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10:10 AM–10:15 AM

LYNX-1: A Pivotal Phase 3 Double-Masked, Randomized Placebo-Controlled Trial of Phentolamine Ophthalmic Solution in Subjects with Dim Light Vision Disturbance

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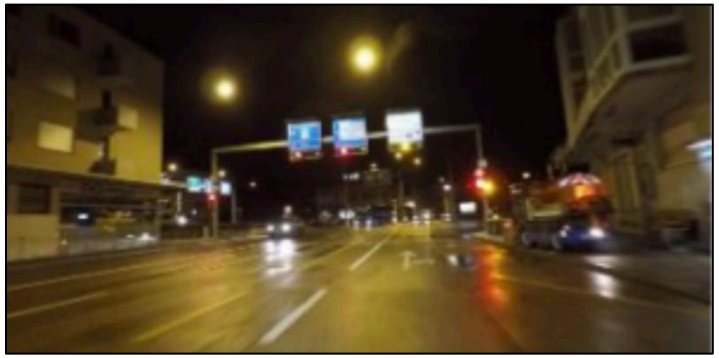
What are Dim Light (DLD) or Night Vision Disturbances (NVD)?

- Night vision disturbances (NVD) describe a decrease in the quality of vision secondary to glare disability, with decreased contrast sensitivity and consequential image degradation.

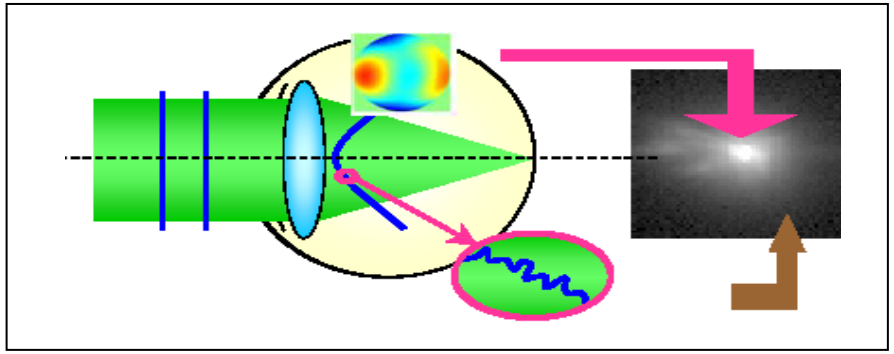


  - *Glare* is light that appears bright and intense.
  - *Ghosting* is to be troubled by a faint, partial, monocular double image.
  - *Starburst* refer to radial or regular radiating scatter of light from a point source.

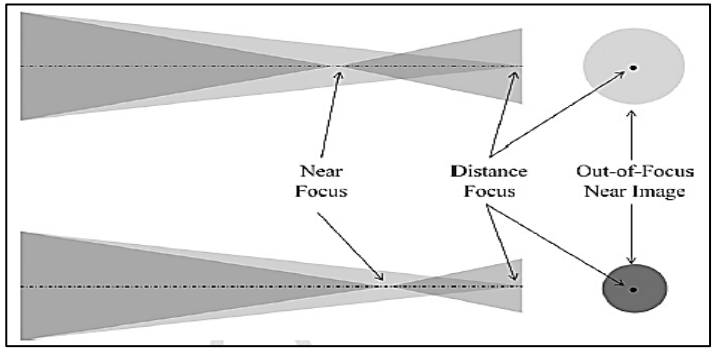
Rosen ES. Night vision disturbance. J Cataract Refract Surg. 2005;31:247-9.

What Causes Dim Light Disturbances?

- *ABERRATIONS*: impact light distribution on a small angular distance



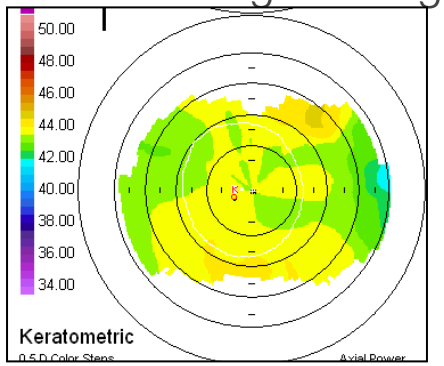
- *SCATTERING: causes uniform distribution of light across a wide region of the retina*
- *INTERNAL REFLECTIONS: within an intraocular lens due to the square edge design*
- *SUPERIMPOSED OUT OF FOCUS RETINAL IMAGE:* with EDOF/multifocal IOLs

