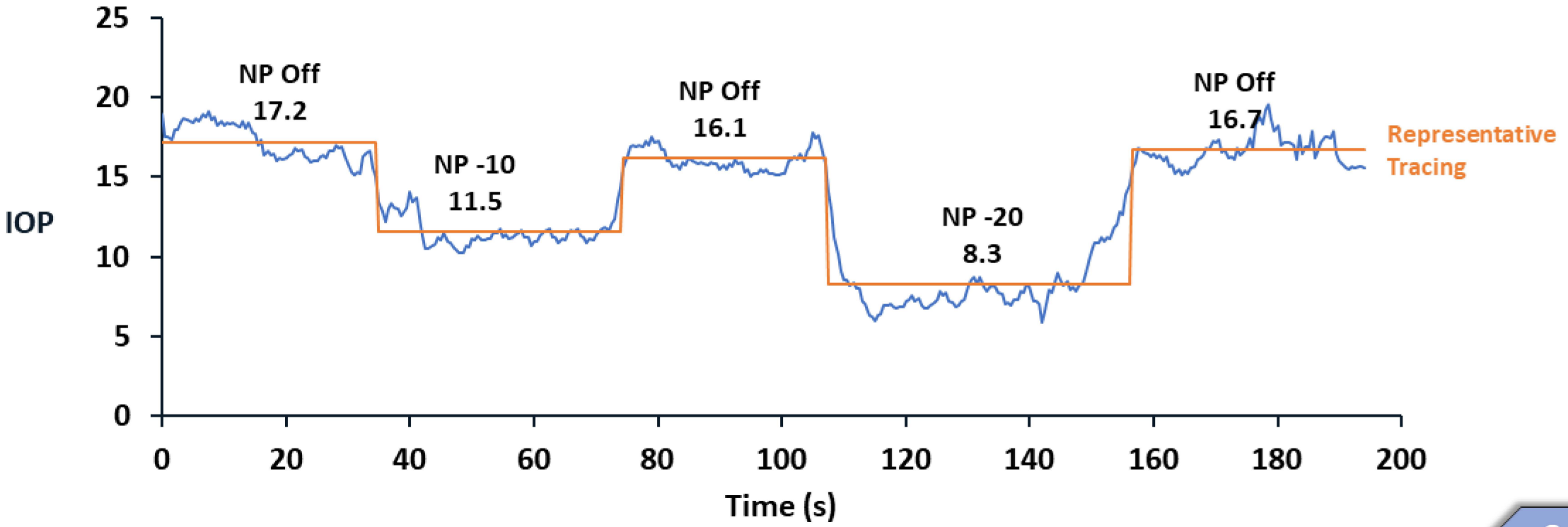
Confirm Study (n = 17): Direct Evidence of IOP Reduction

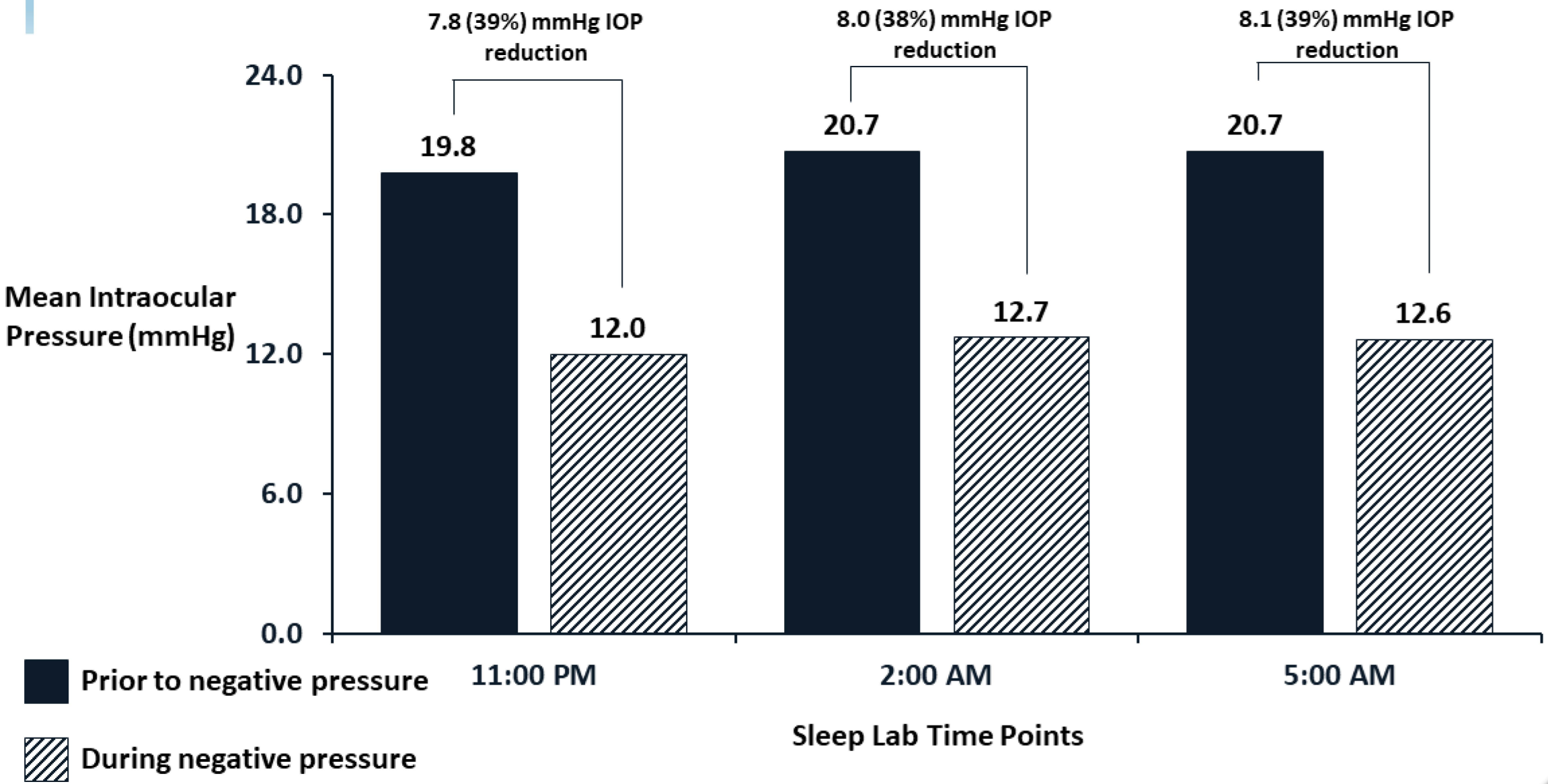
- Data from study in live eyes using manometric IOP measurements confirms that IOP is reduced during negative pressure application
  - Application of -10 mmHg resulted in mean IOP decrease of 5.6 (33%) mmHg
  - Application of -20 mmHg resulted in mean IOP decrease of 8.0 (51%) mmHg



Data provided to FDA, but not yet reviewed

Confirm

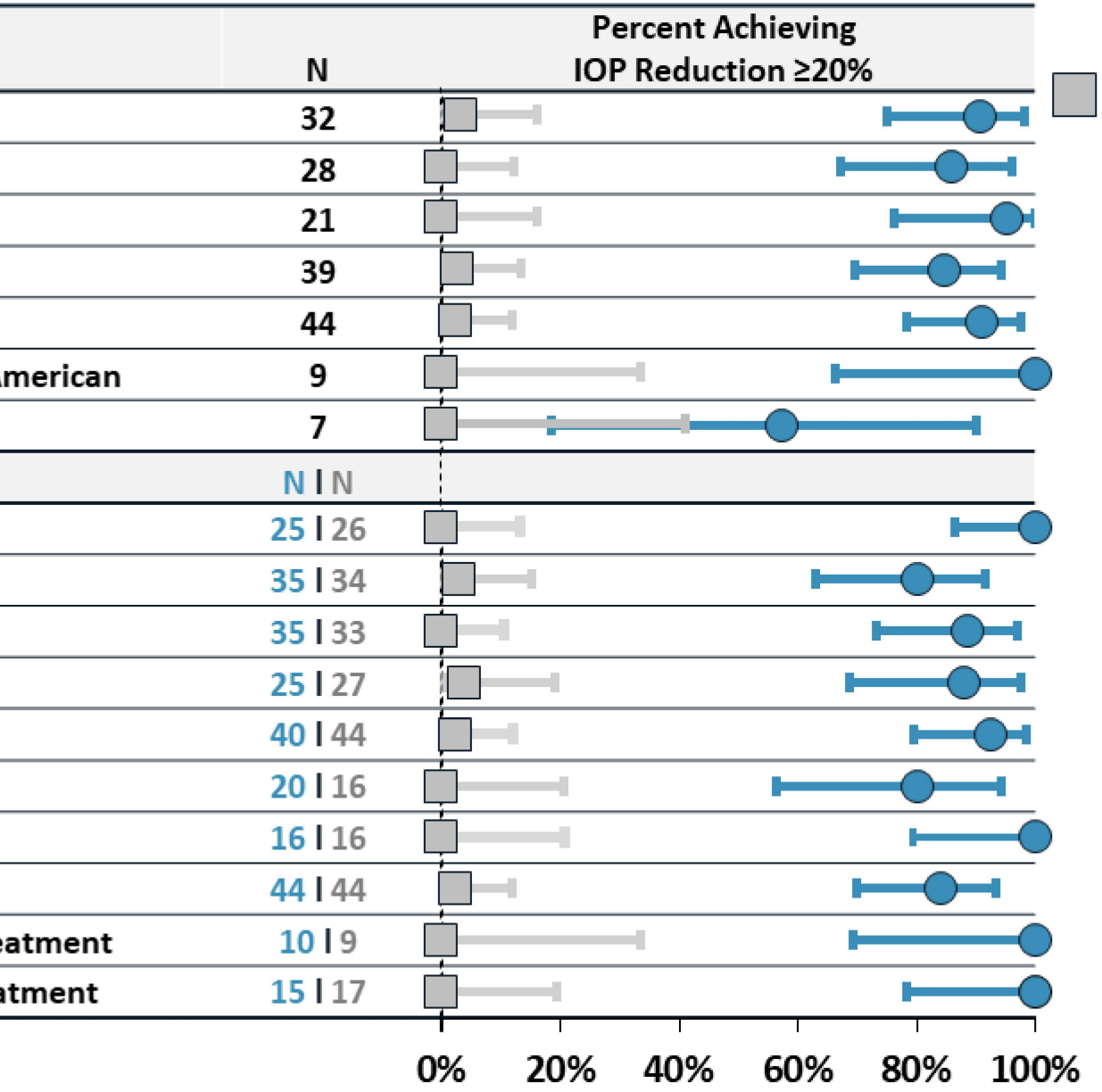
Sleep Lab IOP Reduction – Week 52 (N = 61)



