

Aqueous Humor Dynamics of NCX 470 Ophthalmic Solution (Nitric Oxide-Donating Bimatoprost): A Double-Masked, Placebo-Controlled Phase 3b Clinical Trial

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INTRODUCTION

Elevated intraocular pressure (IOP) is the most important modifiable risk factor for glaucoma, and IOP reduction remains the only proven effective treatment strategy.¹⁻²

IOP reflects the balance between aqueous humor production and drainage through the conventional (trabecular) and uveoscleral outflow pathways and can be described by the modified Goldmann equation:

$$IOP = P_e + (Q - U)/C$$

P_e = episcleral venous pressure (EVP)
 Q = aqueous humor flow rate
 U = uveoscleral outflow rate
 C = outflow facility

The effects of NCX 470 on aqueous humor dynamics (AHD) have been investigated in a preclinical model,³ but have not previously been evaluated in humans.

PURPOSE

NCX 470 (nitric oxide-donating bimatoprost) is designed to lower IOP through complementary effects on the conventional and uveoscleral outflow pathways.

This study characterized the effects of NCX 470 on AHD in healthy adults.

METHODS

- Randomized, double-masked, placebo-controlled Phase 3b study conducted at a single site.
- Healthy adults without glaucoma or other clinically significant ocular disease and with IOP >14 and ≤28 mmHg in both eyes.
- Subjects received NCX 470 0.1% in one eye and placebo (artificial tears) in the fellow eye once daily for 8 days.
- IOP and AHD parameters were evaluated bilaterally at baseline and following treatment.
- The primary efficacy endpoint was change from baseline in AHD following 8 days of NCX 470 treatment compared with placebo.
- Within-treatment and placebo-adjusted changes from baseline were assessed using paired t-tests.

REFERENCES

- Heijl, et al. Arch Ophthalmol. 2002;120:1268-1279.
- Kass MA, et al. Arch Ophthalmol. 2002;120:701-713.
- Galli C, et al. J Ocul Pharmacol Ther. 2024;40:389-396.

CONTACT INFORMATION

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AQUEOUS HUMOR DYNAMICS MEASUREMENTS

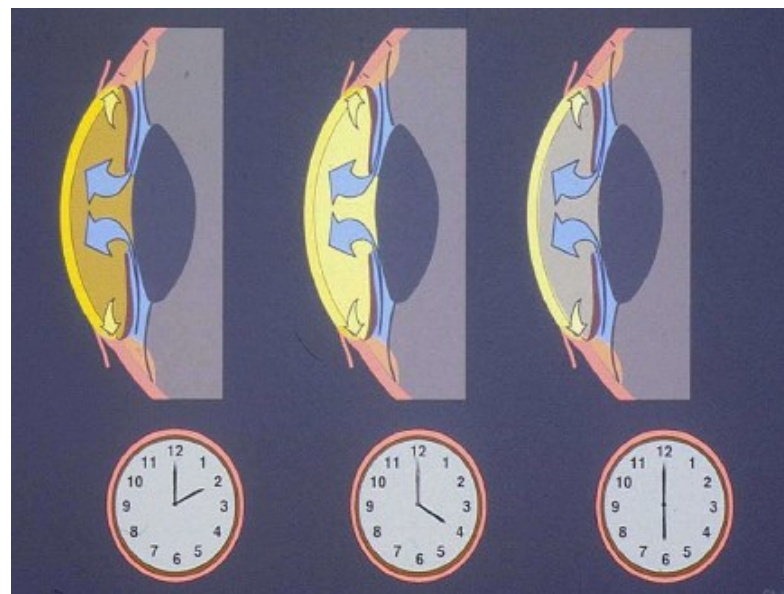


Intraocular Pressure (IOP)

Measured in seated and supine positions by pneumatonometry at 1 PM and 3 PM.

Aqueous Humor Flow Rate

Determined from fluorescein clearance measured by anterior segment fluorophotometry.

