

Phentolamine Ophthalmic Solution Demonstrates Prolonged Duration of Action with Improvement in Distance-Corrected Near Vision for Presbyopic Patients in a Phase 3 Study

Presenter: William Trattler, MD, ABO

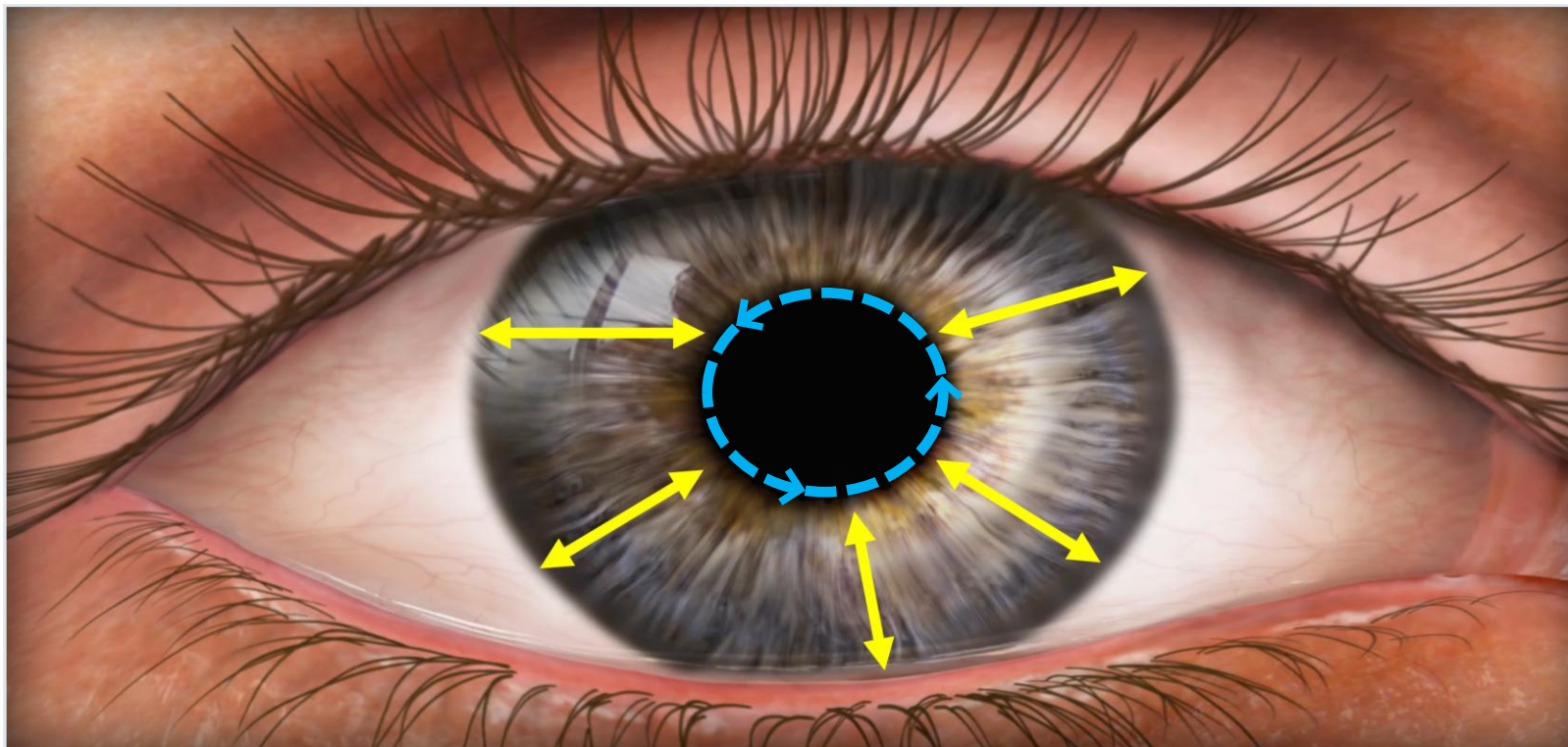
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Disclaimer: MR-141 phentolamine ophthalmic solution is an investigational therapy for presbyopia and is not approved for this use in any country

Phentolamine Ophthalmic Solution (POS) 0.75%

Mechanism of action and clinical rationale

- Differentiated iris dilator inhibition MOA for functional vision improvement
- Phentolamine is a non-selective α_1 antagonist