Artemis CSR Figure 13

Effectiveness in Subgroups In Clinic (Per Protocol)

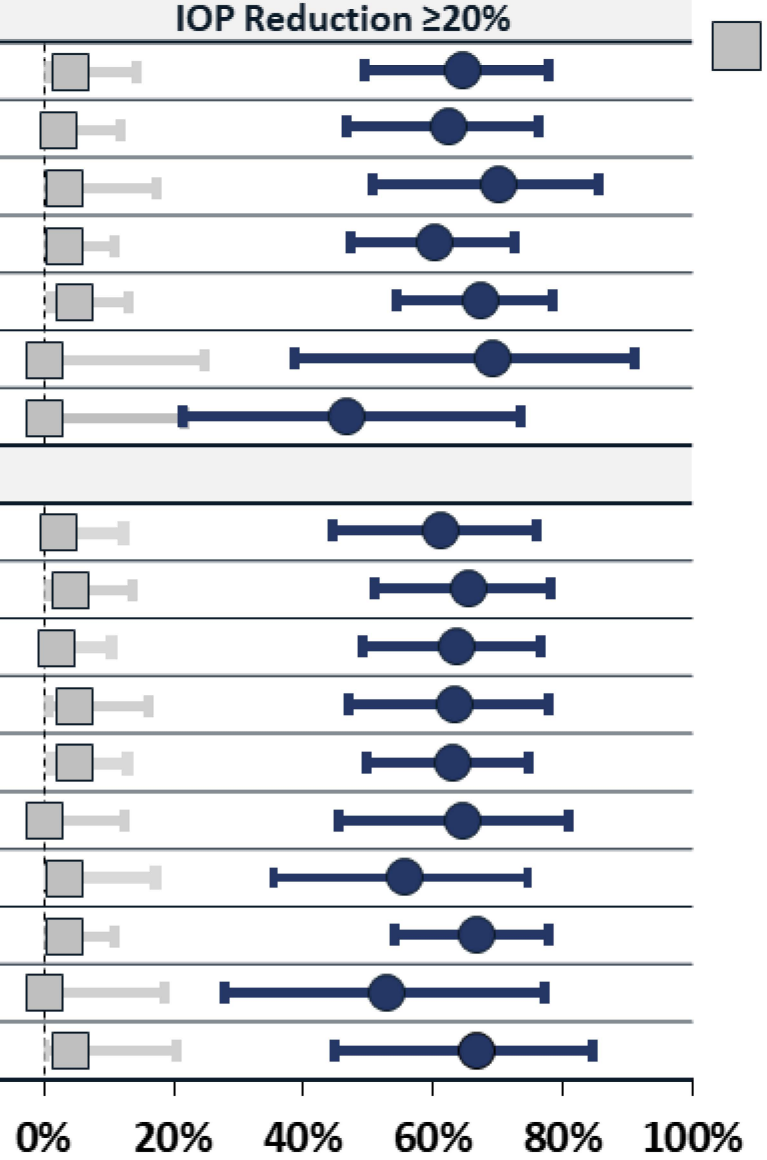
Patient level		N	Percent Achieving IOP Reduction ≥20%
Age	≤ 61	32	
	> 61	28	
Sex	Male	21	
	Female	39	
Race*	White	44	
	Black/African American	9	
	Asian	7	
Eye level		N | N	
Baseline Glaucoma Meds	0	25 | 26	
	≥ 1	35 | 34	
Baseline Goldmann IOP	≤ 14	35 | 33	
	> 14	25 | 27	
Cup-to-Disc Ratio	< 0.8	40 | 44	
	≥ 0.8	20 | 16	
Prior surgical treatment**	Any	16 | 16	
	None	44 | 44	
Prior surgery status if medication free	Any surgical treatment	10 | 9	
	No surgical treatment	15 | 17	



Eye level subgroup analysis not previously reviewed by FDA
*4th category (Mestizo) excluded from covariate analysis (only 1 patient)
**Cataract or glaucoma surgery

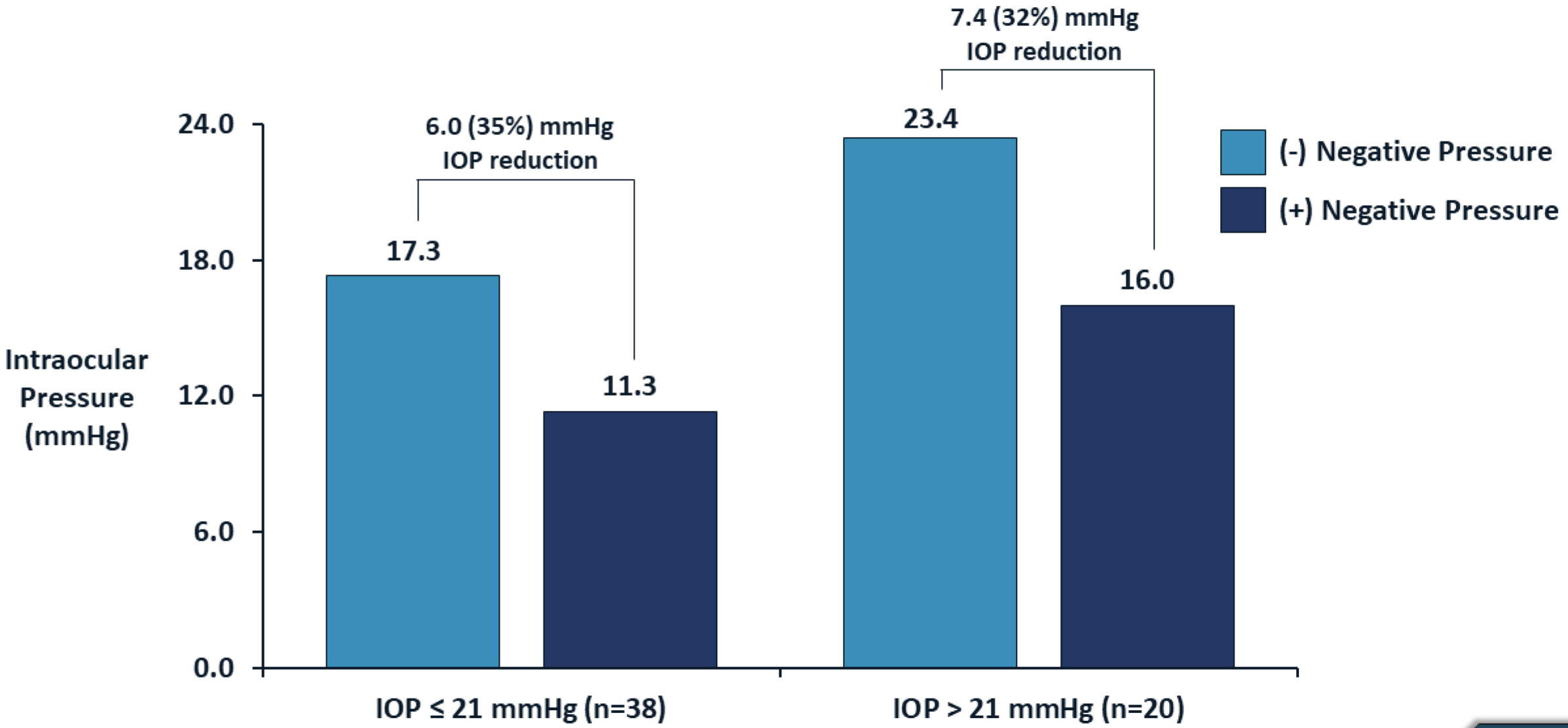
Secondary Endpoint (Sleep Lab): Effectiveness in Subgroups (mITT)