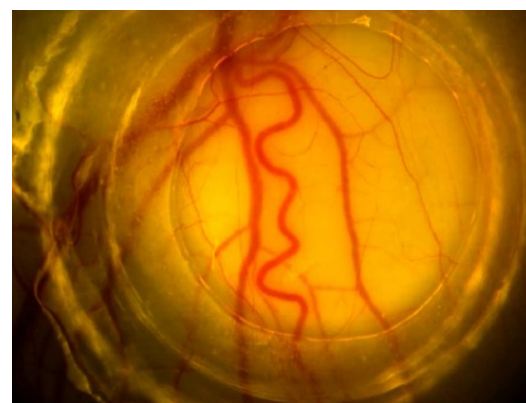


Outflow Facility

Measured non-invasively by constant weight tonography using a 10-g weighted pneumatonometer probe to obtain 2-minute pressure-decay tracings at 1 PM and 3 PM.

Episcleral Venous Pressure (EVP)

Measured non-invasively using a custom-built slit-lamp-mounted venomanometer at 1 PM and 3 PM.



$$U = Q - C (IOP - P_e)$$

Modified Goldmann equation

Uveoscleral Outflow Rate

Calculated from IOP, aqueous humor flow rate, EVP, and outflow facility using the modified Goldmann equation.

RESULTS

N = 18 • Mean age: 46.6 years • Female: 72.2%

Placebo-Adjusted Diurnal Results (NCX 470 vs. Placebo)

Parameter	Placebo-adjusted change from baseline (mean)	p-value
IOP (mmHg)	-2.94	<0.0001
Outflow Facility (μL/min/mmHg)	+0.05	0.0044
Uveoscleral Outflow Rate (μL/min)	+0.68	0.0007
EVP (mmHg)	+0.04	0.7051
Aqueous Humor Flow Rate (μL/min)	+0.19	0.0720

NCX 470 significantly **reduced IOP** and **increased outflow facility and uveoscleral outflow rate** compared with placebo. No statistically significant changes in EVP or aqueous humor flow rate were observed.

RESULTS (continued)