Phentolamine blocks α_1 receptors on the **iris dilator muscle**



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

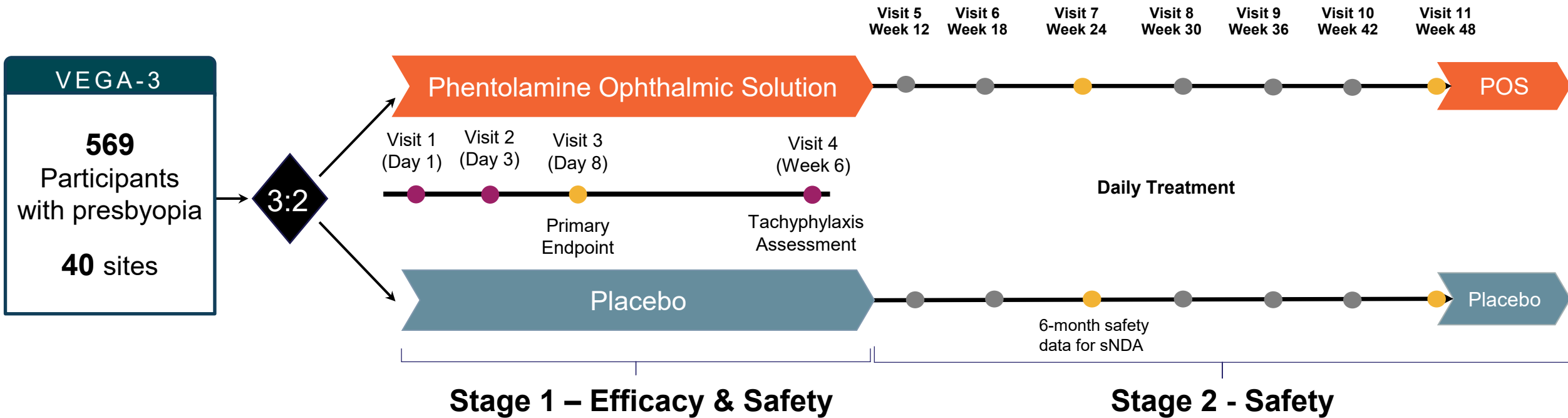
Yellow arrows - iris dilator muscle (alpha antagonists e.g., phentolamine, brimonidine)

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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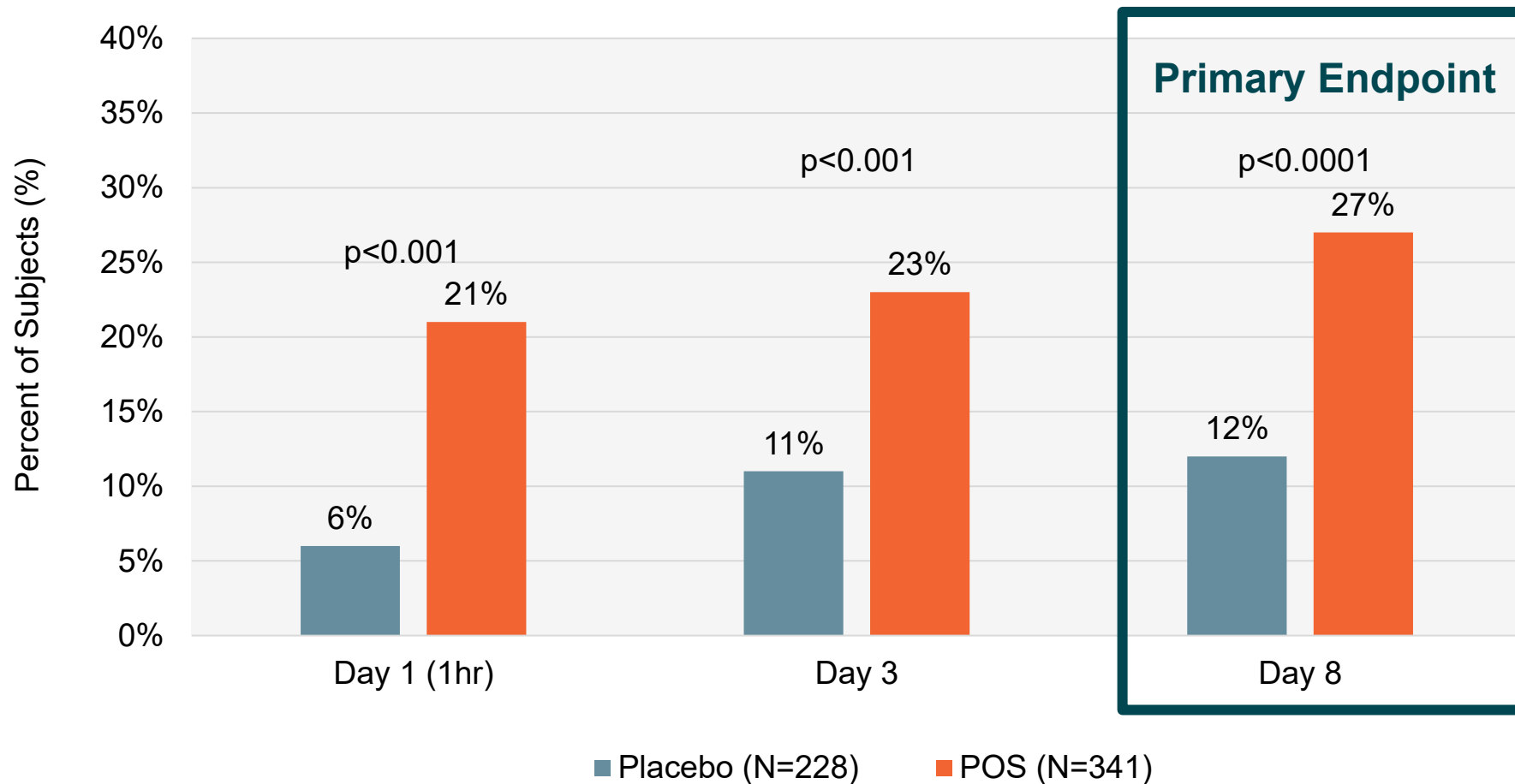
VEGA-3 Study Design



