VisAbility™ Micro Insert System

For the improvement of near vision without compromise to distance vision in patients with presbyopia

November 9, 2020

Refocus Group, Inc.

Ophthalmic Devices Panel

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Mike Judy

President & CEO Refocus Group, Inc.

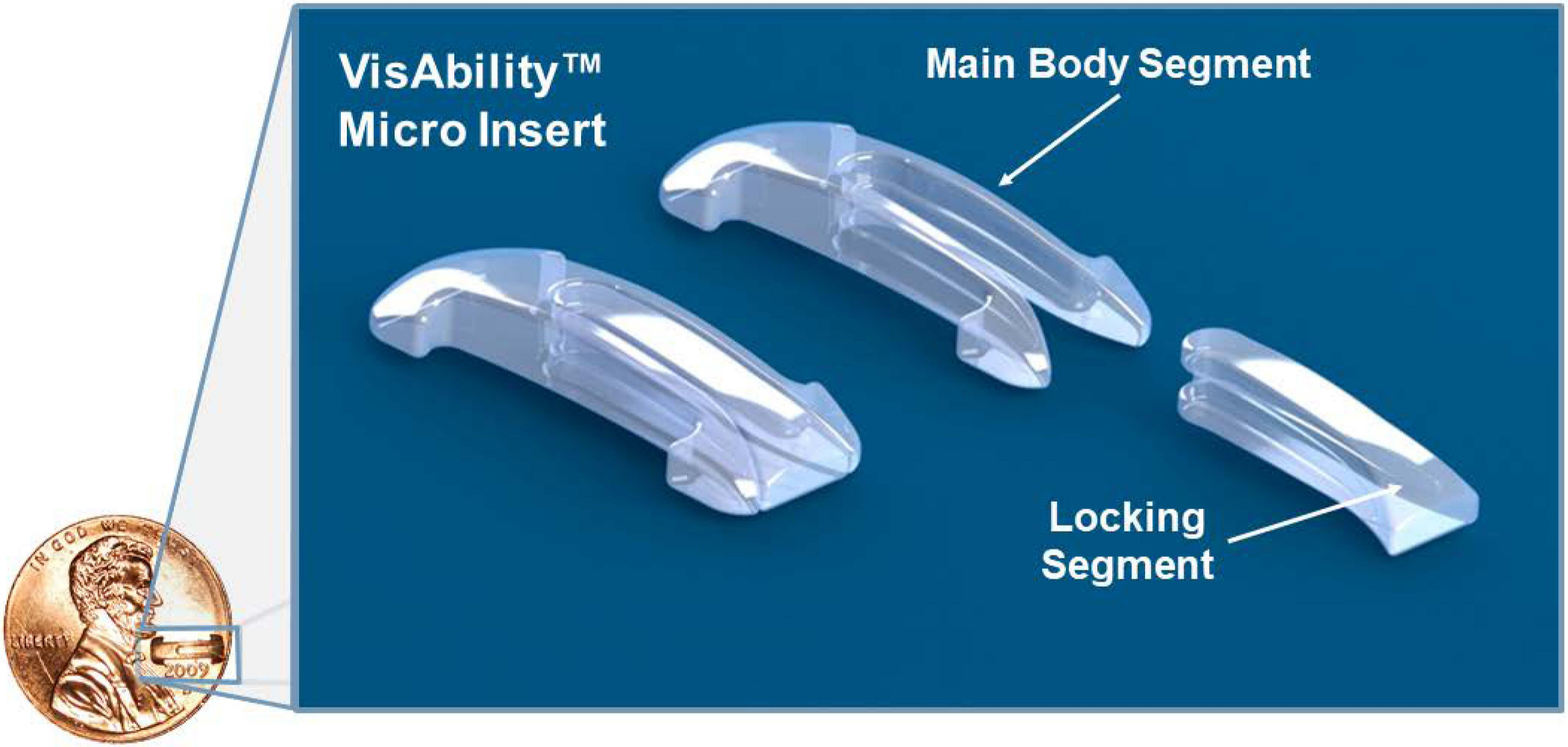
Presbyopia

- A progressive, age-related loss of accommodation, or ability of the eye to focus clearly on objects over a range of intermediate to near distances

VisAbility™ Micro Insert System Treatment for Presbyopia

- Surgical procedure performed outside of visual axis, maintaining cornea and lens integrity
- Allows patients to achieve functional near visual acuity while preserving distance vision

VisAbility™ Procedure



Proposed Indication

VisAbility™ Micro Insert System for bilateral scleral implantation to improve unaided near vision in phakic, presbyopic patients between 45 and 60 years of age, who have a manifest spherical equivalent between -0.75 D and +0.50 D with less than or equal to 1.00 D of refractive cylinder in both eyes, and require a minimum near correction of at least +1.25 D reading add.

FDA-Approved Protocol Established 24-Month Study

3.0 STUDY SYNOPSIS

The objective of this study is to evaluate the safety and effectiveness of the VisAbility implant System (VIS) for the improvement of near visual acuity in presbyopic patients. This is a prospective clinical study that will enroll and determine eligible a total of 360 subjects ranging in age between 45 and 60 years of age at up to 14 clinical sites. Subjects will be implanted with the VisAbility Implant model SGP-046 in the primary eye and then in the fellow eye no sooner than 14 days later. Subjects will be examined at one day, one week and at 1, 2, 3, 6, 12, 18 and 24 months post-operatively.

8.7 Study Completion

Subjects are considered to have completed the study when they complete the 24 month exam regardless of earlier missed visits.

VisAbility™ Micro Insert Provides Clinically Meaningful Improvements in DCNVA

- Clinically significant improvements in Distance Corrected Near Visual Acuity (DCNVA) at all post-operative timepoints
  - DCNVA 20/40 or better AND gain of ≥ 10 letters
    - 12 Months >79% of primary eyes (74.5% lower CI)
    - 24 Months = 84% of primary eyes (79.7% lower CI)

VisAbility™ Micro Insert Provides Unique Benefits and a Favorable Safety Profile

- Procedure performed outside visual axis, avoiding vision loss and aberrations, while preserving distance vision
- Ocular adverse events were typically mild in nature
- All significant ocular adverse events resolved
  - No persistent loss of Best Corrected Distance Visual Acuity (BCDVA) ≥ 2 lines

Post-Approval Plan to Mitigate Risk and Control Access of VisAbility™ Micro Insert

- Select group of surgeons trained and certified in selection of appropriate patients, performance of VisAbility™ Micro Insert surgery, and management of potential complications
- Controlled access of VisAbility™ Micro Insert certified surgeons
- Prospective 3rd party mandatory registry of all patients[1]

1. Protocol of 3rd party registry has not been submitted to the FDA

Agenda

Presbyopia and Current Treatment Options	**Frank Bucci, MD** Founder and President Bucci Laser Vision
Study Design and Effectiveness Results	**Selene Burke, OD** Vice President Clinical Affairs, Refocus Group Inc
Safety Results	**Mark Packer, MD, FACS** Mark Packer MD Consulting Incorporated, President VisAbility™ Study Independent Medical Monitor
Mandatory Training and Certification	**David Schanzlin, MD** Chief Medical Officer, Refocus Group, Inc. Professor of Ophthalmology (Emeritus), University of California, San Diego
Controlled Access and Post-Approval Registry	**Martin Kaufman** Chief Regulatory Officer Refocus Group Inc.
Benefit-Risk Assessment	**Mark Packer, MD, FACS** Mark Packer MD Consulting Incorporated, President VisAbility™ Study Independent Medical Monitor

Presbyopia and Current Treatment Options

Frank Bucci, Jr., MD
Founder and President
Bucci Laser Vision

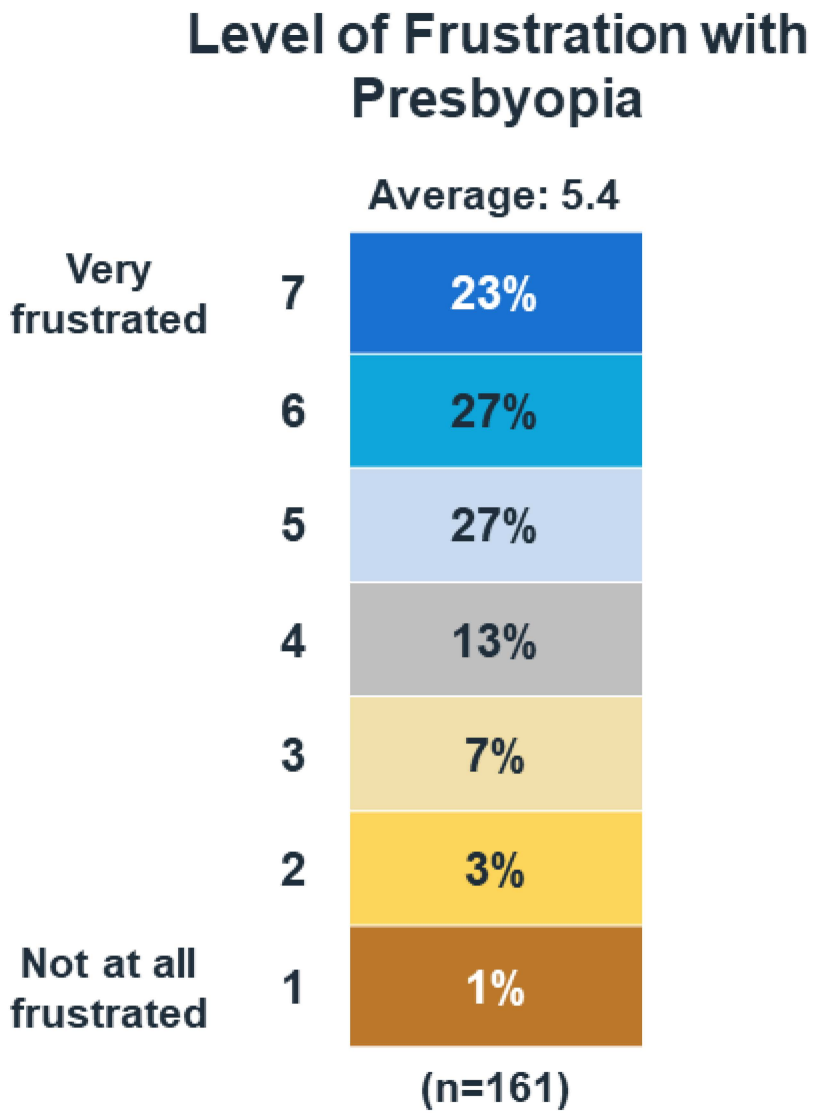
Presbyopia: Most Prevalent of All Visual Deficiencies

- Progressive, age related loss of accommodation
- Ability of unaided eye to focus on near or intermediate distance objects
- 19.1% of US population are ≥ 45 and < 60 years[1]
  - ~61.9 million are likely to experience symptoms of presbyopia[2]

1. Census Report 2018. 2. Luo, et al. 2008.

Presbyopia Reduces Quality of Life

- Presbyopia is associated with substantial, negative effects on vision-targeted health-related quality of life[1]
- Kaiser Associates conducted 2 surveys[2]
  - Scale 1 to 7
  - 50% ranked 6 or 7
  - 40% ranked 4 or 5



1. McDonnell et al., 2003. 2. Kaiser Associates' studies commissioned by Refocus Group, Inc. 2017.

First Line Treatment Options and Limitations

- Eyeglasses or contact lenses
  - Single-vision, bifocals, trifocals, progressive lenses
- Presbyopia corrected with glasses is associated with a decrease in quality of life[1]
- Monovision correction does not fully restore health-related quality of life[2]
- ~10% of patients with presbyopia may be candidates for an intervention other than spectacles to correct the condition[1]

1. Luo et al. 2008;
2. McDonnell et al., 2003.

Surgical Treatment Options and Limitations

- Surgical approaches: Refractive surgery
  - Lens exchange (off-label)
  - Corneal inlays
  - Monovision LASIK
- These methods may result in compromise of distance vision in the effort to improve near vision
- Although monovision correction leads to some improvements in health-related quality of life[1]
  - Compared to single-vision correction, monovision still worse than quality of life prior to developing presbyopia[1]

1. McDonnell et all. 2003

Presbyopia Negatively Impacts Professions and Hobbies

Current Surgical Treatment Options and Limitations

	Performed Outside Visual Axis	Completely Reversible Procedure	Absence of Visual Disturbances	Preserves Distance Vision
Corneal inlays	✗	✗	✗	✗
Lens exchange (off label)	✗	✗	✗	✓
Monovision LASIK	✗	✗	✗	✗

The Ideal Procedure for Presbyopia

- Continuous full range of vision
- Procedure without side effects of halos and glare
- Reversible procedure
- Procedure outside visual axis

Kaiser Associates' studies commissioned by Refocus Group, Inc. 2017.

Presbyopic Patients Want More Treatment Options

- "The large unmet need of willing and able patients has yet to find a surgical solution that fits the lifestyle and high expectations of this group."[1]

Patients need a safe, bilateral procedure that will not negatively impact quality of vision

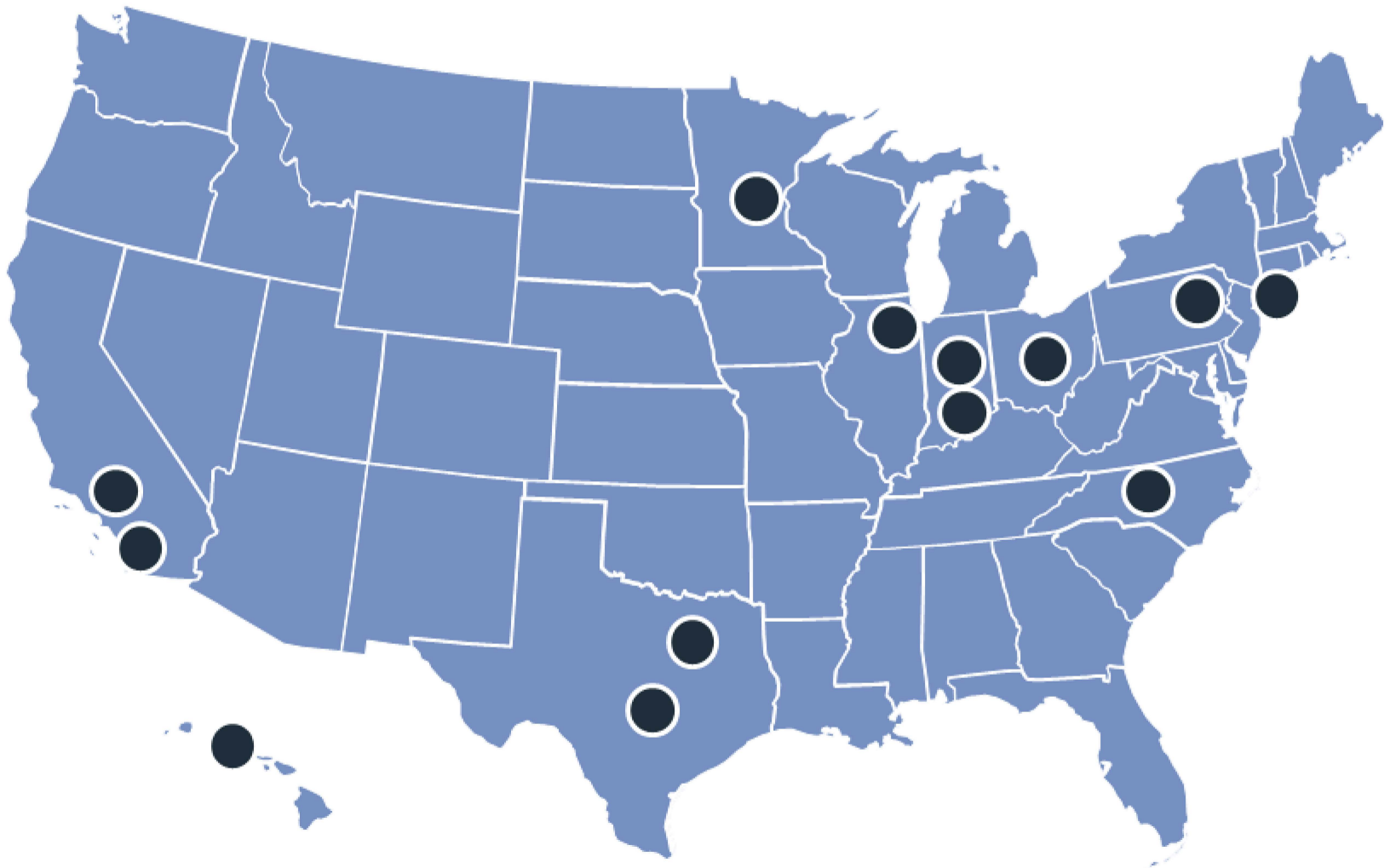
1. https://eyewire.news/articles/market-scope-global-refractive-surgery-demand-continued-to-grow-in-2019/

Study Design and Effectiveness Results

Selene Burke, OD
Vice President Clinical Affairs
Refocus Group, Inc.