Patient level		N	Percent Achieving IOP Reduction ≥20%
Age	≤ 61	48	
	> 61	45	
Sex	Male	30	
	Female	63	
Race*	White	64	
	Black/African American	13	
	Asian	15	
Eye level		**N | N**	
Baseline Glaucoma Meds	0	41 | 43	
	≥ 1	52 | 50	
Baseline Goldmann IOP	≤ 14	52 | 51	
	> 14	41 | 42	
Cup-to-Disc Ratio	< 0.8	62 | 65	
	≥ 0.8	31 | 28	
Prior surgical treatment**	Any	27 | 30	
	None	66 | 63	
Prior surgery status if medication free	Any surgical treatment	17 | 18	
	No surgical treatment	24 | 25	



Eye level subgroup analysis not previously reviewed by FDA
*4th category (Mestizo) excluded from covariate analysis (only 1 patient)
**Cataract or glaucoma surgery

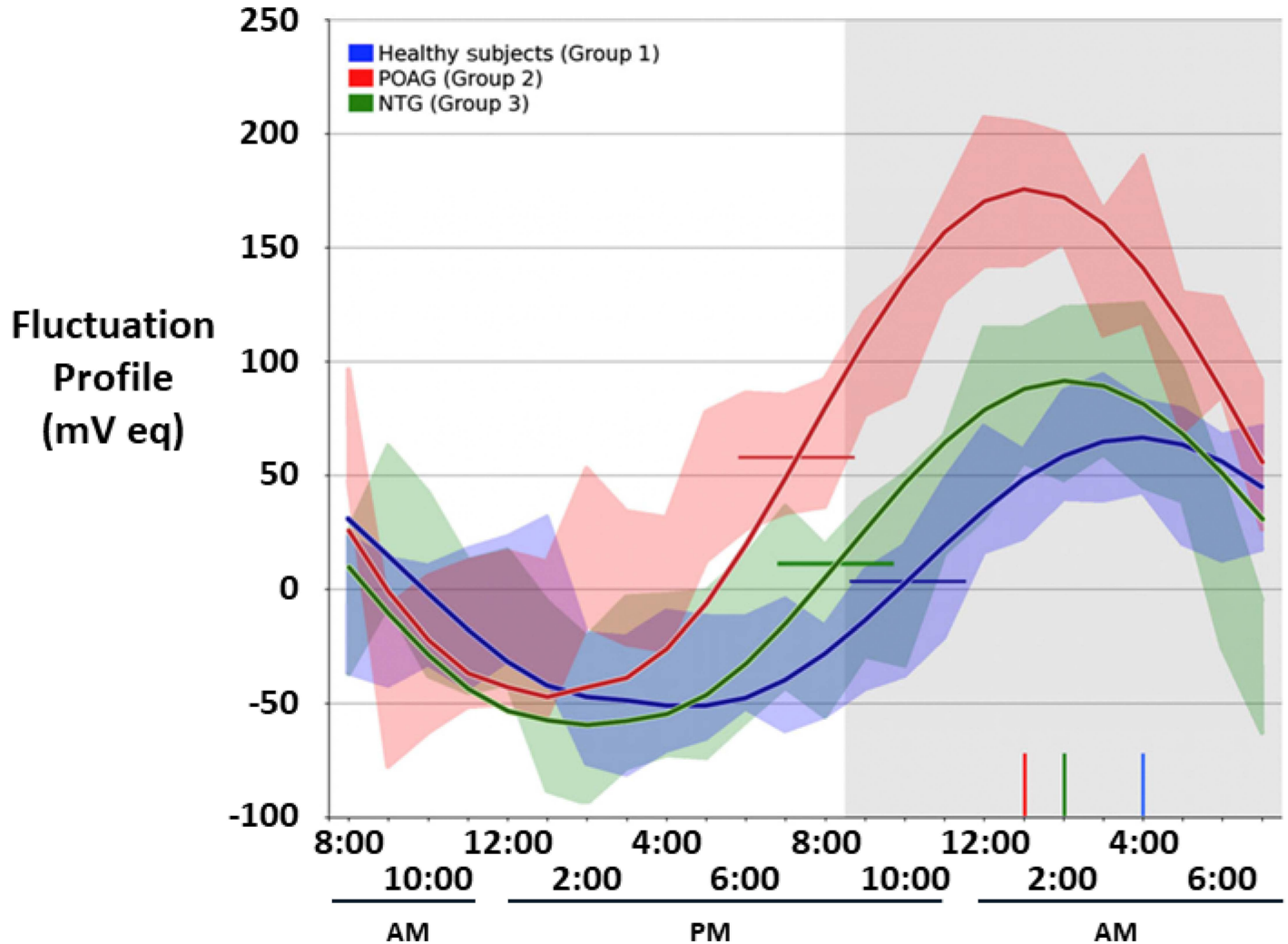
APOLLO Study: OPAP Provided Meaningful IOP Reduction Regardless of Baseline IOP



Analysis not previously reviewed by FDA

Unmet Need in Managing Nocturnal IOP Elevation

- 90% of OAG and 80% of NTG patients experience highest IOP elevations at night



Agnifili, 2015

Proposed HCP Instructions for Use

Determining Program Settings

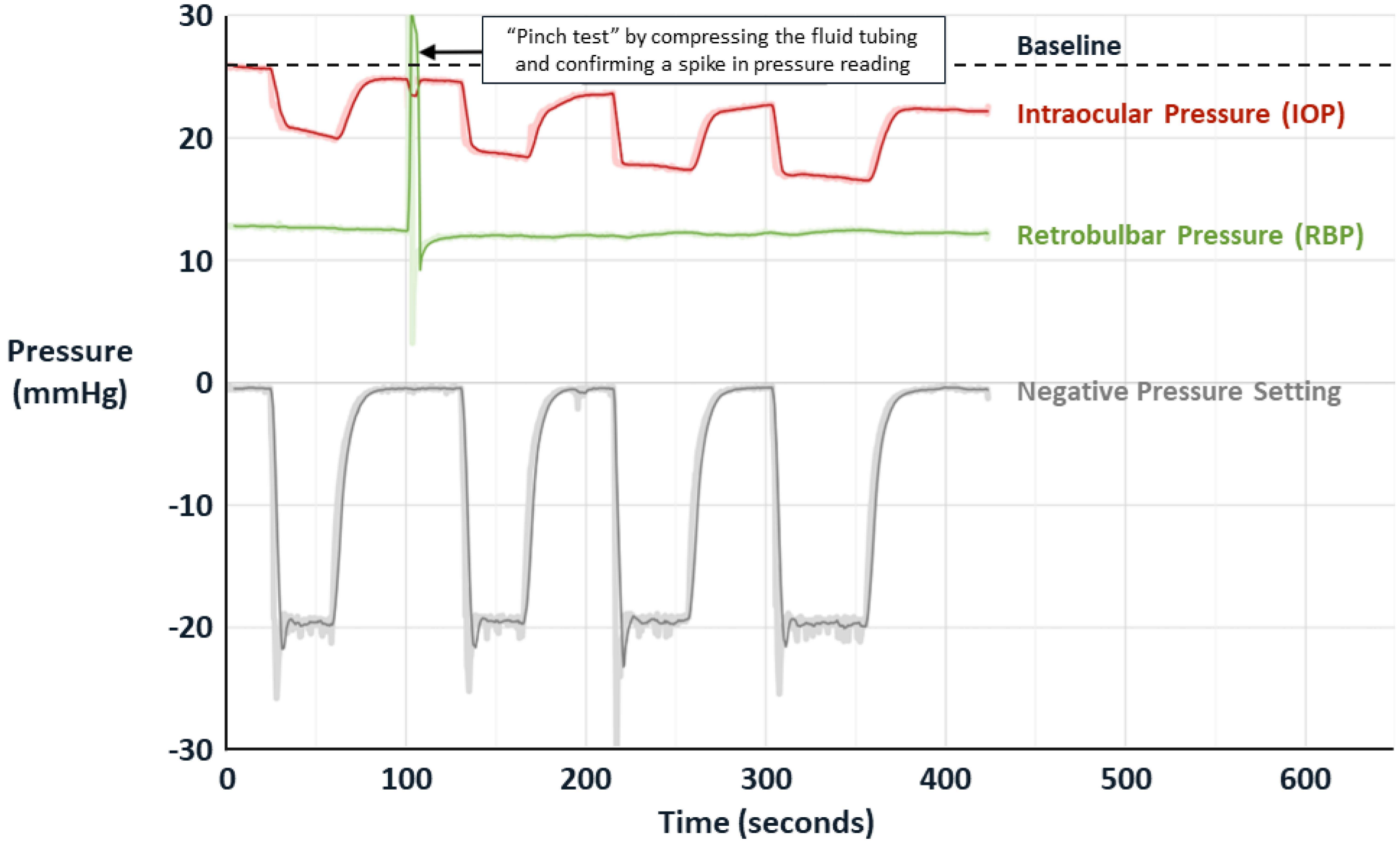
- IOP reduction achieved during OPAP use is typically 40% - 60% of the applied NP programmed
- FSYX OPAP program parameters are based on the patient's current IOP. To determine program parameters, for each eye:
    - Carefully measure IOP
    - Subtract the measured IOP from a reference IOP of 6 mmHg
    - Program the OPAP NP setting as the difference between the measured IOP and 6 mmHg

