Phentolamine Ophthalmic Solution with and without Low Dose Pilocarpine Provides Durable Improvement in Distance Corrected Near Vision for Presbyopic Patients: A Responder Analysis

Presenter:
Mitch Brigell, PhD

Mitchell Brigell PhD, Jay Pepose MD PhD, Kavon Rahmani BS, Louis Haddad MS, Mina Sooch MBA, Eliot Lazar MD

April 23-27, 2023

Disclosures

Consultant

- Ocuphire Pharma
- ONL Therapeutics
- EyePoint Pharmaceuticals
- Design Therapeutics

POS and POS + Low Dose Pilocarpine Presbyopia Eye Drops

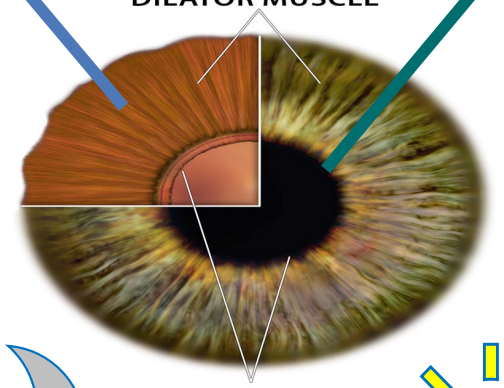
Differentiated MOA with Two Potential Product Labels for Functional Near Vision Improvement

0.75% POS

0.4% LDP

Iris Dilator Muscle **Inhibition**

Iris Sphincter and Ciliary Muscles **Activation**



POS as a Single Agent for Presbyopia

Single Durable Drop

- Phentolamine α1/2 antagonist 505(b)(2)
- Novel MOA on iris dilator with 24 hr durability with moderate pupil reduction
- Well-tolerated with no systemic effects
- Stable, preservative-free, single-use vial

POS with LDP as Adjunctive Therapy for Presbyopia

Two Drops Tunable Option

- Cholinergic agonist 505(b)(2)
- Known MOA on sphincter with potent miotic effects at approved doses (1%, 2%, 4%)
- Low concentration avoids tolerability issues
- Preserved, multi-use vial

