Phase 3 Randomized Controlled Study of Phentolamine Ophthalmic Solution in Post-Refractive Surgery Patients with Impaired Mesopic Vision

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Disclaimer: MR-142 phentolamine ophthalmic solution is an investigational therapy for low-light vision loss after keratorefractive surgery and is not approved for this use in any country

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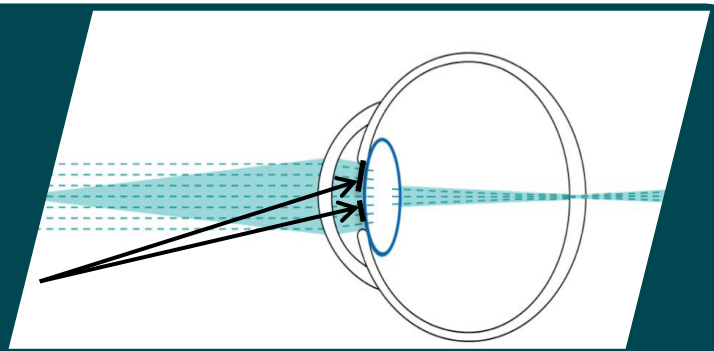
Large Unmet Need in Dim Light Disturbances (DLD)

- **Glare reduces several aspects of nighttime visual performance in older subjects**, and is associated with decreased mesopic visual function[1]
- Peripheral, unfocused rays of light are unmasked when pupils enlarge in dim light, causing **reduced mesopic low contrast vision**[1,2]
- DLD may be caused by **keratorefractive surgery, keratoconus, and cortical cataracts**[1]
- **Symptoms cannot be properly corrected by glasses**

Effects of DLD can be mitigated when a **smaller pupil blocks unfocused, peripheral aberrant rays of light**, selectively allowing passage of more centrally focused rays[2]



DLD, dim light disturbances; LASIK, laser assisted in situ keratomileusis.

1. Kimlin, JA, et al. *Invest Ophthalmol Vis Sci, 58*(5), 2796-2803. **2.** Schallhorn SC, et al. *Ophthalmology*. 2009;116:702-9; 2Xu R, Kollbaum P, Thibos L, Lopez-Gil N, Bradley A. . Ophthalmic Physiol Opt. 2018;38(1):26-36. .

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Reduced Mesopic Vision and Photic Phenomena Associated with Keratorefractive Surgery

800K - 1.4M
PRK and LASIK
procedures performed annually in the U.S.[1]

~40M
keratorefractive
procedures performed each year globally[1]

- Keratorefractive surgery has evolved since the approval of PRK in 1995 and LASIK in 1999[2-4]
- Previous versions of LASIK, prior to laser flaps and wavefront-guided and optimized treatments, **were associated with decreased night driving performance**[2-4]
- Substantial number of patients who underwent legacy keratorefractive procedures have **debilitating reduced mesopic best spectacle corrected low contrast vision and photic phenomena** and are **more likely to be involved in motor vehicle collisions**[2-4]

No Commercially-Available Treatment for Dim Light Disturbances[1]

FDA, Food and Drug Administration; LASIK, laser assisted in situ keratomileusis; PRK, photorefractive keratectomy.

1. Ting DSJ, et al. *Curr Opin Ophthalmol*. 2024;35:4-10. **2.** Schallhorn SC, et.al, *Ophthalmology*. 2009;116:702-709. **3.** Tahzib NG, et al. J *Cataract Refract Surg*. 2005;31:1943-1951. **4.** Schein OD, et al. *J Cataract Refract Surg*. 2001;27:665-673.