Example:

- Measured IOP = 16 mmHg
- Reference IOP = 6 mmHg
- NP setting programmed = -10 mmHg (16 - 6 = 10)

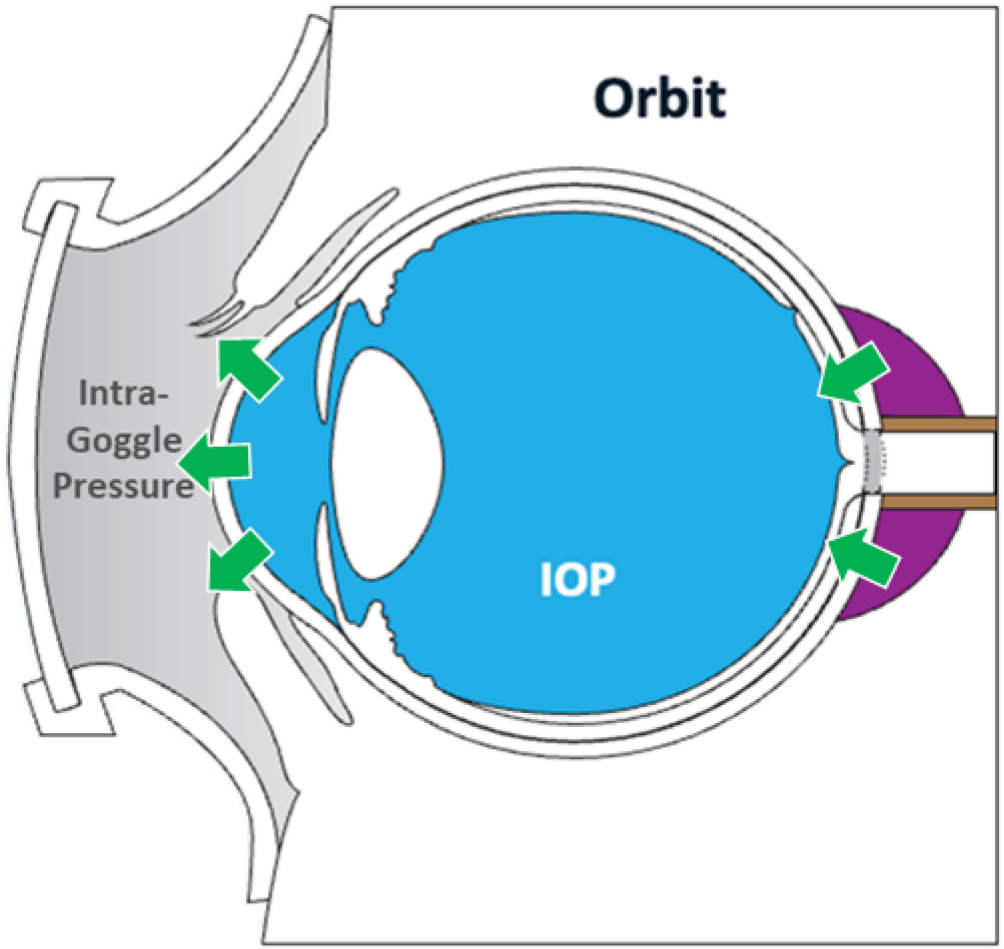
- Patient comfort should be considered when determining program settings. After NP setting has been determined, program OPAP and test the setting in clinic with patient to confirm it can be tolerated by patient. If patient cannot tolerate NP setting, decrease NP until patient is comfortable and can tolerate settings
- If a lower IOP is desired than that calculated using algorithm above, consider increasing NP setting, if tolerable

Retrobulbar Pressure Remains Stable with Negative Pressure Application



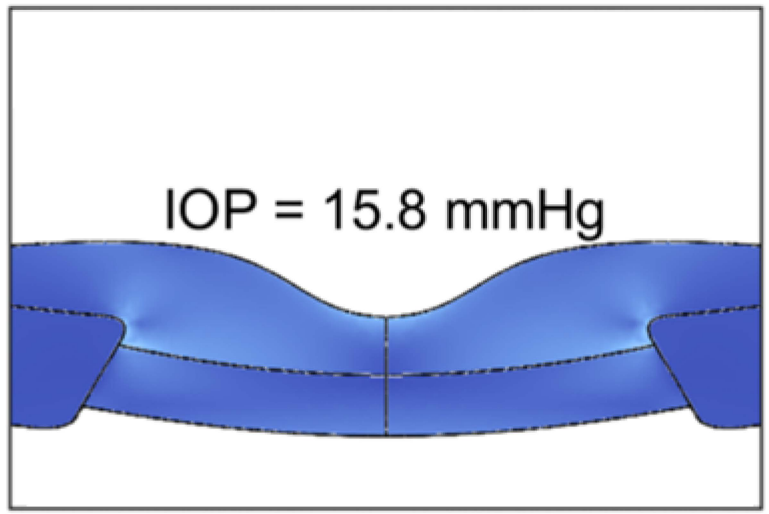
Shafer, 2022; Cadaver Study: Subject 1 Run2 – Pre-NP IOP of 25 mmHg

Mechanism of Decreased Strain

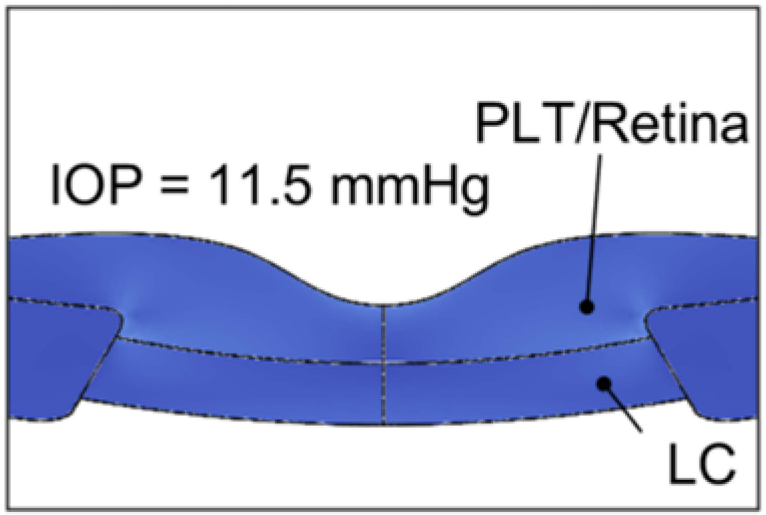


54% decrease in tissue strain at ONH

Normotensive Case



Goggle Case



OCT Mean RNFL Analysis

Study Eye

- Baseline: 77.9 ± 13.6 µm
- 52 Week: 77.9 ± 13.6 µm

Control Eye

- Baseline: 77.3 ± 14.5 µm
- 52 Week: 77.5 ± 14.8 µm

No Eyes with > 5um OCT thinning had VF Loss at end of study

- In study eyes, 57/62 (92%) had thinning ≤ 5 µm
- In control eyes, 55/62 (89%) had thinning ≤ 5 µm
- 5 µm is test–retest variability.

- One instance of OCT RNFL thinning ≥ 10 µm occurred in control eye but OCT quality was poor (signal strength 4/10 at Week 52 versus 8/10 at Baseline)

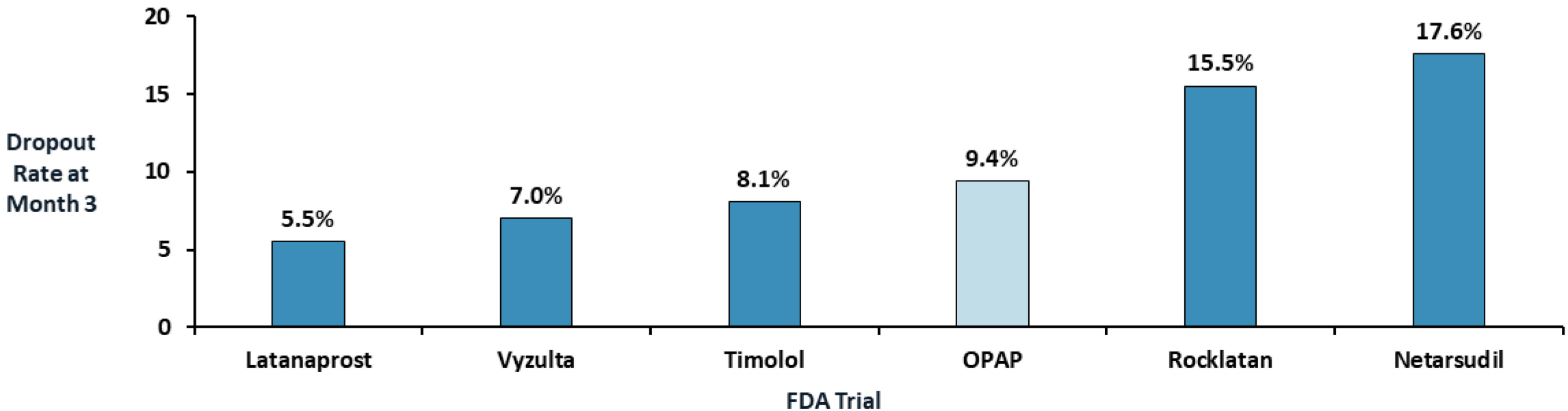
Periorbital AEs by Severity (> 1 Patient in Either Arm)