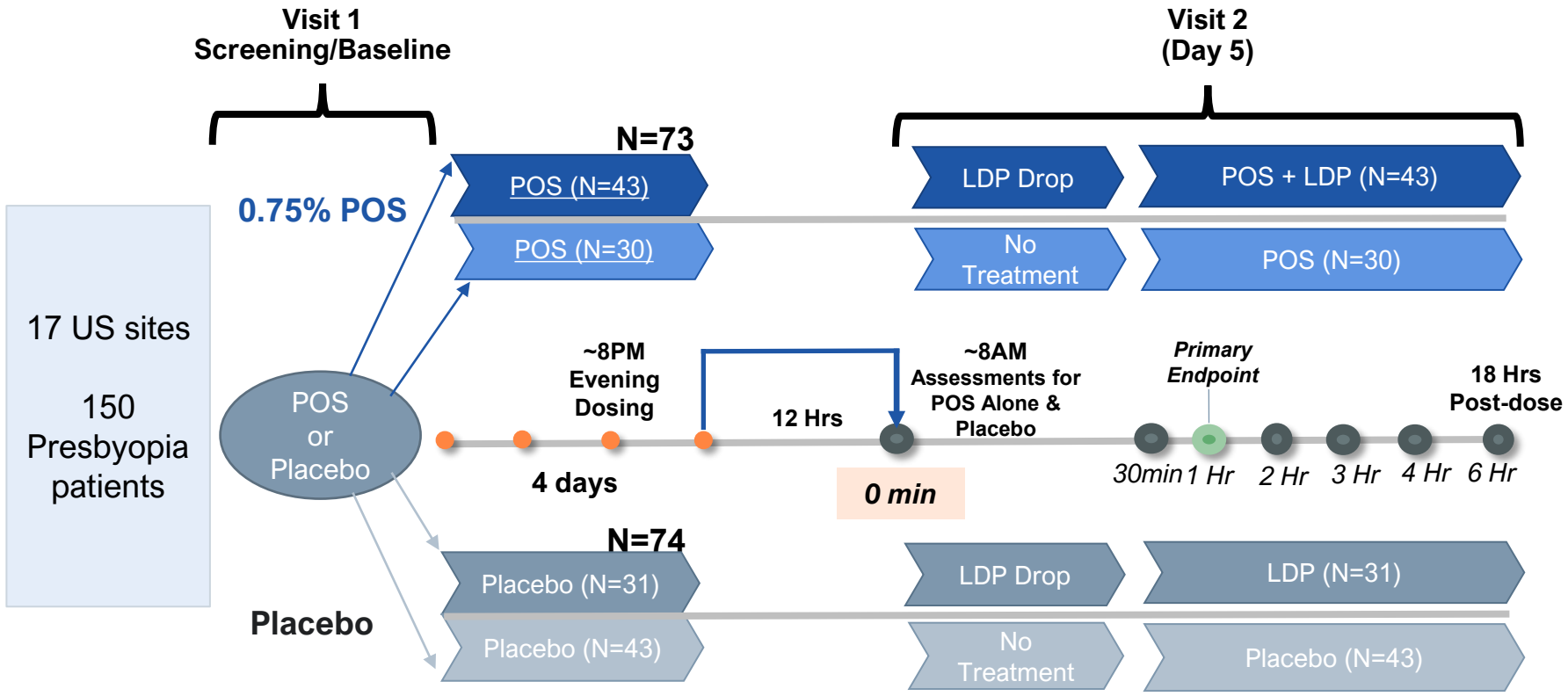
Evening drop ***Daytime drop***

Target Pupil Size is 2-3 mm

Source: POS data from 12 completed trials; Pilocarpine product label and literature

VEGA-1 (NCT# 04675151) Phase 2 Design

Randomized, Double-Masked, Placebo-Controlled Multi-Center One-Week Trial



Eligibility Criteria

- Males or females ≥ 40 and ≤ 64years of age
- BCDVA of 20/20 or better in each eye under photopic conditions
- DCNVA of 20/50 worse under photopic conditions in each eye & binocularly

Endpoints

Primary: % of subjects with ≥ 3 lines of improvement in distance-corrected near visual acuity comparing POS + LDP vs placebo alone at 1 hour

Secondary:

- % of subjects with ≥ 2 and ≥ 3 lines gained at time points from 30 min to 6 hours in photopic and mesopic lighting comparing POS + LDP vs placebo, POS alone, and LDP alone
- No loss of distance vision
- Pupil diameter at time points
- Safety and tolerability (redness)

Baseline Demographics and Baseline Characteristics

