

LYNX-2: A Pivotal Phase 3 Trial of Phentolamine Ophthalmic Solution in Post-Keratorefractive Surgery Subjects with Decreased Mesopic Visual Acuity

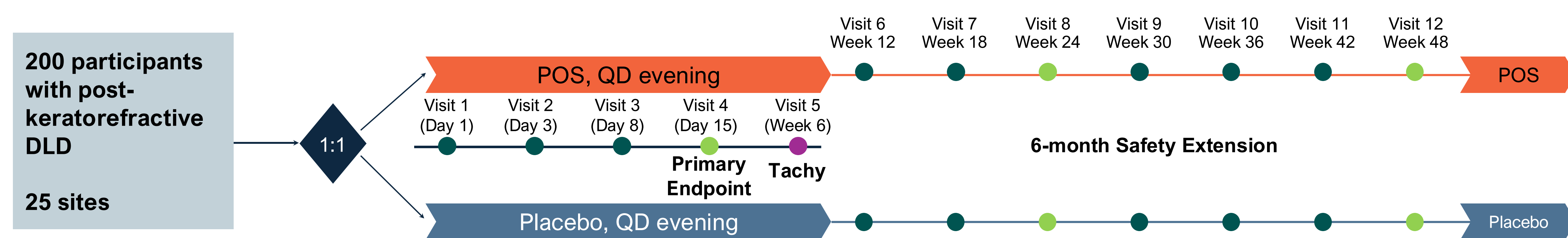
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Purpose

- Dim light disturbances (DLD), such as glare, halos, and starburst are caused by peripheral, unfocused rays of light when pupils enlarge in dim light, leading to reduced mesopic low contrast vision.^{1,2}
- DLD may be caused by keratorefractive surgery, keratoconus, and cortical cataracts, and symptoms cannot be properly corrected by glasses.¹
- Glare reduces several aspects of nighttime visual performance in older adults and is associated with decreased mesopic visual function.³
- Phentolamine Ophthalmic Solution (POS) 0.75% is a potential treatment option for DLD. It works by inhibiting the iris dilator muscle, which decreases pupil size moderately without affecting the iris sphincter or ciliary muscles. This allows for functional vision improvement in conditions like pharmacologically-induced mydriasis, presbyopia, and DLD.
- LYNX-2 is a multicenter, randomized, double-masked Phase 3 study of the safety and efficacy of POS versus placebo in adult participants with DLD after keratorefractive surgery.

Methods



Key Inclusion Criteria

- Previous history of refractive surgery (e.g., PRK, LASIK, SMILE, and RK) and have subject-reported night vision disturbances (e.g., glare, halos, and/or starbursts); Symptoms must have been first noted within 2 months following refractive surgery
- Pupil diameter (PD) ≥ 5 mm under mesopic conditions in at least 1 eye
- Mesopic low-contrast visual acuity (mLCVA) ≤ 30 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (20/63 Snellen or worse) in at least 1 eye
- ≥ 10 ETDRS letters improvement in mLCVA in at least 1 eye during illumination of the contralateral eye