Preferred term, n (%)	Study Eyes N = 93			Control Eyes N = 93		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Periorbital AEs	14 (15%)	3 (3%)	0	7 (8%)	0	0
Periorbital edema	10 (11%)	2 (2%)	0	1 (1%)	0	0
Periorbital contact dermatitis	4 (4%)	0	0	3 (3%)	0	0
Periorbital folds above eyebrows	1 (1%)	0	0	1 (1%)	0	0
Ocular AE	19 (20%)	5 (5%)	1 (1%)	12 (13%)	1 (1%)	0
Lid Edema	9 (10%)	1 (1%)	1 (1%)	1 (1%)	0	0

Artemis Study CSR Table 36

Comparable Dropout Rates at 3 Months

- Recently approved trials leading to approval of topical OHT options reported variable dropout rates at 3 & 6 months
  - Latanoprostene bunod (LBN) 7.1% at 3 months[1]
  - Netarsudil/latanoprost 15.5% at 3 months[2]
  - Netarsudil 30.8% at 6 months[3]
- CPAP use data show adherence rates 30 – 60%[4]



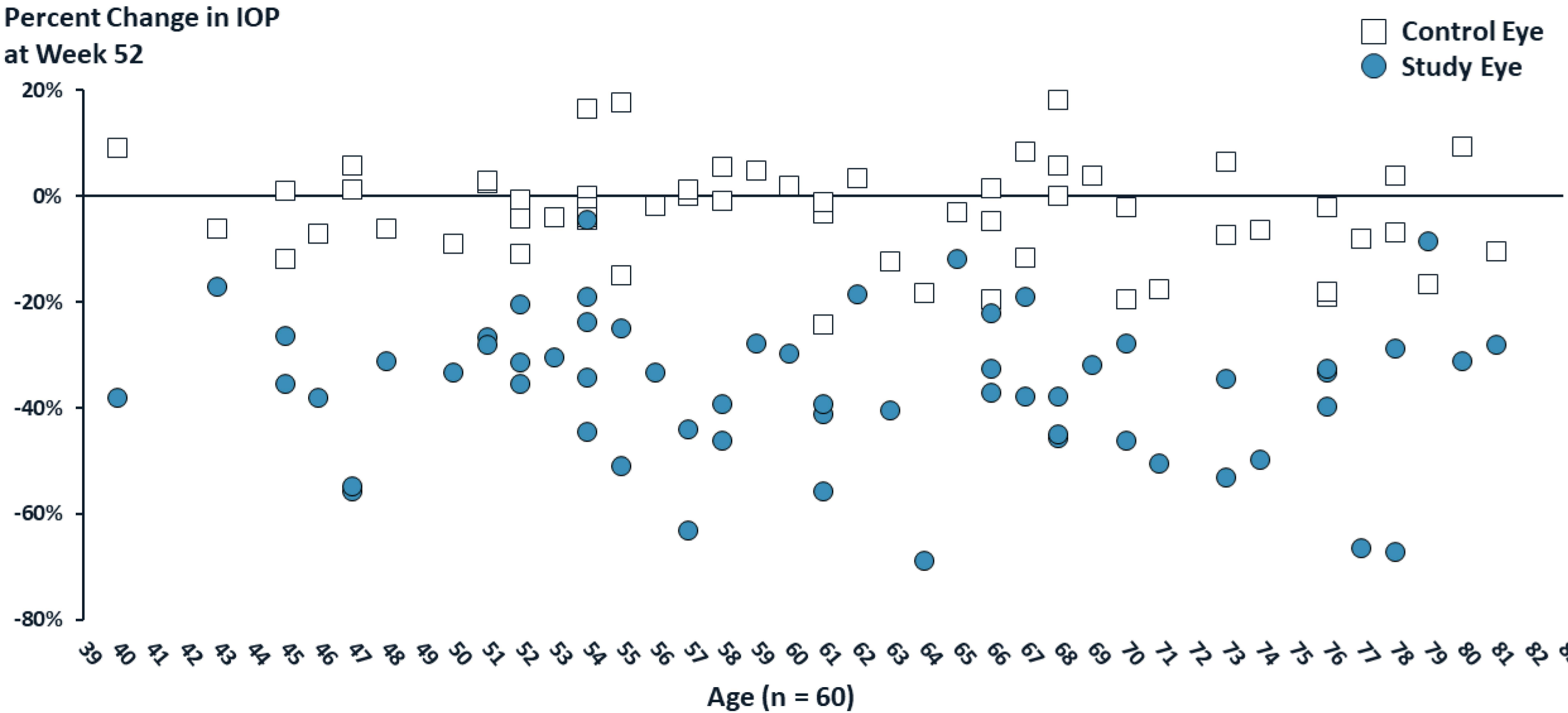
1. Weinreb RN et al. 2016; 2. Asrani S et al. 2019 ; 3. Khouri AS et al. 2019 4. Rotenberg, 2016

Pachymetry Values During NP Application (n=12 eyes)

Parameter	NP = 0mmHg	NP = -20 mmHg	Difference	P-value
Central Corneal Thickness (CCT)	511.5 µm	510.9 µm	0.57 µm	0.336
Anterior Chamber Depth (ACD)	3.66 mm	3.66 mm	< 0.01 mm	0.844
Axial Length	24.59 mm	24.60 mm	-0.01 mm	0.026

Kamalipor et al 2020

IOP Lowering at Week 52 by Age (In Clinic, Per Protocol)



Effectiveness and Safety in Patients by Age > 65

- N = 40 randomized over age 65
- 15 did not complete study
- 15 patients had device-related AEs (21 total)
  - 2 periorbital edema
  - 8 lid edema
  - 3 periorbital contact dermatitis
  - 3 conjunctival hyperemia
  - 1 myokymia
  - 1 dry eye
  - 1 periorbital pain
  - 1 visual disturbance
  - 1 lid erythema

- Study eyes
  - Mean in clinic IOP reduction -37.2%
  - Mean sleep lab IOP reduction -36.4%

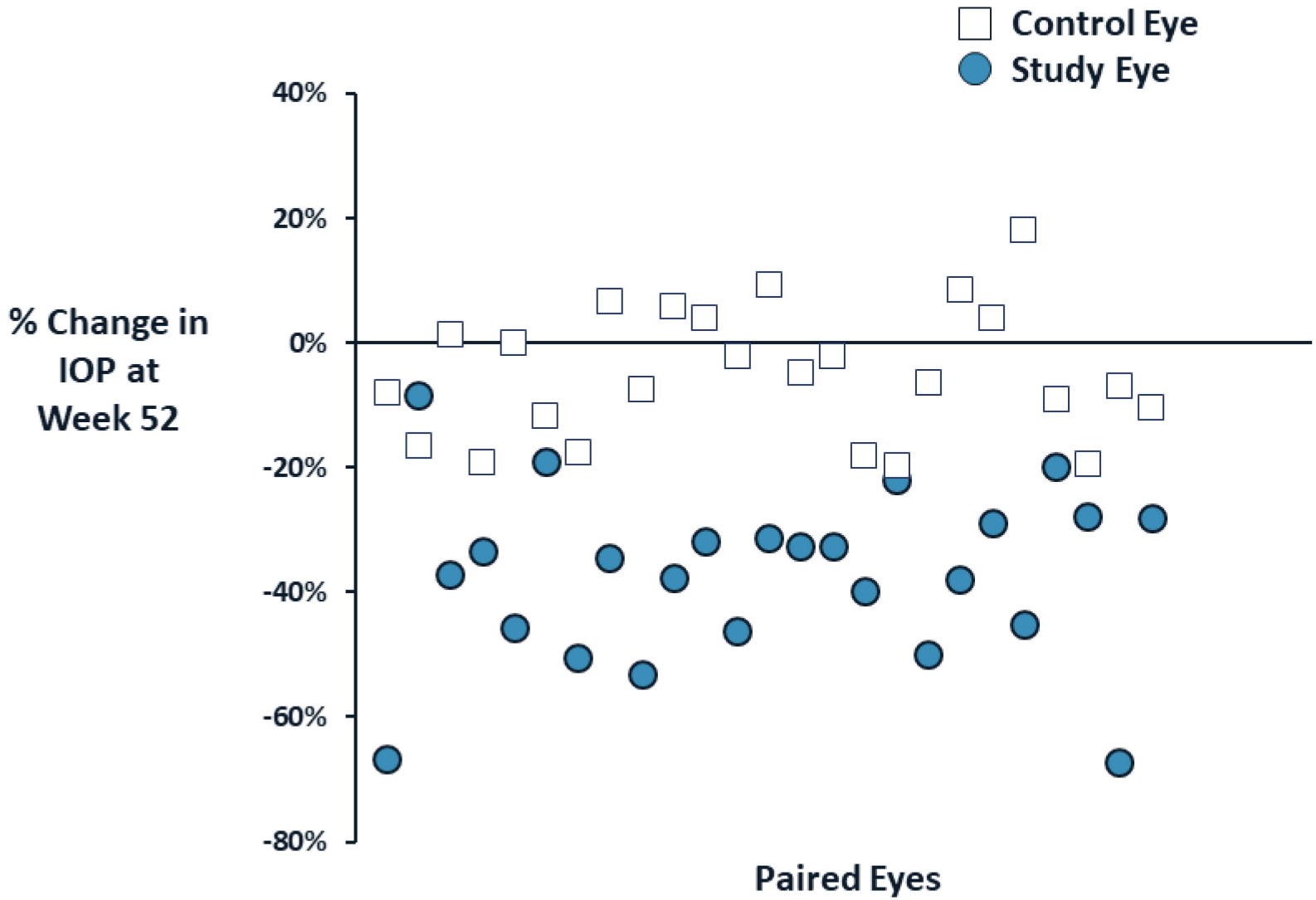


Table 33 (CP-X19): Summary of Device Wear Time at Home in Subjects with NP Settings between -17 to -20 mmHg (Inclusive) for ≥ 26 Weeks