Key Inclusion Criteria

- Males or females ≥ 45 and ≤ 64 years of age
- Best-corrected distance VA of 20/20 or better in each eye
- Distance-corrected near VA between 20/50 and 20/100 in photopic conditions in each eye and binocularly
- Binocular best-corrected near VA 20/25 or better
- Photopic PD of ≥ 4 mm in either eye

Primary Endpoint: Percent of Subjects Gaining ≥ 15 Letters Binocular DCNVA at Day 8 Without Loss of ≥ 5 Letters Binocular BCDVA

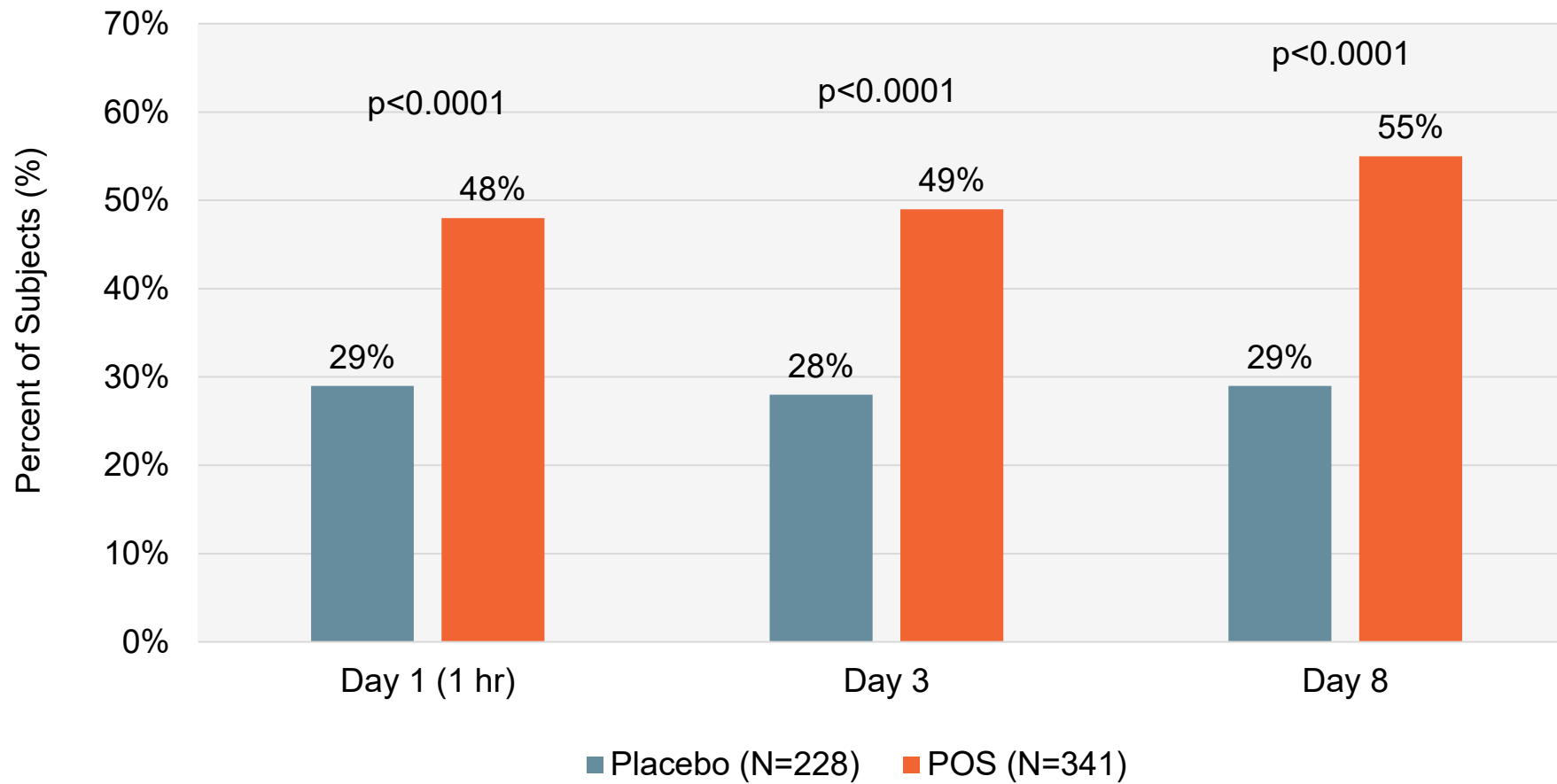


BCDVA, best-corrected distance visual acuity; DCNVA, distance-corrected near visual acuity; POS, phentolamine ophthalmic solution 0.75%.

Source: Data on file, Opus/Viatris.