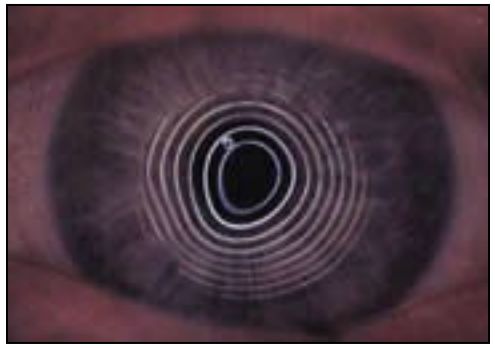


Liao X, Lin J, Tian J, et al. Curr Eye Res 2018;43:696-701; Nochez Y, Majzoub S, Pisella PJ. J Cataract Refract Surg 2012;38:633-40.
Adapted from slide courtesy of Jack T. Holladay, MD, MSEE, FACS

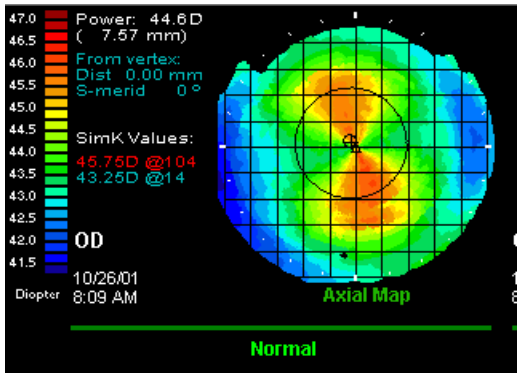
Complex Corneas with Irregular Astigmatism and Peripheral Aberrations

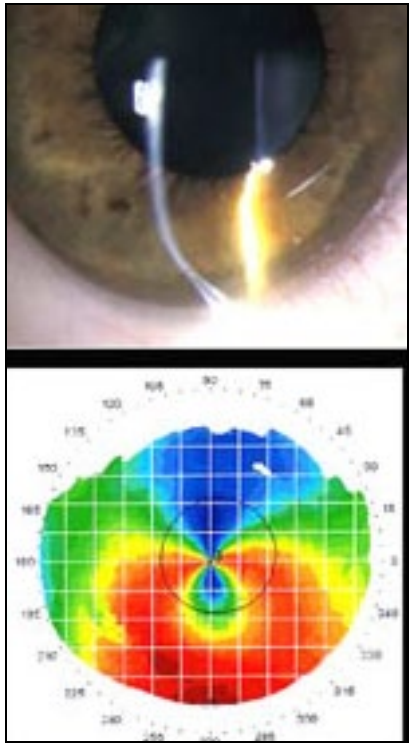
- Anterior Basement Membrane Dystrophy
- RK, PRK, LASIK
- Pterygium, Salzman's nodular degeneration
- Keratoconus
- Pellucid Marginal Degeneration, ectasia