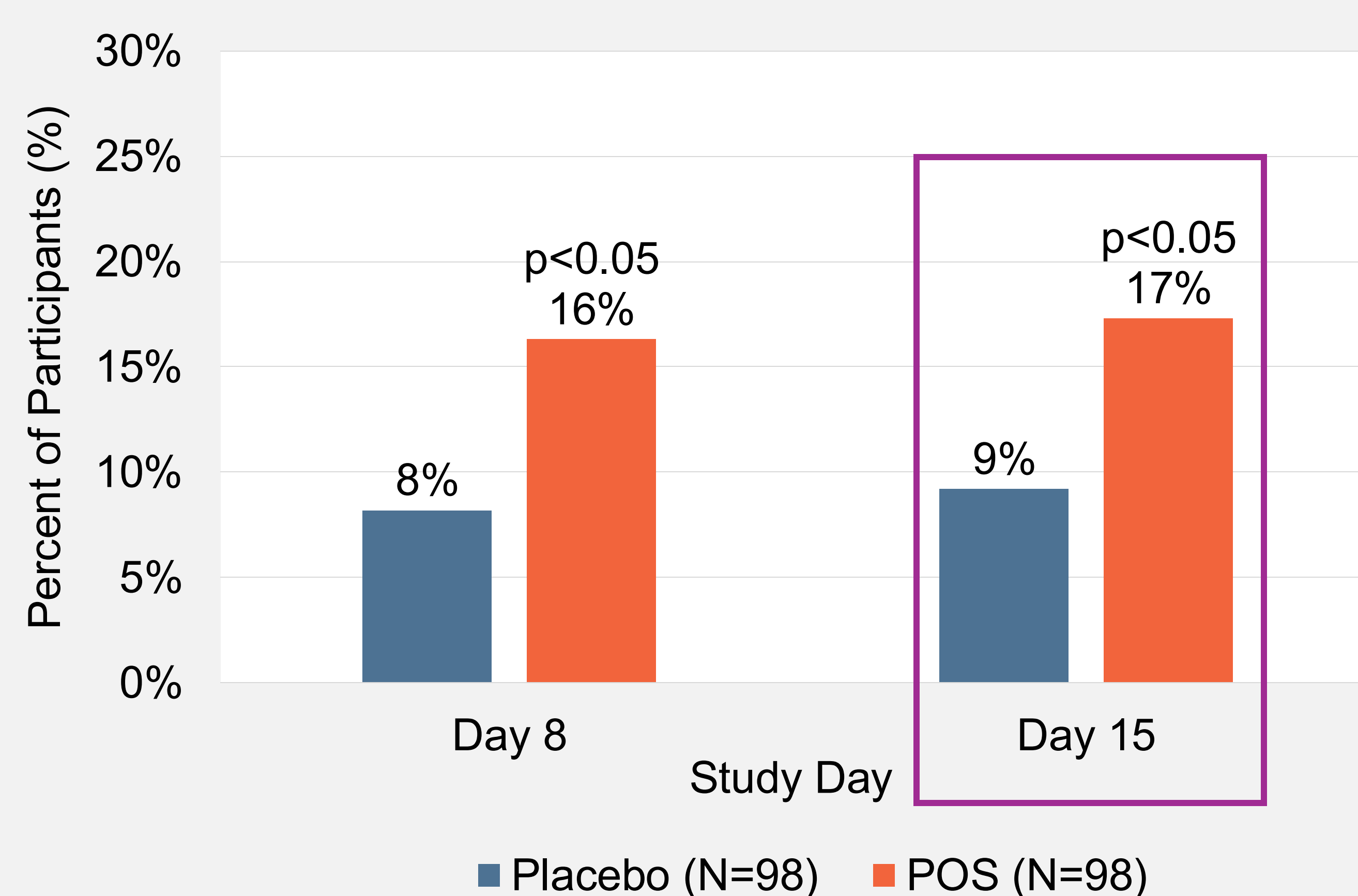
Results

Demographics and Baseline Characteristics were Balanced Between Groups

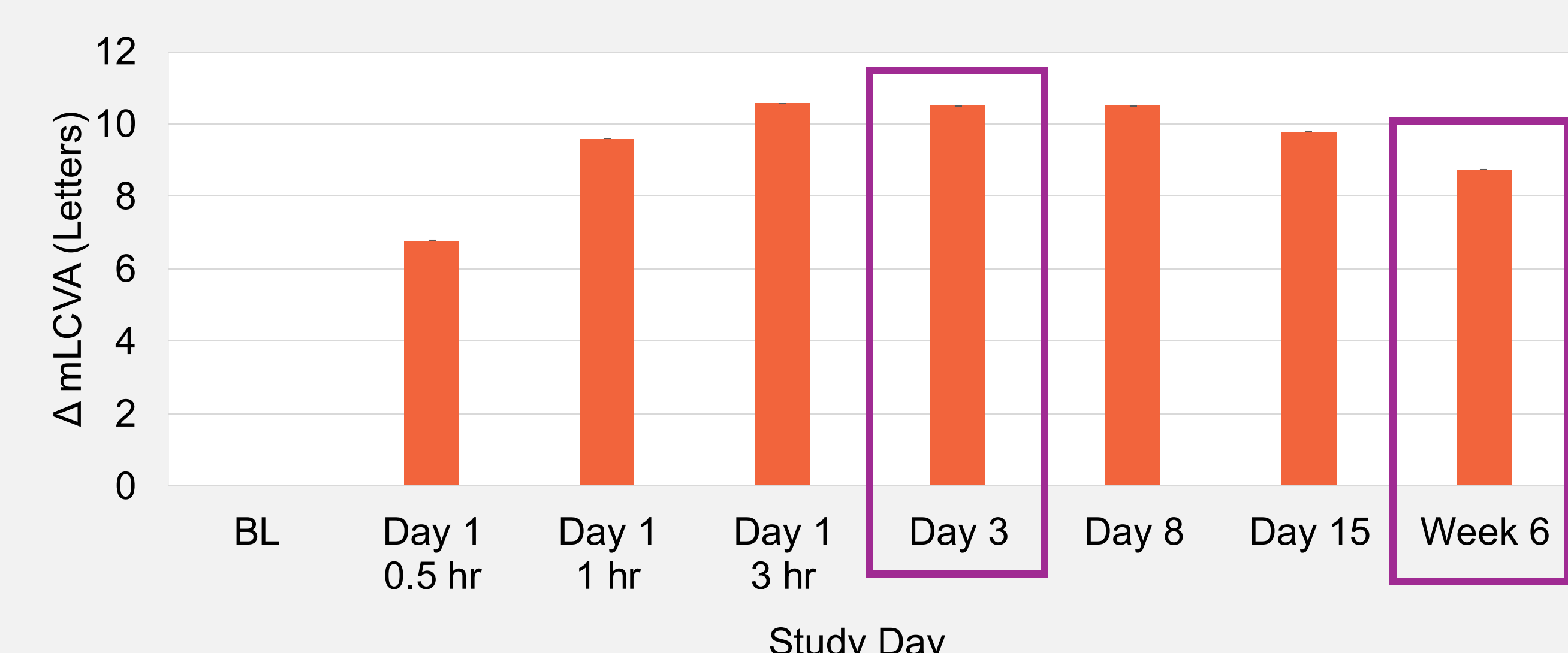
| | POS (n=99) | Placebo (n=100) |
|--------------------------------------------------------|----------------|-----------------|
| Demographics | | |
| Age (years) Mean (SD) | 45.3 (9.86) | 45.5 (10.92) |
| Male | 30 (30.3) | 35 (35.0) |
| Female | 69 (70.7) | 65 (65.0) |
| Race, n (%) [a] | | |
| American Indian or Alaska Native | 1 (1.0) | 1 (1.0) |
| Asian | 12 (12.1) | 10 (10.0) |
| Black or African American | 7 (7.1) | 8 (8.0) |
| Other | 1 (1.0) | 0 |
| White | 80 (80.8) | 83 (83.0) |
| Ethnicity, n (%) | | |
| Hispanic or Latino | 13 (13.1) | 9 (9.0) |
| Not Hispanic or Latino | 86 (86.9) | 91 (91.0) |
| Irides type, n (%) | | |
| Light | 47 (47.5) | 47 (47.0) |
| Dark | 52 (52.5) | 53 (53.0) |
| Baseline Characteristics | | |
| mLCVA in the study eye, letters Mean (SD) ^A | 19.2 (6.00) | 17.8 (6.68) |
| Mesopic PD in the study eye, mm | 5.985 (0.7857) | 5.849 (0.6820) |