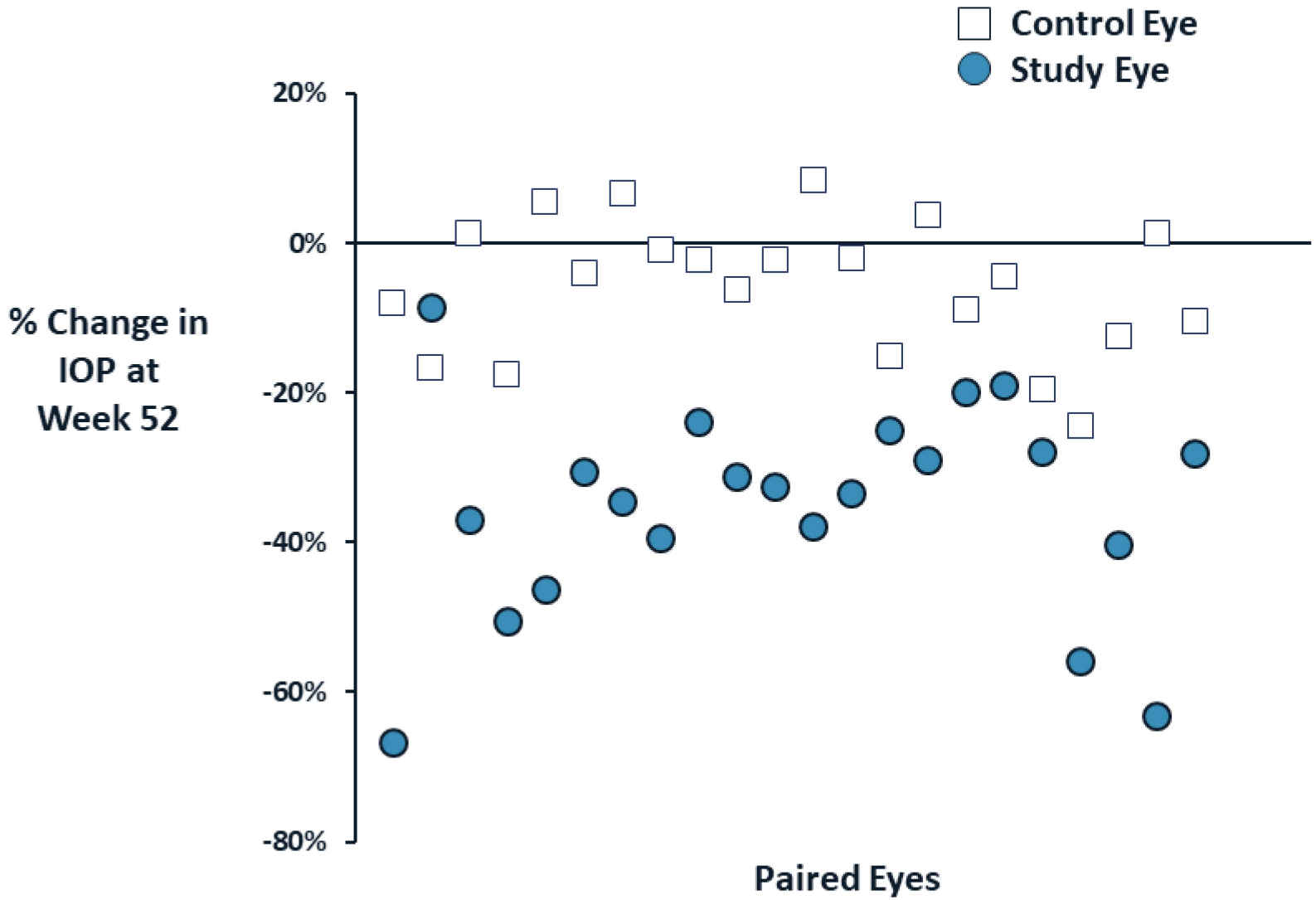
Subject ID, hours:	Day 0 to Week 6	Week 6 to Week 12	Week 12 to Week 26	Week 26 to Week 38	Week 38 to Week 52	Device-Related AEs Reported
(b)(6)	6.0	5.7	6.1	6.5	6.5	None
	3.7	4.0	4.6	4.3	5.3	None
	2.8	2.0	2.2	2.0	2.5	Mild periorbital edema
	5.3	5.5	5.9	5.5	6.0	None
	7.2	7.8	7.8	7.6	7.0	None
	5.5	6.7	6.5	6.5	6.6	Mild periorbital edema, Mild symptoms & signs of dry eye
	6.2	5.9	5.8	5.4	5.9	None
	6.3	6.3	6.1	6.2	6.2	Mild periorbital edema

AE=adverse event.

Effectiveness and Safety in Patients with Any Anti-Hypertensive Medication

- N = 32 patients on any anti-hypertensive medication
- 10 did not complete study
- 9 patients had device-related AEs (12 total)
  - 4 periorbital edema
  - 3 lid edema
  - 2 periorbital contact dermatitis
  - 1 conjunctival hyperemia
  - 1 myokymia
  - 1 dry eye

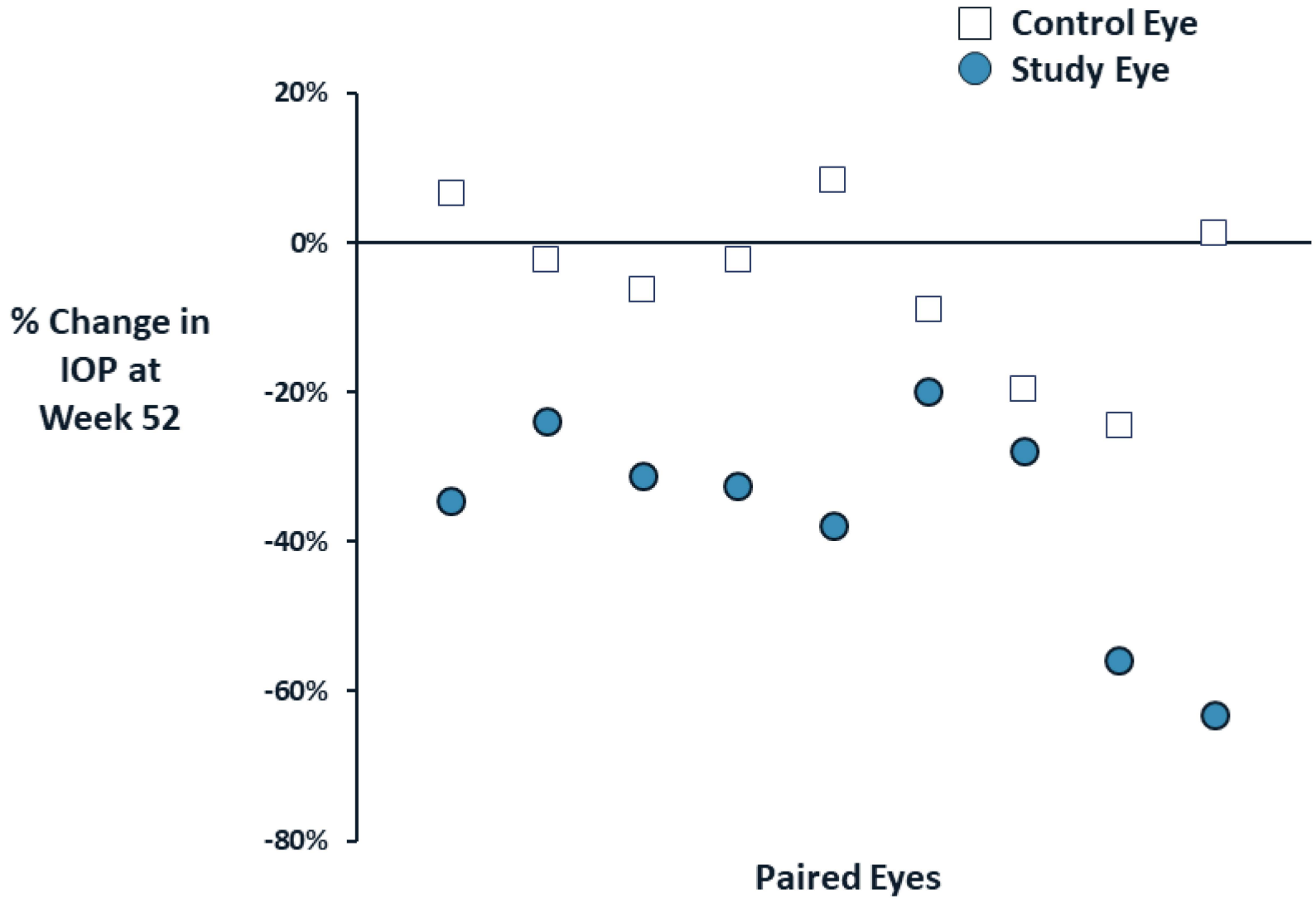
- Study eyes
  - Mean in clinic IOP reduction 35.6%
  - Mean sleep lab IOP reduction 37.3%



