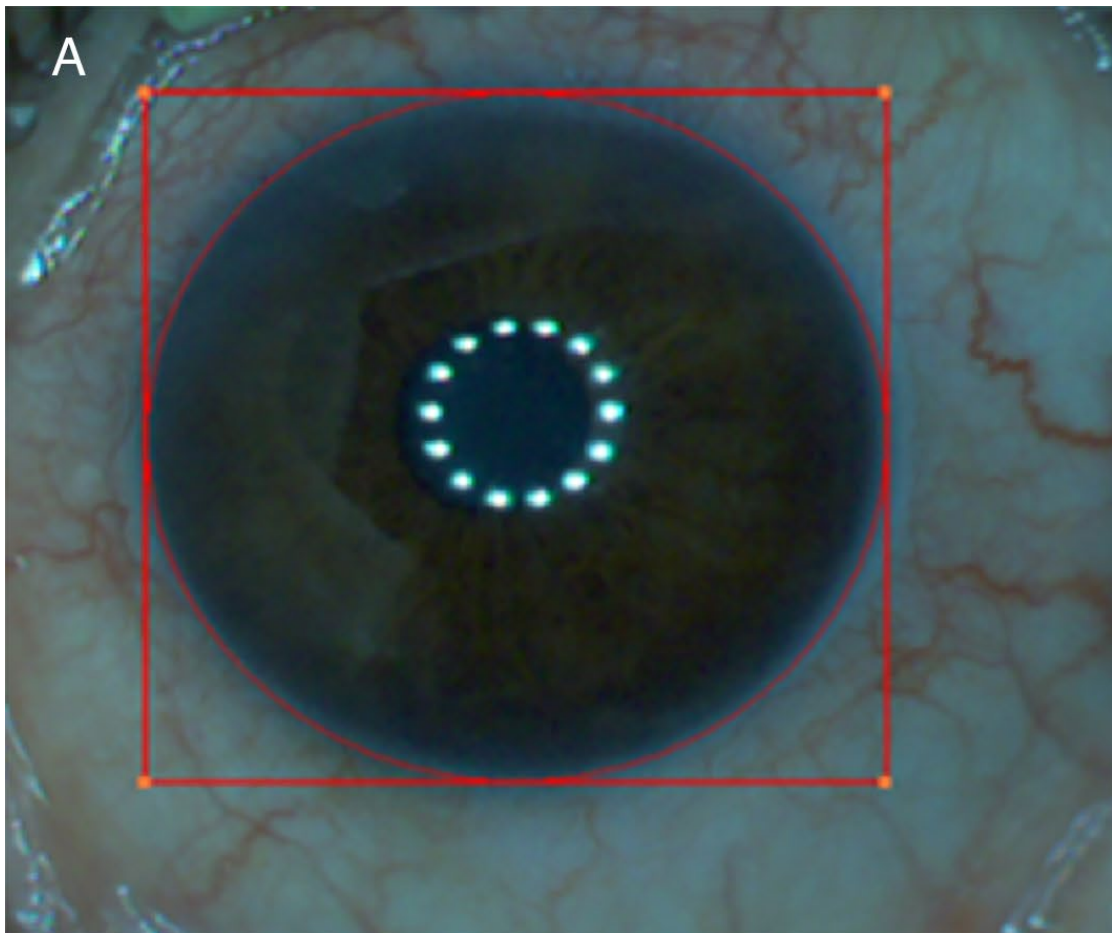
Belkin DSLT

- Rapid, non-contact Direct SLT
 - Delivers similar energy as traditional SLT
 - Automated delivery of energy through limbus (transconjunctival)
 - Without Gonioscopy
-
- Will be approved in US within months!!

DSLT Data

- Baseline IOP 26.7-
 - Patients were washed out of all meds
 - Some pxs were treatment naïve
- After tx IOP
 - 1 mth – 21.7mm Hg (18.1% reduction)
 - 3 mth- 20.8mm HG (21.4%)
 - 6 mth 21.5mm Hg (18.8% reduction)
- At 6 mths medication need reduced from 1.6 to 0.4

Automated Direct SLT





#This Is A BFD!!