Well-Balanced Across Arms

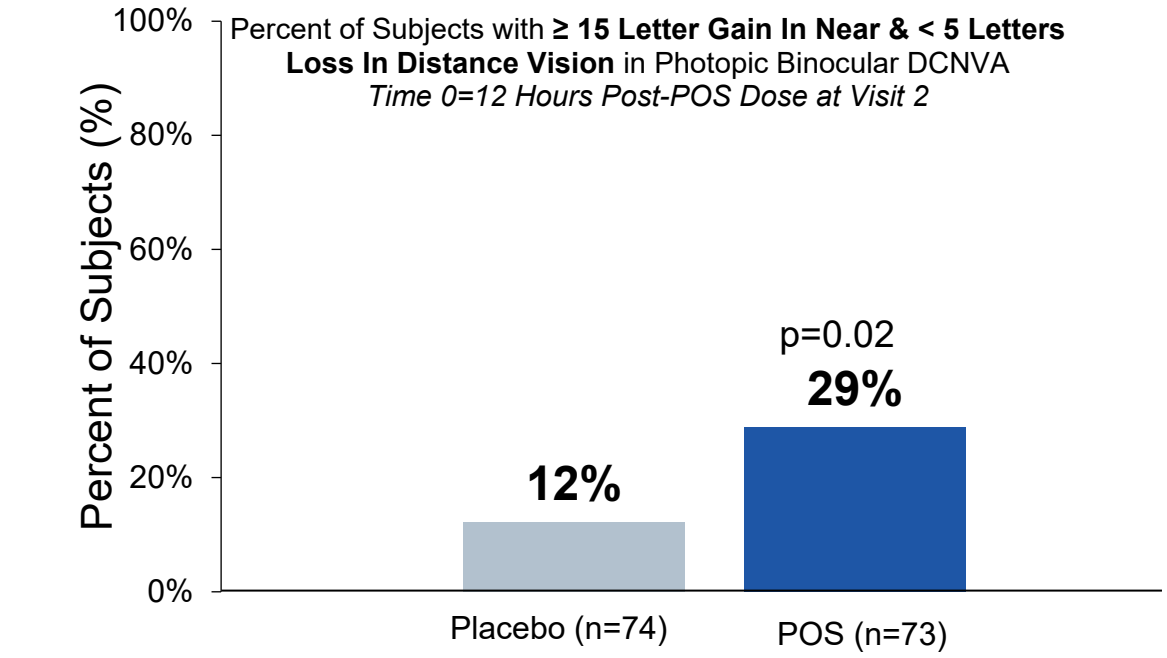
	Placebo Alone N=43	POS Alone N=30	LDP Alone N=31	POS+LDP N=43	Total N=147
Age (years): Median (Range)	52 (42-62)	54 (41-60)	52 (44-64)	53 (43-63)	53 (41-64)
Sex: Male n (%) **Female** n (%)	15 (35%) 28 (65%)	7 (23%) 23 (77%)	13 (42%) 18 (58%)	5 (12%) 38 (88%)	40 (27%) 107 (73%)
Race: White n (%) **Other*** n (%)	37 (86%) 6 (14%)	26 (87%) 1 (3%)	28 (90%) 3 (10%)	40 (93%) 3 (7%)	131 (89%) 15 (11%)
Dark Iris Color: n (%)	18 (42%)	12 (40%)	12 (39%)	18 (42%)	60 (41%)
Light Iris Color: n (%)	25 (58%)	18 (60%)	19 (61%)	25.1 (58%)	87 (59%)
Photopic DCNVA Mean Letters read-Binocular *(Snellen Equiv.)* *70 letters = 20/20*	46 (20/63)	45 (20/63)	48 (20/63)	46 (20/63)	46 (20/63)
Photopic BCDVA Mean Letters read-Binocular *(Snellen Equiv.)* *55 letters = 20/20*	62 (20/15)	61 (20/15)	60 (20/15)	61 (20/15)	61 (20/15)
Photopic Pupil Diameter Mean (mm)	4.3	4.5	4.3	4.3	4.3
Mesopic Pupil Diameter Mean (mm)	5.1	5.0	5.0	5.1	5.1
IOP (mmHg)	13.5	14.8	13.9	14.4	14.1