Effectiveness and Safety in Patients with Beta Blockers

- N = 15 patients on a Beta Blocker
- 6 did not complete study
- 5 patients had device-related AEs
  - 2 periorbital contact dermatitis
  - 1 lid edema
  - 1 periorbital edema
  - 1 dry eye

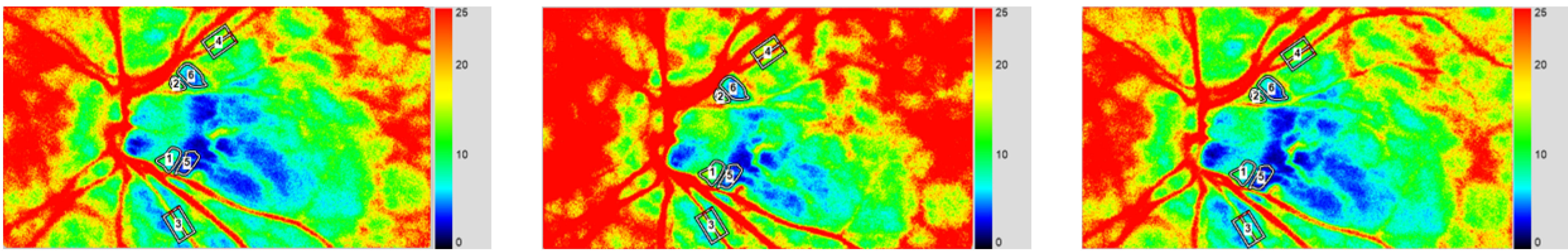
- Study eyes
  - Mean in clinic IOP reduction 36.4%
  - Mean sleep lab IOP reduction 34.7%



Laser Speckle Flowgraphy

- 7 eyes with glaucoma
- Increase of 20-30% blood flow in all four measured vascular beds
  - Retinal arterioles
  - ONH tissue
  - Peripapillary choroid and outside
  - Watershed zone of greater than 20-30%
- Increased blood flow in both area of RNFL defect and intact tissue

Baseline **Vacuum** **Post**



Hashimoto et al. 2020; Kardon et al. 2022

FDA / AGS Joint Meeting on MIGS Stated "1-Year Clinical Trial Should be Sufficient…"

American Academy of Ophthalmology
The Eye M.D. Association

Special Commentary: Supporting Innovation for Safe and Effective Minimally Invasive Glaucoma Surgery

Summary of a Joint Meeting of the American Glaucoma Society and the Food and Drug Administration, Washington, DC, February 26, 2014

Joseph Caprioli, MD,[1] Julie H. Kim, MD,[2] David S. Friedman, MD, PhD,[3] Tina Kiang, PhD,[2] Marlene R. Moster, MD,[4] Richard K. Parrish II, MD,[5] Eva M. Rorer, MD,[2] Thomas Samuelson, MD,[6] Michelle E. Tarver, MD, PhD,[2] Kuldev Singh, MD, MPH,[7] Malvina B. Eydelman, MD[2]

Panelists agreed that a 1-year clinical trial should be sufficiently long to identify severe adverse outcomes associated with MIGS devices. Although some panelists believed that a minimum of 1 year also would be sufficient to demonstrate effectiveness, others believed that 2 years may be needed to evaluate effectiveness for MIGS devices inhabiting the suprachoroidal space.

Consistency of IOP Response with Negative Pressure Application

	Ethier Modeling[1]	ARTEMIS N = 60 (In Clinic, PP)	APOLLO N = 58 (In Clinic, PP)	CONFIRM N = 17
Mean IOP Reduction, mmHg (%)	6.4 (41%)	6.6 ± 3.1 (36%)	6.5 ± 2.4 (33%)	5.6 ± 1.3 (33%)
Ratio of IOP Reduction to NP Application	**54%**	**58%** (±24%)	**56%** (±18%)	**56%** (±13%)

Consistency of response (56-58% ratio of IOP reduction: NP application) demonstrates that with -10 mmHg of negative pressure, expect 5-6 mmHg of IOP reduction

1. Safa, 2023; Table not previously reviewed by FDA

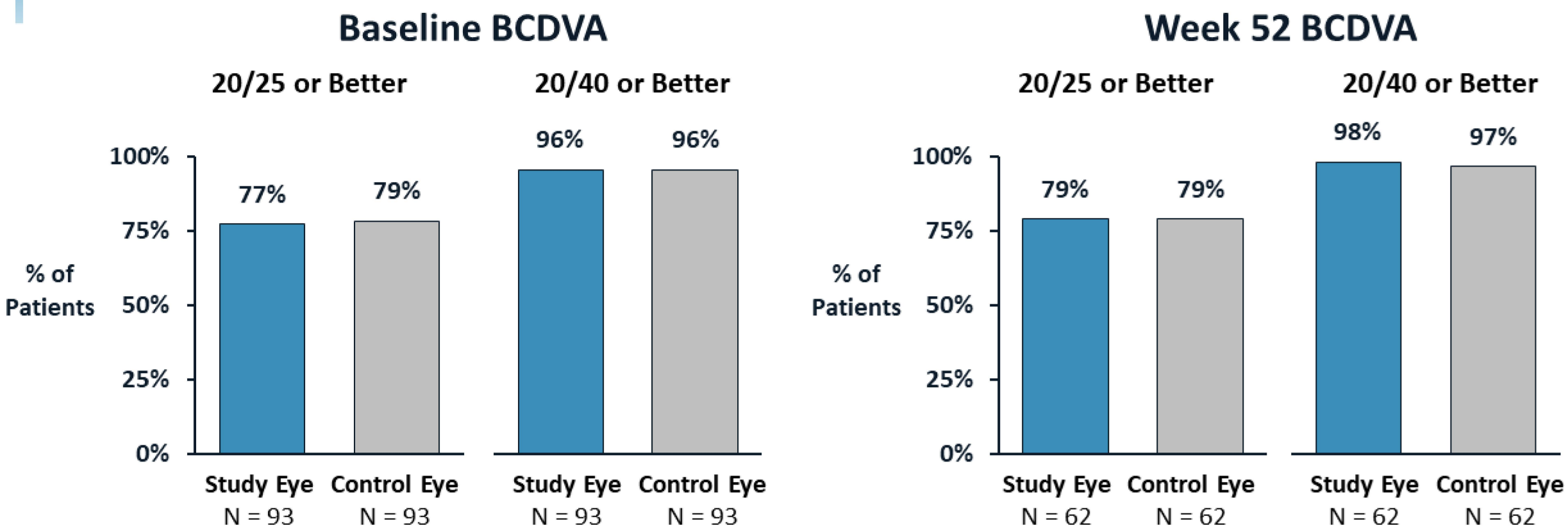
Patients with ≥ 2.5 dB MD Loss: Detailed Breakdown

			VF MD (dB)		Week 52 IOP and NP Setting						VFRC Evaluation of Progression		
PT. #	Eye		Baseline	Week 52	Off	On	CHG	PCHG	NP	Device Related AEs	VF Alone	VF + OCT	Progression Relative to Contralateral Eye
VF MD worsening ≥ 2.5 dB as compared to baseline													
1	OD	Treatment	-8.99	-12.12	15.8	10.5	-5.3	-33.54	-9	None	No	No	No
	OS	Control	-20.37	-28.15							Indeterminable	No	Indeterminable
2	OS	Treatment	-4.02	-7.32		9.5			-7	None	Insufficient	No	Insufficient
	OD	Control	-4.44	-3.47							Insufficient	No	Insufficient
3	OS	Treatment	-5.76	-12.49	18.3	6	-12.3	-67.21	-20	None	No	No	Insufficient
	OD	Control	-5.62	-12.76							Insufficient	No	Insufficient
4	OS	Treatment	-22.59	-24.9	18.5	6.8	-11.7	-63.24	-20	None	Insufficient	No	Insufficient
	OD	Control	-19.28	-24.05							Insufficient	No	Insufficient
VF MD worsening < 2.5 dB as compared to baseline													
5	OD	Treatment	-0.16	-2.18	16	11	-5	-31.25	-6	None	Yes	No	No
	OS	Control	-1.84	-3.59							Yes	No	No