A: 55 letters = 20/20 Snellen acuity

Primary Endpoint: Percent of Participants Gaining ≥ 15 Letters mLCVA at Day 15

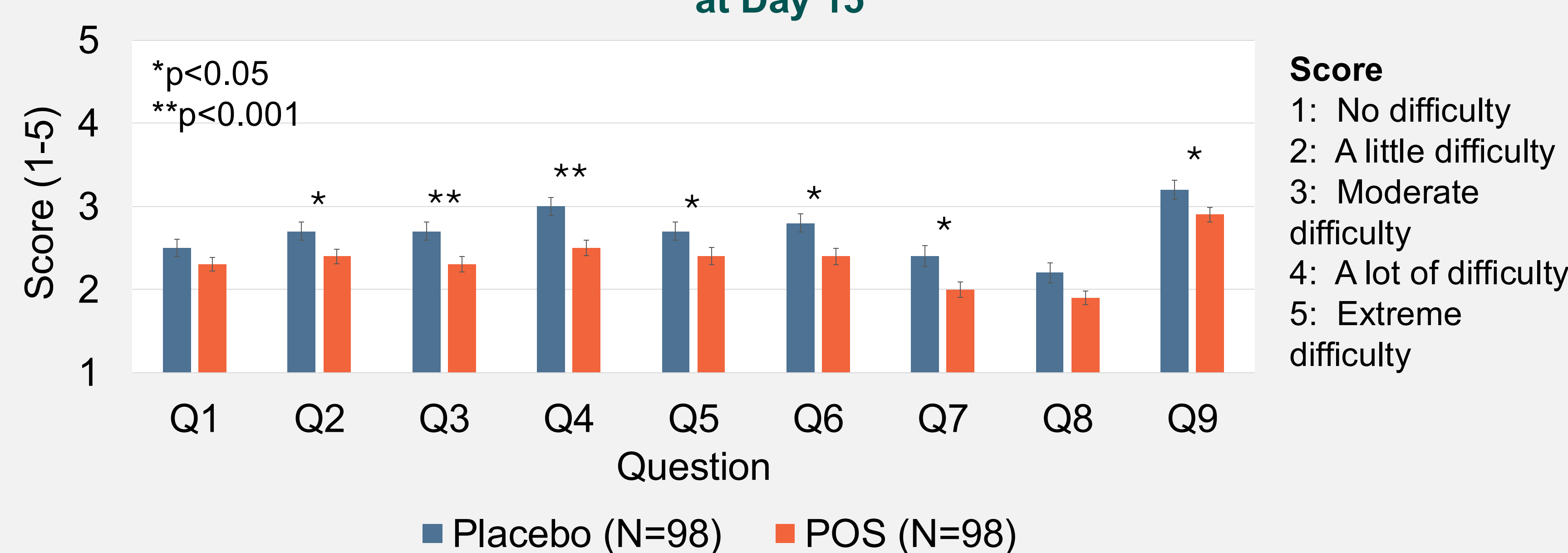


Tachyphylaxis Endpoint: Change from Baseline in mLCVA at Week 6 versus Visits Through Day 15 in POS-Treated Participants



- 95% confidence interval does not include or exceed a prespecified criterion of -5 letters in comparing the best mLCVA (Day 3) to Week 6
- 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
- Difference between best mLCVA (Day 3) and Week 6 – 1.85 letters
- Results do not show evidence of tachyphylaxis

Patient-reported Outcomes (Vision and Night Driving Questionnaire or VNDQ) at Day 15