Prospective, Multi-Center Study

Oday Alsheikh, San Antonio, TX
Ken Beckman, Columbus, OH
Frank Bucci, Wilkes-Barre, PA
Ralph Chu, Bloomington, MN
Alan Faulkner, Honolulu, HI
Jim Katz, Des Plaines, IL
Jodi Luchs, Wantagh, NY
John Meyer, Louisville, KY
David Schanzlin, San Diego, CA
Karl Stonecipher, Greensboro, NC
Dan Tran, Orange County, CA
Jeff Whitman, Dallas, TX
Kevin Waltz, Indianapolis, IN



Study Objectives

- Evaluate safety and effectiveness of VisAbility™ Micro Insert for improvement of near vision in presbyopes
- Two co-primary endpoints
  1. Achievement of DCNVA 20/40 or better and gain ≥ 10 letters DCNVA in 75% of primary (dominant) implanted eyes at 12 months
     - Per protocol, data collected at all visits including through 24 months
  2. Achievement of statistically significant difference in proportion of primary eyes with DCNVA 20/40 or better and gain of ≥ 10 letters at 6 months, in patients randomized to treatment vs control (Randomized Substudy)

DCNVA: Distance Corrected Near Visual Acuity

VisAbility™ Key Inclusion Criteria

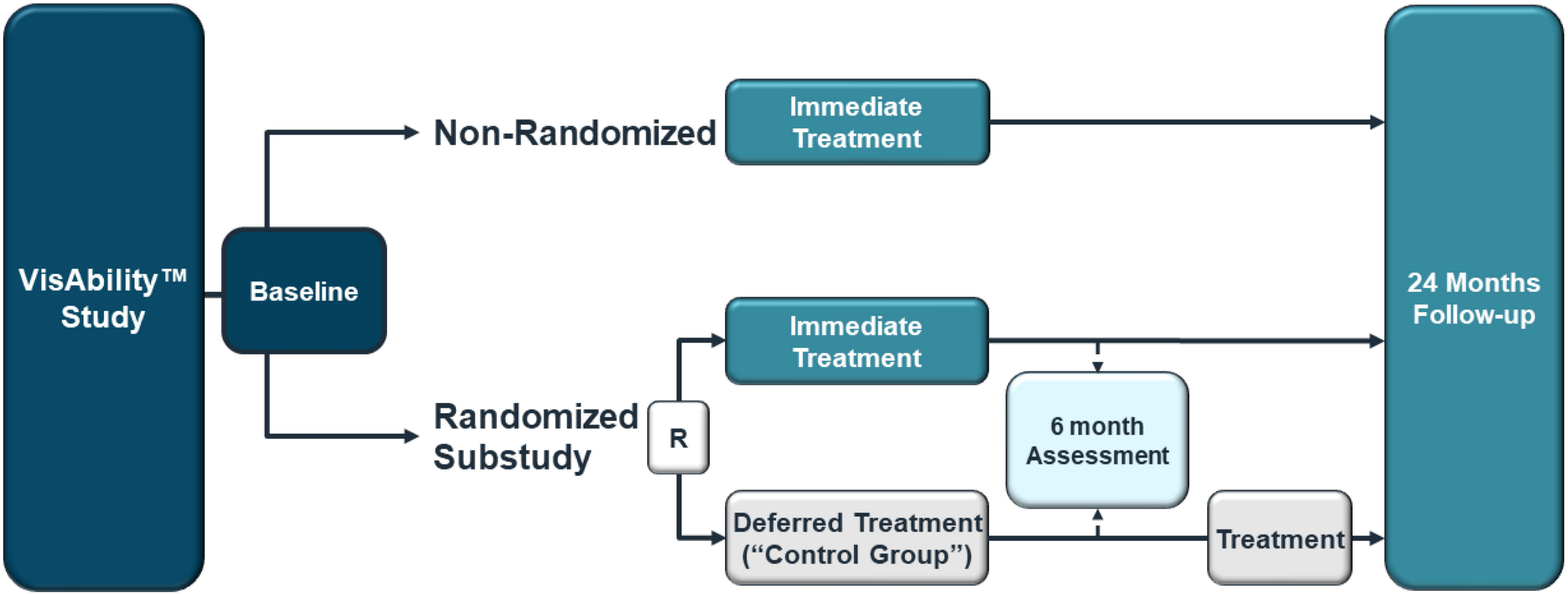
- Between 45 - 60 years old
- BCDVA of 20/20
- DCNVA and UCNVA at 40 cm of 20/50 to 20/80
- MRSE
  - -0.75 to +0.50 diopters
  - ≤ 1.00 diopter of astigmatism
- Minimum near add: ≥ +1.25 to read 20/20 at near

BCDVA: Best Corrected Distance Visual Acuity; DCNVA: Distance Corrected Near Visual Acuity; UCNVA: Uncorrected Near Visual Acuity

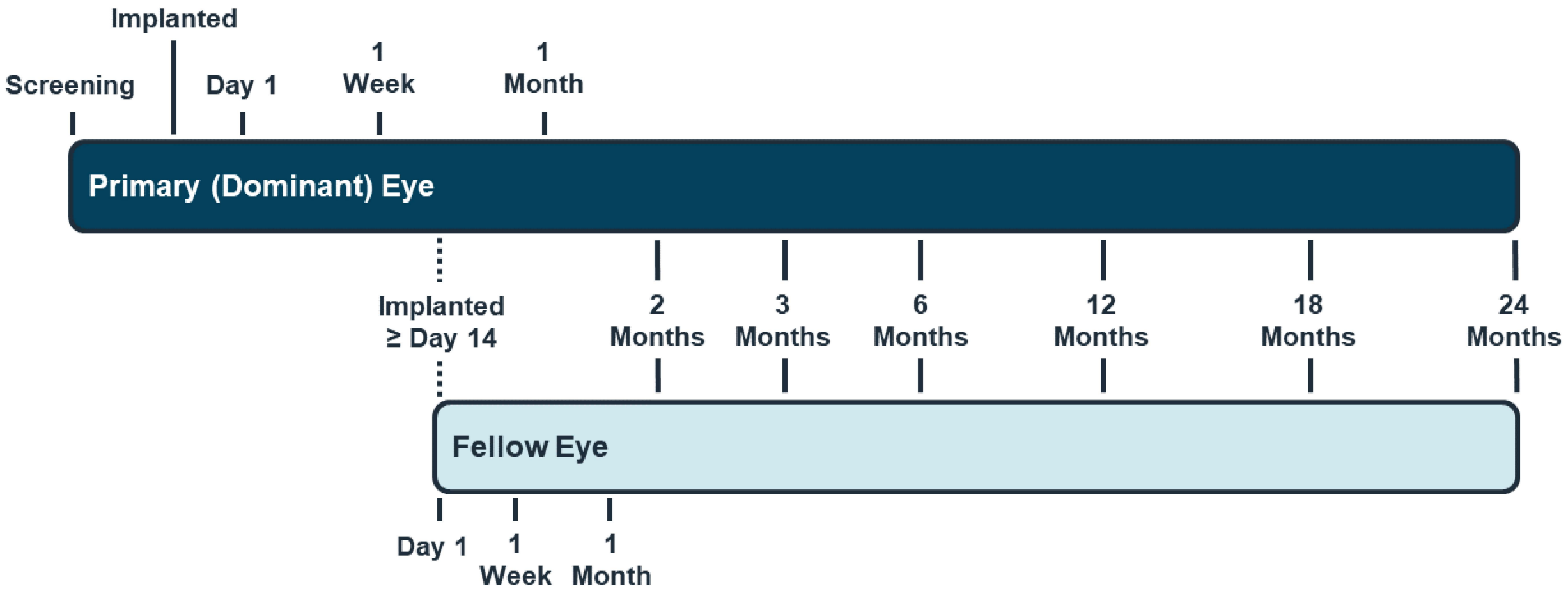
VisAbility™ Key Exclusion Criteria

- Abnormal pupil function
- Ocular or systemic inflammatory disease
- Prior intraocular or refractive procedures
- Prior muscle surgery
- Scleral thickness less than 530 microns
- Chronic ocular or systemic disease

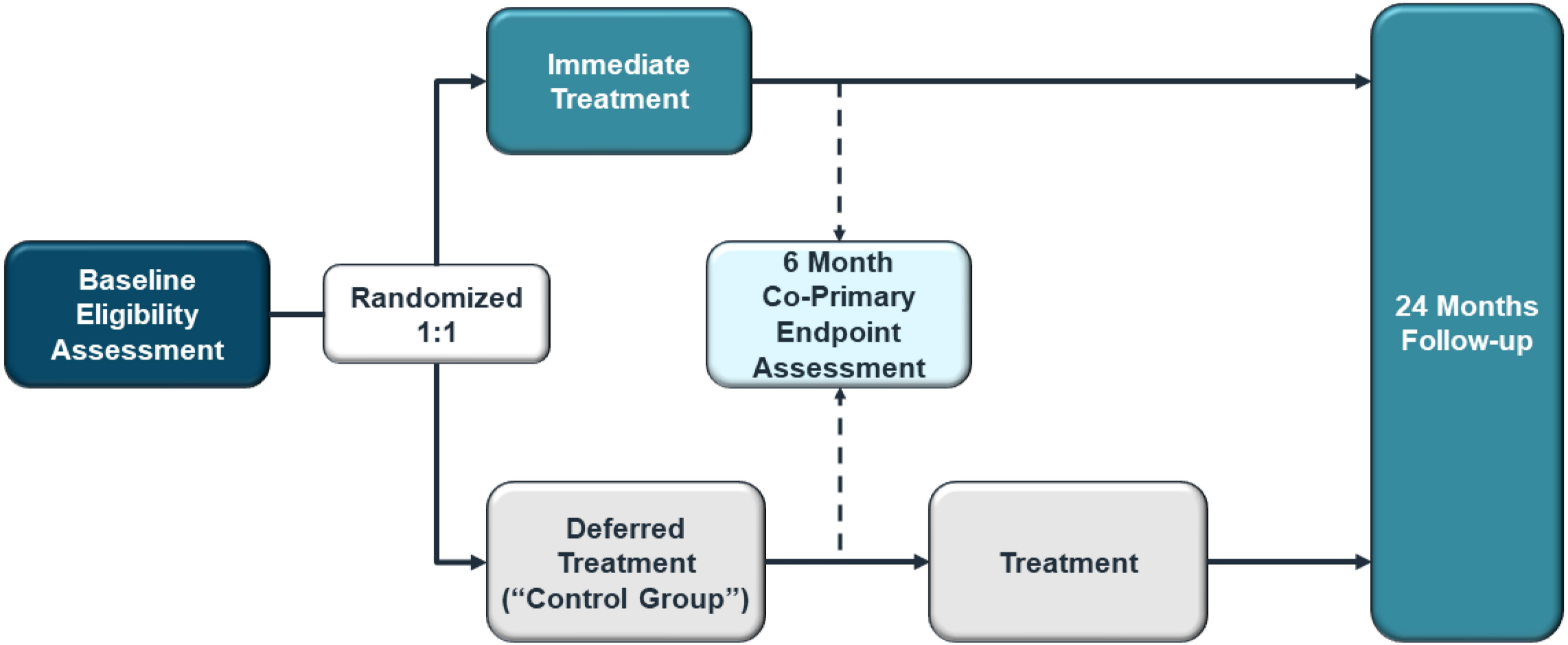
VisAbility™ Study Design



VisAbility™ Non-Randomized Arm

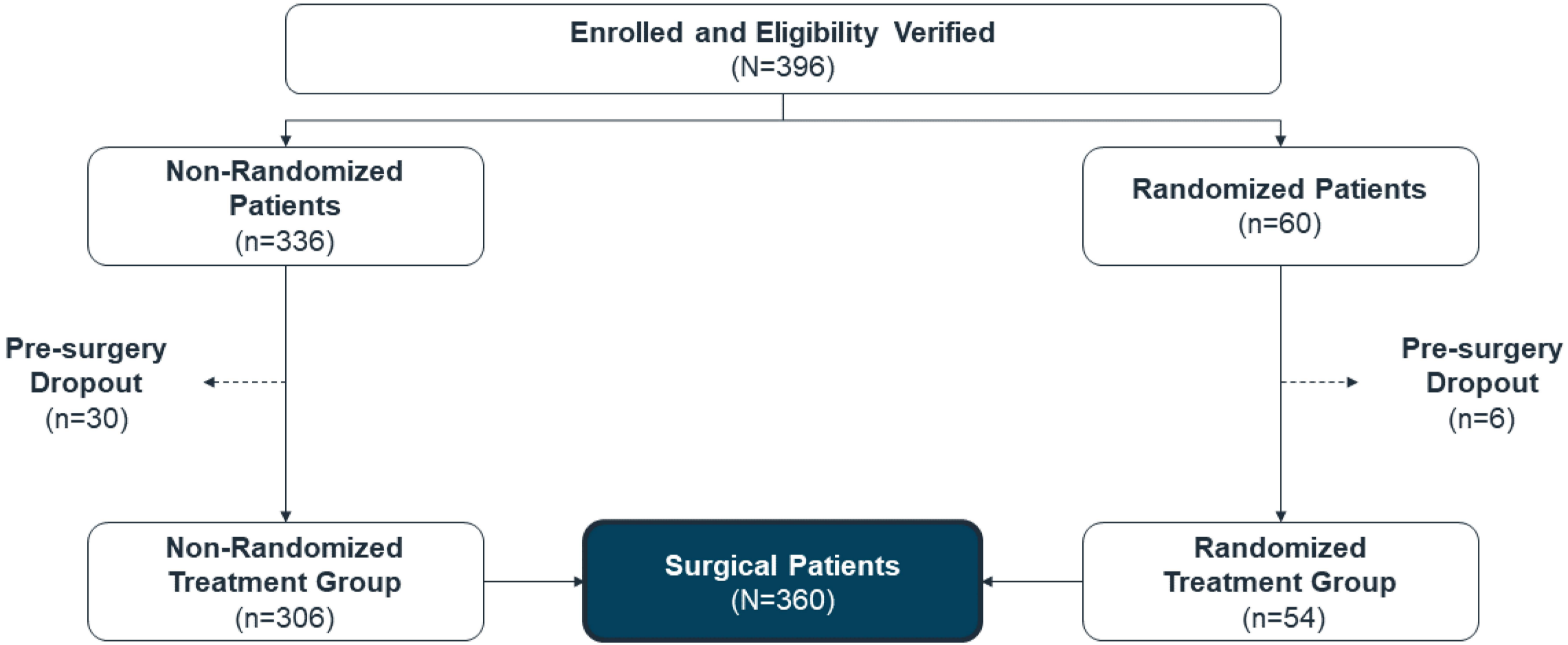


VisAbility™ Randomized Substudy Arm

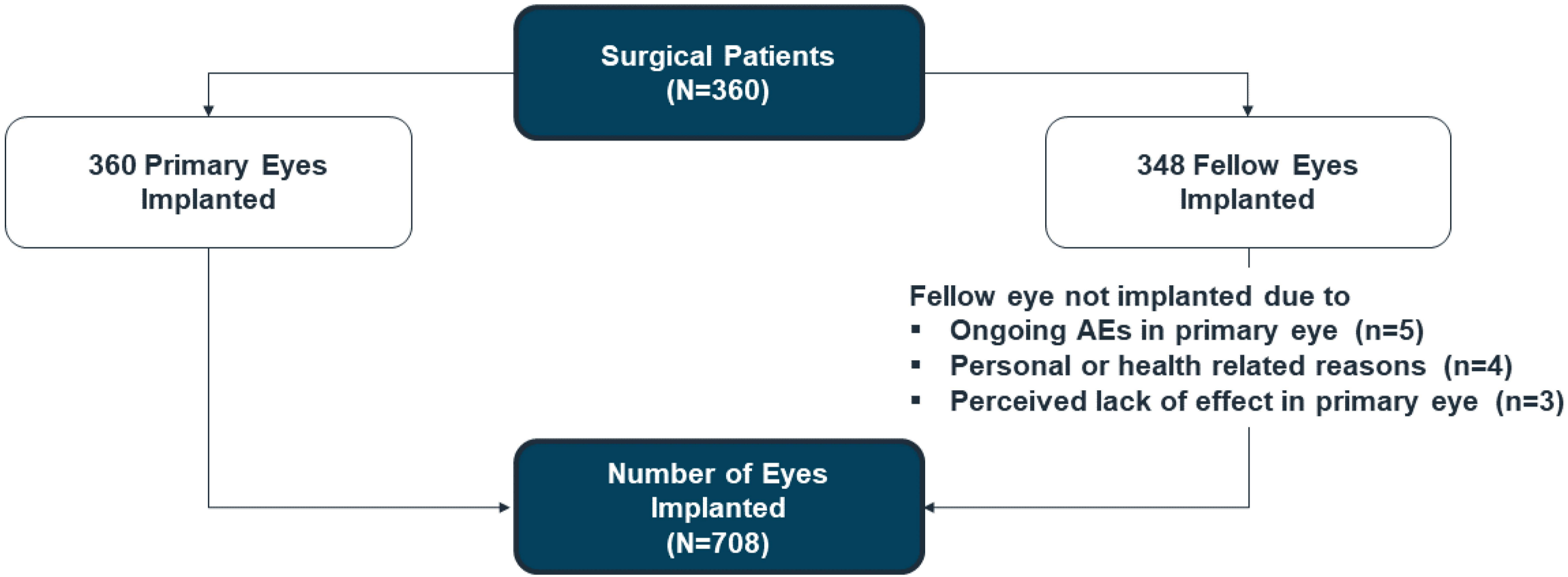


Patients in VisAbility™ randomized substudy and non-randomized cohort had same visit schedule.