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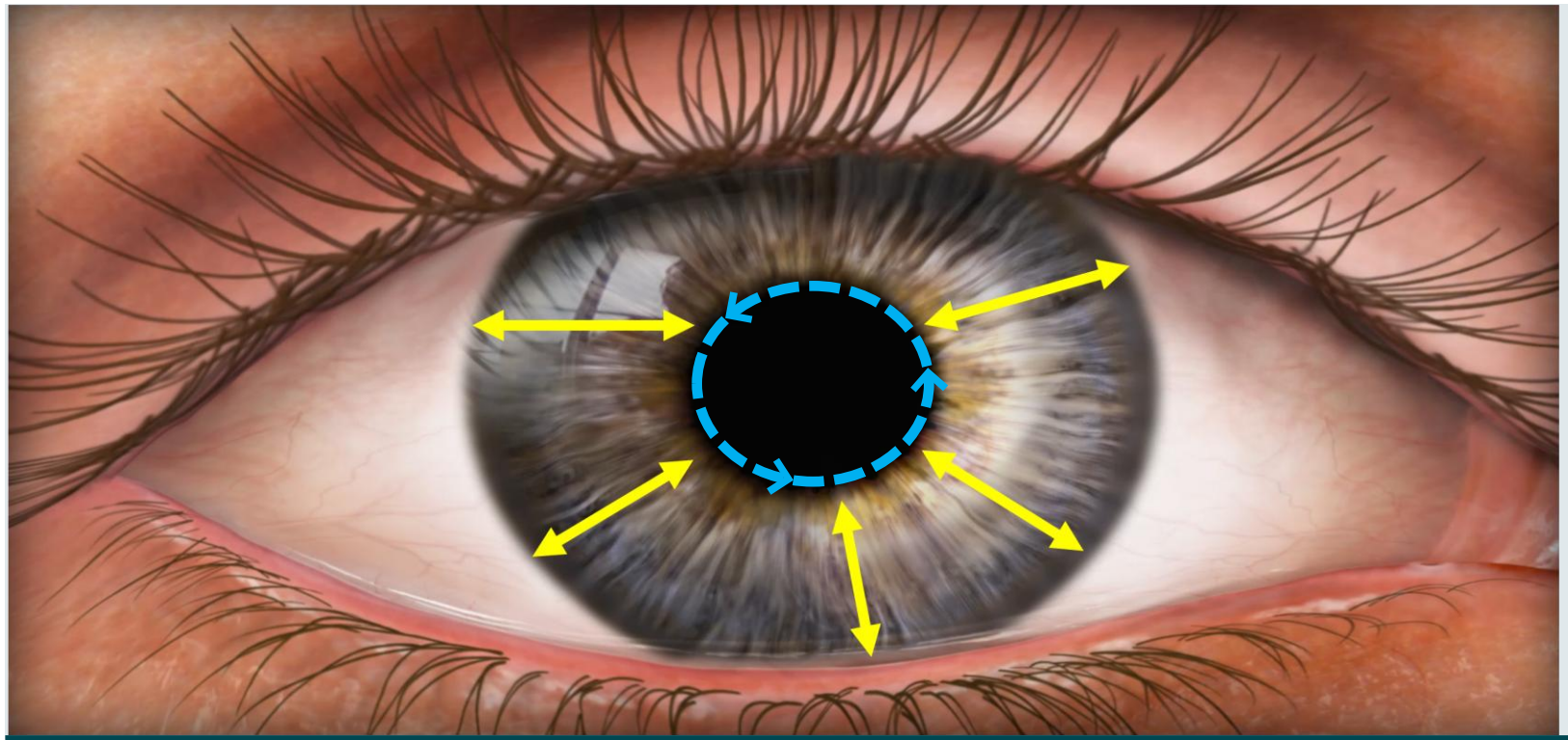
Potential Treatment Option: Phentolamine Ophthalmic Solution 0.75%

- Differentiated mechanism of action via iris dilator inhibition
- 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**

Yellow arrows - iris dilator muscle (alpha antagonists e.g., phentolamine, brimonidine)
Blue circle - iris sphincter muscle (cholinergic agonists e.g.; pilocarpine, carbachol, aceclidine)

* This indication is already FDA approved. DLD, dim light disturbances; POS, phentolamine ophthalmic solution 0.75%.