FIGURE 1. EFFECT ON MEAN DIURNAL IOP

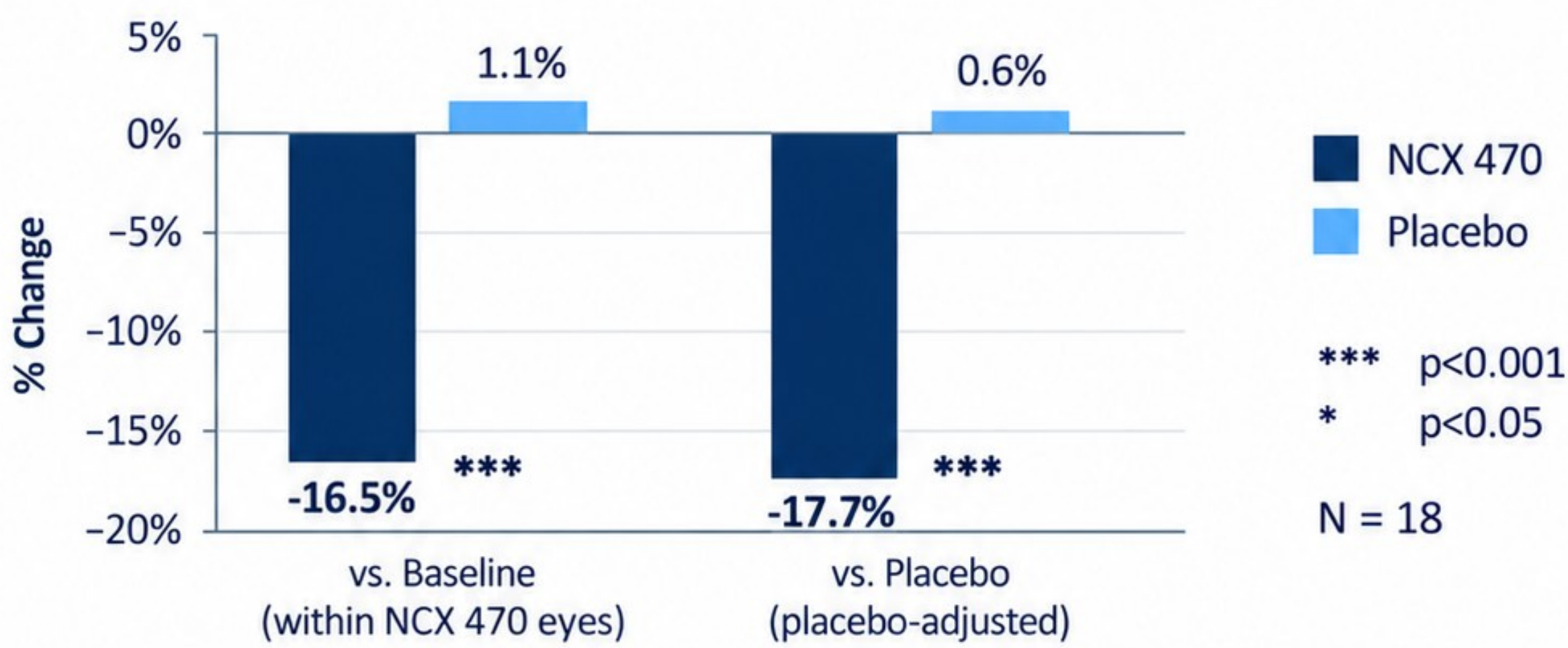


FIGURE 2. EFFECT ON MEAN DIURNAL OUTFLOW FACILITY

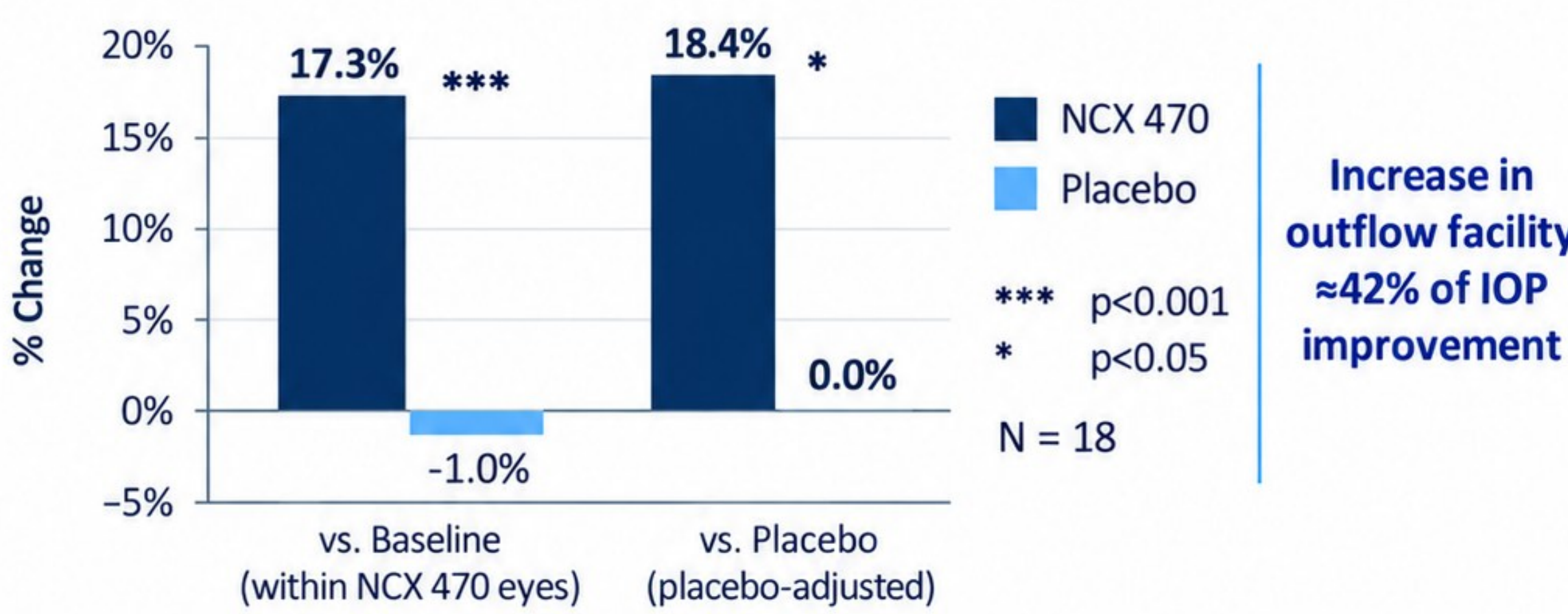
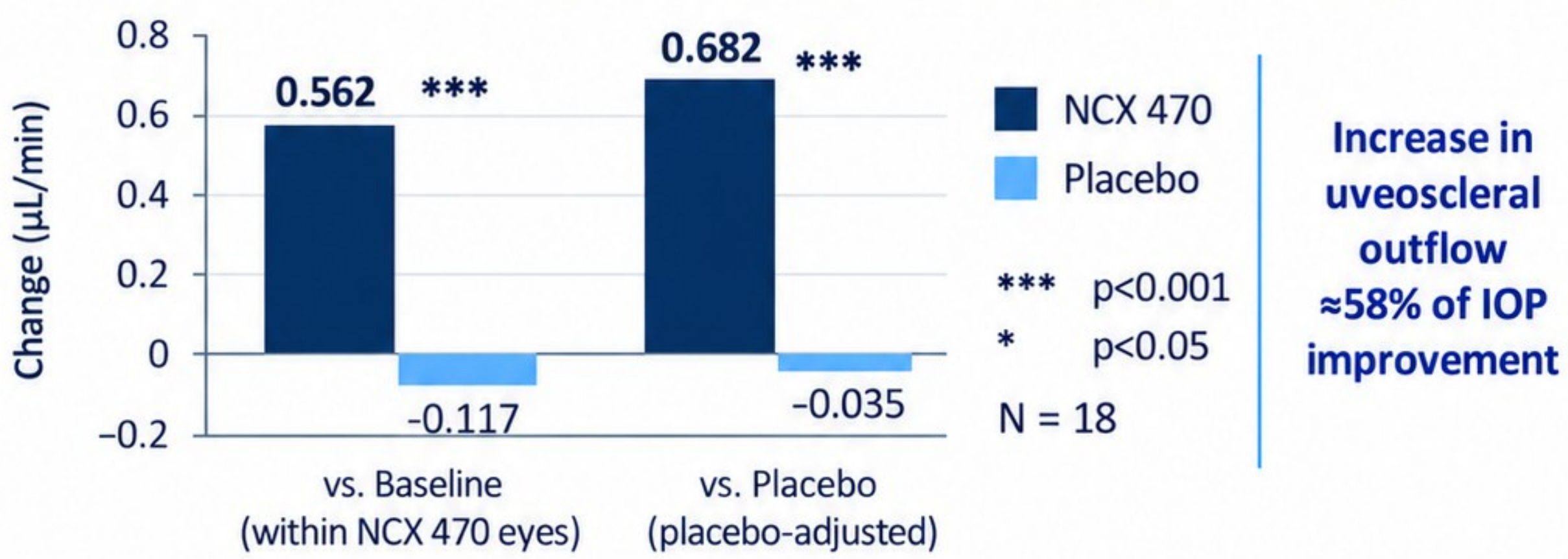