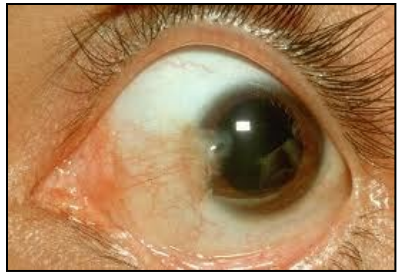




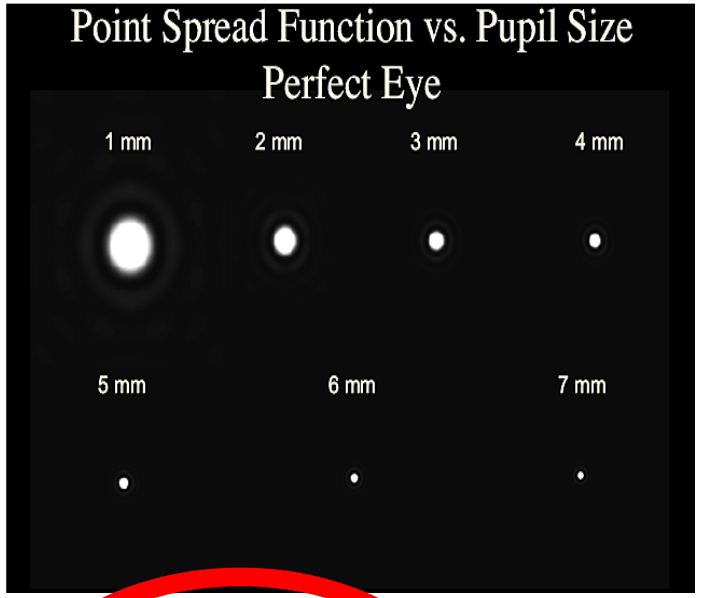
Regular astigmatism

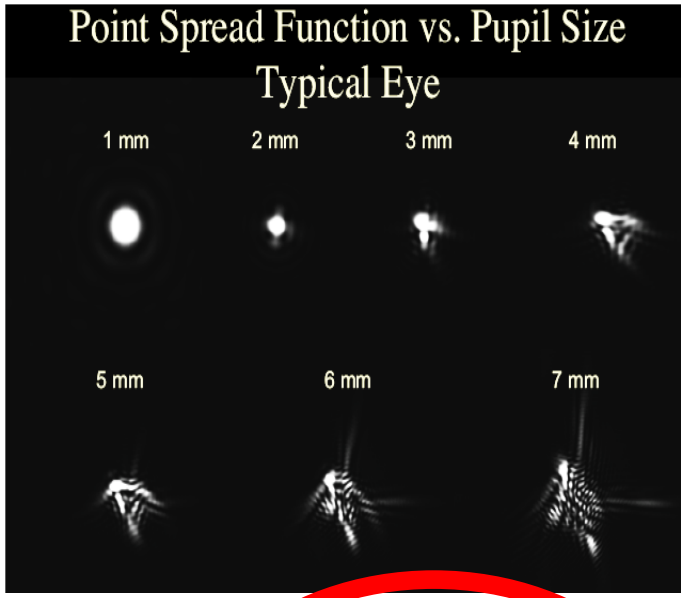


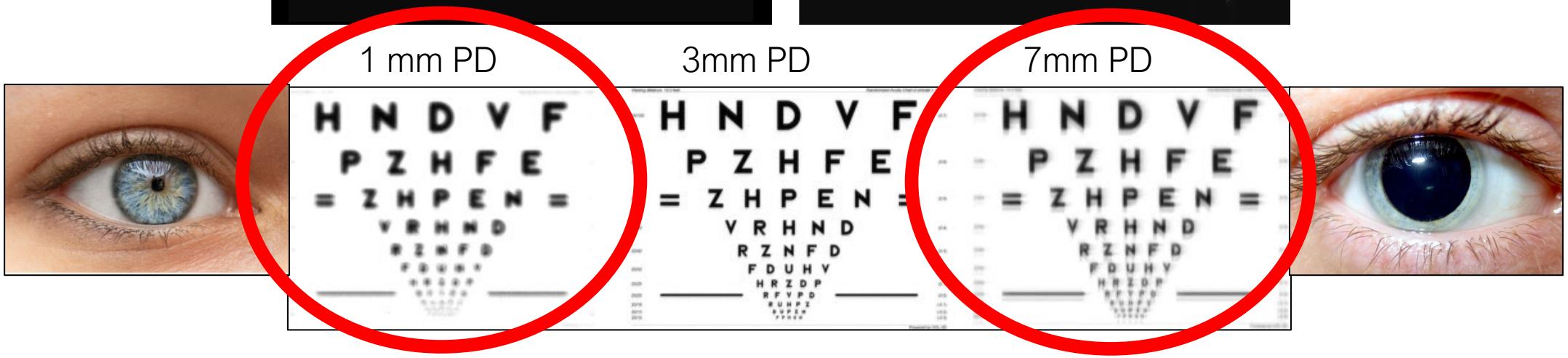




Effect of Pupil Size on Ocular Aberrations and Visual Quality







Pepose JS, Applegate RA. Making sense out of wavefront sensing. Am J Ophthalmol. 2005;139(2):335-43.