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Secondary Endpoint: Percent of Subjects Gaining ≥ 10 Letters Binocular DCNVA

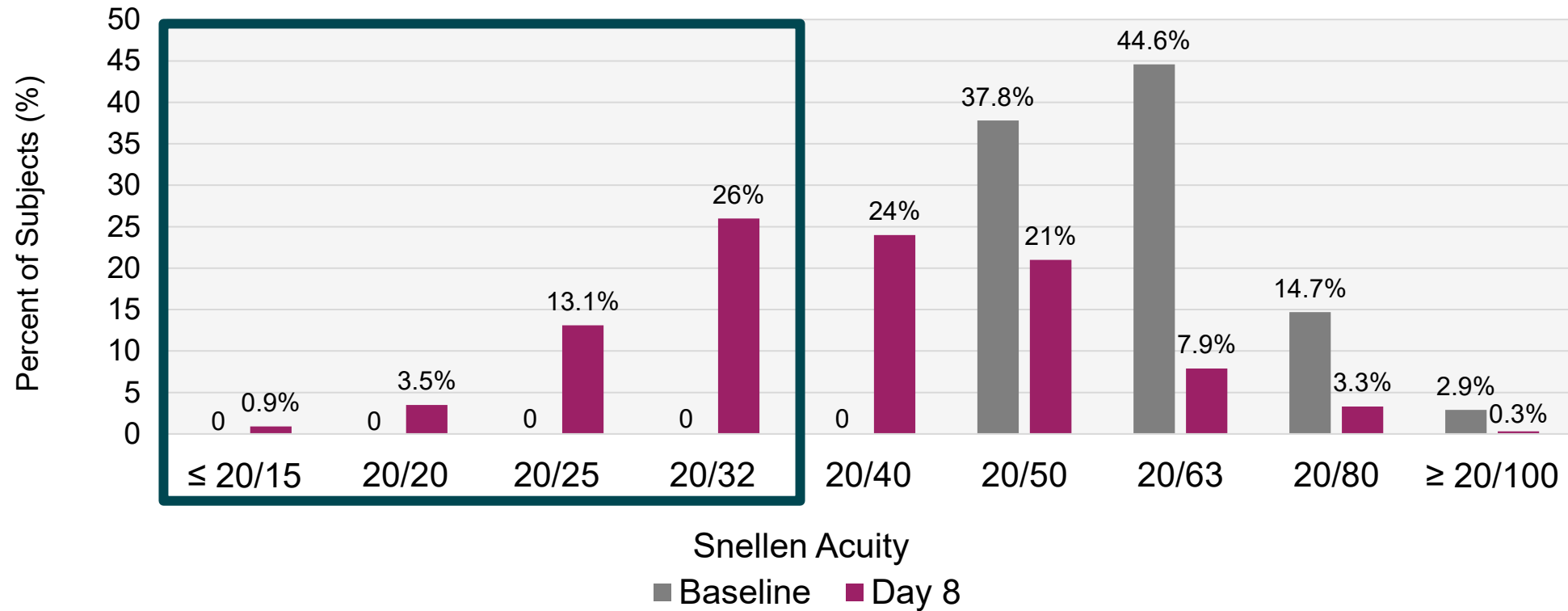


DCNVA, distance-corrected near visual acuity; POS, phentolamine ophthalmic solution 0.75%.

Source: Data on file, Opus/Viatris.

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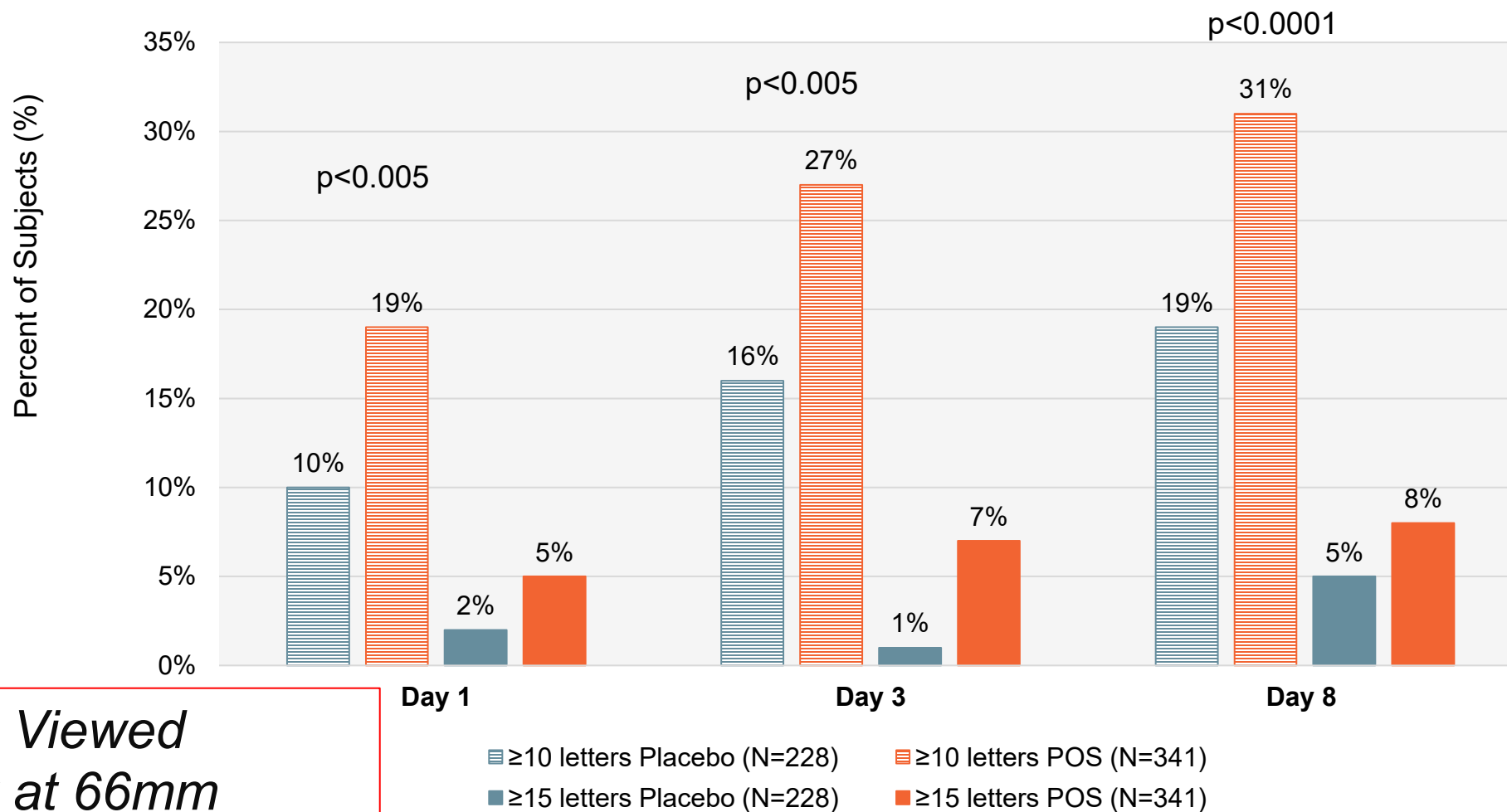
Secondary Endpoint: Distribution of DCNVA in POS-treated Subjects at Baseline and Day 8