FIGURE 3. EFFECT ON MEAN DIURNAL UVEOSCLERAL OUTFLOW RATE



Results at 1 PM and 3 PM were generally consistent with the diurnal analyses; the placebo-adjusted increase in outflow facility did not reach statistical significance at 1 PM (p=0.0815).

SAFETY: the most common ocular treatment-emergent adverse event (TEAE) was **ocular hyperemia (33.3% vs 5.6%)** in NCX 470- vs placebo-treated eyes. No serious adverse events were reported and no TEAEs led to discontinuation.

CONCLUSIONS

In healthy adults, NCX 470 0.1% dosed once daily **significantly lowered IOP, with increases in outflow facility and uveoscleral outflow**. No statistically significant effects on EVP or aqueous humor flow were observed. These findings support the **dual mechanism of action** of NCX 470 through enhancement of both trabecular and uveoscleral outflow.

DISCLOSURES

Garbutt: Nicox Ophthalmics, Inc. (E, I)
Kazemi: (N)
Hubatsch: Nicox Ophthalmics, Inc. (E, I)
Sponseller: Kowa Pharmaceuticals Americas, Inc. (E)
Sit: Alcon, Inc. (F); Globe Biomedical, Inc. (C); Injectsense, Inc. (C); Kowa Pharmaceuticals America, Inc. (C); Nicox Ophthalmics, Inc. (F); PolyActiva Pty (C); Qlaris Bio, Inc. (C, F); Santen Pharmaceuticals Asia Pty (C)