Are we ready???

1 More Topic – Autologous Serum





Autologous Serum – The How

More aptly called Eye-Platelet Rich Plasma (EPRP)

Eyedrops created from patient's own blood

Blood is drawn and spun down

WBC and RBC are all removed by centrifugation; platelets and growth factors remain

Plasma is placed in sterile eyedrop bottle





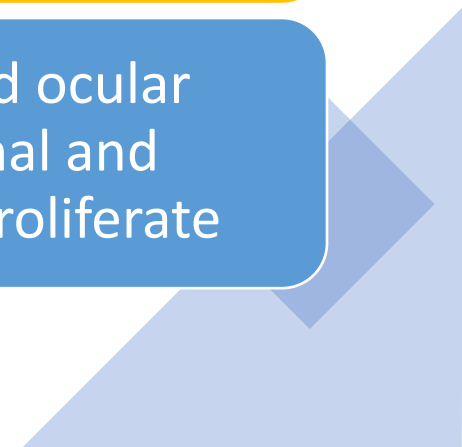
Autologous Serum – The Why

Autologous plasma is rich in platelets and growth factors

Growth factors enhance proliferation and wound healing

Effective on hard and soft tissues

Growth factors restore damaged ocular surface by inducing mesenchymal and epithelial cells to migrate and proliferate



Autologous Serum – The What For?

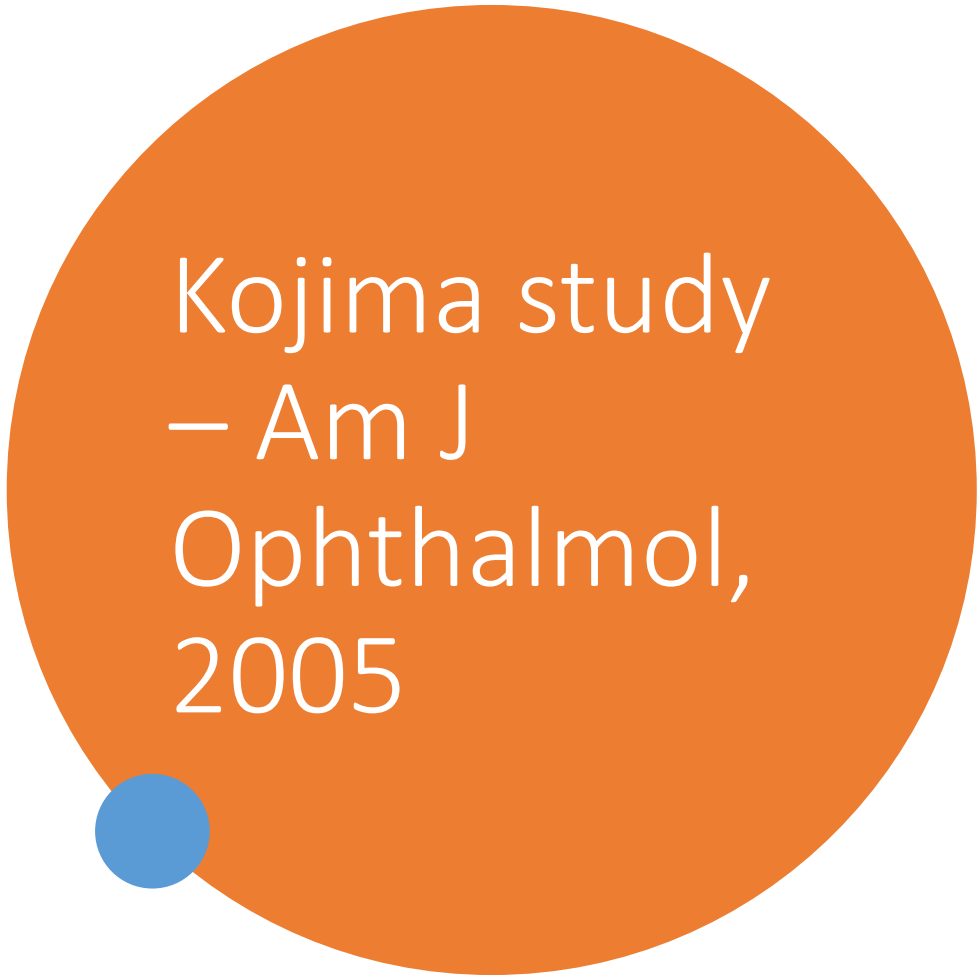
Severe Dry Eye

Corneal Ulcers (especially if dormant)