Potential Treatment Option: 0.75% Phentolamine Ophthalmic Solution

Differentiated Iris Dilator Inhibition MOA for Functional Vision Improvement

Phentolamine is the Active Ingredient in POS: a non-selective α1 Antagonist

Phentolamine blocks α1 receptors on the **Iris Dilator Muscle**

↓

Decreases pupil size (moderately) **without affecting the iris sphincter or ciliary muscles**

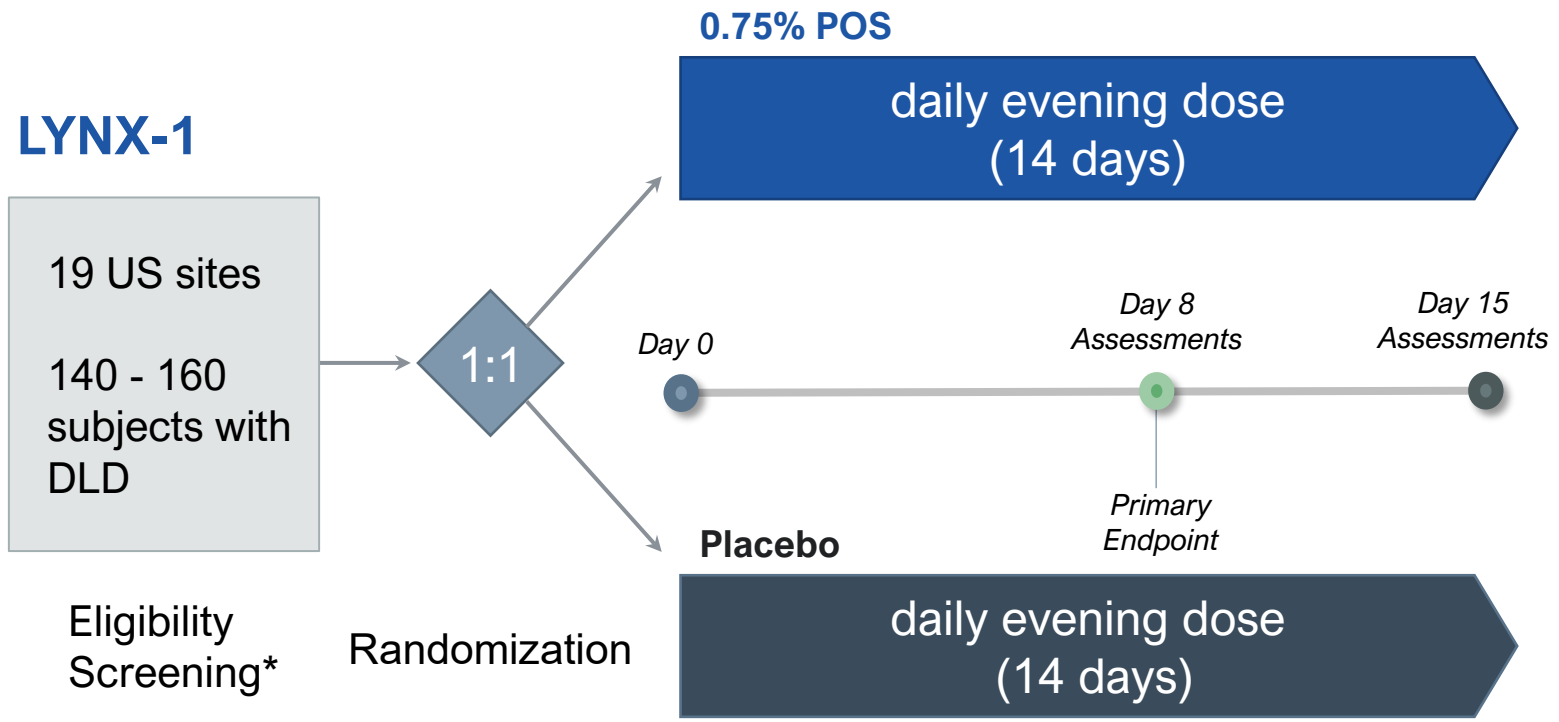
↓

Allows for 3 indications:
RM, Presbyopia and DLD

POS is not approved by any regulatory agency. Illustration for educational purposes

Study Design

Randomized, Double-Masked, Placebo-Controlled Two-Week Trial



Phase 3 Initiated in Dec 2020; 145 Subjects Enrolled

Top Line Results Reported May 19, 2022

Inclusion Criteria - Subjects with baseline mesopic LCVA of 20/63 or worse

Endpoints

Primary: % of subjects with ≥ 15 letters of improvement in mesopic low contrast best-corrected distance visual acuity (Day 8)