VisAbility™ Patient Disposition



VisAbility™ Number of Eyes Implanted



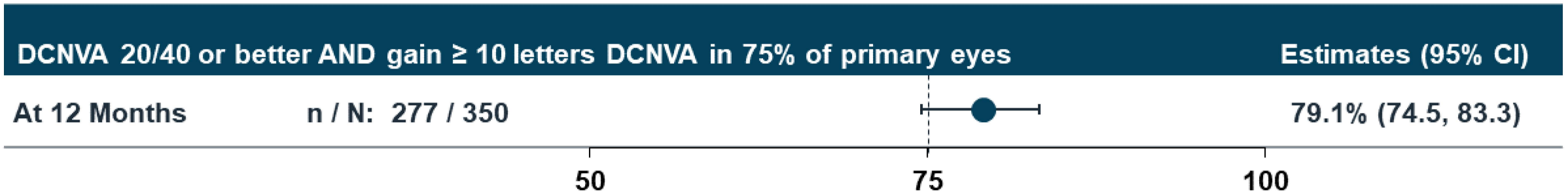
98% accountability at 12 months
96% accountability at 24 months

VisAbility™ First Co-Primary Effectiveness Endpoint

- Achievement of DCNVA 20/40 or better AND gain ≥ 10 letters DCNVA in 75% of primary eyes implanted at 12 months
  - Lower bound of the 95% CI ≥ 75%

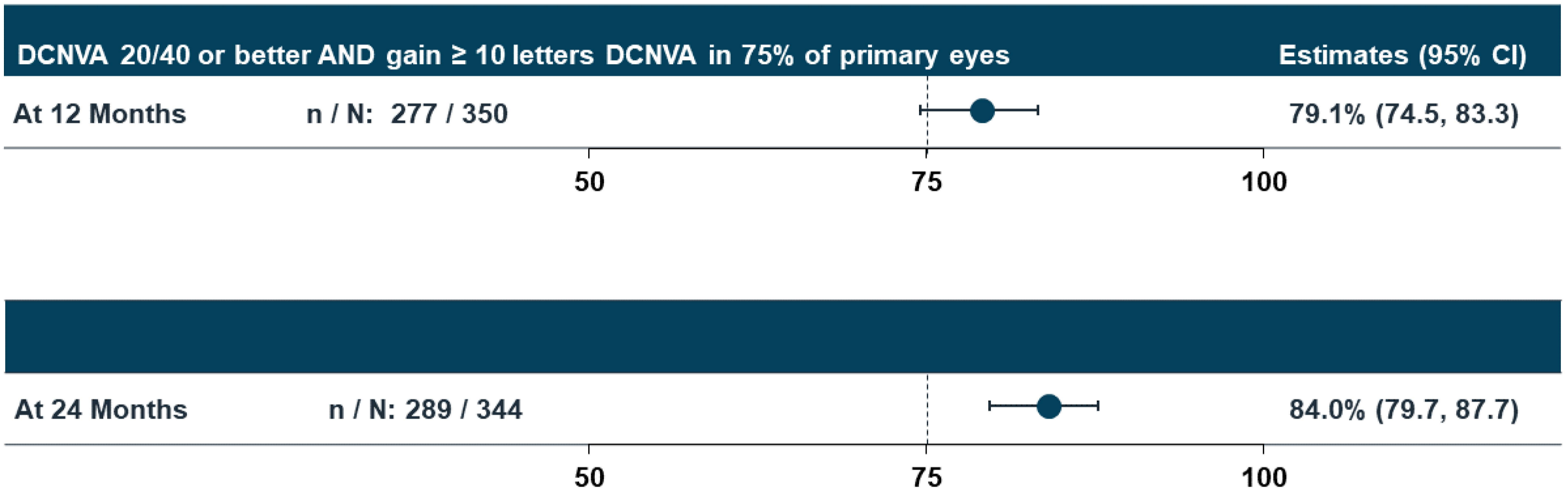
DCNVA: Distance Corrected Near Visual Acuity

First Co-Primary Effectiveness Endpoint: Clinically Meaningful Improvement at 12 Months



DCNVA: Distance Corrected Near Visual Acuity

Clinically Meaningful Improvement at 12 and 24 Months



DCNVA: Distance Corrected Near Visual Acuity

Results for First-Co-Primary Endpoint Criteria and Individual Components at 12 and 24 Months

	12 Months (N=350)	24 Months (N=344)
	%, n, 95% CI	%, n, 95% CI
First Co-Primary Endpoint Criteria: DCNVA 20/40 or better AND gain ≥ 10 letters DCNVA	**79.1%** n=277 74.5, 83.3	**84.0%** n=289 79.7, 87.7
DCNVA 20/40 or better[1]	**89.4%** n=313 85.7, 92.4	**91.3%** n=314 87.8, 94.0
Gain ≥ 10 letter DCNVA[1]	**80.0%** n=280 75.4, 84.1	**85.5%** n=294 81.3, 89.0

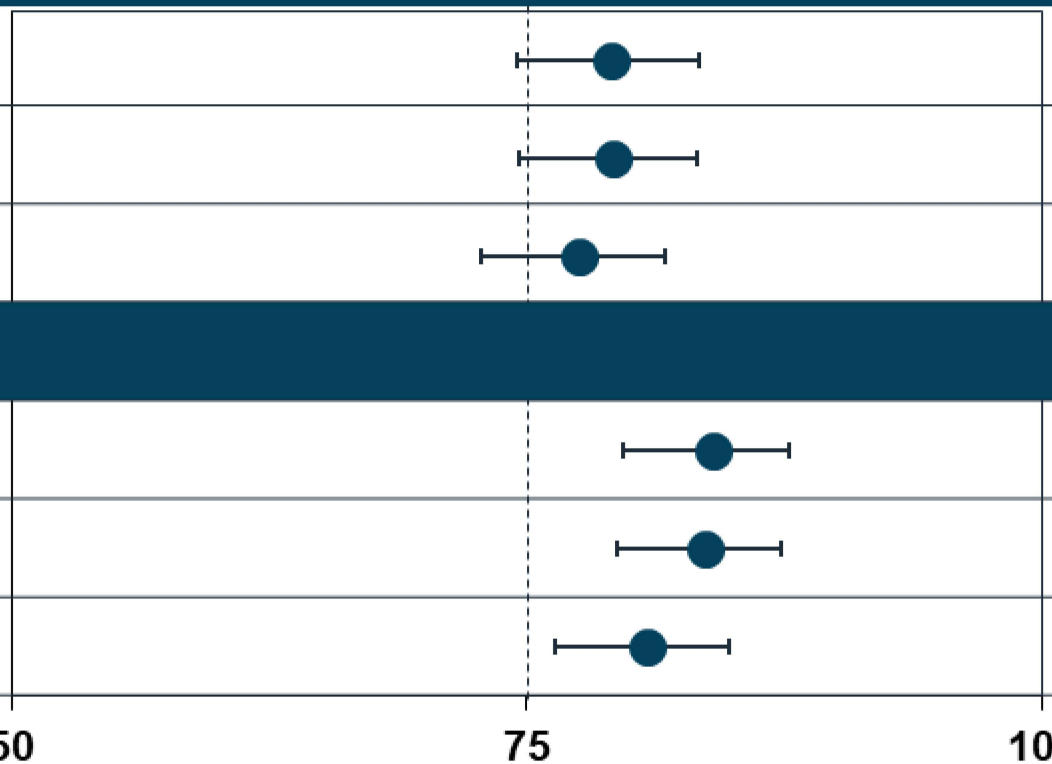
1 Analysis was not prespecified or presented to the FDA

DCNVA: Distance Corrected Near Visual Acuity

Clinically Meaningful Improvement at 24 Months Even in Worst Case Sensitivity Analysis

DCNVA 20/40 or better and gain ≥ 10 letters DCNVA in 75% of primary eyes

12 Months	n / N	Estimates (95% CI)
Primary Analysis	277 / 350	79.1% (74.5, 83.3)
Best Case Analysis	285 / 360	79.2% (74.6, 83.2)
Worst Case Analysis	279 / 360	77.5% (72.8, 81.7)
24 Months		
Primary Analysis	289 / 344	84.0% (79.7, 87.7)
Best Case Analysis	301 / 360	83.6% (79.4, 87.3)
Worst Case Analysis	291 / 360	80.8% (76.4, 84.8)



Best Case: missing data imputed using best value from any protocol scheduled visit at 1 month or after.
Worst Case: missing data imputed using worst value from any protocol scheduled visit at 1 month or after.
Discontinued primary eyes imputed as effectiveness failures in both cases.

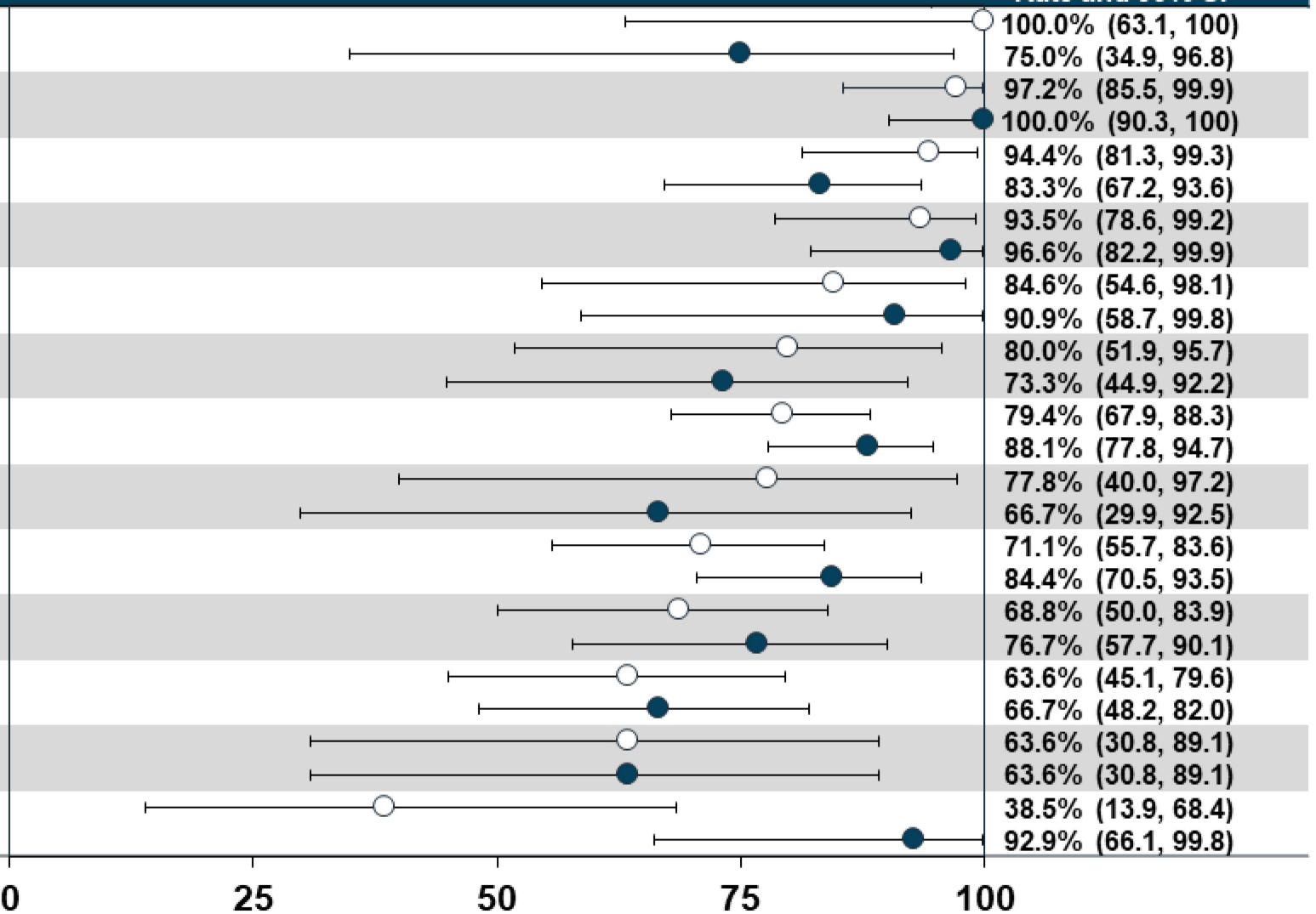
Site Variability

Poolability & Variation Across Sites

- Observed variation in effectiveness outcomes across sites
- No covariates identified to account for the variation
- Analyses excluding site performance can induce selection bias
- Meeting the endpoint at site level was not a pre-specified goal
  - Study sample size was not selected to achieve such a goal
- All patients and sites contribute to evidence of effectiveness

DCNVA 20/40 or Better and Gain ≥ 10 Letters of Primary Eyes by Clinical Site at 12 and 24 Months

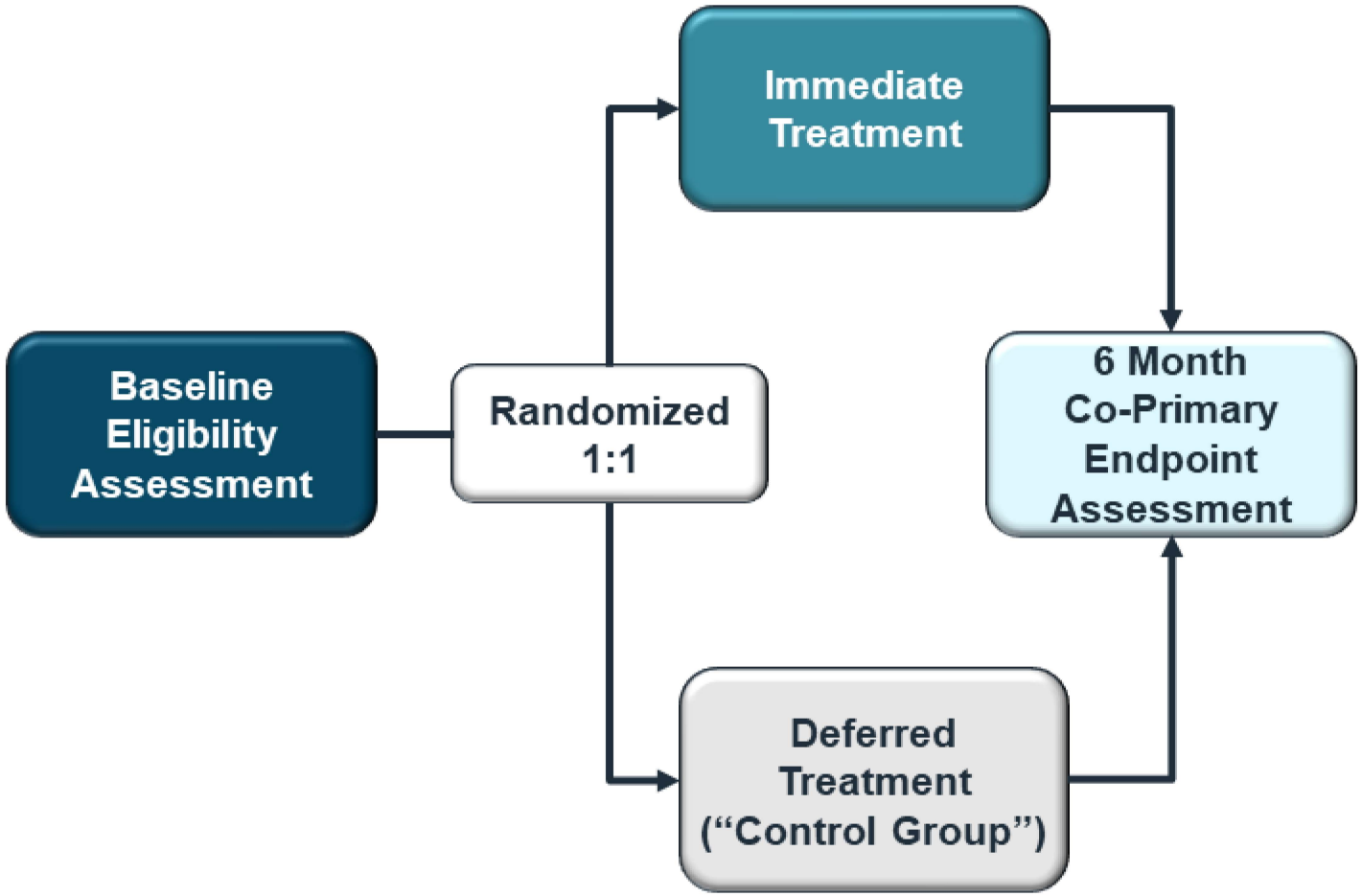
Site	Months	N	Rate and 95% CI
001	12	8	100.0% (63.1, 100)
	24	8	75.0% (34.9, 96.8)
009	12	36	97.2% (85.5, 99.9)
	24	36	100.0% (90.3, 100)
006	12	36	94.4% (81.3, 99.3)
	24	36	83.3% (67.2, 93.6)
003	12	31	93.5% (78.6, 99.2)
	24	29	96.6% (82.2, 99.9)
005	12	13	84.6% (54.6, 98.1)
	24	11	90.9% (58.7, 99.8)
012	12	15	80.0% (51.9, 95.7)
	24	15	73.3% (44.9, 92.2)
008	12	68	79.4% (67.9, 88.3)
	24	67	88.1% (77.8, 94.7)
014	12	9	77.8% (40.0, 97.2)
	24	9	66.7% (29.9, 92.5)
002	12	45	71.1% (55.7, 83.6)
	24	45	84.4% (70.5, 93.5)
013	12	32	68.8% (50.0, 83.9)
	24	30	76.7% (57.7, 90.1)
007	12	33	63.6% (45.1, 79.6)
	24	33	66.7% (48.2, 82.0)
004	12	11	63.6% (30.8, 89.1)
	24	11	63.6% (30.8, 89.1)
010	12	13	38.5% (13.9, 68.4)
	24	14	92.9% (66.1, 99.8)



DCNVA: Distance Corrected Near Visual Acuity; error bars represent 95% CI

VisAbility™ Randomized Substudy

VisAbility™ Randomized Substudy Arm Second Co-primary Endpoint



Primary Eyes 20/40 or Better
AND
Gain of ≥ 10 Letters

Second Co-Primary Effectiveness Endpoint at 6 Months Achieved (Randomized Substudy)

	Deferred Treatment (Control)[1] (N=29)	Immediate Treatment[2] (N=28)
Primary Eyes 20/40 or Better, and Gain of ≥ 10 Letters	7%	64%
95% CI[3]	0.8%, 22.8%	44.1%, 81.4%
Fisher's Exact Test p-value	<0.001	

[1] For (2) patients missing Month 6 values, since no data observed between Month 3 and Month 6, patients were excluded.
[2] No explants at or before Month 6. For (3) patients missing Month 6 values, value closest to Month 6 collected from protocol schedule visits after Month 6 up to and including Month 12 was used.
[3] Exact binomial 95% confidence interval (CI).