43.5% of POS-treated subjects achieved near vision of 20/32 or better at Day 8

DCNVA, distance-corrected near visual acuity; POS, phentolamine ophthalmic solution 0.75%.
Source: Data on file, Opus/Viatris.

Secondary Endpoint: Percent of Subjects with Improvement in DCIVA by Visit



*Near Chart Viewed
Binocularly at 66mm*

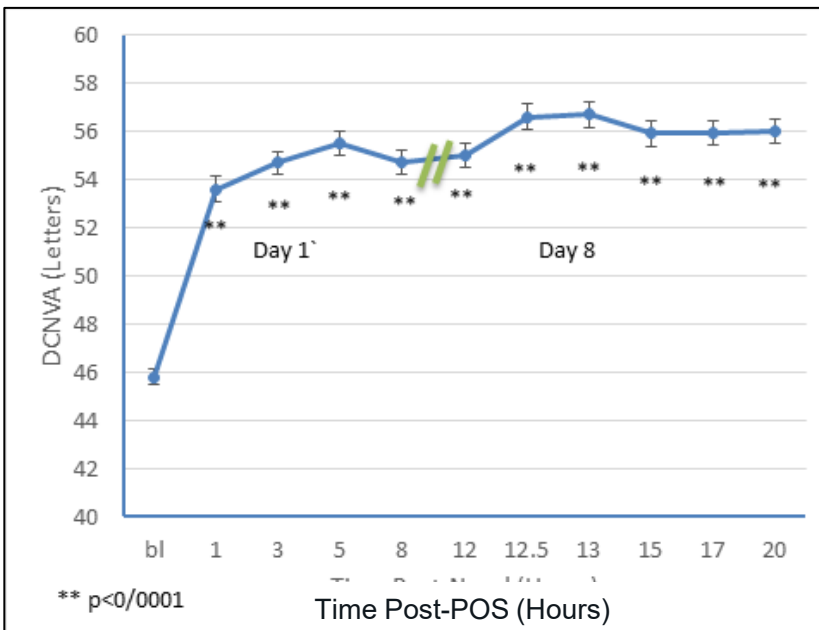
DCIVA, distance-corrected intermediate visual acuity; POS, phentolamine ophthalmic solution 0.75%.

Source: Data on file, Opus/Viatris.

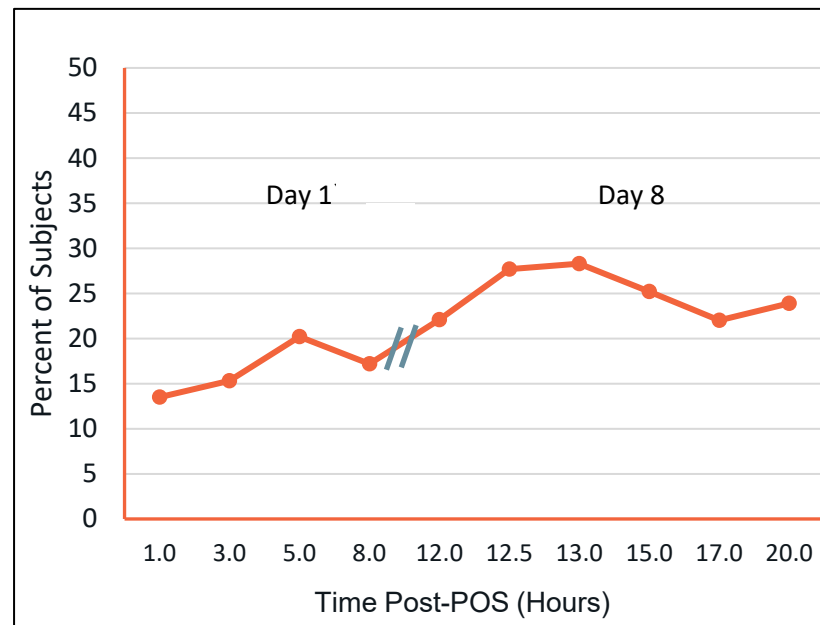
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POS 20-Hour Duration of Effect Data in VEGA-2 Phase 3 Study