Secondary (Days 8 & 15):

- Pupil diameter
- Visual acuity measures (distance and near)
- Safety and tolerability (redness)

Demographics and Baseline Characteristics

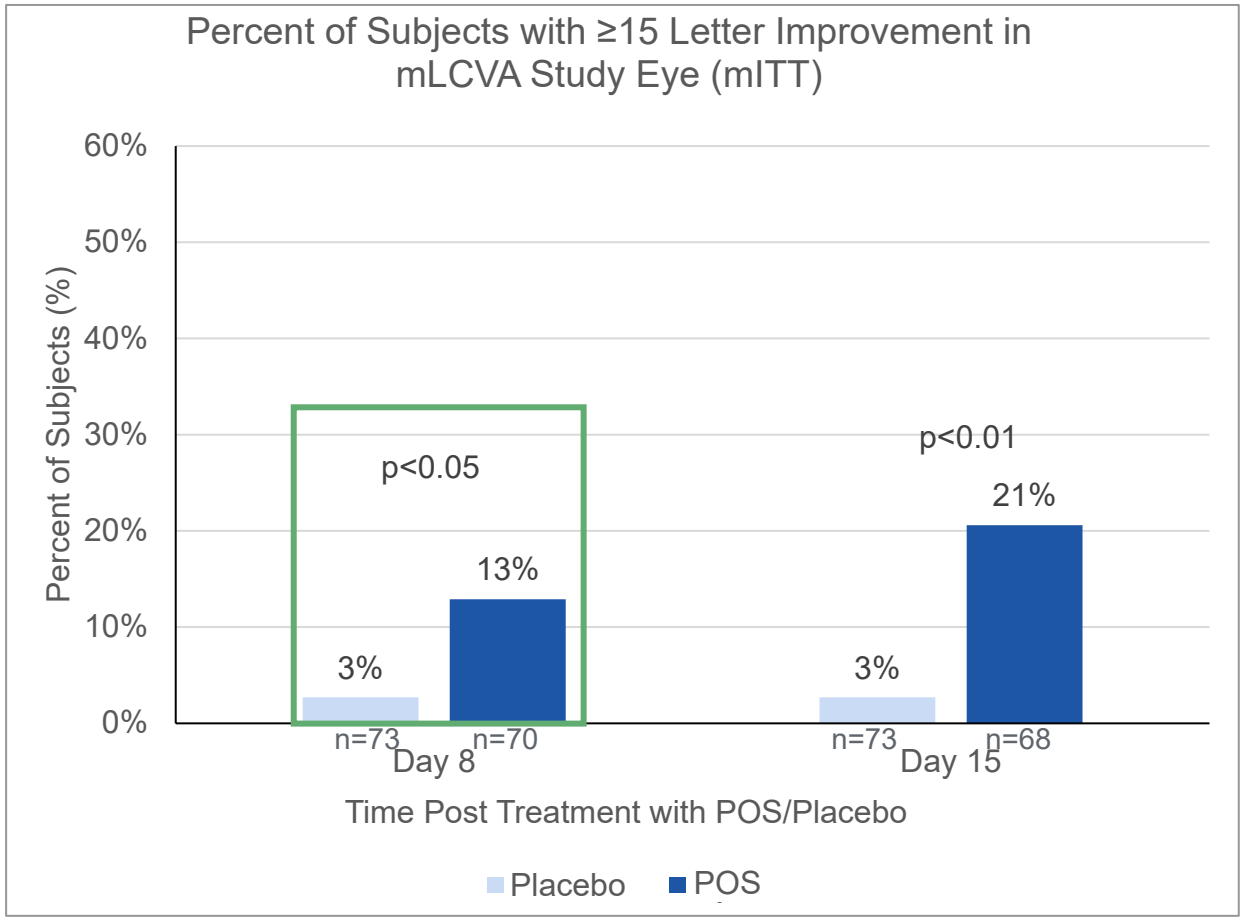
Treatment and Placebo Arms Were Well-Balanced