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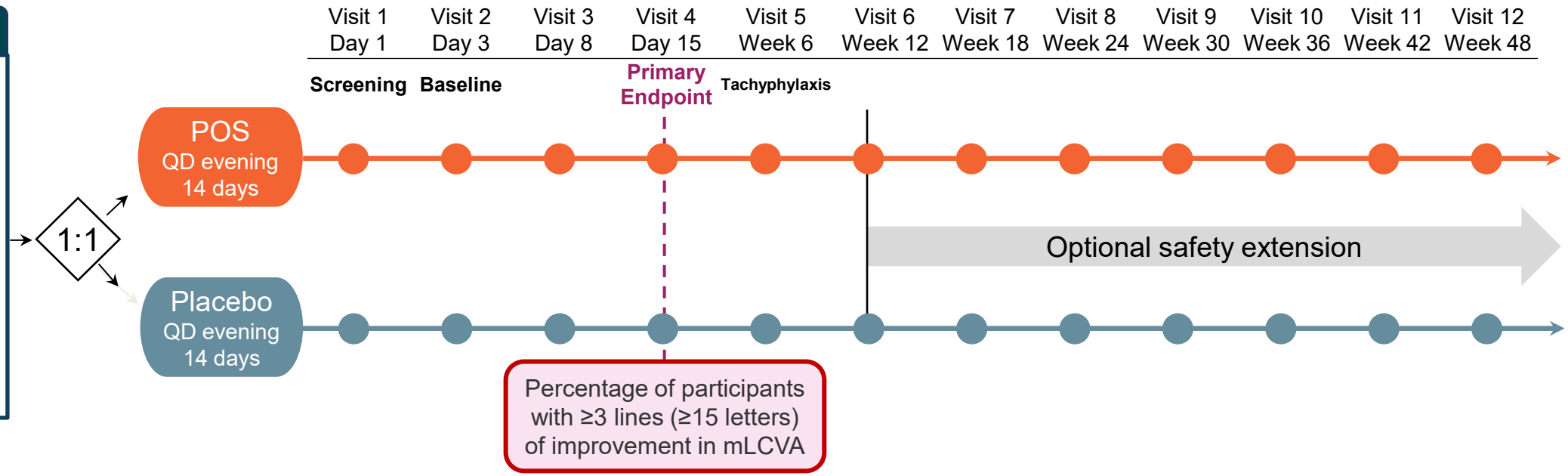
MR-141 phentolamine ophthalmic solution is an investigational therapy for presbyopia and is not approved for this use in any country.

LYNX-2 Phase 3 Pivotal Study Design

LYNX-2

200 Participants post-keratorefractive surgery with DLD

40 U.S. Sites



Eligibility Criteria

- Males or females ≥ 18 years of age
- Participant self-reported DLD and previously undergone keratorefractive surgery
- Baseline mLCVA impairment (Snellen 20/63 or worse) in at least one eye
- ≥ 10 letters improvement in mLCVA during illumination of contralateral eye with a BAT system
- PD ≥ 5mm under mesopic conditions in at least one eye
- Participants with no recent (6 months) ocular procedures or clinically significant ocular disease

DLD, dim light disturbances; FDA, Food and Drug Administration; mLCVA mesopic low contrast best-corrected distance visual acuity; PD, pupil diameter; QD, once daily; SPA, Special Protocol Assessment.
Source: Clinicaltrials.gov ID: NCT06349759