Source: VEGA-1 Results

Planned P3 Efficacy Endpoint Met by POS and POS+LDP

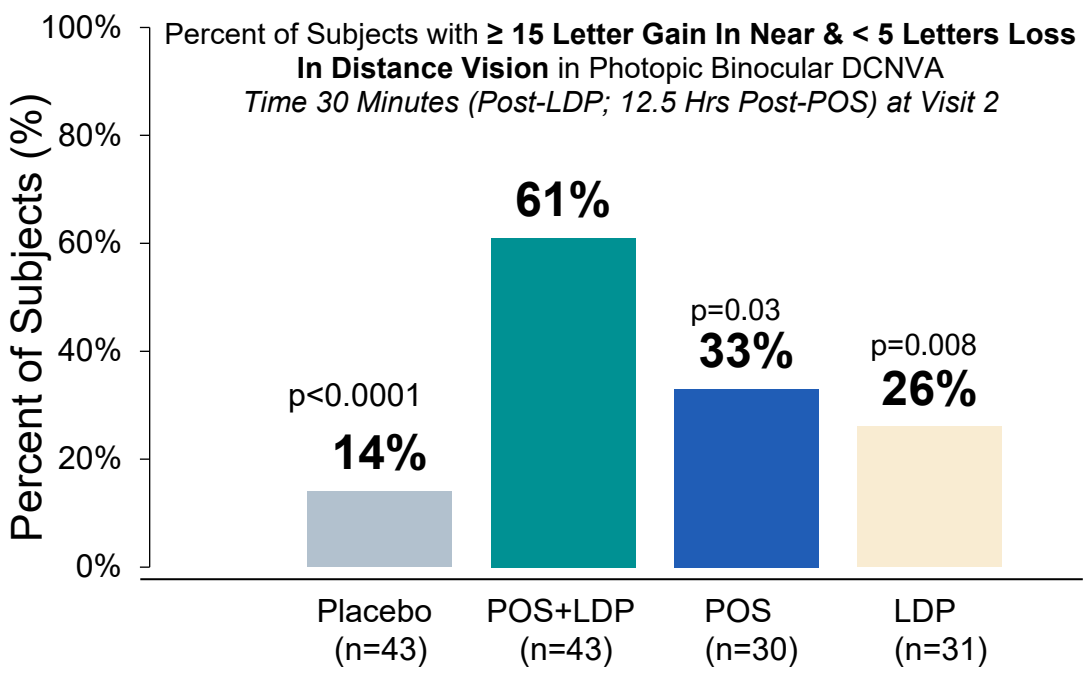
POS Single Drop and LDP Combination Provide Statistically Significant Near Vision Gain

1 **POS as a Single Drop for Presbyopia**



53% of subjects achieved ≥ 10 letter improvement in DCNVA at 12 hours (p=0.005 vs placebo) and a similar trend at other time points