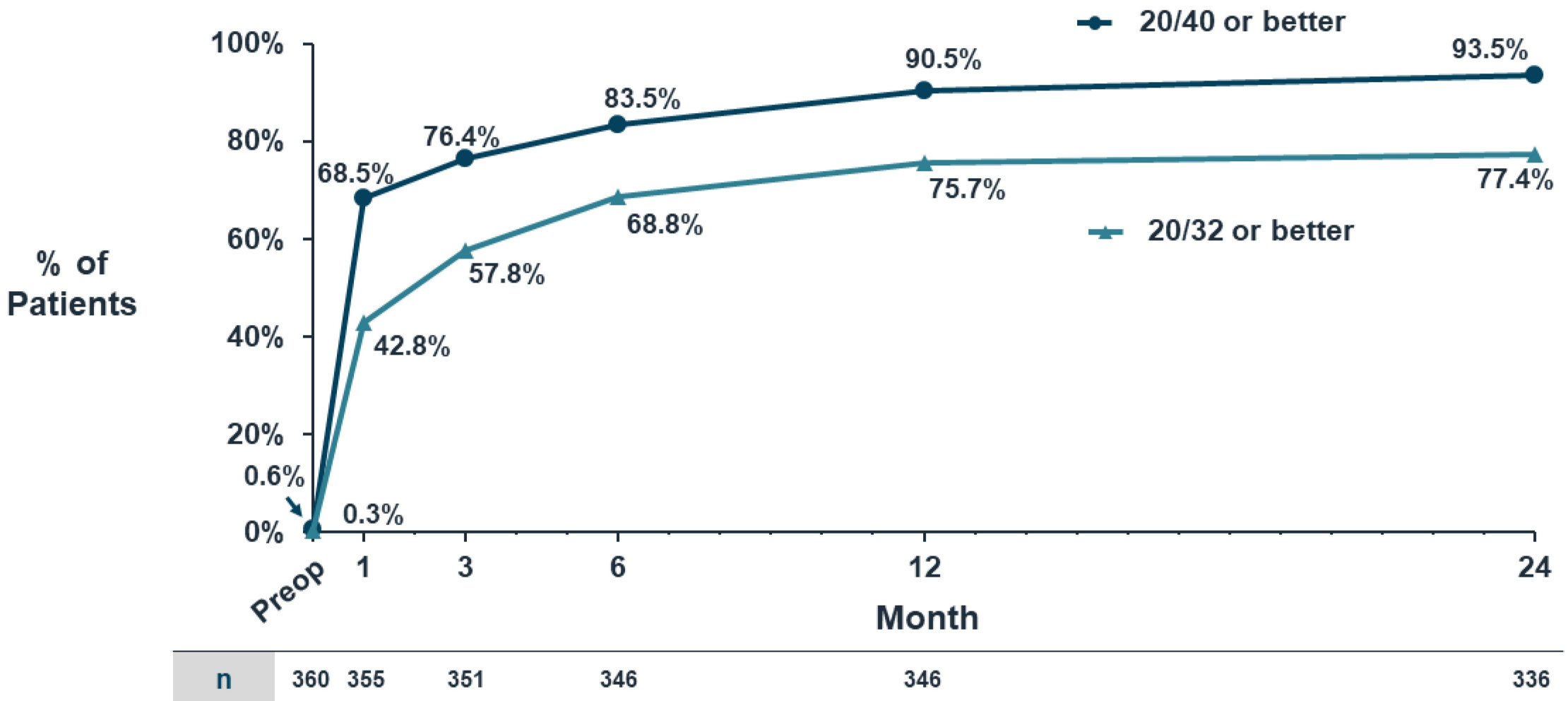
Additional Measures of Clinical Benefit

Distance Corrected Near Visual Acuity (DCNVA)

Binocular Uncorrected Near Visual Acuity (UCNVA)

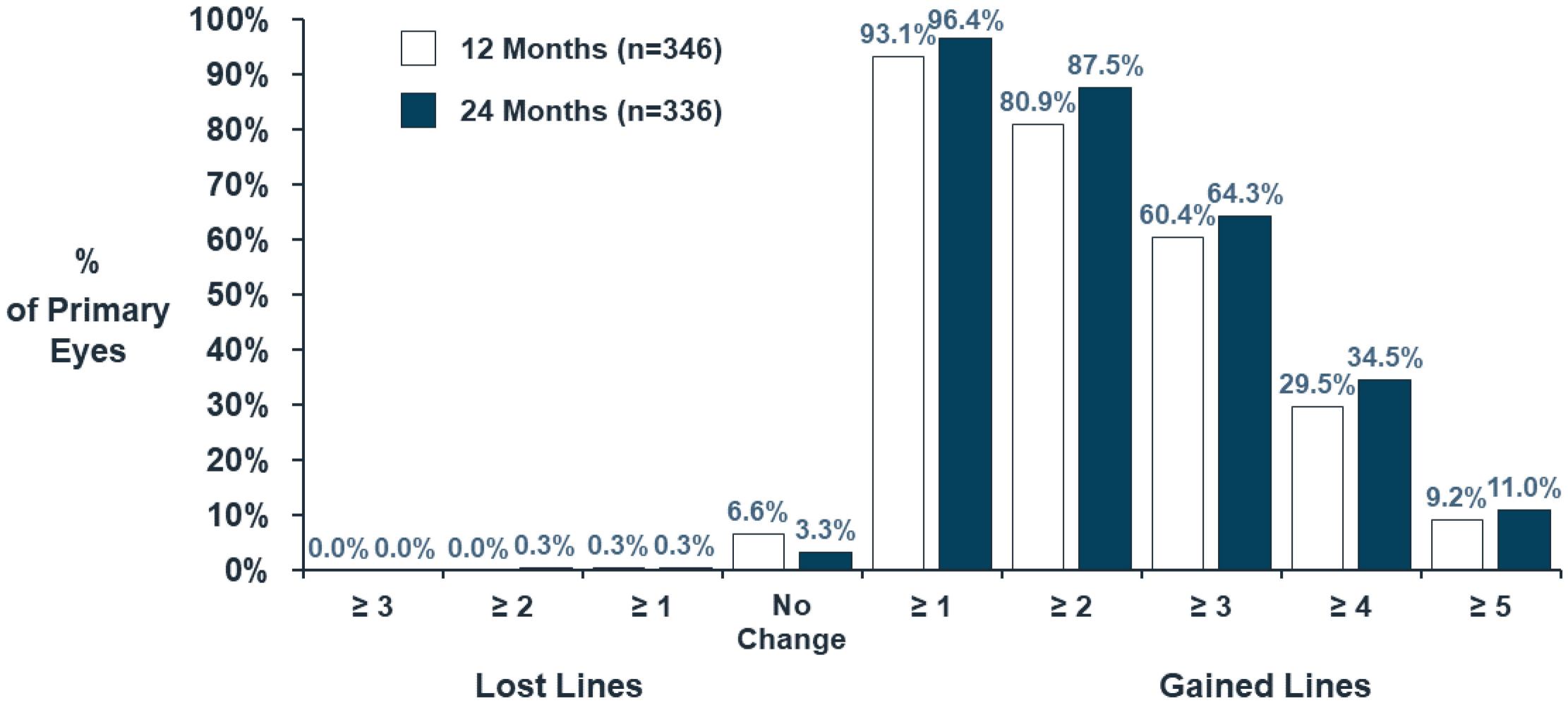
Patient Preferred Reading Distance

DCNVA for Primary Eyes



Preoperatively, <1% of study patients had DCNVA of 20/40 or better in primary eye due to 6-month observation data used as baseline analyses, per study design.
Observed data, no imputation

Clinically Meaningful Improvement in DCNVA at 12 and 24 Months



Percentage is based on the number of eyes reported with data. Observed data, no imputation

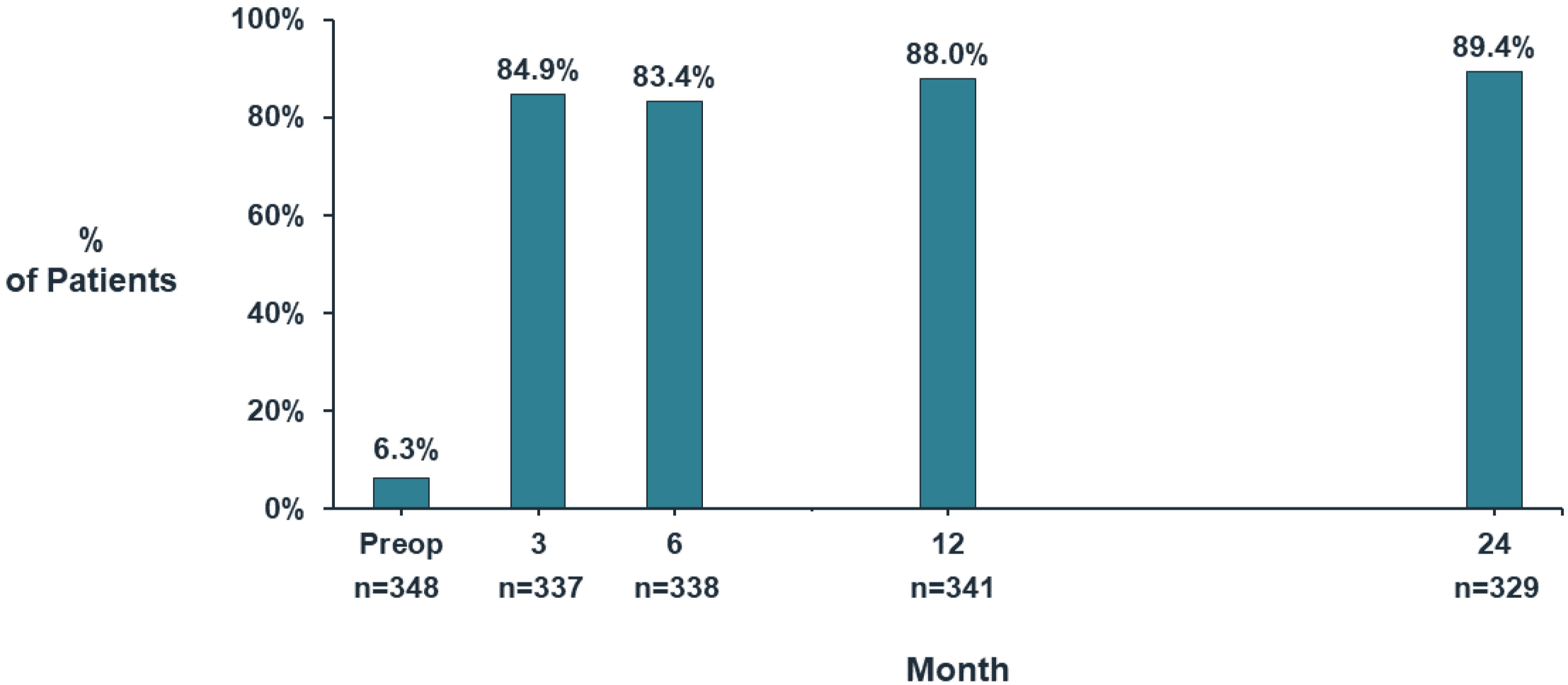
Additional Endpoints of Clinical Benefit

Distance Corrected Near Visual Acuity (DCNVA)

Binocular Uncorrected Near Visual Acuity (UCNVA)

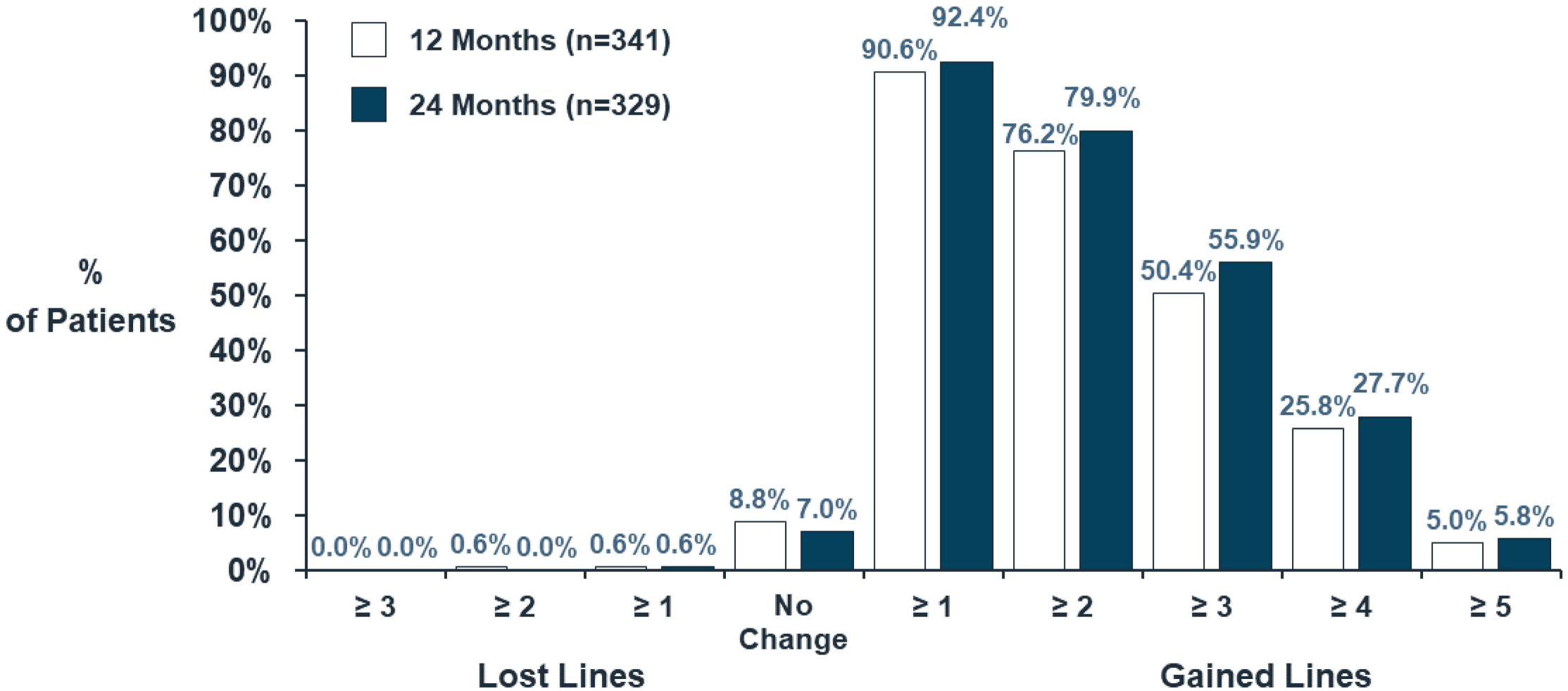
Patient Preferred Reading Distance

Real World Patient Benefit: Binocular UCNVA, 20/32 or Better



Observed data, no imputation

> 90% of Eyes Experienced ≥ 1-Line Improvement in Binocular UCNVA at 12 and 24 Months



Percentage is based on the number of eyes reported with data. Observed data, no imputation

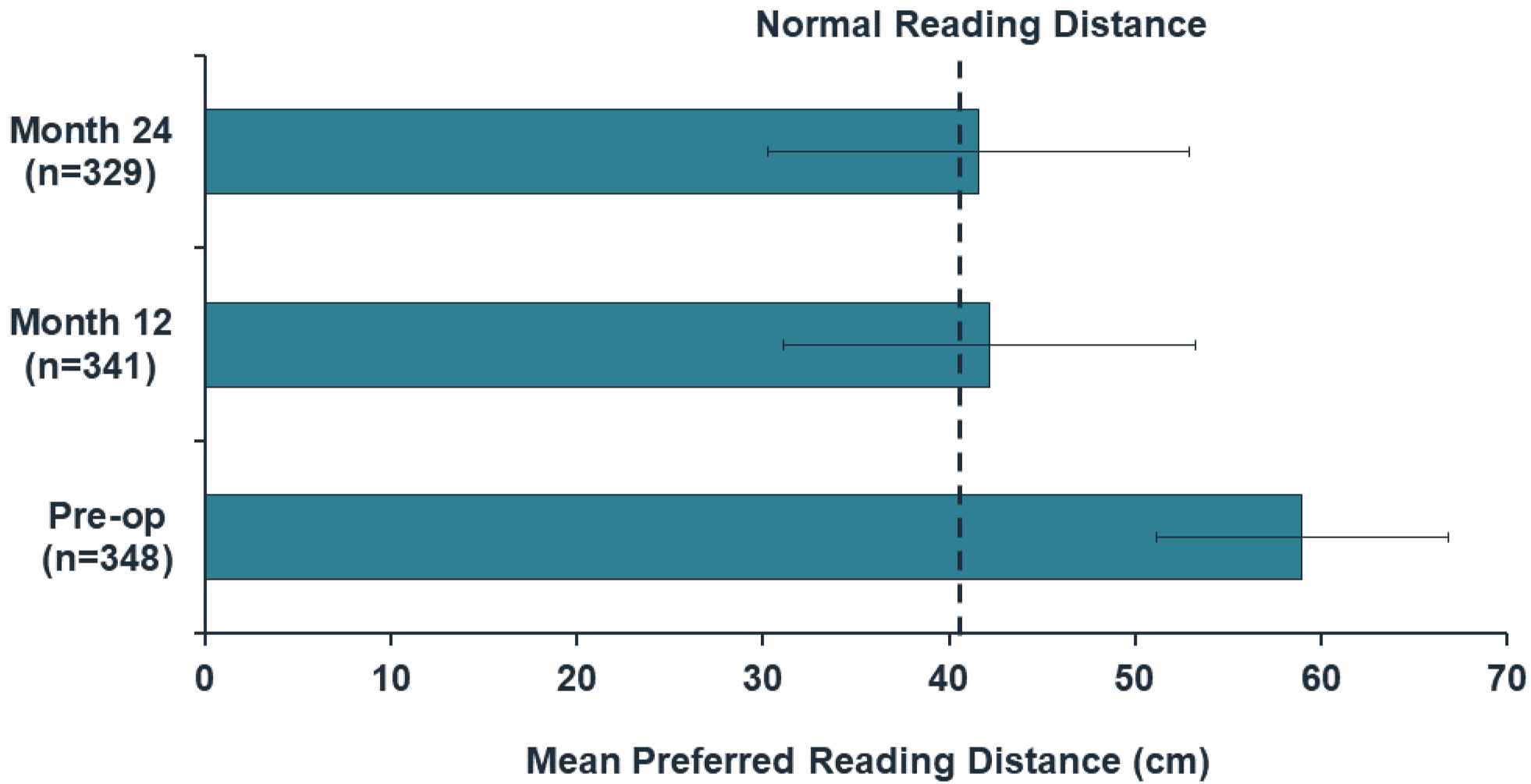
Additional Effectiveness Data

Distance Corrected Near Visual Acuity (DCNVA)