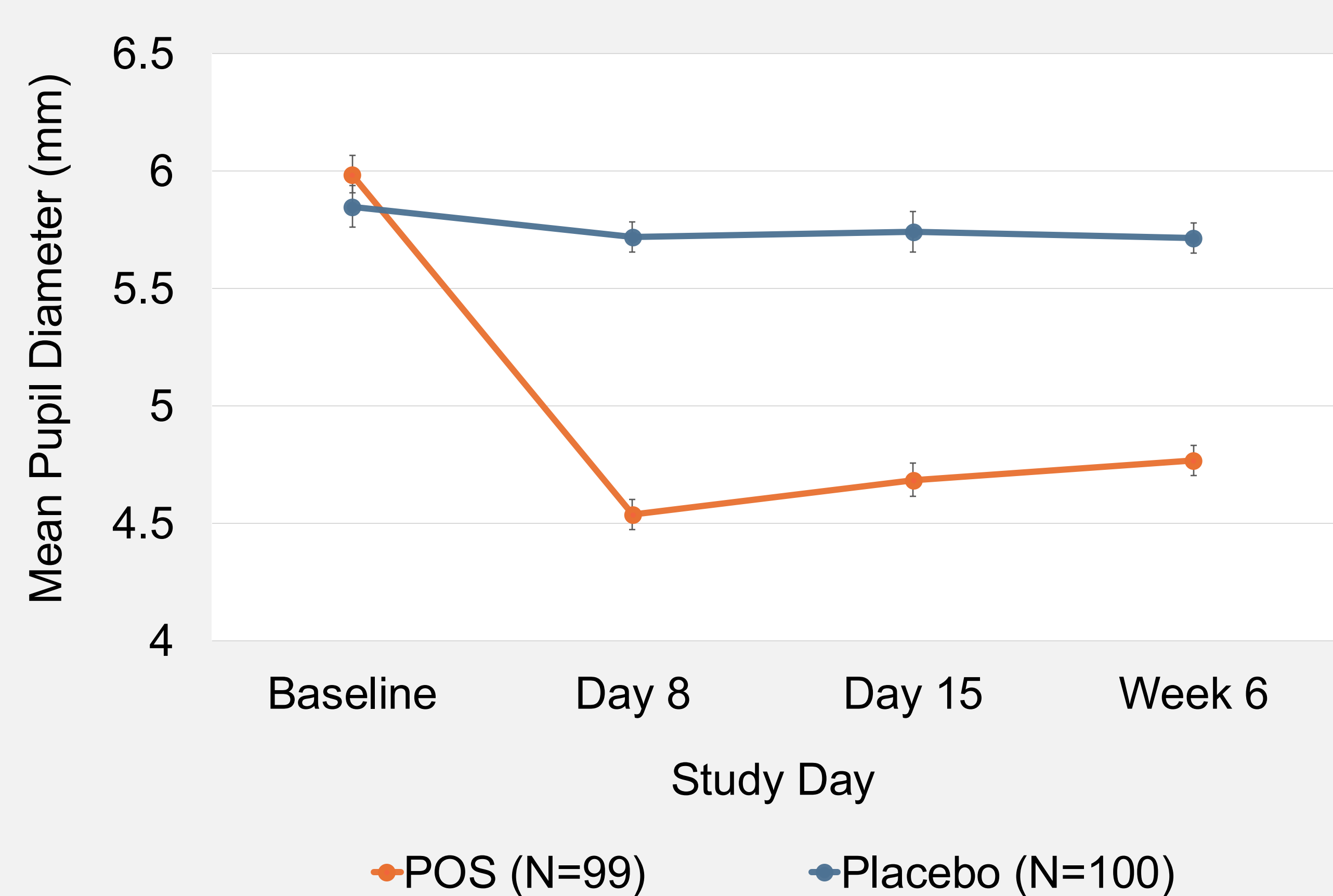


1. Seeing dark cars when driving at night
2. Seeing pedestrians on the roadside when driving at night
3. Reading street signs when driving at night
4. Seeing the road because of oncoming headlights
5. Seeing because of glare when driving at day or dusk
6. Adjusting after passing headlights from oncoming cars
7. Judging the distance to your turnoff or exit while driving at night
8. Judging the distance between you and another moving cars when driving at night
9. Seeing the road in rain or poor weather when driving at night

Safety and Tolerability

| | POS (n=99) | Placebo (n=100) |
|-----------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------|
| Total AEs | 233 | 46 |
| Total treatment-related AEs | 51 | 23 |
| AEs occurring in $\geq 5\%$ of subjects | | |
| Conjunctival hyperemia | 35% (86% mild) | 4% |
| Instillation site irritation | 19% (all mild) | 0% |
| Dysgeusia | 11% (all mild) | 1% |
| Headache | 1% | 0% |
| Withdrew due to AE | | |
| Conjunctival hyperemia | 8 (8.1%) | 1 (1%) |
| Conjunctivitis | 3 | 0 |
| Allergic conjunctivitis | 2 | 0 |
| Eye pain | 1 | 0 |
| Eyelid edema | 1 | 0 |
| Noninfective conjunctivitis | 1 | 0 |
| Eyelid pruritic | 1 | 0 |
| Punctate keratitis | 1 | 0 |
| Vision blurred | 0 | 1 |
| Serious AE | | |
| | 1 (melanoma in situ non-ocular; unrelated to study drug) | 1 (retinal detachment; unrelated to study drug) |
| Death | 0 | 0 |

Mean Change from Baseline in Mesopic Pupil Diameter



Conclusions

- The primary outcome of the study was met, with significantly more POS-treated subjects gaining ≥ 15 letters of mesopic LCVA compared to placebo at Day 15
- POS-treated subjects also had a significant reduction in subjective difficulty with nighttime driving discomfort at Day 15 compared to placebo
- No POS-treated subject lost one or more lines of mLCVA at any timepoint
- No evidence of tachyphylaxis over 6 weeks of repeated dosing
- As with previous studies, POS displayed a favorable safety profile
- A second Phase 3 registrational study in this patient population is currently underway (LYNX-3)

References

1. Pepose J, Brigell M, Lazar E, et al. *BMC Ophthalmol.* 2022;22:402.
2. Rosen ES. *J Cataract Refract Surg.* 2005;31:247-9.
3. Kimlin, JA, et al. *Invest Ophthalmol Vis Sci.* 2017;58:2796-2803.

Disclaimer: Phentolamine is not an FDA-approved product for keratorefractive subjects with reduced mesopic vision and photic phenomena.