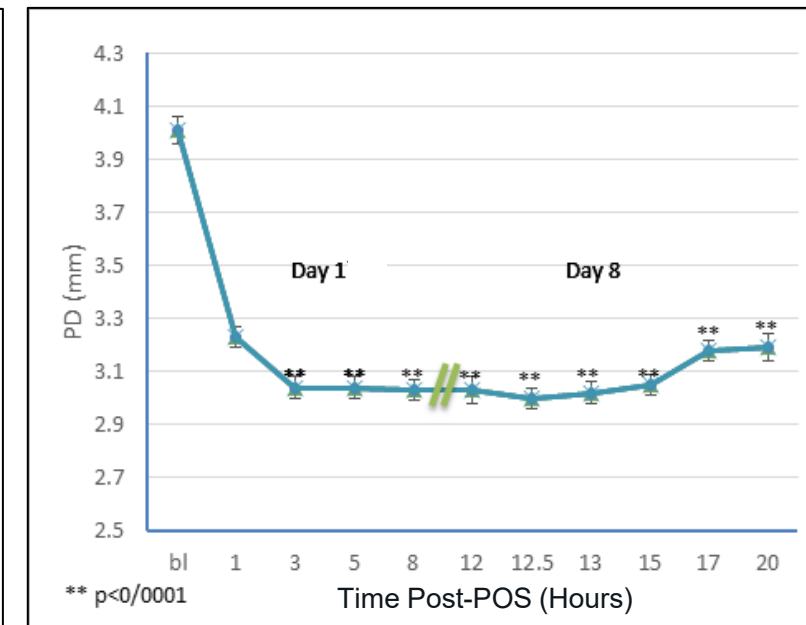
Mean DCNVA¹



Subjects With ≥ 15 -Letter Improvement in DCNVA Without Loss of ≥ 5 Letters of BCDVA²