Binocular Uncorrected Near Visual Acuity (UCNVA)

Patient Preferred Reading Distance

Patient Preferred Reading Distance: Binocular DCNVA

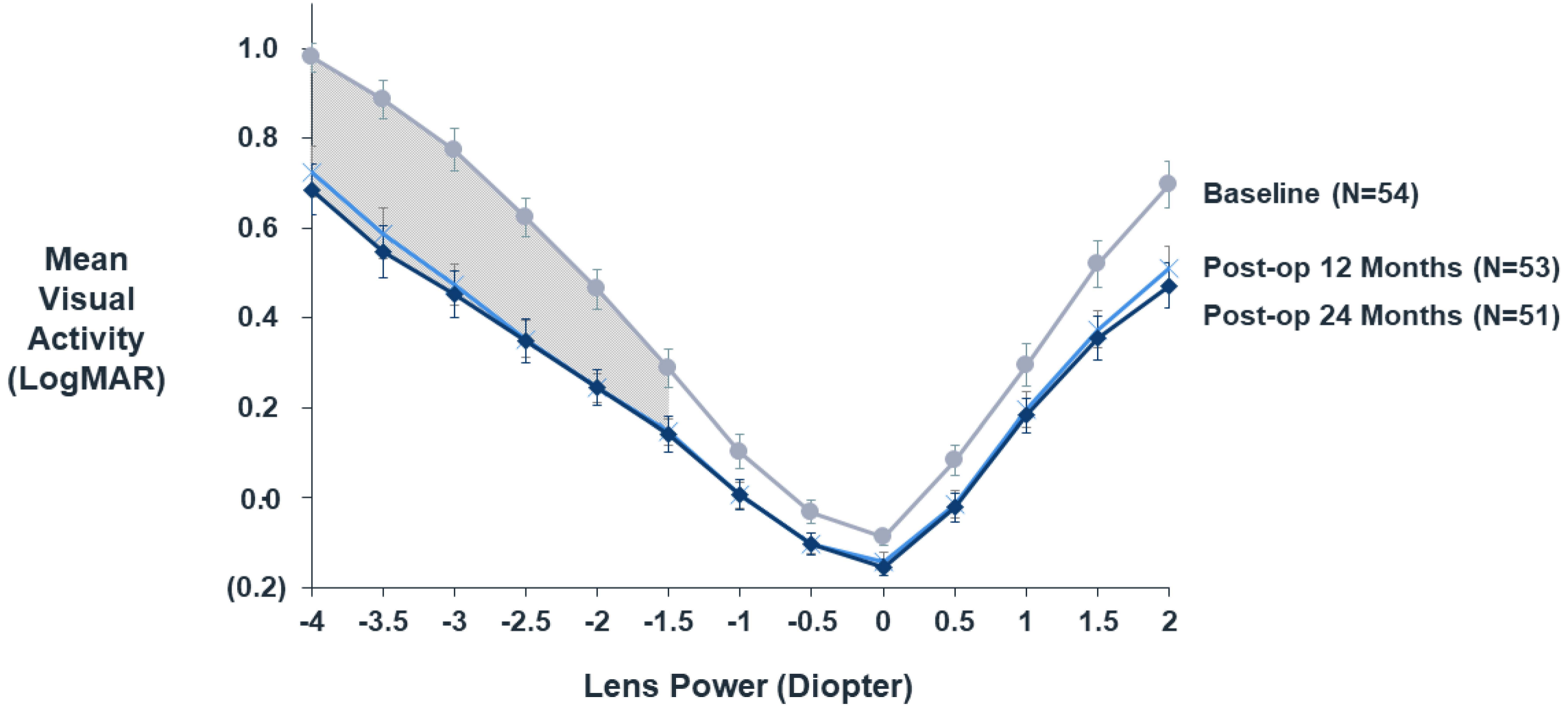


Exploratory Studies Tested in Randomized Substudy

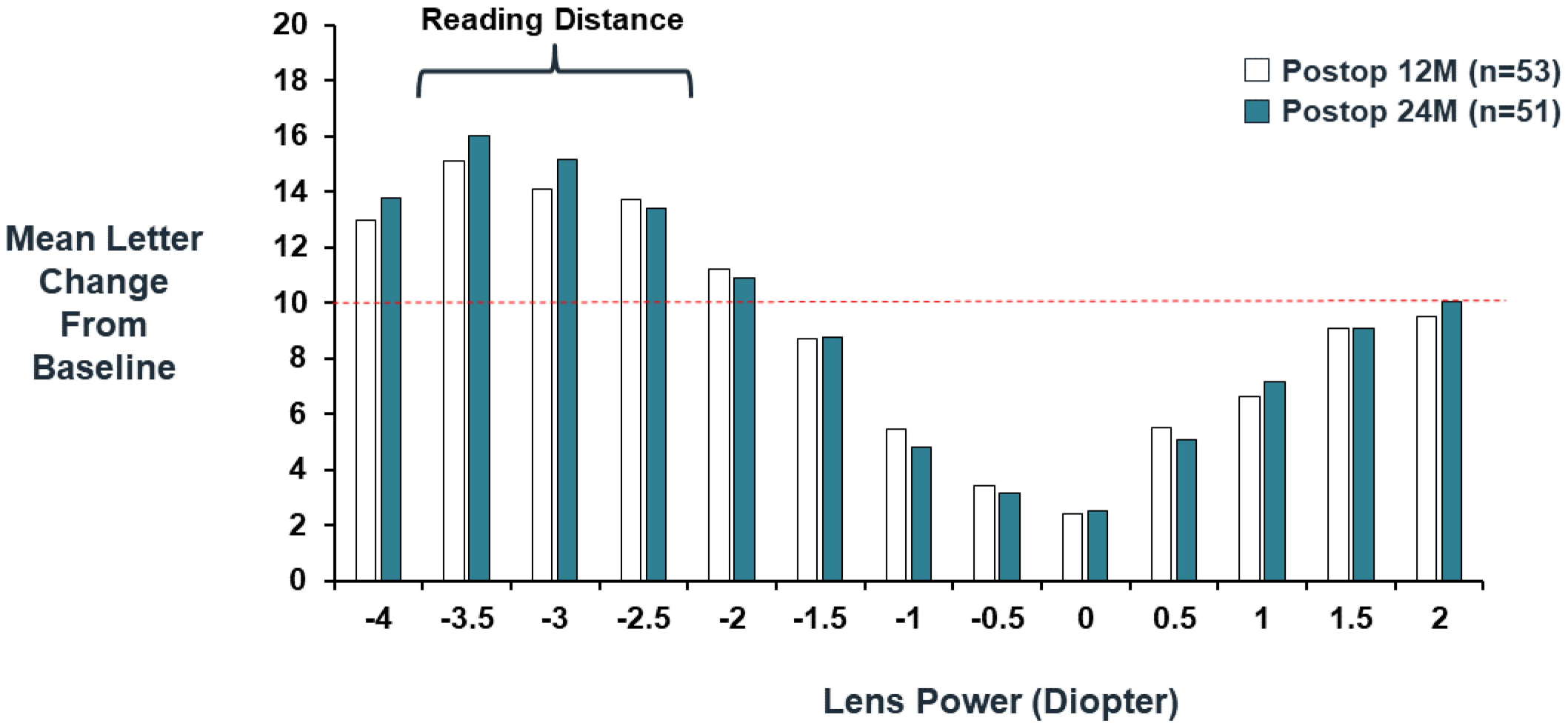
Defocus Curve

iTrace Wavefront Aberrometry

Defocus Curve: Exploratory Substudy Demonstrates Clinically Meaningful Improvement in Near Vision



Defocus Curve Demonstrates Clinically Meaningful Improvement in Near Vision



Wavefront Aberrometry Results

- No clinically significant change in lower order terms from baseline to 24 months
  - Objective measure supports stability in distance refraction over course of study
- No clinically significant mean changes in higher order terms from baseline to 24 months (often associated with glare or halos)

VisAbility™ Implant System Demonstrates Clinically Meaningful Improvements

- DCNVA 20/40 or better AND gain of ≥ 10 letters in primary eye
  - 79% at 12 months
  - 84% at 24 months
- Binocular UCNVA 20/32 or better
  - 88% at 12 months
  - 89% at 24 months
- VisAbility™ provides clinically meaningful improvement in near visual acuity in presbyopic patients

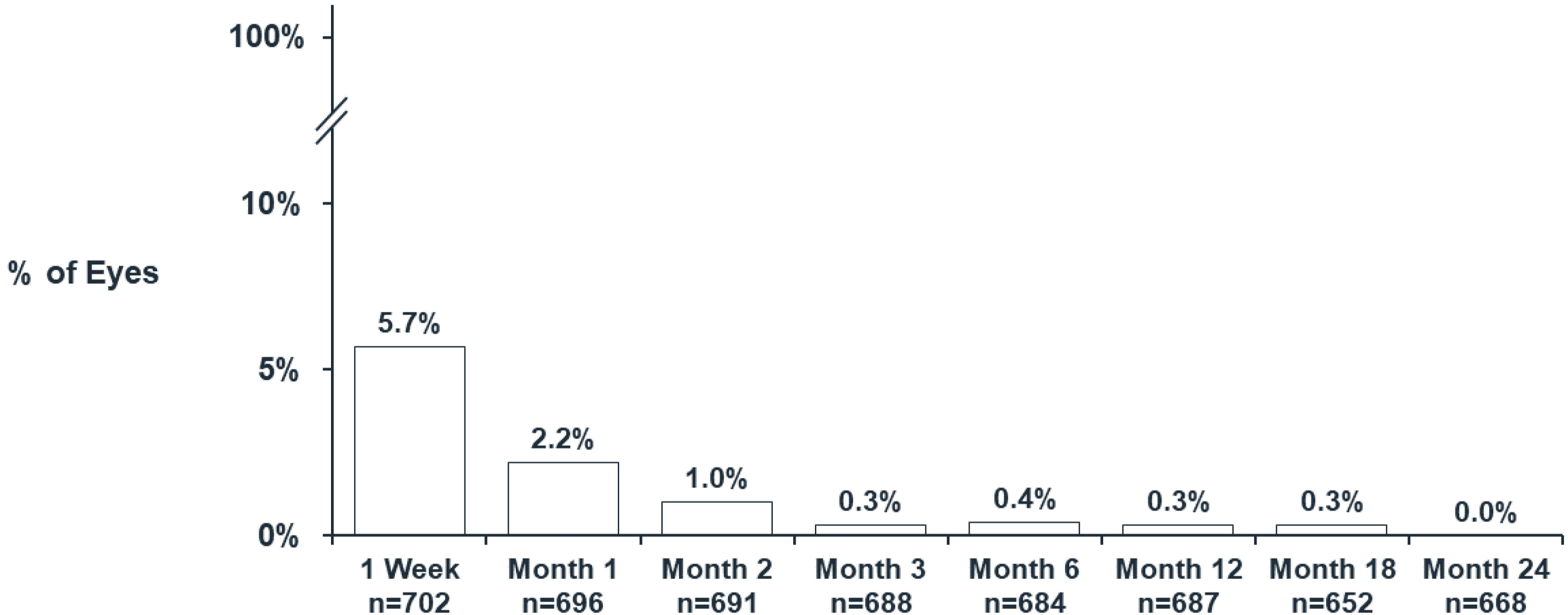
Safety of VisAbility™ Micro Insert System

Mark Packer, MD, FACS
VisAbility™ Independent Medical Monitor

VisAbility™ Safety Agenda

- Best corrected distance visual acuity (BCDVA)
- Ocular surface findings and events
- Specific ocular adverse events
  - Anterior segment ischemia (ASI)
  - Scleral perforation
  - Explantation
  - Retinal events
  - Conjunctival retraction

Loss of ≥ 2 lines BCDVA at Any Time Point



Number of eyes	40	15	7	2	3	2	2	0

Percentage based on number of eyes reported with data.

≥ 2 Line Decrease in BCDVA at 3 Months or Later Post Procedure

- 5 eyes (4 patients): decreased BCDVA secondary to ocular surface findings - resolved following treatment
- 1 eye*: corneal abrasion secondary to metal foreign body - treated w/ topical antibiotic
- 1 eye: hypertensive optic neuropathy (systemic HTN)
- 2 eyes (2 patients): cataract - resolved after cataract surgery
- 1 eye: decrease BCDVA and no associated etiology - 20/12.5 at baseline to 20/20 at 6 months, returning to 20/16 at 12 months

*Unscheduled visit after 3 months

VisAbility™ Safety Agenda

- Best Corrected Distance Visual Acuity (BCDVA)
- Ocular surface findings and events
- Review of specific ocular adverse events
  - Anterior Segment Ischemia (ASI)
  - Scleral perforation
  - Explantation
  - Retinal events
  - Conjunctival retraction

Ocular Surface Findings

Cornea Superficial Punctate Keratitis	Preop N=708	Month 12 N=687	Month 24 N=668
None	97%	90%	92%
Trace	3%	8%	6%
Mild	<1%	2%	2%
Moderate	0%	<1%	0%
Marked/Severe	0%	0%	0%
Conjunctival Injection			
None	81%	57%	70%
Trace	17%	33%	24%
Mild	2%	9%	6%
Moderate	0%	<1%	0%
Marked/Severe	0%	0%	0%

Slit Lamp – Lid Findings

Blepharitis	Preop N=708	Month 12 N=687	Month 24 N=668
None	83%	88%	92%
Trace	15%	10%	8%
Mild	2%	3%	1%
Moderate	0%	0%	<1%
Marked/Severe	0%	0%	0%
Not Reported	0%	0%	0%
Meibomian Gland Dysfunction			
None	70%	64%	69%
Trace	26%	30%	28%
Mild	4%	6%	2%
Moderate	0%	<1%	<1%
Marked/Severe	0%	0%	0%
Not Reported	0%	0%	0%

Ocular Surface Adverse Events

Events	Through 12 Months		Cumulative Through 24 Months	
	% of Patients (N=360)	% of Eyes (N=708)	% of Patients (N=360)	% of Eyes (N=708)
Any ocular adverse events	31%	22%	47%	37%
Conjunctiva / cornea	15%	12%	25%	20%
Dry eye requiring prescription medication after 6 months	7%	7%	12%	12%
Conjunctival injection - moderate or severe at ≥ 3 months	4%	3%	6%	5%
Eyelids	3%	3%	9%	9%
Onset of or worsening to severe of clinically significant lid margin disease after 3 months	3%	3%	9%	9%

VisAbility™ Safety Agenda

- Best Corrected Distance Visual Acuity (BCDVA)
- Ocular surface findings and events
- Review of specific ocular adverse events
  - Anterior Segment Ischemia (ASI)
  - Scleral perforations
  - Explantation
  - Retinal events
  - Conjunctival retraction

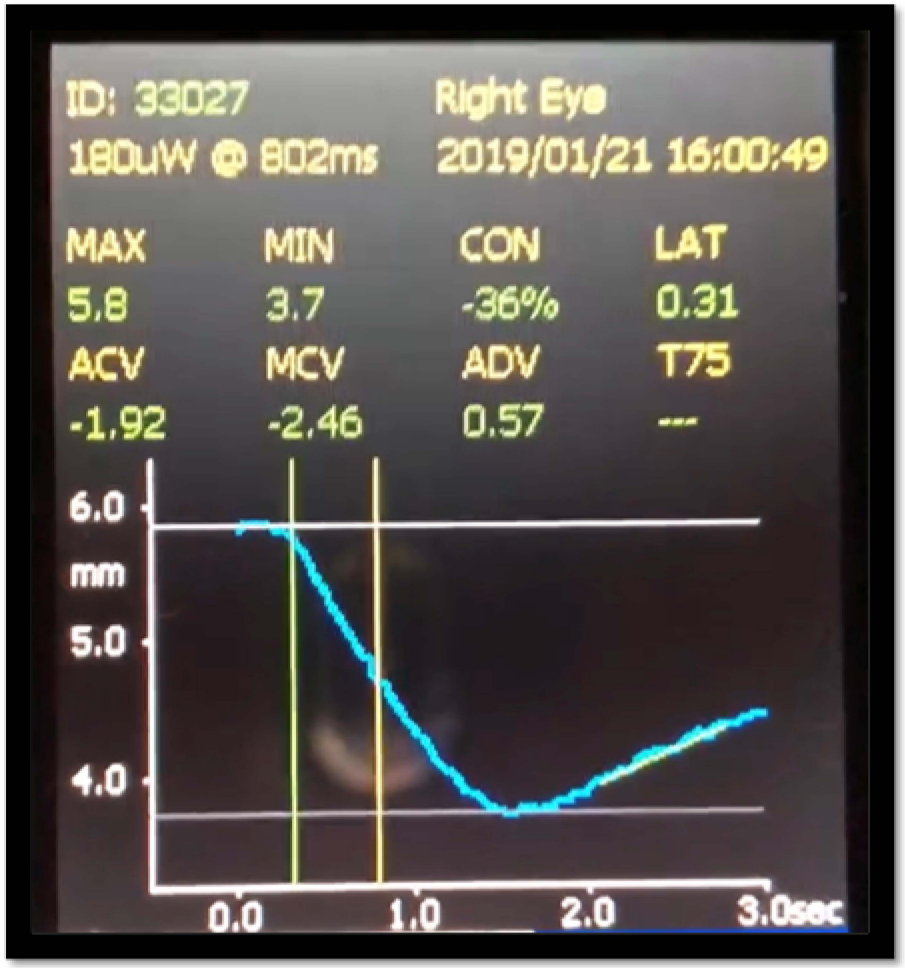
Anterior Segment Ischemia (ASI): an Acute, Self-Limited Event