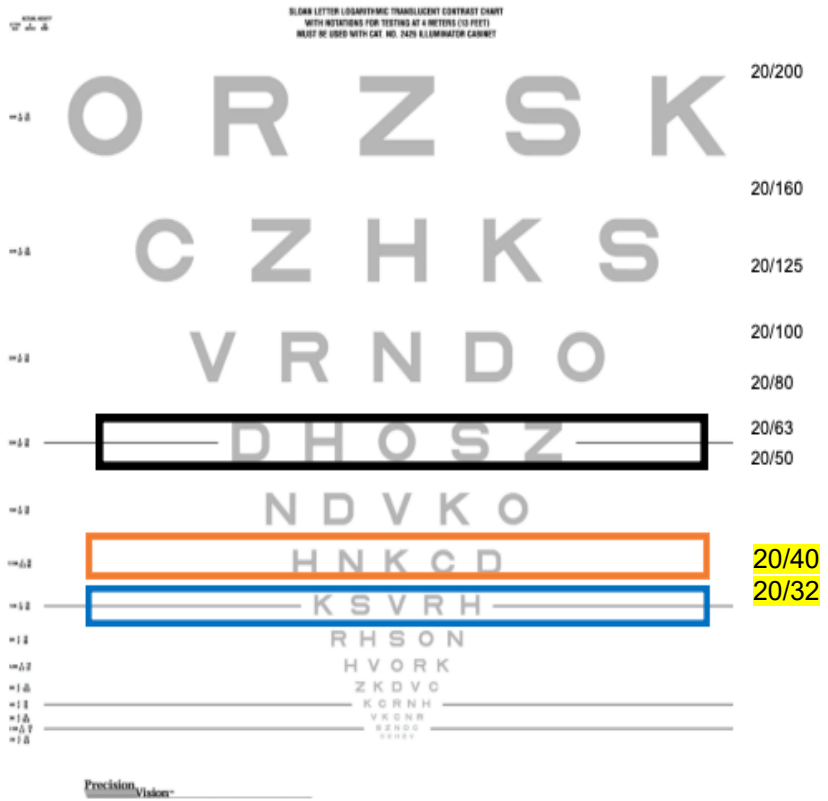
	POS n=70	Placebo n=73	Total n=143
Baseline Characteristic			
Age (years): Mean (Range)	47 (19-70)	45 (19-69)	46 (19-70)
Sex: Male n (%) **Female** n (%)	9 (13%) 61 (87%)	14 (19%) 59 (81%)	23 (16%) 120 (84%)
Race: White n (%) Other* n (%)	67 (96%) 4 (5%)	65 (89%) 9 (12%)	132 (92%) 13 (9%)
Light Iris Color: n (%)	43 (61%)	44 (60%)	87 (61%)
Dark Iris Color: n (%)	27 (39%)	29 (40%)	56 (39%)
Mesopic Baseline Pupil Diameter (PD) Mean (mm)	6.1	6.1	6.1
Photopic Baseline PD Mean (mm)	4.7	4.7	4.7
Mesopic Low Contrast BCDVA letters *55 letters = 20/20*	16	17	17
Photopic Low Contrast BCDVA letters	34	34	34
Mesopic High Contrast BCDVA letters	46	46	46
Mesopic High Contrast DCNVA letters *70 letters = 20/20*	50	49	50
Subjects with LASIK n (%)	14 (20%)	11 (15%)	25 (17%)

Source: LYNX-1 Results

Primary Endpoint: Percentage of Subjects with ≥15 Letter Improvement in mLCVA

Statistically Greater % of Subjects Treated with had ≥15 Letter *Improvement Compared to Placebo*