Mean PD³

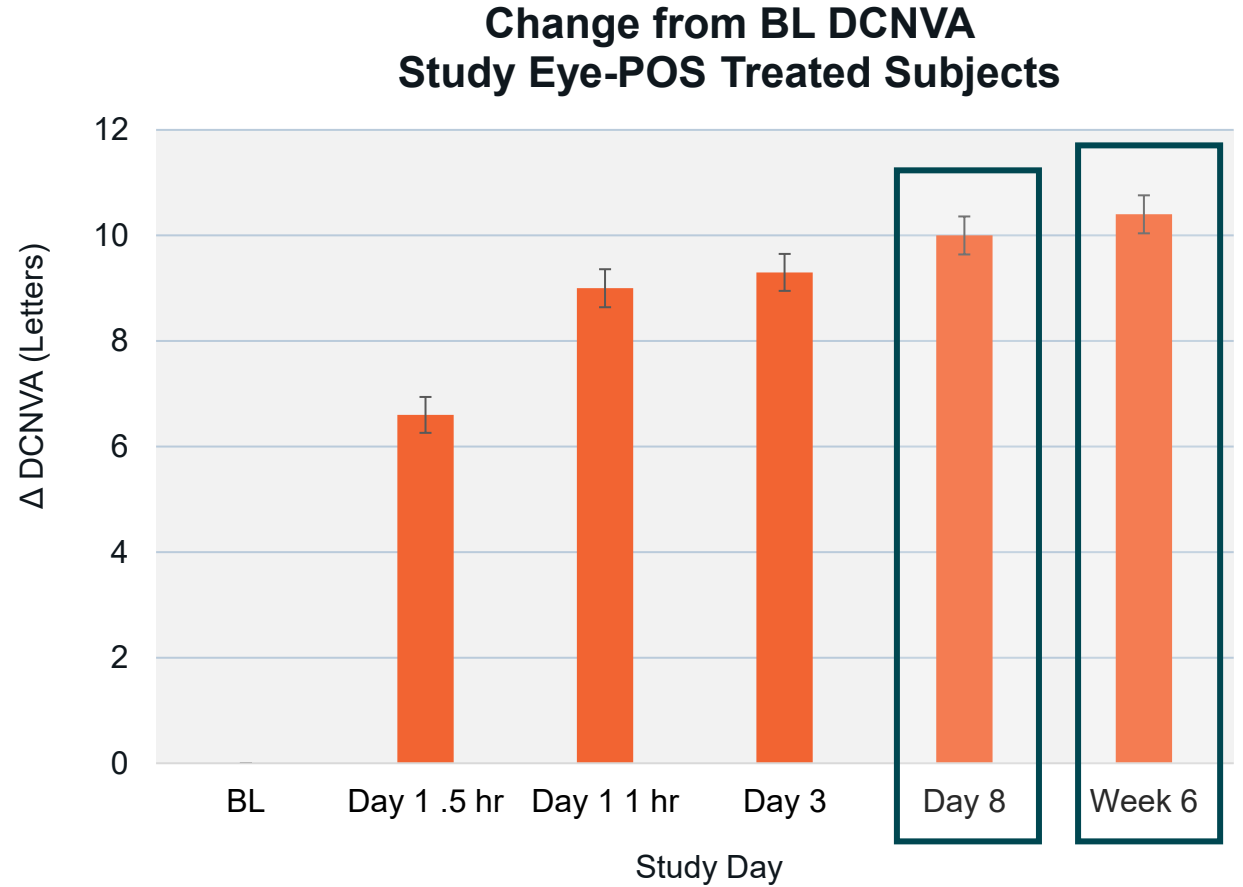


POS-treated subjects reported a statistically significant improvement in satisfaction with near vision upon awakening compared to placebo at Day 8 (p<0.0001)

DCNVA, distance-corrected intermediate visual acuity; DCNVA, distance-corrected near visual acuity; PD, pupil diameter; POS, phentolamine ophthalmic solution 0.75%.
Sources: 1. Data on File, Opus/Viatrix Table 14.2.3.1.1. 2. Data on file, Opus/Viatrix Table 14.2.1.1.1. 3. Data on file, Opus/Viatrix Table 14.2.13.1.

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 9-10.5 letters of DCNVA at all time points from 1-hour after the first dose to Week 6 of daily dosing
- Results showed no evidence of tachyphylaxis through Week 6
- Best DCNVA was observed at Week 6
- Day 8 showed the best DCNVA prior to Week 6
- 95% CI -0.29 to +1.06 remained above the prespecified criterion of -5 letters, indicating no meaningful loss of effect



CI, confidence interval; DCNVA, distance-corrected near visual acuity; POS, phentolamine ophthalmic solution 0.75%.
Source: Data on file, Opus/Viatris.

Safety

	Placebo (n=228)	POS (n=341)
Total AEs	153 (67.1%)	190 (55.7%)
AEs occurring in ≥5% of subjects		
Conjunctival hyperemia	1%	26% (90% mild)
Eye irritation	0	5.6% (63% mild)
Instillation site irritation	1.3%	15% (98% mild)
Dysgeusia	0.4%	5.9% (all mild)
Headache	0	2.6%
Withdrew due to AE	3 (1.3%) Most due to conjunctival problems	60 (17.6%) Most due to conjunctival problems
Serious AE	2 (unrelated to study drug)	2 (unrelated to study drug)
Death	0	0