2 **POS with LDP Adjunctive Therapy**

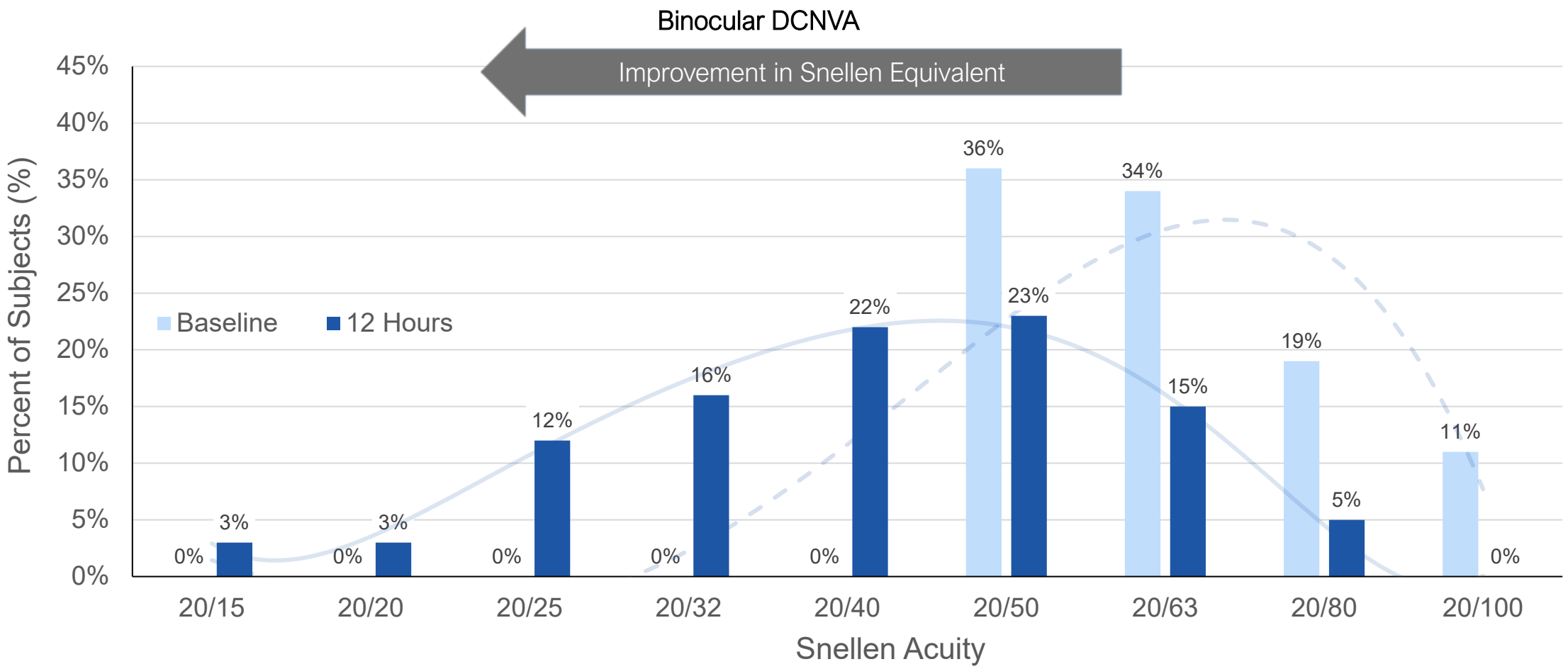


79% of subjects achieved ≥10 letter improvement in DCNVA at 1 Hour (p=0.005 vs placebo) and a similar trend at other time points

Source: VEGA-1 Results

Binocular DCNVA Baseline vs. 12 Hour Post POS Monotherapy

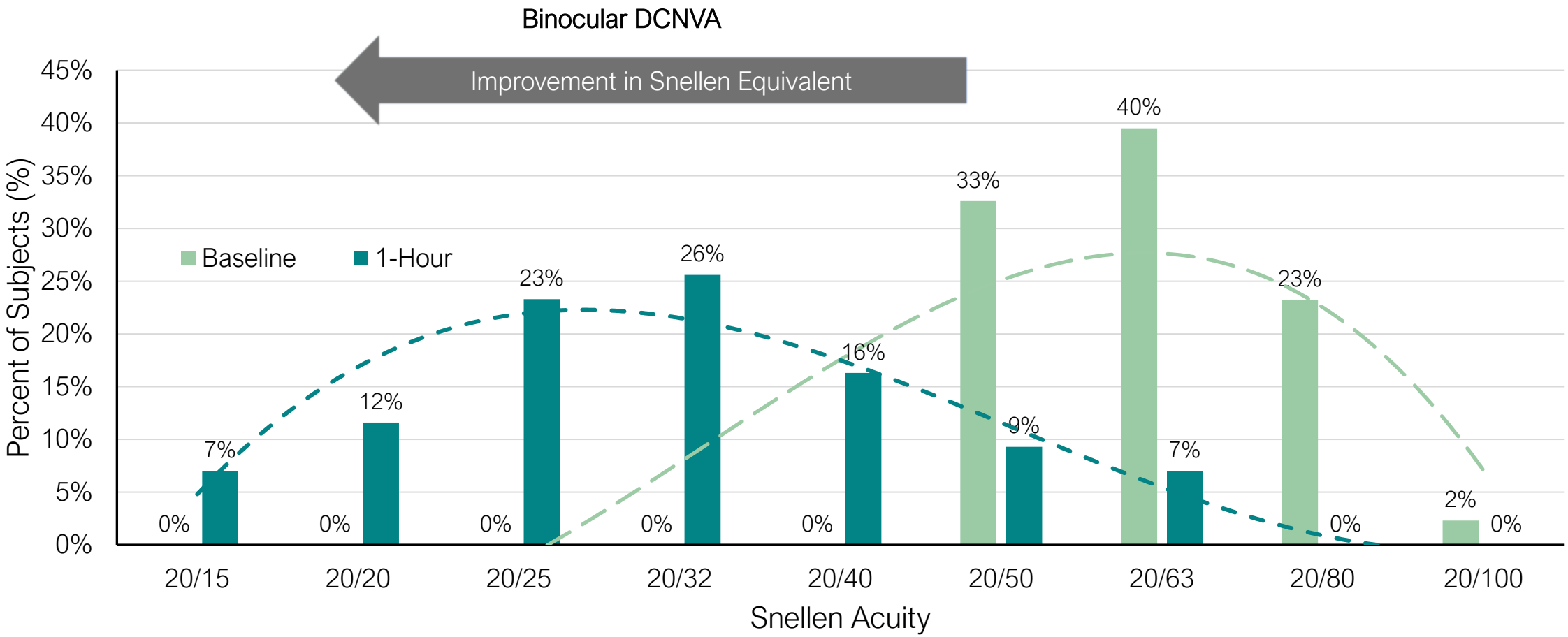
56% Achieved 20/40 or Better at 12 hours (Post-POS) Compared to Baseline