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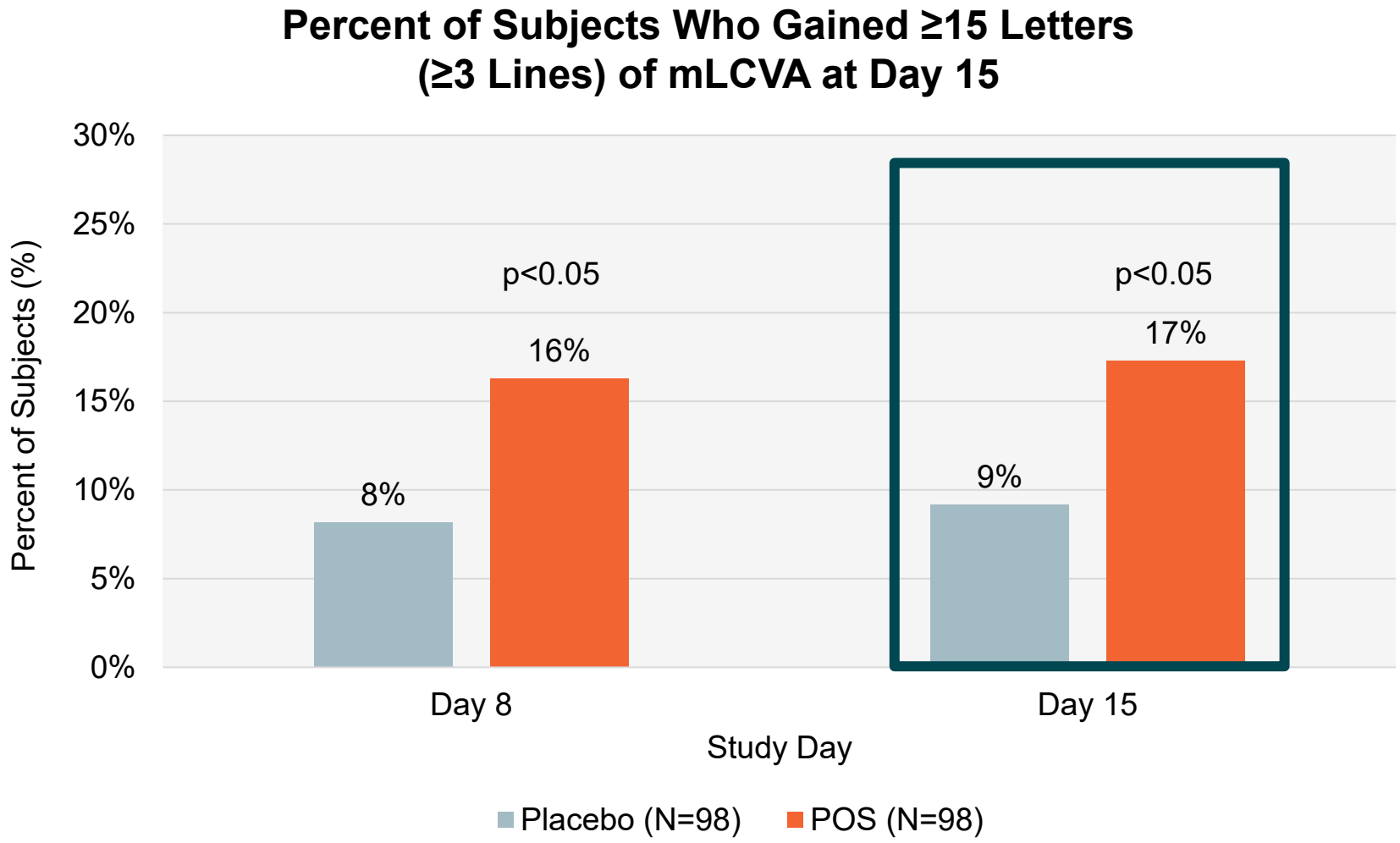
Primary Endpoint Was Met
Percent of Subjects Gaining ≥15 Letters mLCVA at Day 15



mLCVA, mesopic low contrast visual acutiy; POS, phentolamine ophthalmic solution 0.75%.
Source: Data on File, Opus/Viatris.

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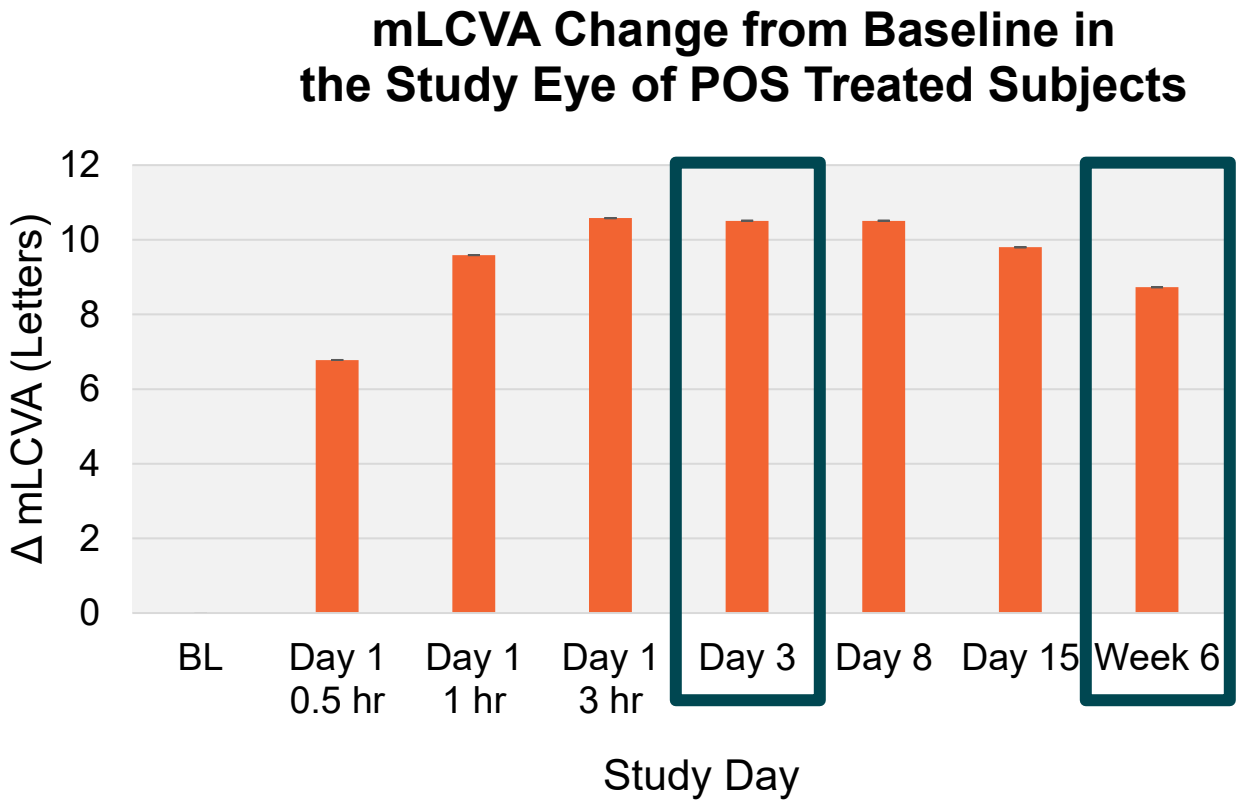
Tachyphylaxis Endpoint: Change from Baseline in DCNVA at Week 6 vs Visits Through Day 15 in POS-treated Eyes