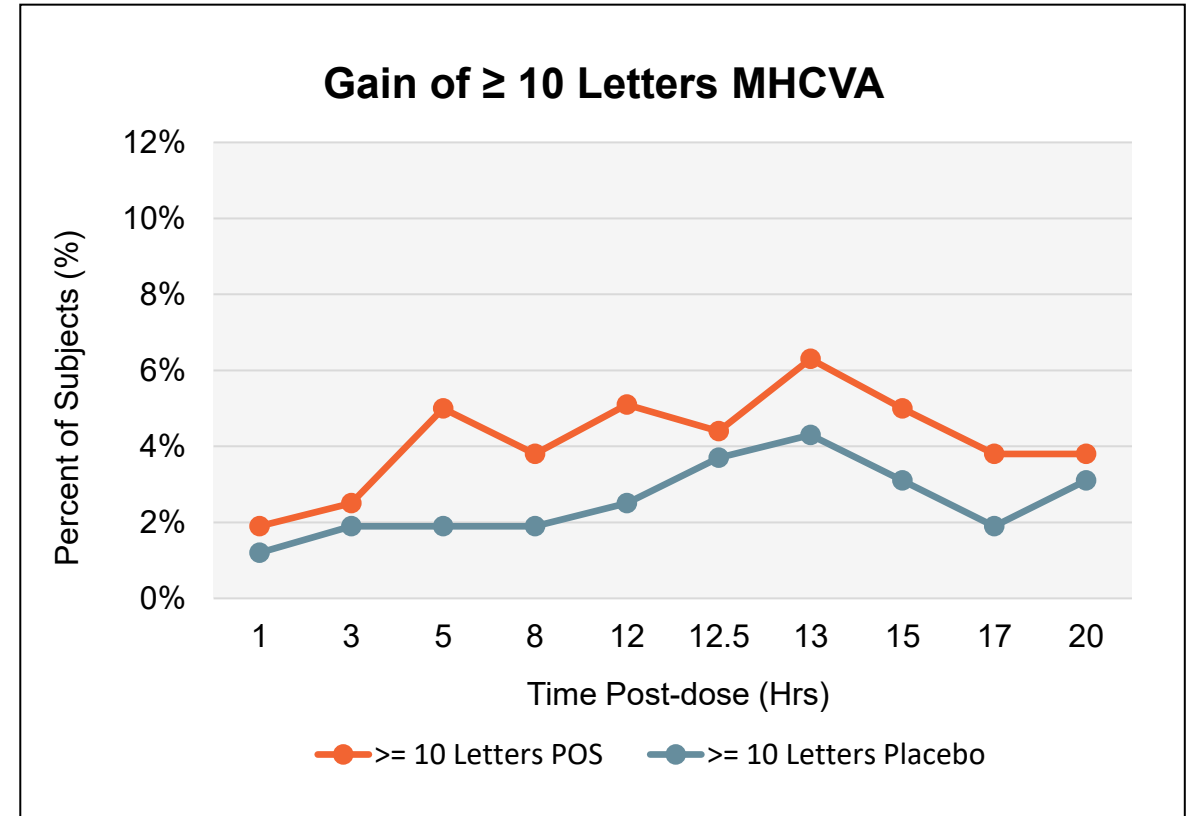
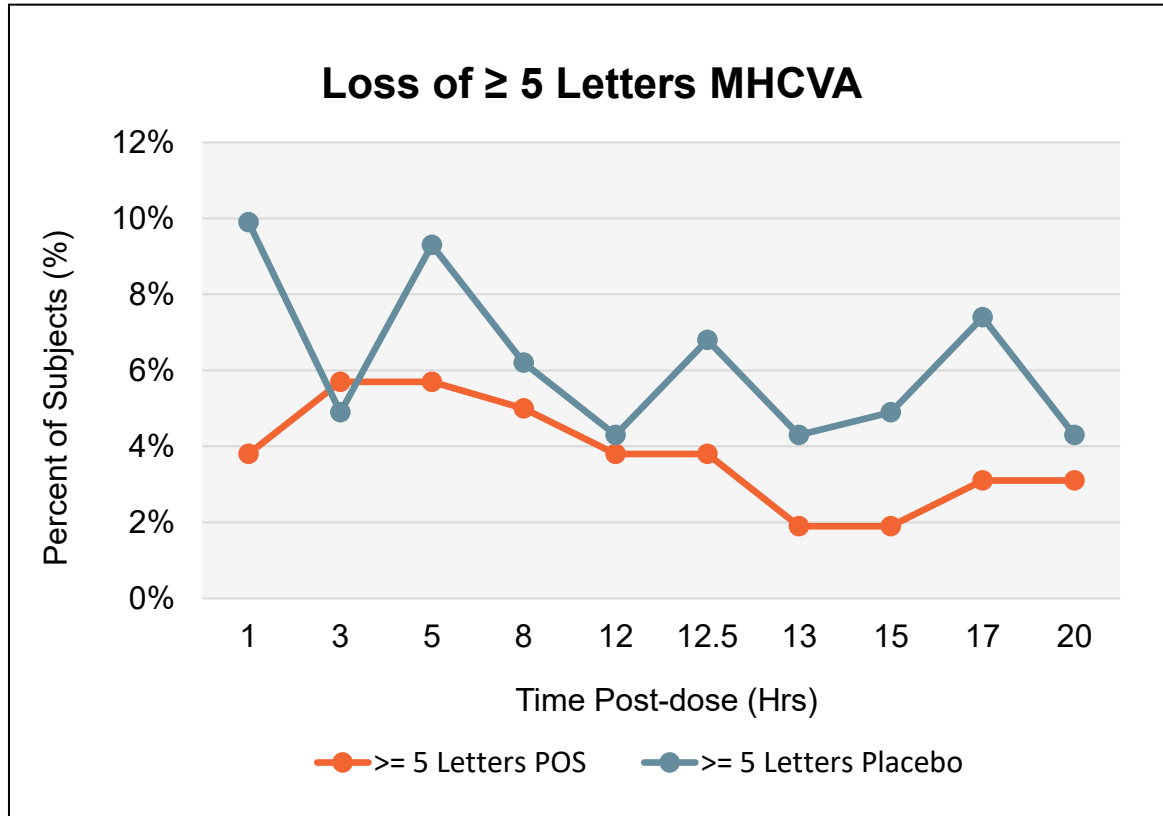
● In both groups, majority of AEs were mild in severity and related to drug instillation (discomfort, conjunctival hyperemia)

AE, adverse event; DCNVA, distance-corrected near visual acuity; POS, phentolamine ophthalmic solution 0.75%.

Source: Data on File, Opus/Viatris.

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Secondary Endpoint: Change from Baseline Mesopic High-Contrast Visual Acuity Over 20 Hours in the VEGA-2 Phase 3 Study



MHCVA, mesopic high contrast visual acuity; POS, phentolamine ophthalmic solution 0.75%.
Mesopic is defined as conditions under dim or low-light
Source: Data on File, Opus/Viatriis.

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Summary

- **POS improved near vision in presbyopic patients**
 - Effects were experienced within **1-hour of dosing with a single drop and persisted over 20 hours**
 - Nighttime dosing affords near vision upon awakening, due to duration of effect
- **No evidence of tachyphylaxis** over 6 weeks of repeated dosing
- **No clinically meaningful decrease in mesopic high contrast visual acuity (MHCVA)** was observed in POS-treated subjects
- Most common adverse events ($\geq 5\%$) were conjunctival hyperemia (26%), instillation site irritation (15%), dysgeusia (5.9%), and eye irritation (5.6%), with the majority mild in severity; **no drug-related serious adverse events occurred**
- POS does not act on the ciliary muscle; headache was reported in 2.6% of subjects