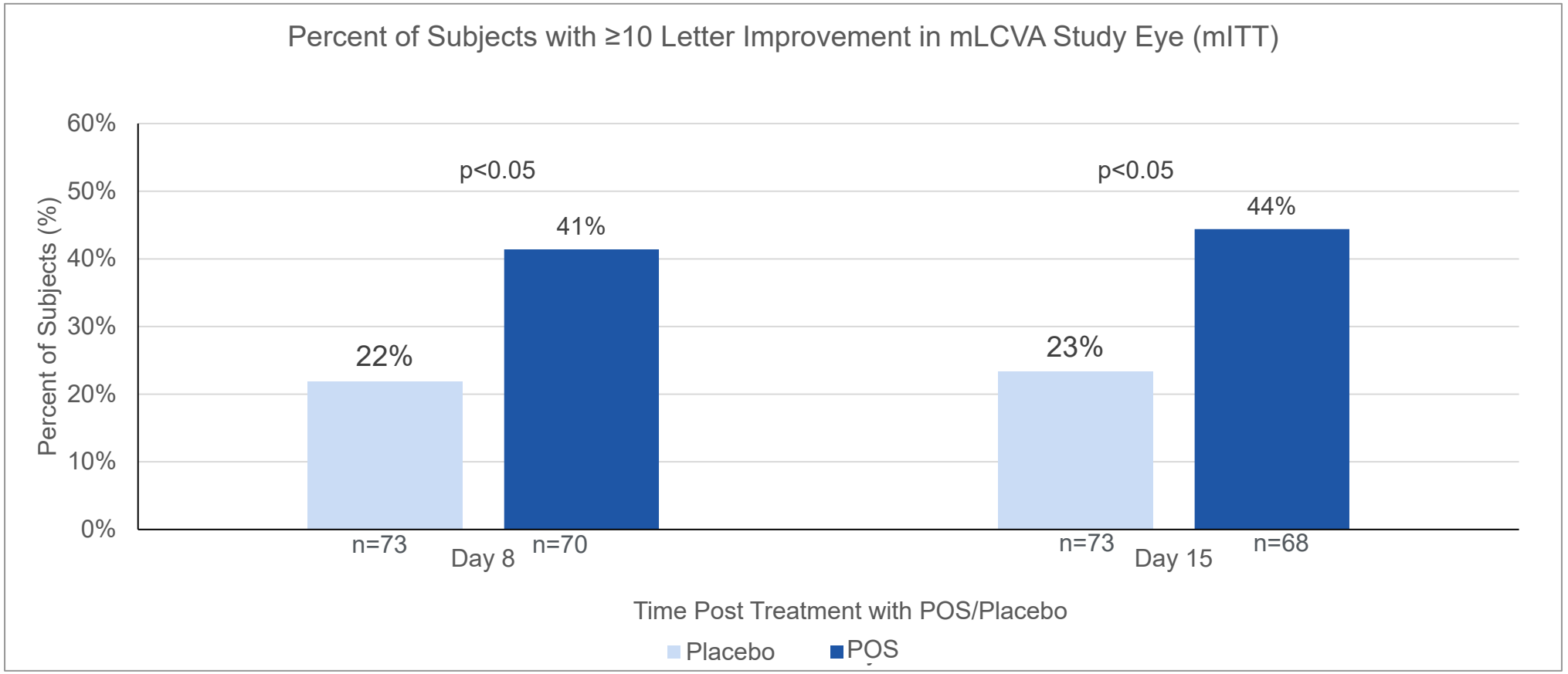


Source: LYNX-1 Results

mLCVA = Mesopic Low Contrast Best-corrected Distance Visual Acuity

Percentage of Subjects with ≥10 Letter Improvement in mLCVA

Statistically Greater % of POS Treatment Showed Clinically Meaningful Improvement in mLCVA



Source: LYNX-1 Results

mLCVA = Mesopic Low Contrast Best-corrected Distance Visual Acuity

POS Safety and Tolerability

Data Support a Favorable Benefit/Risk Profile For Subjects with DLD

- No deaths or serious AEs; No withdrawals due to AEs
- AEs occurring in >5% of POS-treated subjects included: instillation site irritation (9% vs 0% placebo), installation site pain (13% vs 0% placebo), dysgeusia (11% vs 0% placebo) and conjunctival hyperemia (9% vs 3% placebo)
- 84% of the AEs considered related to POS were mild
- No statistical difference in conjunctival hyperemia between treatment arms with evening dosing at Day 8 and Day 15

Source: LYNX-1Results

Key Takeaways

- POS showed a statistically significant and clinical meaningful 15 letter (3 line) and 10 letter (2 line) improvement in mesopic low contrast distance visual acuity (mLCVA) at days 8 and 15 compared to placebo in subjects with dim light disturbance (DLD)
- POS has demonstrated a favorable safety and tolerability profile
- These positive LYNX-1 Phase 3 data in DLD support a second Phase 3 for potential NDA submission
- POS does not engage the ciliary muscle and so no increased risk of retinal tears or detachment
- With no approved treatment options, POS has the potential to be the first Rx eye drop for millions of patients suffering from halos, glares, starbursts and other dim light vision disturbances

We thank all the LYNX-1 study participants, investigators and their staff !!!

Source: LYNX-1 Results