Patients with ≥ 2.5 dB MD Loss: Detailed Breakdown

PT. #	Eye		VF MD (dB) Baseline	VF MD (dB) Week 52	Device Related AEs	VFRC Evaluation of Progression: VF Alone	VFRC Evaluation of Progression: VF + OCT	VFRC Evaluation of Progression: Progression Relative to Contralateral Eye
VF MD worsening ≥ 2.5 dB as compared to baseline								
1	OD	Treatment	-8.99	-12.12	None	No	No	No
	OS	Control	-20.37	-28.15		Indeterminable	No	Indeterminable
2	OS	Treatment	-4.02	-7.32	None	Insufficient	No	Insufficient
	OD	Control	-4.44	-3.47		Insufficient	No	Insufficient
3	OS	Treatment	-5.76	-12.49	None	No	No	Insufficient
	OD	Control	-5.62	-12.76		Insufficient	No	Insufficient
4	OS	Treatment	-22.59	-24.9	None	Insufficient	No	Insufficient
	OD	Control	-19.28	-24.05		Insufficient	No	Insufficient
VF MD worsening < 2.5 dB as compared to baseline								
5	OD	Treatment	-0.16	-2.18	None	Yes	No	No
	OS	Control	-1.84	-3.59		Yes	No	No

BCDVA Unchanged Between Baseline and Week 52



- BCDVA loss ≥ 2 lines from baseline: 2 study eyes and 2 control eyes in 4 patients
  - Considered unrelated to study device; **all cases resolved prior to or at study exit**

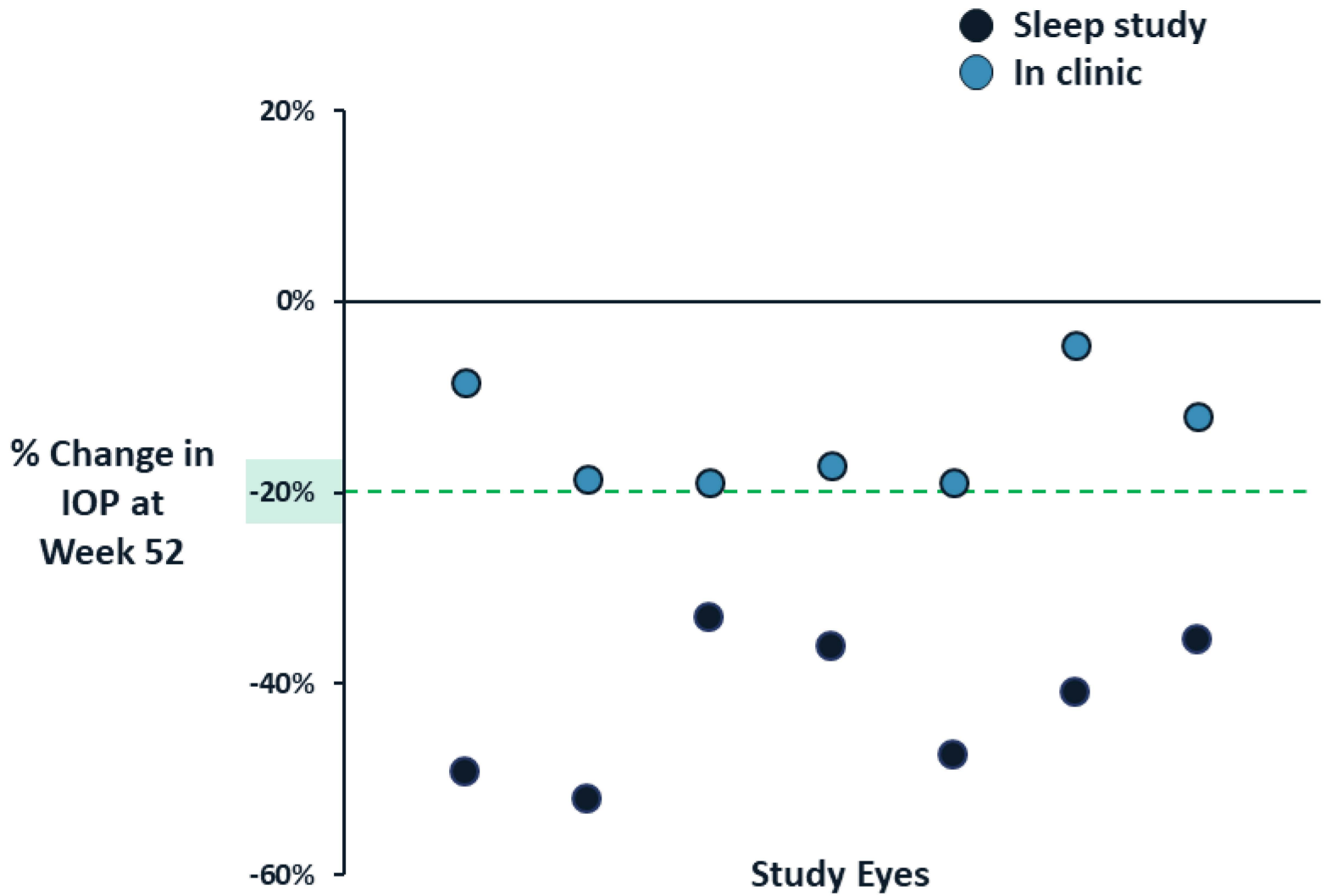
Artemis Study CSR Table 39

BCDVA (Best Corrected Distance Visual Acuity)

Effectiveness and Safety in "Non-responders" (In Clinic, mITT)

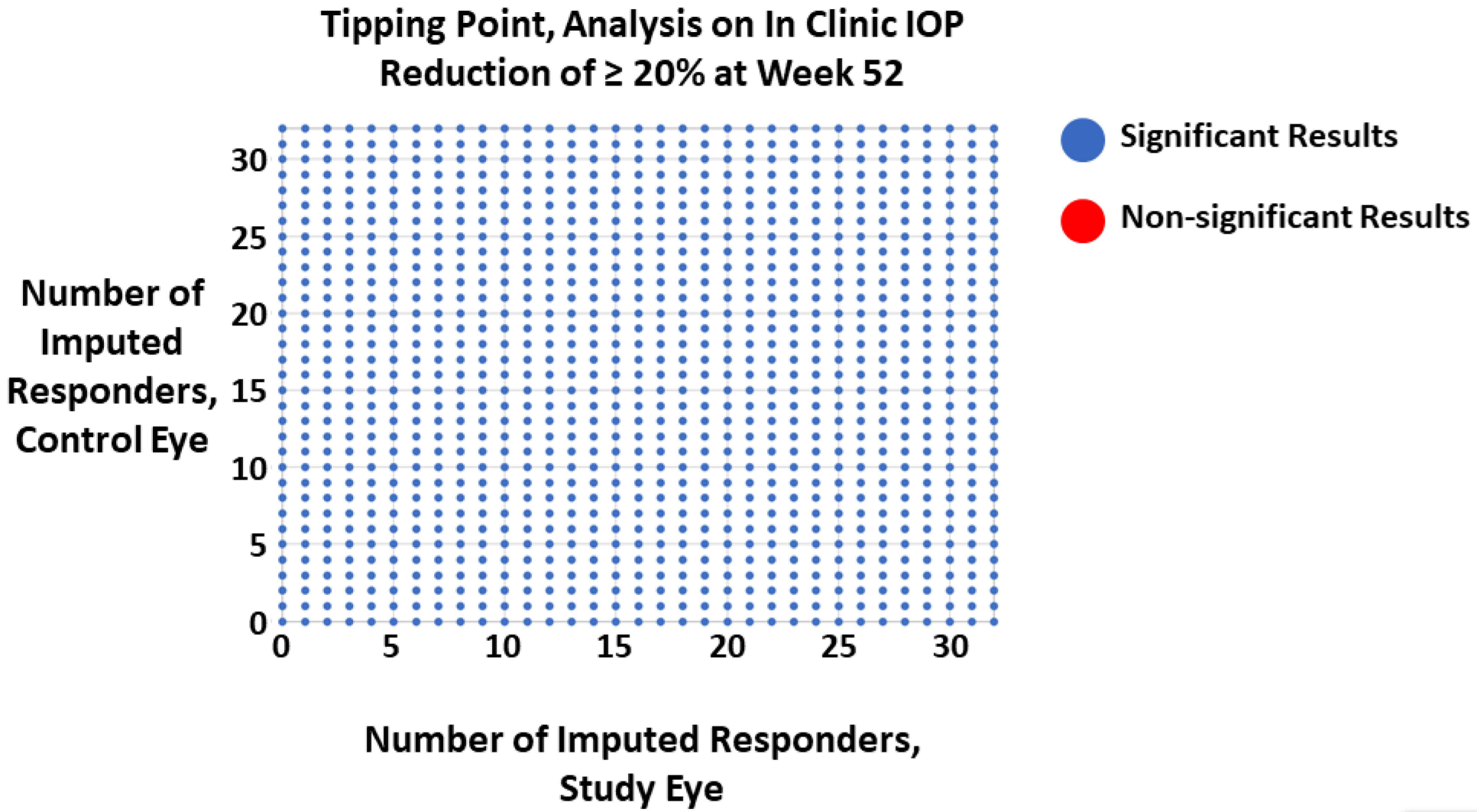
- N = 7 patients did not meet the primary endpoint (≥ 20% in clinic IOP ↓)

- Mean in clinic IOP reduction of 14.2%
- Mean sleep lab IOP reduction of 42.1%
  - All 7 eyes had ≥ 30% IOP reduction at final sleep lab



Analysis not previously reviewed by FDA

Tipping Point Sensitivity Analysis Confirmed Robustness of Primary Endpoint (N = 61)



Artemis CSR Figure 8