- Only occurs during immediate postoperative period
- Resolves spontaneously over time
- Severe (Grade 4) ASI is "followed by a period of gradual clinical improvement, with return of preoperative acuity, usually within nine weeks."[1]
- Literature (1960): 1 case of phthisis reported
  - 65-year-old male, retinal detachment, 4 muscle disinsertion, scleral buckle, hyphema, IOP 60 mmHg[2]
- Common sequela of ASI is pupillary abnormality

1. Saunders RA, et. al. 1994. 2. Girard LJ, et. al. 1960.

ASI: Systematic Evaluation and Reporting

- Earliest reliable clinical sign of ASI is decreased pupillary response
- Pupil response systematically evaluated in VisAbility™ Study
- Iris angiography (Grade 1) variable and not predictive of clinical course
- Findings and adverse events associated with ASI systematically collected and evaluated



ASI Outcomes: Acute, Benign, Self-limited Events That Resolved Completely

5 Patients	Eyes N	Eyes %	Disposition	BCDVA
Total	**5**	**0.7%**		
Pupillary abnormality	1	0.1%	Recovered by Month 24 Sequela - 1 to 2 clock hours of stable iris transillumination	20/16 (24 mo)
Grade 2 ASI	2	0.3%	Explanted, recovered fully without sequelae by Day 7	20/20 (3 mo) 20/16 (3 mo)
Grade 3 ASI	1	0.1%	Recovered fully without sequelae by Month 6	20/12.5 (24 mo)
Grade 4 ASI	1	0.1%	Recovered fully without sequelae by Month 6	20/12.5 (24 mo)

Grade 2: decreased pupil reactivity
Grade 3: decreased pupil reactivity + anterior chamber reaction
Grade 4: decreased pupil reactivity + anterior chamber reaction + corneal edema

Mitigation of ASI Risk

- Mandatory surgeon training and certification
- Postoperative pupillometry and explantation within 6 hours of eyes not meeting threshold criteria
  - Percent change ≥ 25% constriction in operative eye at two distinct time points ≥ 5 minutes apart
  - Demonstrated immediate effective reversal of decreased pupillary response
- Controlled Access following approval

VisAbility™ Safety Agenda

- Best Corrected Distance Visual Acuity (BCDVA)
- Ocular surface findings and events
- Review of specific ocular adverse events
  - Anterior Segment Ischemia (ASI)
  - Scleral perforations
  - Explantation
  - Retinal events
  - Conjunctival retraction

Intraoperative Scleral Perforation 8 Patients, 8 Eyes (~1% of Implanted Eyes)

- All perforations resolved
- Micro-perforations
  - Vitreous presentation as evidenced by the presence of pigment
  - No vitrectomies were required
- No cases of choroidal hemorrhage
- No cases resulted in endophthalmitis
  - Micro Insert tamponade
  - Conjunctival covering

Safety and Effectiveness Results for Intraoperative Scleral Perforation Cases

	Sequelae	DCNVA Baseline	DCNVA 24 months	BCDVA 24 months
1	Inadvertent bleb, low IOP, cataract removal; Multifocal IOL at 6 months	20/50	20/25*	20/20*
2	ST quadrant not implanted, Day 1 A/C cell/flare & hypotony/IOP 5mmHg; Posterior vitreous detachment, retinal hemorrhage; Resolved within one month	20/63	20/63	20/12.5
3	Residual inflammation, posterior iris synechiae post-op, Day 6 and 7; Resolved Day 11	20/50	20/20	20/16
4	None	20/80	20/25	20/16
5	None	20/63	20/40	20/16
6	None	20/63	20/20	20/16
7	None	20/63	20/32	20/12.5
8	None	20/50	20/25	20/12.5

*VA with Multifocal IOL—not included in primary effectiveness analysis; DCNVA at 18 months (no 24 months DCNVA)

Newly Proposed Mitigation of Scleral Perforation Risk

- Mandatory surgeon training and certification
  - Enhanced antibiotic prophylaxis
  - Retinal consultation
- Controlled access following approval

Newly proposed training program has not been submitted to FDA

VisAbility™ Safety Agenda

- Best Corrected Distance Visual Acuity (BCDVA)
- Ocular surface findings and events
- Review of specific ocular adverse events
  - Anterior Segment Ischemia (ASI)
  - Scleral perforations
  - Explantation
  - Retinal events
  - Conjunctival retraction

Low Rate of Explants

- 13 eyes, 8 patients through 24 months
  - 1.8% of implanted eyes
- Post explant BCDVA 20/20 or better in all eyes
- No persistent complications or sequelae of explantation
- Rate of explantation can be reduced by patient selection and patient education

Explantation Through 5-Years

	Devices Explants (Eyes)	Patients
Year 1	5	4
Year 2	8	4
Year 3	14	7
Year 4	2	1
Year 5	2	1
Total	31	17

Primary Reason for Explant Through 24 Months

Reason for Explant	Patients (n=8)	Eyes (n=13)
Inadequate pupil response (day of surgery)	2	2
Foreign body sensation	2	4
Redness / cosmesis	2	3
Perceived lack of effect	1	2
Residual refractive error	1	2

VisAbility™ Safety Agenda

- Best Corrected Distance Visual Acuity (BCDVA)
- Ocular surface findings and events
- Review of specific ocular adverse events
  - Anterior Segment Ischemia (ASI)
  - Scleral perforations
  - Explantation
  - Retinal events
  - Conjunctival retraction

Low Rate of Retinal Holes / Tears (2 Eyes – 0.3% of Implanted Eyes)

- Neither case believed to be related to device or procedure
- Case 1: retinal tear associated with posterior vitreous detachment
  - 8 months post-op
- Case 2: asymptomatic round hole
  - One-week post-op
  - Location distant from implant site
- Both eyes treated, stabilized and maintained BCDVA 20/20 or better at 12 and 24 months

VisAbility™ Safety Agenda

- Best Corrected Distance Visual Acuity (BCDVA)
- Ocular surface findings and events
- Review of specific ocular adverse events
  - Anterior Segment Ischemia (ASI)
  - Scleral perforations
  - Explantation
  - Retinal events
  - Conjunctival retraction

Conjunctival Retraction Requiring Secondary Surgical Intervention Occurred at Low Rate (~2% of Implanted Eyes)

- Re-approximation of retracted conjunctiva
  - Risk of infection mitigated by concomitant prophylactic antibiotics
- N=15 eyes, 15 patients with re-approximation due to retraction (2.1% of implanted eyes)
  - 5 eyes with exposure of one VisAbility™ Micro Insert segment
  - 10 eyes with no exposure
- All cases resolved within 10 days without sequelae

Conjunctival Retraction Related to Surgical Technique

- Appropriate suturing at limbus prevents retraction
- Once conjunctiva has healed, retraction no longer a risk
- Mitigation will include surgeon training, certification, and controlled access

Summary of Ocular Adverse Events

Anterior segment ischemia	▪ Only occurs immediate post-operative ▪ Acute, self-limited; all events of ASI resolved
Scleral perforation	▪ Mitigated by surgical training, enhanced antibiotic prophylaxis and retinal consultation
Explantation	▪ Uncomplicated, without sequalae
Retinal events	▪ Unrelated to device or procedure
Conjunctival retraction	▪ Solely early post-operative event, easily corrected

Safety Conclusions: Favorable Safety Profile

- Procedure performed outside visual axis, maintaining the integrity of the cornea and lens, thus preserving distance vision
- No persistent loss of ≥ 2 lines of BCDVA
- Common ocular adverse events were effectively managed
- Low rate of surgical complications
  - Events can be mitigated through surgeon training and education

VisAbility™ Micro Insert System: Mandatory Training and Certification

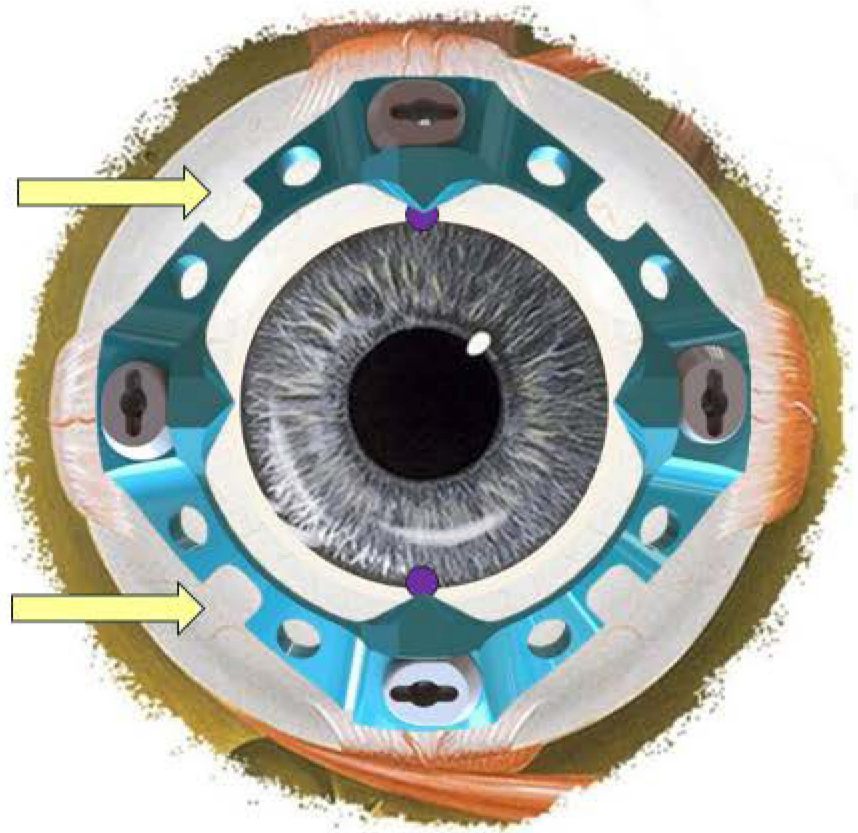
David Schanzlin, MD
Chief Medical Officer, Refocus Group, Inc.
Professor of Ophthalmology (Emeritus),
University of California, San Diego

Mandatory Post-Approval Certification Program

	Clinical Study Investigators	Post-Market Surgeons
Formal didactic with testing		
Best practices from clinical trial experience		✓
Pearls to avoid complications		✓
Wet lab training		
Demonstration of proficiency	✓	✓
Review surgery & proctoring		
Minimum 5 eyes for proctoring	✓	✓
Post-operative support & monitoring		
Clinical specialist monitoring		✓
Surgeon trainer “sign off” & mentorship		✓
Reporting requirements		✓
3rd party registry		✓

Analysis of and Training to Avoid ASI

- **Avoiding ASI**
  - Proper placement of VisAbility™ Micro Insert
- **Training points**
  - Identify superior and inferior rectus muscle
  - Properly mark the limbus
  - Align docking station correctly
  - Position notch between rectus muscles
  - Postoperative pupillometry



Training to Avoid Perforations

- Keep feeder tube along roof of tunnel
  - Don’t allow leading edge to be directed posteriorly
- Should exit tunnel at 4mm mark
- Be mindful of Main Body Segment orientation as it enters tunnel
- Back out and reload when necessary
- Topical antibiotic and dilated peripheral retinal exam, if necessary

Training to Avoid Conjunctival Retraction and Explants

- Conjunctival retraction
  - Proper suture technique
- Explants
  - Majority due to redness or irritation secondary to partial interpalpebral placement
  - Avoid patients with lagophthalmos, lateral lid laxity, or untreated ocular surface disease

VisAbility™ Micro Insert System: Controlled Access

Martin Kaufman
Chief Regulatory Officer
Refocus Group, Inc.

VisAbility™ Micro Insert System Controlled Access

- Access granted to ophthalmic surgeons with proven track record of demonstrating excellence through certification program
  - 3 to 6 months post-approval access limited to VIS-2014 Study surgeons
  - 6 to 9 months post-approval, access limited to 3 select cities around three centers of excellence

5-Year Continuation Study and Post-Approval Study

- Ongoing 5-year continuation study
  - Follow existing VIS-2014 pivotal study patients
  - Approved by FDA (November 2018)
- Post-Approval Study
  - Prospective, 1-year, multi-center, single arm
  - Up to 150 subjects
  - Submitted to FDA for review

3rd Party Registry

- Mandatory for all patients
- Prospectively collect data on both safety and effectiveness
- Provide practice support to identify trends and provide corrective feedback
- Participation in registry required to maintain certification

FDA has not reviewed the 3rd party registry

Post-Marketing Data Thresholds

- Monitoring of clinical performance through post-approval registry to support continuous improvement
- VIS-2014 Pivotal Study results will establish initial performance thresholds[1]
- "Real-world" device performance will be used to refine these thresholds[1]
- FDA adverse event reporting requirements will be followed

1. These data have not been submitted to FDA

VisAbility™ Micro Insert System: Benefit-Risk Analysis

Mark Packer, MD, FACS

VisAbility™ Independent Medical Monitor

Near Activity Visual Questionnaire (NAVQ) for Assessment of Presbyopia

- NAVQ: best validated questionnaire available
- NAVQ administered preop, 6, 12, 18 and 24 months
- Patients rated level of difficulty performing 10 near vision tasks
- 4-point response scale of no difficulty to extreme difficulty

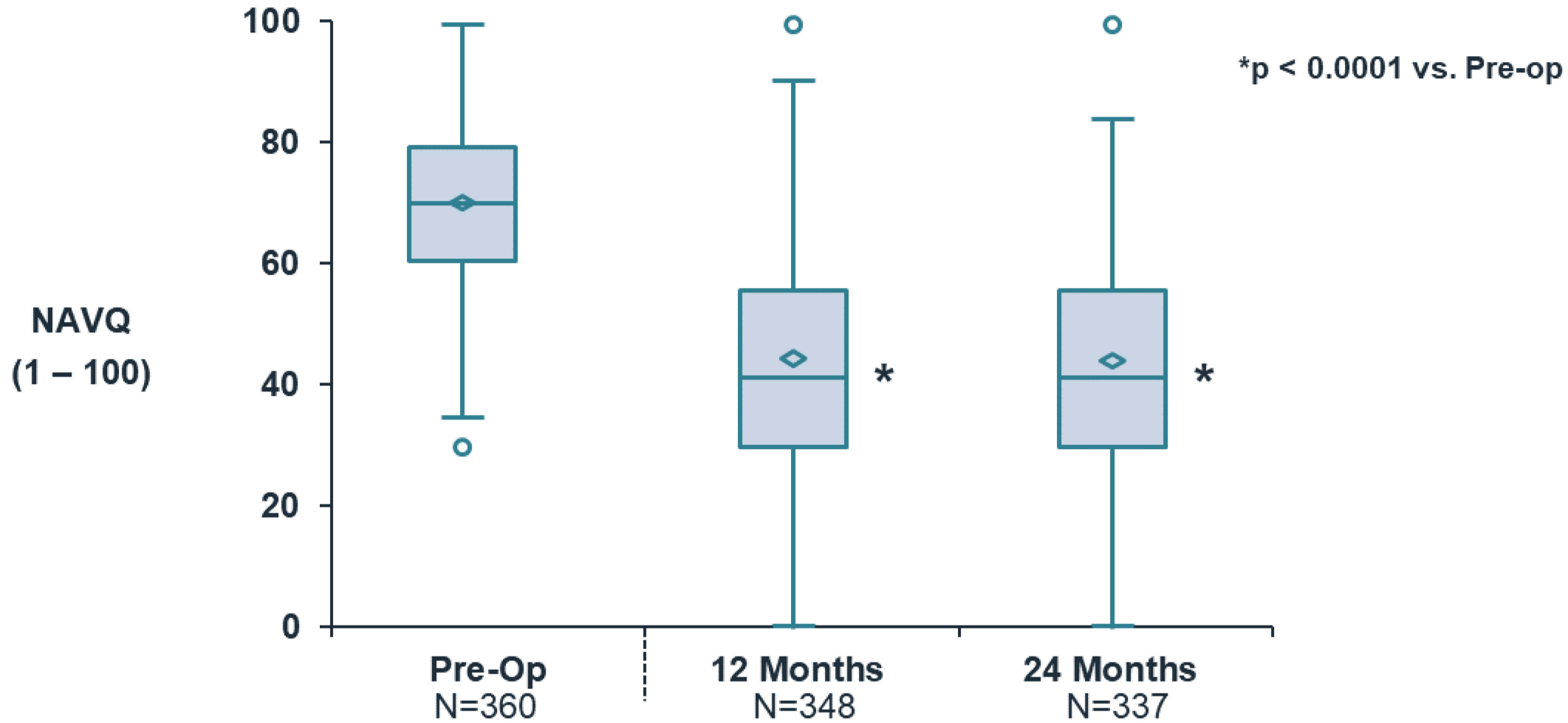
Tasks Assessed

1. Reading small print, such as newspaper articles, items on a menu, telephone directories
2. Reading labels/instructions/ingredients/prices, such as on medicine bottles, food packaging
3. Reading your post/mail, such as electric bills, greeting cards, bank statements, letters from friends and family
4. Writing and reading own writing, such as greeting cards, notes, letters, filling in forms, checks, signing one's name
5. Seeing display and keyboard on computer or calculator
6. Seeing display and keyboard on mobile or fixed telephone
7. Seeing objects close and engaging in hobbies, such as playing card games, gardening, seeing photographs
8. Seeing objects close in poor or dim light
9. Maintaining focus for prolonged near work
10. Conducting near work without spectacles

NAVQ #10. Conducting Near Work Without Spectacles

	Pre-Op (N=360)		12 Months (N=348)		24 Months (N=337)	
	n	%	n	%	N	%
No difficulty	3	1%	50	14%	60	18%
A little difficulty	20	6%	130	37%	121	36%
Moderate difficulty	88	24%	105	30%	84	25%
Extreme difficulty	247	69%	63	18%	71	21%
Missing	2	1%	0	- %	1	<1%

NAVQ Scores: Statistically Significant Reduction in Difficulty with Near Vision



How satisfied are you with your near vision?