Source: VEGA-1 Results

Binocular DCNVA Baseline vs. 1 Hour Post POS+LDP

84% of Subjects Achieved Near Acuity of 20/40 or Better

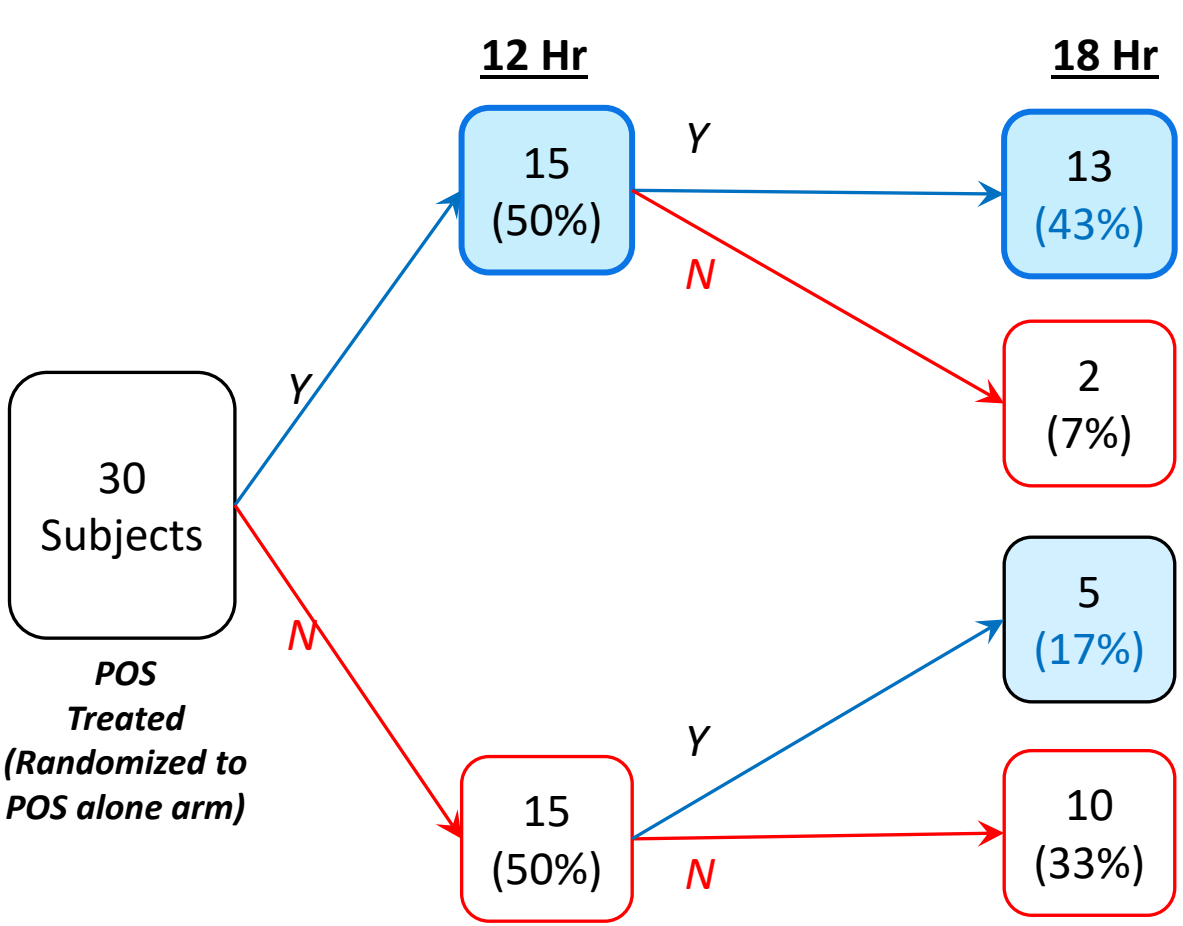


Source: VEGA-1 Results

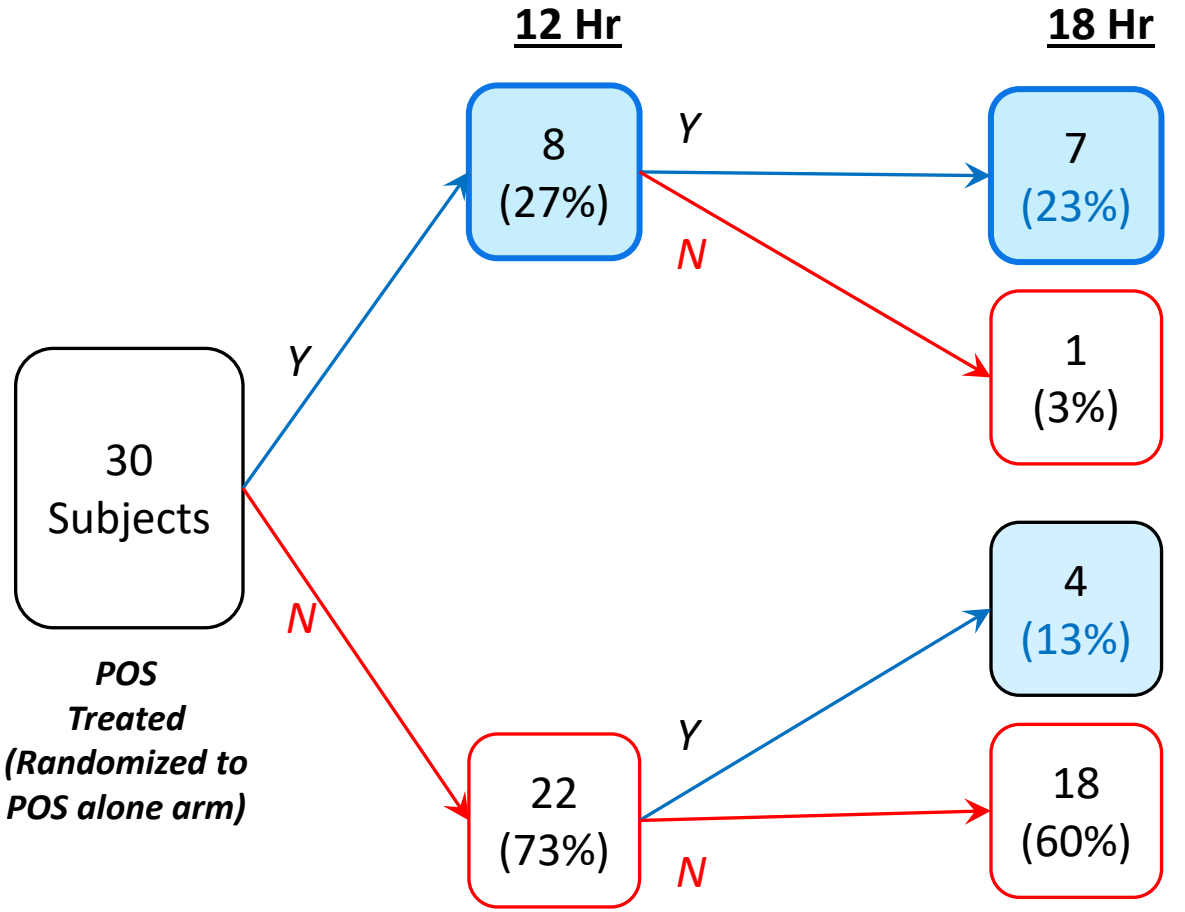
POS Monotherapy Gain of ≥ 2 or 3 Lines Binocular DCNVA Over Time

85%+ Responders Have a Durable Effect Out 12 to 18 Hours, With Even More POS Responders at 18 Hours