Non-healing epithelial defects

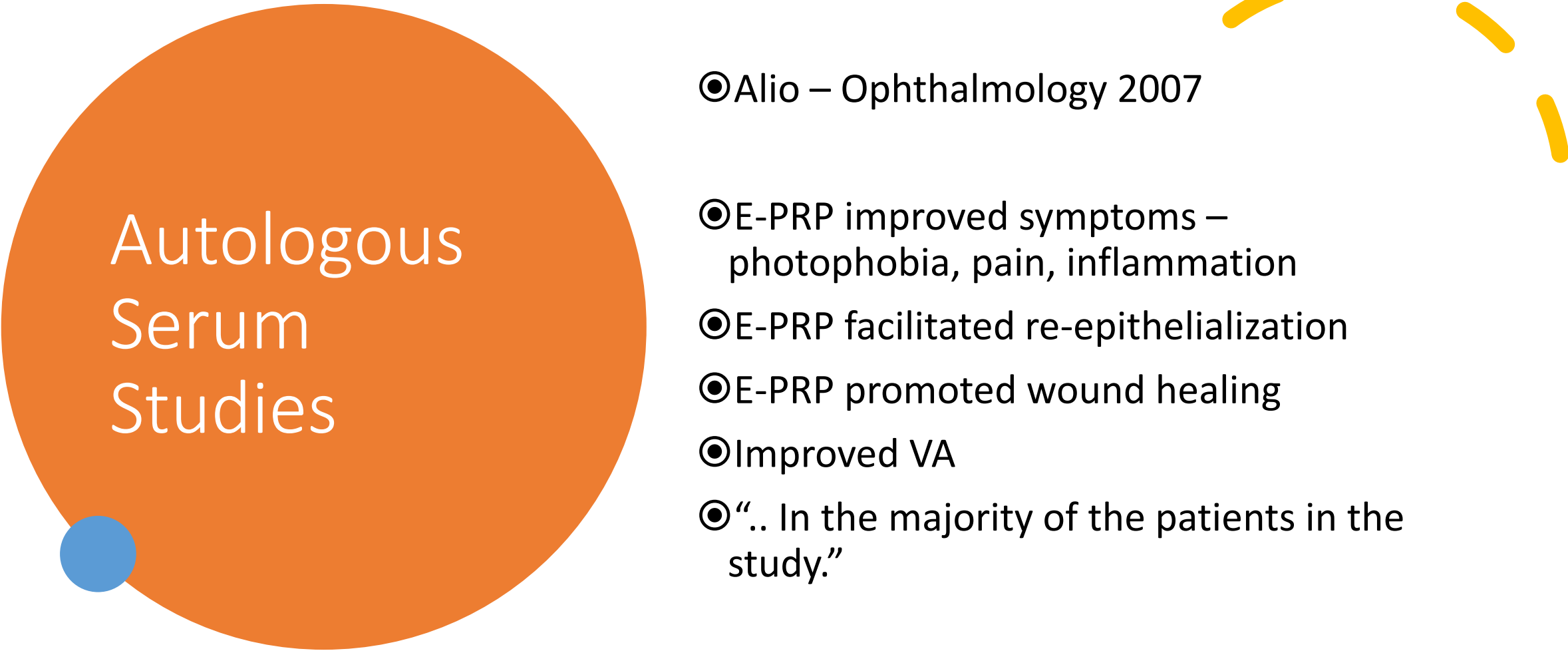
LASIK complications

Chronic Dystrophies (EBMD)