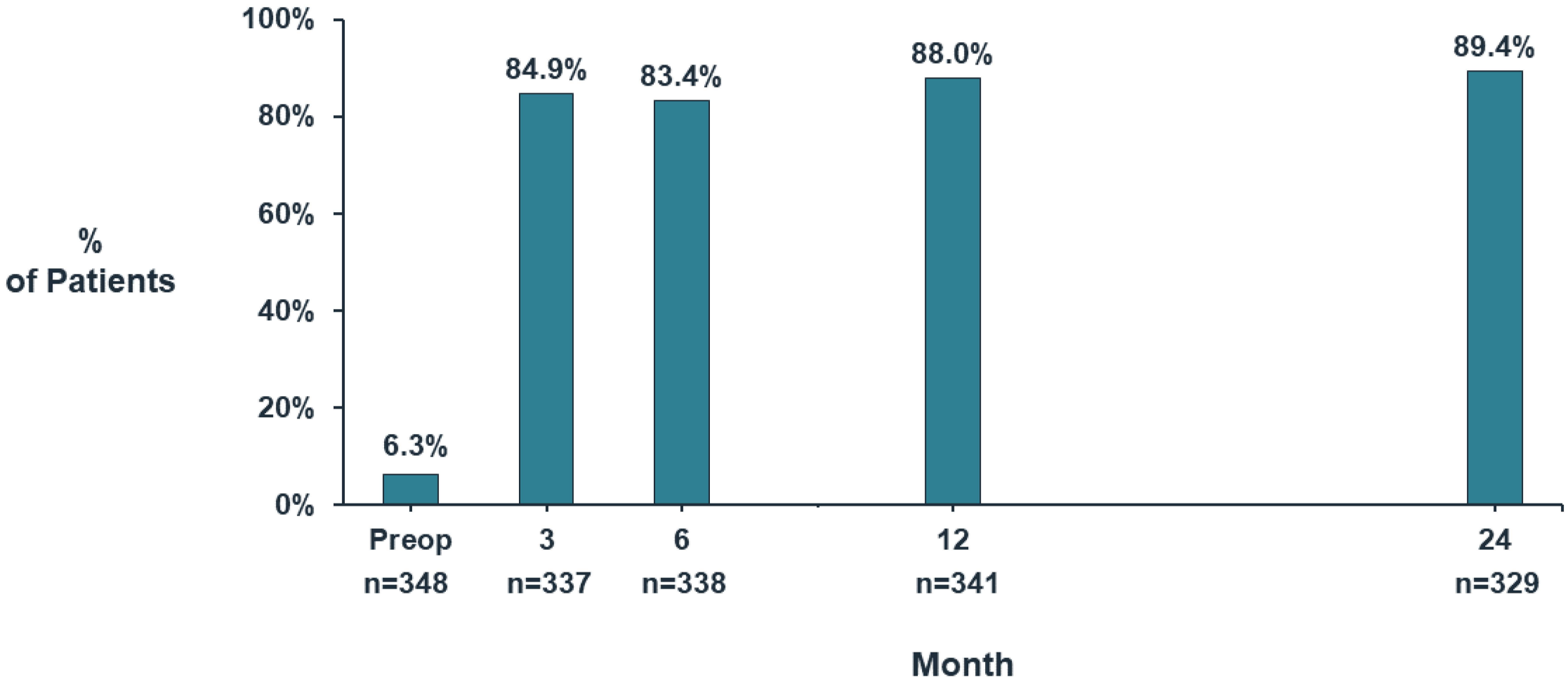
	Pre-Op (N=360)		12 Months (N=348)		24 Months (N=337)	
	n	%	n	%	N	%
Completely Satisfied	1	<1%	17	5%	28	8%
Very Satisfied	0	-	88	25%	89	26%
Moderately Satisfied	6	2%	118	34%	106	31%
A Little Satisfied	53	15%	71	20%	65	19%
Completely Unsatisfied	299	83%	53	15%	49	15%
Missing	1	<1%	1	<1%	0	-

Summary of Evidence for Favorable Benefit-Risk Profile

Safety Overview

- Adverse events of clinical interest (anterior segment ischemia, scleral perforations, conjunctival retraction, explantation and retinal events)
  - Incidence in pivotal trial very low
  - No lasting symptoms
  - Occurrence can be mitigated, and potential sequelae managed
- Speculative sequelae (endophthalmitis, phthisis bulbi) not observed; evidence in literature suggests vanishingly low rates

Real World Patient Benefit: Binocular UCNVA 20/32 or Better



Near Vision Requirements

Acuity	Print Size Comparison	Example
20/20	3-point font	medicine bottle labels
20/30	5-point font	small print paperback; footnotes
20/40	6-point font	want ads; telephone directory

"Near Vision Test Chart" by the Low Vision Clinic, N.C. Memorial Hospital Dept. of Ophthalmology, University of North Carolina School of Medicine, Chapel Hill, NC.

VisAbility™ Micro Insert System Fills an Unmet Need for a Surgical Option to Treat Presbyopia

	Performed Outside Visual Axis	Reversible Procedure	Absence of Visual Disturbances	Preserves Distance Vision
Corneal inlays	✗	✗	✗	✗
Lens exchange (off-label)	✗	✗	✗	✓
Monovision LASIK	✗	✗	✗	✗

VisAbility™ Micro Insert System:

- Performed outside the visual axis
- Segments can be removed
- Lens and cornea remain intact
- Preserves distance vision

Safety and Effectiveness Outcomes Support Favorable Benefit Risk Assessment

- Effectiveness data: compelling and robust results
- Safety outcomes:
  - Ocular adverse events were effectively managed
  - Mitigations designed to further enhance safety profile[1]
  - Refocus committed to thoughtful and conservative commercialization strategy

1. These data have not been submitted to FDA

VisAbility™ Micro Insert System

For the improvement of near vision without compromise to distance vision in patients with presbyopia

November 9, 2020

Refocus Group, Inc.

Ophthalmic Devices Panel

Back-up Slides Shown On Screen

No Difference in Effectiveness by Age

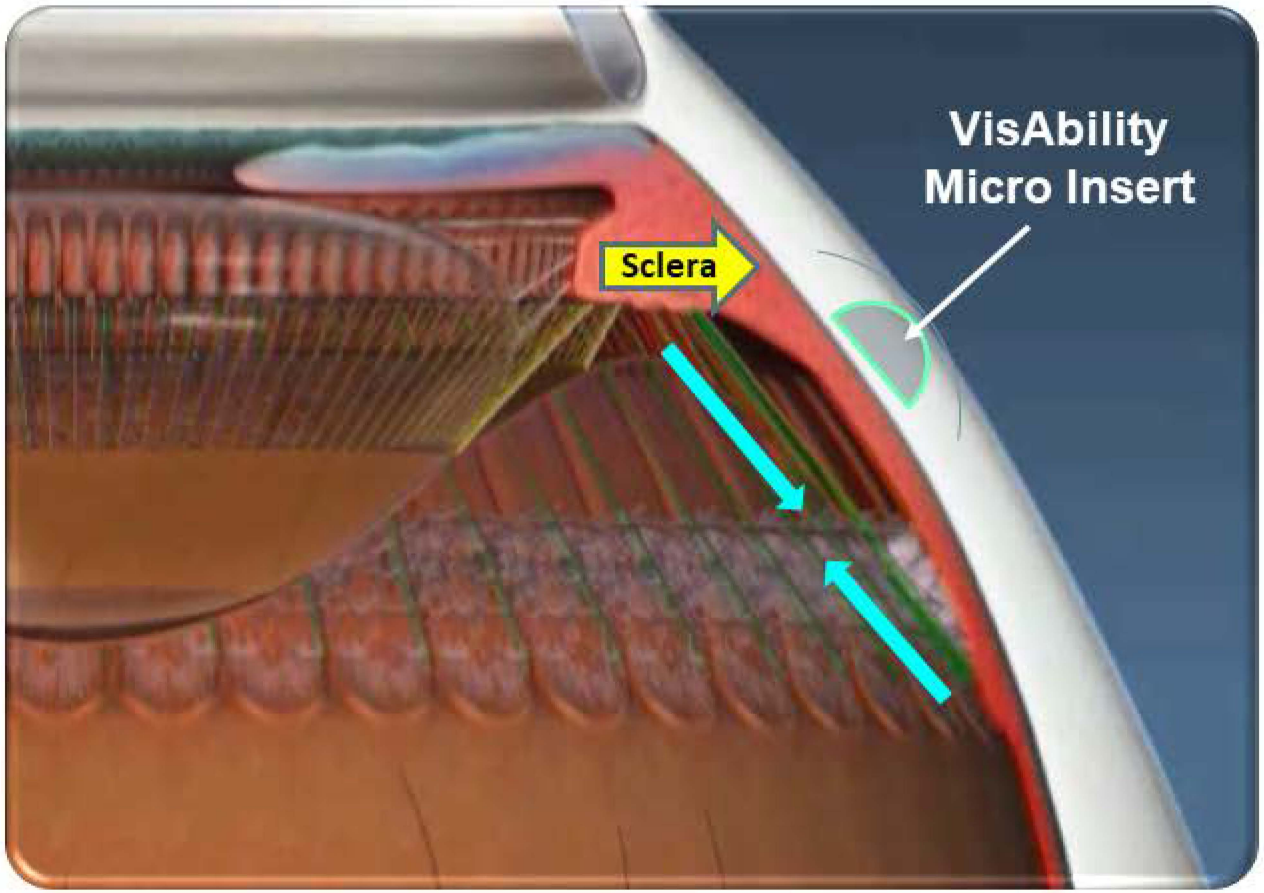
- First Co-Primary Effectiveness Endpoint at 24 Months by Age
  Intent-to-Treat Population

Age	DCNVA 20/40 or Better and Gain of ≥ 10 Letters		
	N	n (%)	95% CI
45 - 49	99	88 (88.9%)	81.0%, 94.3%
50 - 54	171	141 (82.5%)	75.9%, 87.8%
55 - 60	74	60 (81.1%)	70.3%, 89.3%
p-value			0.281
Average over Age		84.1%	80.1%, 88.2%

VisAbility Micro Insert Mechanism of Action Hypothesis

Micro Insert alters local anatomy

- Gently tents out the sclera
  - Expands extralenticular space & tightens zonules
  - Relaxes the tension on the posterior vitreous zonule
- Restores ciliary muscle movement



Pupillometry – Maximum Pupil Size Safety Cohort

Maximum Pupil Size (mm)	Preop (N=708)	Month 12 (N=687)	Month 24 (N=668)
n (Reported)	708	683	664
Mean (SD)	5.50 (0.77)	5.38 (0.78)	5.28 (0.79)
Median	5.6	5.4	5.3
Min, Max	2.9, 7.5	2.9, 8.0	2.6, 7.5

Axial Length and Change in Axial Length from Baseline Safety Cohort

	Preop (N=708)	Month 12 (N=687)	Month 24 (N=668)
Axial Length (mm)			
n (Reported)	708	683	666
Mean (SD)	23.548 (0.733)	23.530 (0.727)	23.535 (0.731)
Median	23.56	23.54	23.55
Min, Max	21.60, 25.76	21.55, 25.77	21.55, 25.77
Not Reported	0	4	2
Change in Axial Length (mm)			
n (Reported)		683	666
Mean (SD)		-0.006 (0.124)	-0.002 (0.123)
95% CI[1]		(-0.015, 0.004)	(-0.011, 0.008)
Median		0.00	0.00
Min, Max		-1.43, 2.58	-0.56, 2.69
Not Reported		4	2

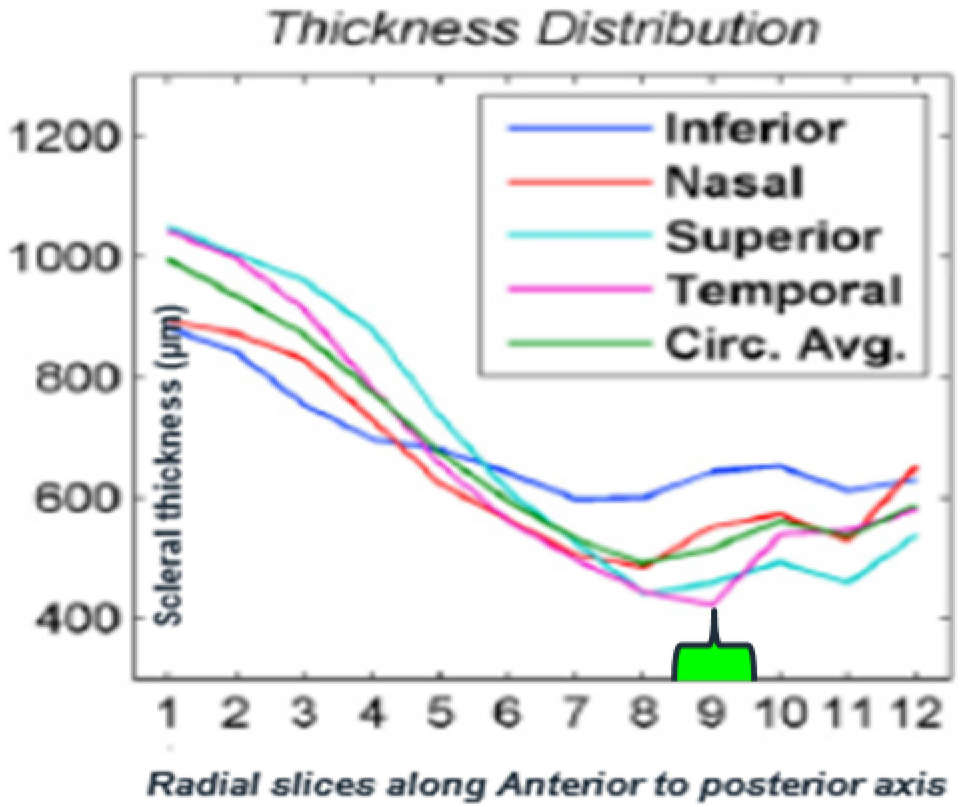
[1] 95% confidence interval was based on t-distribution

FDA Table 86: First Co-Primary Effectiveness Endpoint at 12 Months by Baseline Scleral Thickness – Effectiveness Cohort

Scleral Thickness	N	20/40 or Better and Gain of ≥ 10 Letters[1] n (%)	95% CI[2]
≤ 530 um	57	46 (80.7%)	68.1%, 90.0%
>530 - 560 um	130	115 (88.5%)	81.7%, 93.4%
>560 - 580 um	67	55 (82.1%)	70.8%, 90.4%
>580 um	87	59 (67.8%)	56.9%, 77.4%
p-value[3]			0.003
Average over Scleral Thickness[4]		79.8%	75.3%, 84.2%

Deriving Location of Scleral Thickness Measurement

- UBM Scleral thickness measurements taken in Superior Temporal Quadrant
  - Corresponds to thinnest quadrant at 3.5-4.0 mm implant location



(Norman, R.E., et al. Dimensions of the human sclera: thickness measurement and regional changes with axial length. Experimental Eye Research. 2010 (90):277-284)

Near Vision (DCNVA) Before and After Explant in Those Patient's Who Requested Explants-VIS-2014-2YR

Age	Eye	Primary Reason for Explant	Pre op DCNVA	Last DCNVA Prior to Explant	Post Explant DCNVA	Latest Post Explant BCDVA	Time After Explant
52	1	Inadequate pupil recovery day of surgery	20/80	-	-	20/20	3 months
53	2	Inadequate pupil recovery day of surgery	20/63	-	-	20/16	5 months
50	3	Cosmesis	20/50	20/32 (+9)	20/50 (+4)	20/16	33 months
50	4 5	Residual refractive error	20/63 20/50	20/40 (+8) 20/50 (+0)	20/80 (-5) 20/40 (+2)	20/12.5 20/16	32 months
51	6 7	Foreign body sensation	20/50 20/50	20/32 (+9) 20/20 (+18)	- -	20/16 20/16	3 months
47	8 9	Foreign body sensation	20/63 20/63	20/32 (+15) 20/32 (+14)	20/63 (+3) 20/63 (+0)	20/12.5 20/12.5	24 months
52	10 11	Cosmesis	20/80 20/80	20/63 (+9) 20/63 (+4)	20/80 (+1) 20/50 (+7)	20/20 20/16	35 months
50	12 13	Perceived lack of effect	20/50 20/80	20/50 (+3) 20/50 (+7)	20/50 (+1) 20/63 (+3)	20/16 20/16	25 months