POS Gain of ≥ 2 Lines Binocular DCNVA ➔ 60% 18Hrs



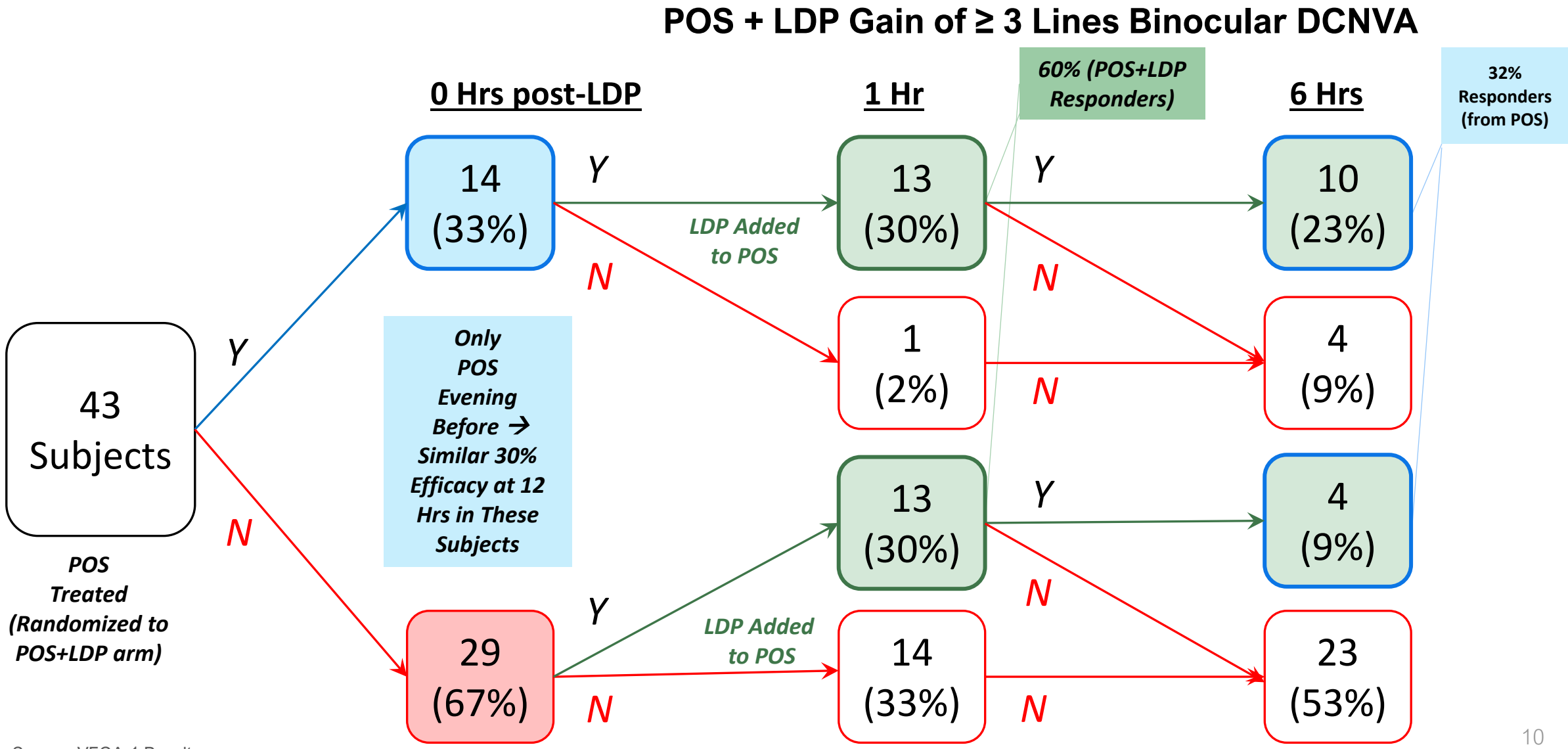
POS Gain of ≥ 3 Lines Binocular DCNVA ➔ 36% 18Hrs