Kojima study
– Am J
Ophthalmol,
2005

- E-PRP for Dry Eye
- Conclusion- Autologous plasma is superior to conventional treatment for improving ocular surface health and subjective comfort
- E-PRP improved tear stability and vital staining scores (RB)



Autologous Serum Studies

◎Alio – Ophthalmology 2007

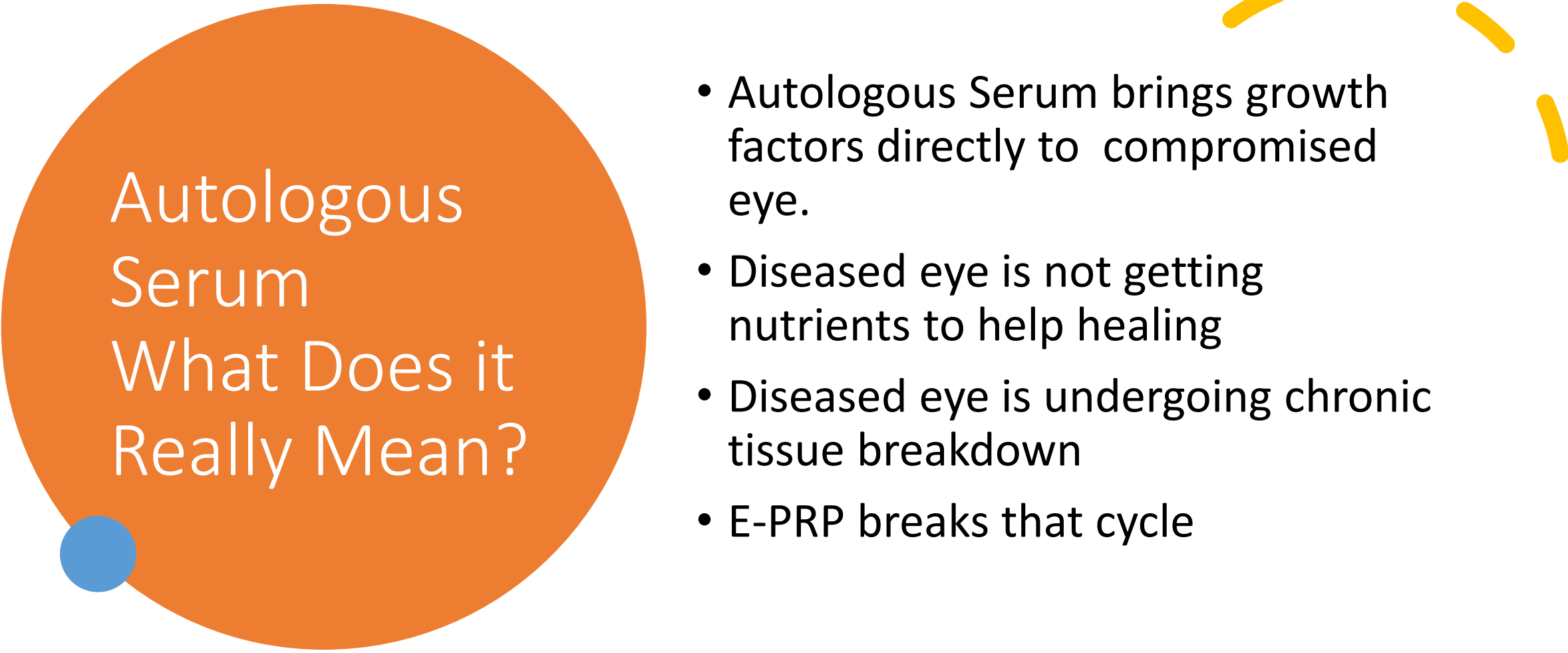
◎E-PRP improved symptoms –
photophobia, pain, inflammation