Analysis not previously submitted to, or reviewed by, FDA

Sample Size: Second Co-Primary Endpoint (Randomized Sub-Study)

- Sample size of 30 immediate treatment and 30 deferred treatment/control subjects
- Two-sided α=0.05, power > 90%
- Randomized data in previous studies used to set responder rates
  - 6-month control responder rate ~ 10%
  - Assumed 6-month surgery responder rate ~ 75%

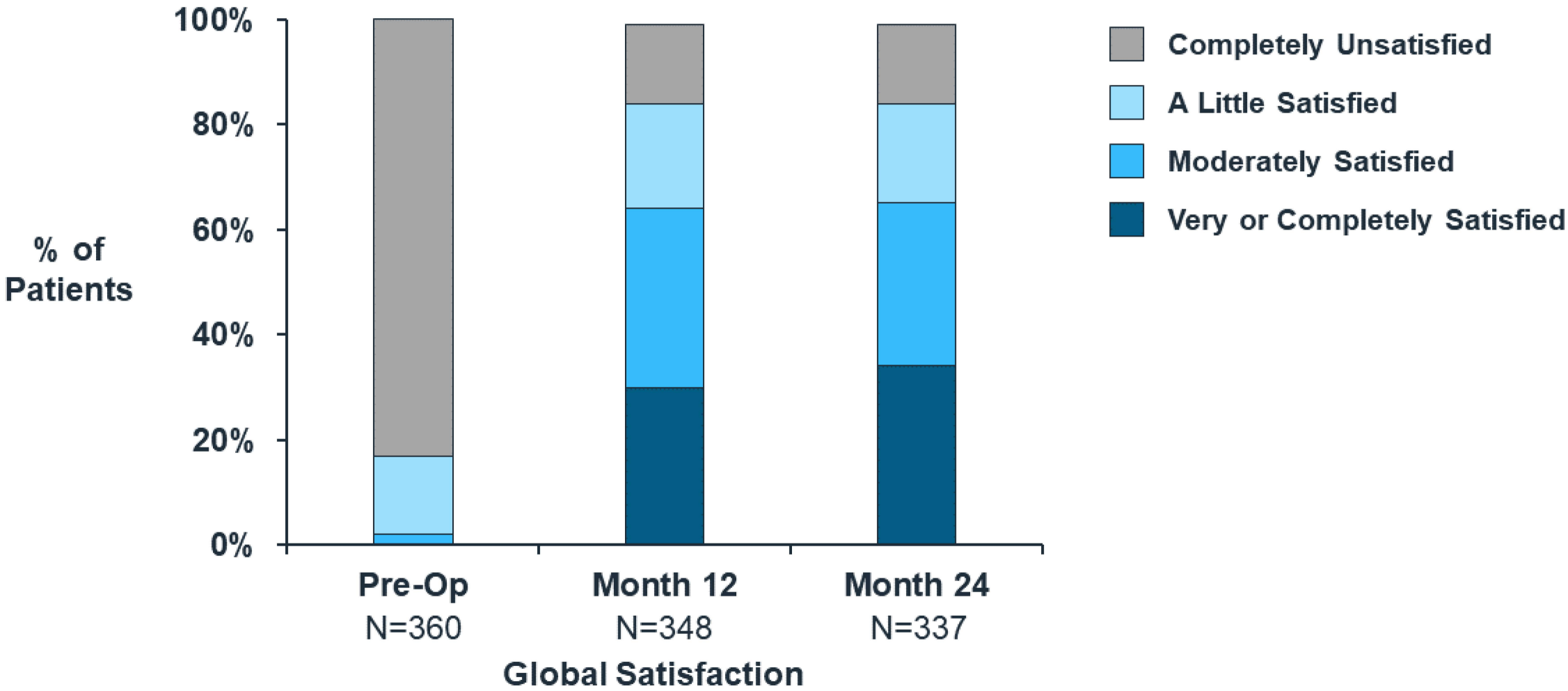
Sample Size: First Co-Primary Endpoint and Safety

- 333 implanted primary eyes:
  - First co-primary effectiveness endpoint, two-sided α=0.05, power = 90%
    - Expected responder rate of 0.825 based on previous Refocus clinical studies
  - > 95% probability to detect adverse events with population occurrence of 1%

VisAbility: iTrace Results

- **Static Change (distance targets)**
  - No significant change in aberrations of the eye from baseline to 12 and 24 months
- **Dynamic Change (near targets)**
  - Statistically significant C04 defocus across all zones at all near distances
    - VisAbility Substudy – Z(4,0), statistically significance across all zones ($p<0.01$) between 0.04μ and 0.07μ (0.1 and 0.25D)

NAVQ Item 11: Satisfaction with Near Vision Preop, 12, and 24 Months



Pupillometry – Minimum Pupil Size Safety Cohort

Minimum Pupil Size (mm)	Preop (N=708)	Month 12 (N=687)	Month 24 (N=668)
n (Reported)	708	683	664
Mean (SD)	3.16 (0.55)	3.12 (0.55)	3.08 (0.57)
Median	3.1	3.1	3.0
Min, Max	1.5, 4.9	1.6, 5.5	1.4, 5.3

VIS-2014-5YR Study Long Term Safety Data: Ocular Adverse Events

Events	Number (%) of Subjects N = 282	Number (%) of Eyes N = 556	Number of Events
Any Ocular Adverse Events	**27 (9.6%)**	**38 (6.8%)**	**41**
Lids and Lashes	**2 (0.7%)**	**3 (0.5%)**	**3**
Chalazion	1 (0.4%)	1 (0.2%)	1
Onset or worsening to severe clinically significant lid margin disease	1 (0.4%)	2 (0.4%)	2
Cornea	**1 (0.7%)**	**2 (0.4%)**	**2**
Dry Eye signs requiring prescription	1 (0.4%)	2 (0.4%)	2
Conjunctiva/Sclera	**6 (2.1%)**	**9 (1.6%)**	**9**
Conjunctival cyst	1 (0.4%)	1 (0.2%)	1
Conjunctival erosion	1 (0.4%)	1 (0.2%)	1
Subconjunctival hemorrhage (not associated w/ an explant, concomitant procedure, etc.)	1 (0.4%)	1 (0.2%)	1
Conjunctivitis (allergic, bacterial, viral)	3 (1.1%)	6 (1.1%)	6
Anterior Segment, Iris, Lens	**3 (1.1%)**	**3 (0.5%)**	**3**
Lens opacity- two grade change as compared to preoperative baseline	3 (1.1%)	3 (0.5%)	3

Study and enrollment are open

Database lock July 2020

VisAbility: Demographics

	ITT Population (N=360)
Age at Consent (years)	
Mean (SD)	51.6 (3.5)
Male	60%
Race	
Caucasian	85%
Asian	5%
Black or African American	4%
Other	6%
Ethnicity	
Hispanic or Latino	11%
Not Hispanic or Latino	89%

*As per protocol, the primary eye is the dominant eye

Presbyopia Prevalence: No Racial Differences in Treatment Success

- First Co-Primary Effectiveness Endpoint at 24 Months by Race Intent-to-Treat Population

	DCNVA 20/40 or Better and Gain of ≥ 10 Letters		
Race	N	n (%)	95% CI
Caucasian	294	246 (83.7%)	78.9%, 87.7%
Non-Caucasian	50	43 (86.0%)	73.3%, 94.2%
p-value			0.835
Average over Race		84.8%	79.6%, 90.1%

No Anatomical Racial/Ethnic Differences

- No significant racial differences in anterior scleral thickness[1,2]
- No significant differences in relative lens position of Asians, Hispanics or African Americans (within 0.01mm of Caucasian eyes)[3]
- Eyelid and orbital anatomy related to implant position evaluated preoperatively
- No significant differences in onset and progression of presbyopia in White and African American populations[4]

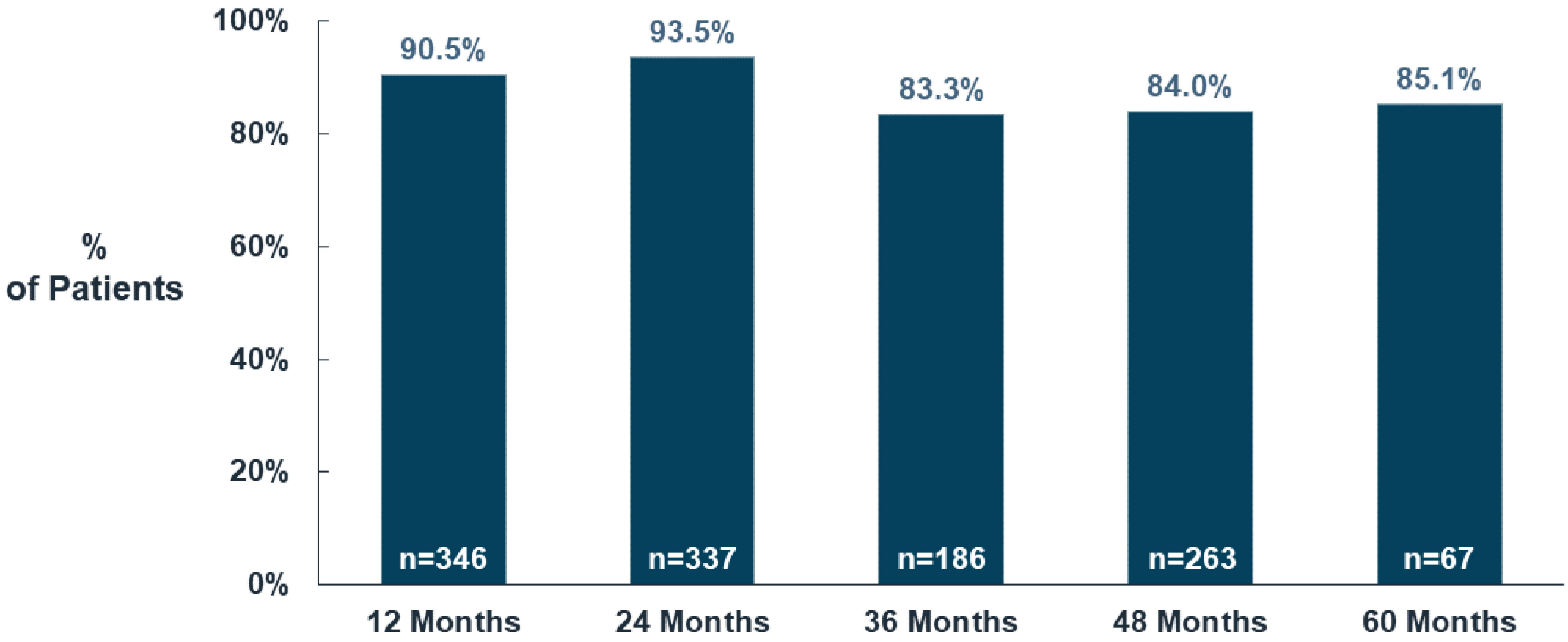
1. Buckhurst HD, et. Al. 2015. 2. Grytz R, et. al. 2014. 3. Wang D, et. Al. 2017. 4. Hunter H Jr, et. Al. 1997.

Presbyopia Prevalence: No Sex Differences in Treatment Success

- First Co-Primary Effectiveness Endpoint at 12 Months by Sex Intent-to-Treat Population

Sex	20/40 or Better and Gain of ≥ 10 Letters		
	N	n (%)	95% CI
Male	210	166 (79.0%)	72.9%, 84.3%
Female	140	111 (79.3%)	71.6%, 85.7%
p-value			1.000
Average over Sex		79.2%	74.8%, 83.5%

DCNVA 20/40 or Better Primary Eyes 5 Year Study



Near Vision (DCNVA) Before and After Explant in Those Patient's Who Requested Explants-VIS-2014-2YR

Eye	Age	Site	Ethnicity	Sex	Primary Reason for Explant	Pre op DCNVA	Last DCNVA Prior to Explant	Post Explant DCNVA	Latest Post Explant BCDVA	Time After Explant
1	52	003	Hispanic	M	Inadequate pupil recovery day of surgery	20/80	-	-	20/20	3 months
2	53	004	Caucasian	M	Inadequate pupil recovery day of surgery	20/63	-	-	20/16	5 months
3	50	008	Caucasian	M	Cosmesis	20/50	20/32 (+9)	20/50 (+4)	20/16	33 months
4 5	50	008	Caucasian	F	Residual refractive error	20/63 20/50	20/40 (+8) 20/50 (+0)	20/80 (-5) 20/40 (+2)	20/12.5 20/16	32 months
6 7	51	014	African American	F	Foreign body sensation	20/50 20/50	20/32 (+9) 20/20 (+18)	- -	20/16 20/16	3 months
8 9	47	014	Hispanic	M	Foreign body sensation	20/63 20/63	20/32 (+15) 20/32 (+14)	20/63 (+3) 20/63 (+0)	20/12.5 20/12.5	24 months
10 11	52	002	Caucasian	M	Cosmesis	20/80 20/80	20/63 (+9) 20/63 (+4)	20/80 (+1) 20/50 (+7)	20/20 20/16	35 months
12 13	50	002	Caucasian	F	Perceived lack of effect	20/50 20/80	20/50 (+3) 20/50 (+7)	20/50 (+1) 20/63 (+3)	20/16 20/16	25 months

Analysis not previously submitted to, or reviewed by, FDA

No pre-disposing health conditoins in patient population

Change in Control Group Prior to Implant

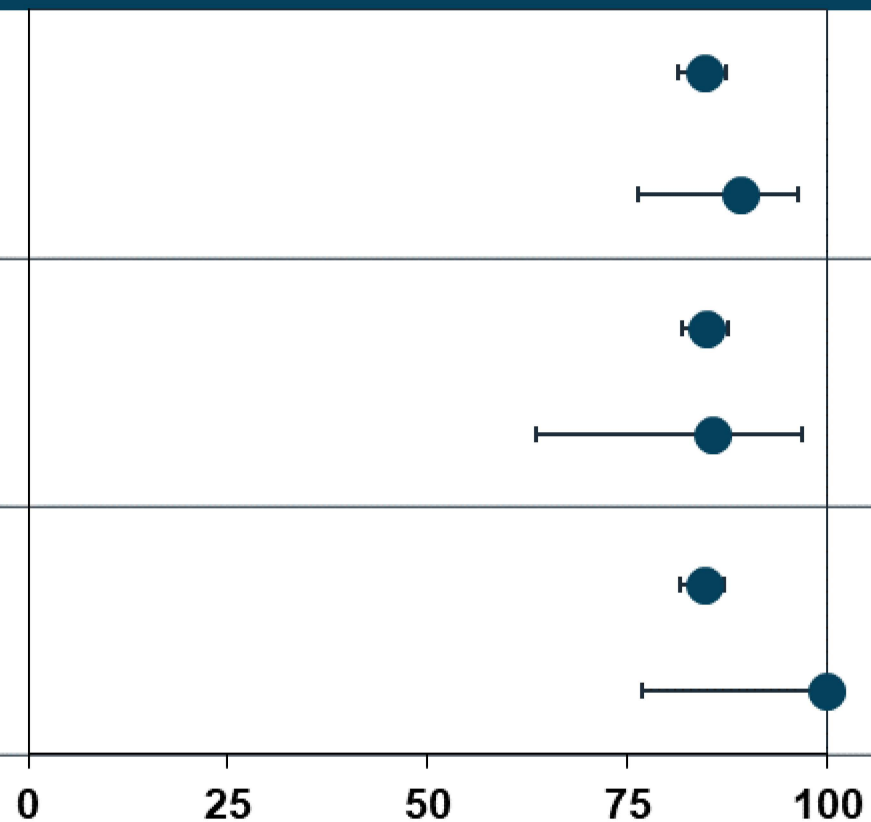
	BCDVA	DCNVA
Loss 2 lines	0	1
Loss 1 – 2 lines	0	4
Less than 1 line change	25	13
Gained 1 – 2 lines	4	7
Gained 2 lines	0	3
Gained > 2 lines	0	1

Proposed IFU Contraindications

- Scleral thickness <530 microns
- Pupil change from scotopic to photopic of <30%, or absolute difference of <1.00 mm
- Chronic ocular surface disease
- Ocular inflammatory disease
- Acute or chronic ocular disease
- Prior intraocular, extraocular, or orbital surgery
- Chronic systemic diseases which may affect the eye
- Uncontrolled systemic disease
- Anti-coagulation

Effectiveness by Implant Location: DCNVA 20/40 or Better and Gain ≥ 10 letters at 24 Months

24 Months	As Intended	Eyes n / N	Estimates (95% CI)	P-Value
Depth	Yes	523 / 619	84.5% (81.4, 87.3)	0.52
	No	41 / 46	89.1% (76.4, 96.4)	
Distance	Yes	546 / 644	84.8% (81.8, 87.5)	1.00
	No	18 / 21	85.7% (63.7, 97.0)	
Position	Yes	550 / 651	84.5% (81.5, 87.2)	0.14
	No	14 / 14	100% (76.8, 100.0)	



Analysis not previously submitted to, or reviewed by, FDA.
P-values from Fisher's exact test not adjusted for multiple comparisons

Micro Insert Segment Placement and AEs

- **Cumulative 24 Months**: 116 Eyes / 75 Subjects with unintended position
  - **Ocular Surface Events**
    - Dry eye: 24 events / 17 eyes / 17 subjects
    - Conjunctival Injection: 5 events / 5 eyes / 4 subjects
  - **Explants**
    - Perceived lack of effect: 1 eye
    - Foreign Body Sensation: 4 eyes / 2 subjects

Underlying data previously submitted to the FDA in tabular format - not submitted to FDA in displayed format.