Source: VEGA-1 Results

POS + LDP Gain of ≥ 3 Lines Binocular DCNVA Over Time

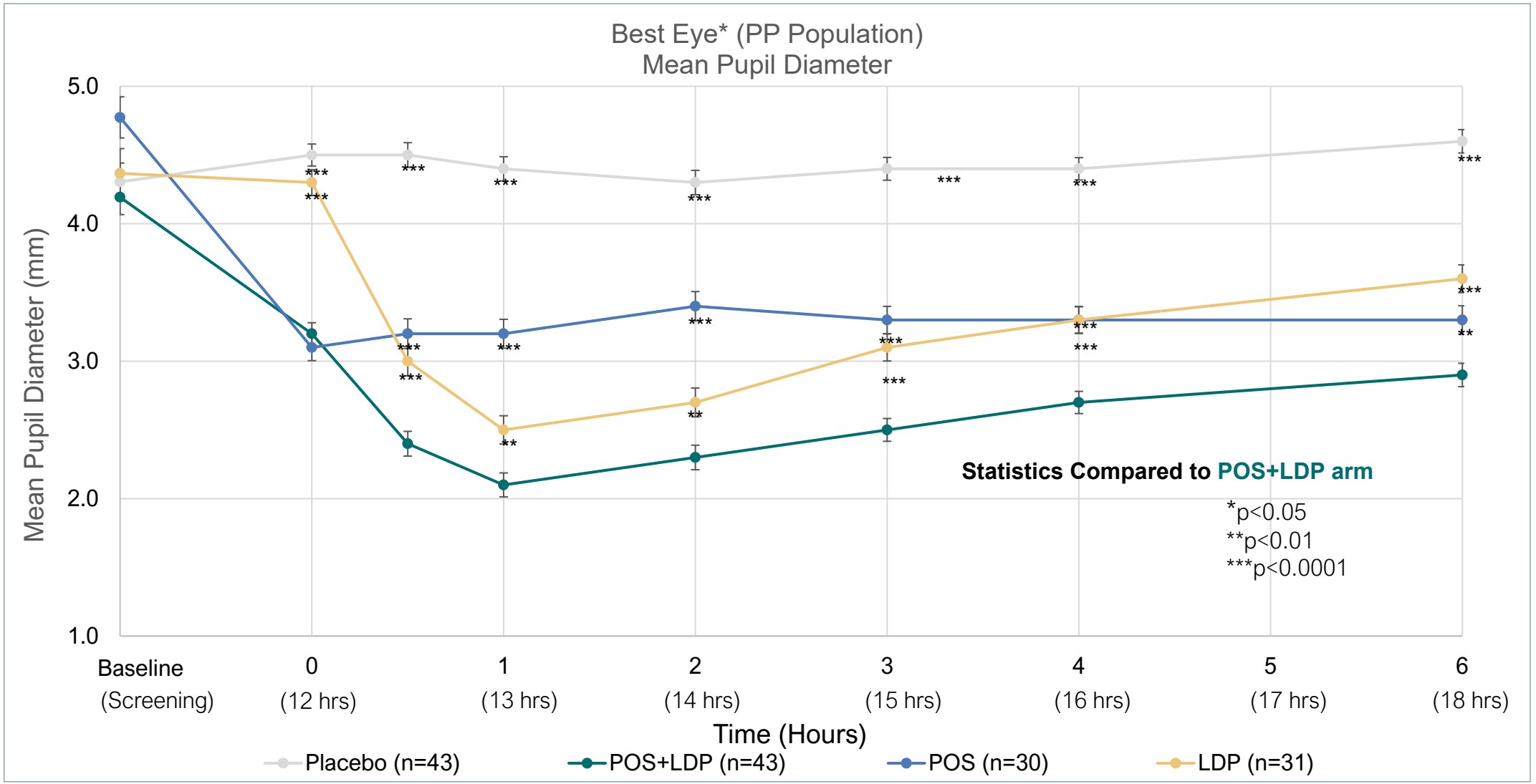
Low Dose Pilocarpine Provides Doubling of % Responders at 1 hour; LDP Response Reduced at 6 hours



Source: VEGA-1 Results

VEGA-1: Mean Pupil Diameter Over Time

POS+LDP Reduced Pupil Diameter to 2-3 mm, Consistent With Improvement in Near Vision



Source: VEGA-1 Results

*Defined as eye tested with greatest reduction in diameter between Study Eye and Fellow Eye: Note; PP population differs from mITT by only one subject; results were essentially identical

Safety Findings Across All Arms

POS and POS+LDP Combination were Well-Tolerated with a Favorable Safety Profile

- No serious AEs
- Most AEs were mild
  - No systemic AEs were observed in >5% subjects
  - No headaches, no brow aches, and no blurry vision AEs reported
  - Only mild, transient conjunctival hyperemia observed in <5% of subjects
- No significant loss in distance vision loss (≥ 5 letters):
  - In photopic lighting (160 cd/m^2): 0% placebo, 3% POS, 0% POS+LDP and 7% LDP
  - In mesopic lighting (3 cd/m^2): 7% placebo, 0% POS, 5% POS+LDP and 7% LDP
- No change in IOP

Source: VEGA-1 Results

Conclusions

- Phentolamine Ophthalmic Solution 0.75% (POS) provides a durable increase in near vision in presbyopic subjects
  - 56% of subjects achieve 20/40 or better near vision without correction
  - 30% of subjects gained 3 or more lines of near vision 12-hours post-dose
  - 85+% of subjects maintain their improved vision over 18 hours
- Low Dose Pilocarpine (LDP) provides transient improvement when added to POS treatment
  - 84% of subjects achieve 20/40 or better near vision without correction
  - 60% of subjects gain 3 or more lines of near vision 1-hour post-dose
    - LDP gains over POS monotherapy is transient (4 to 6 hours) as expected with pilocarpine MOA
- POS with adjunctive pilocarpine offers a tunable option for presbyopes of all ages
  - Many will get adequate benefit from phentolamine alone
  - Others can get needed transient gain from adjunctive pilocarpine treatment

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