- Subjects in the POS group **gained 8-11 letters of mLCVA at all time points** from 1-hour after the first dose to 6 weeks of daily dosing
- Results show **no evidence of tachyphylaxis**
- Difference between best mLCVA Day 3 and Week 6 was **-1.85 letters**
- 95% CI -2.73 to -0.97 does not include the prespecified criterion of -5 letters



BL, baseline; mLCVA, mesopic low contrast visual acutiy; POS, phentolamine ophthalmic solution 0.75%.
Source: Data on File, Opus/Viatris.

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Percentage of Subjects With Loss or Gain of 5, 10, or 15 letters of mLCVA by Treatment Group

	POS (N=99)	Placebo (N=100)
Day 15	98	98
≥15 letters	17 (17.3%)	9 (9.2%)
≥10 letters	51 (52.0%)	42 (42.9%)
≥5 letters	83 (84.7%)	76 (77.6%)
≥-4 to ≤4 letters	15 (15.3%)	19 (19.4%)
≤-5 letters	**0**	**3 (3.1%)**
≤-10 letters	**0**	**1 (1.0%)**
≤-15 letters	**0**	**1 (1.0%)**

mLCVA, mesopic low contrast visual acuity; POS, phentolamine ophthalmic solution 0.75%.
Source: Data on File, Opus/Viatris.

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Safety

Category	Placebo (n=100)	Phentolamine 0.75% (n=99)
Total AEs	46	233
Total treatment-related AEs	23	59
AEs occurring in ≥5% of subjects		
Conjunctival hyperemia	4%	35% (86% mild)
Instillation site irritation	0%	19% (all mild)
Dysgeusia	1%	11% (all mild)
AEs occurring in ≤1% of subjects		
Headache	0%	1%
Withdrew due to AE	**1 (1%)**	**8 (8.1%)**
Conjunctival hyperemia	0	3
Conjunctivitis	0	2
Allergic conjunctivitis	0	2
Eye pain	0	1
Eyelid edema	0	1
Noninfective conjunctivitis	0	1
Eyelid pruritic	0	1
Punctate keratitis	0	1
Vision blurred	1	0
Serious AE	1 (retinal detachment; unrelated to study drug)	1 (melanoma in situ non-ocular; unrelated to study drug)
Death	0	0

POS, phentolamine ophthalmic solution 0.75%.
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Summary

- The LYNX-2 primary study outcome was met
  - **Significantly more POS treated post-keratorefractive subjects gained ≥ 15 letters of mesopic LCVA compared to placebo at Day 15**
- POS treated subjects also had a **significant reduction in mesopic vision associated visual disturbances** such as glare, halos and starbursts
- **No evidence of tachyphylaxis** over 6 weeks of repeated dosing
- Consistent with previous studies, the most common adverse events (≥5%) in POS-treated subjects were conjunctival hyperemia (35%), instillation site irritation (19%), and dysgeusia (11%), **with the majority being mild in severity**.
- **No POS treated subjects lost one or more lines of mLCVA** at any timepoint

LASIK, laser assisted in situ keratomileusis; mLCVA, mesopic low contrast distance visual acuity; POS, phentolamine ophthalmic solution 0.75%.
Source: Data on File, Opus/Viatris.