◎E-PRP facilitated re-epithelialization

◎E-PRP promoted wound healing

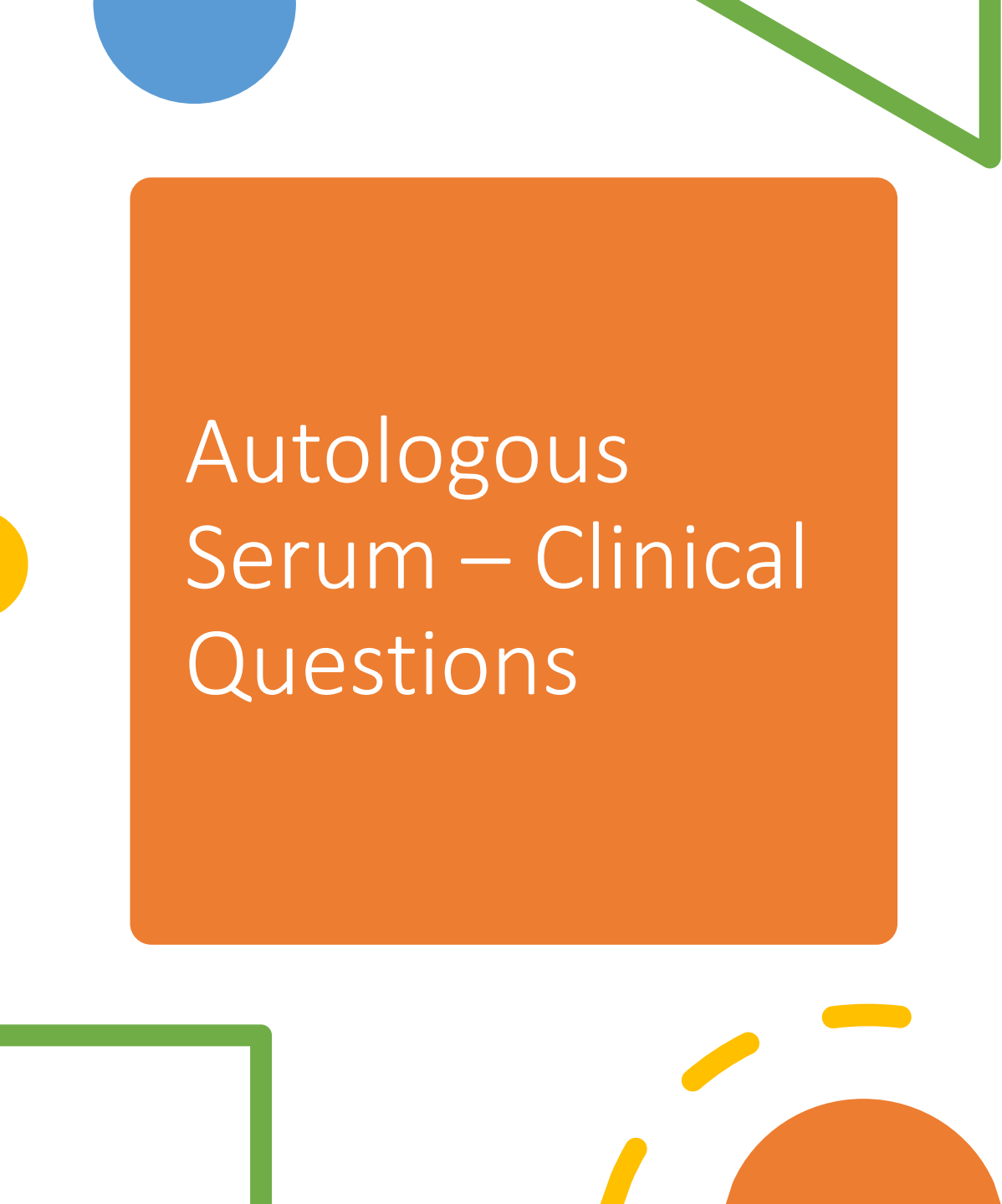
◎Improved VA

◎“.. In the majority of the patients in the
study.”



Autologous Serum What Does it Really Mean?

- Autologous Serum brings growth factors directly to compromised eye.
- Diseased eye is not getting nutrients to help healing
- Diseased eye is undergoing chronic tissue breakdown
- E-PRP breaks that cycle



Autologous Serum – Clinical Questions

- What is the dosage?
- Where should it be kept?
- When should it be Rx'd?
- How Can I actually Acquire It???