NCX 470, a Nitric Oxide Donating Bimatoprost versus Latanoprost Has Greater Proportion of Subjects Achieving ≥10 mmHg IOP Decrease in Phase 3 Trial

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INTRODUCTION

Glaucoma is the number one cause of irreversible vision loss and the second leading cause of blindness worldwide.[1] As the population ages, the number of people expected to be diagnosed with glaucoma is expected to exceed 111 million by 2040.[2] Intraocular pressure (IOP) is the primary risk factor for glaucoma and lowering IOP is currently the only proven effective treatment.[1] While prostaglandin analogues have been the mainstay of topical medical management for glaucoma for many years, drugs with greater IOP reduction is still an unmet need for patients with open-angle glaucoma (OAG) and ocular hypertension (OHT).[3]

Nicox Ophthalmics, Inc. is developing NCX 470, a nitric-oxide (NO) donating bimatoprost prostaglandin analog, as new therapy for lowering IOP in patients with OAG or OHT. When exposed to esterases in the eye, NCX 470 is cleaved into its active metabolites, the prostamide bimatoprost, which in turn is converted to bimatoprost acid, a prostaglandin F2α receptor agonist, and into 6-(nitrooxy)-hexanoic acid, a NO-donating moiety.

The topline results of the phase 3 trial were presented at AGS 2023.[4] The results of a secondary analysis of this large, multi-regional trial to evaluate the proportion of subjects with at least a 10mmHg reduction from baseline will be presented here.

AIM

The purpose of this phase 3 clinical trial was to compare the safety and IOP-lowering efficacy of NCX 470 ophthalmic solution vs latanoprost ophthalmic solution in adult subjects with open-angle glaucoma or ocular hypertension.

In this analysis, we evaluated the proportion of subjects with substantial IOP reduction (≥ 10 mmHg).

METHOD

This trial was a randomized, double-masked, multi-center, parallel group trial conducted at 56 sites in the United States and one site in China.

- Subjects dosed NCX 470 0.1% or latanoprost 0.005% once daily in the evening for 3 months
- Subjects were evaluated at 8AM, 10AM, 4PM at Week 2, Week 6 and Month 3.
- The primary efficacy objective was to demonstrate non-inferiority to latanoprost in mean IOP from baseline at each visit in the 3-month study.
- This analysis is an evaluation of the proportion of subjects with substantial IOP reduction (≥ 10 mm Hg).

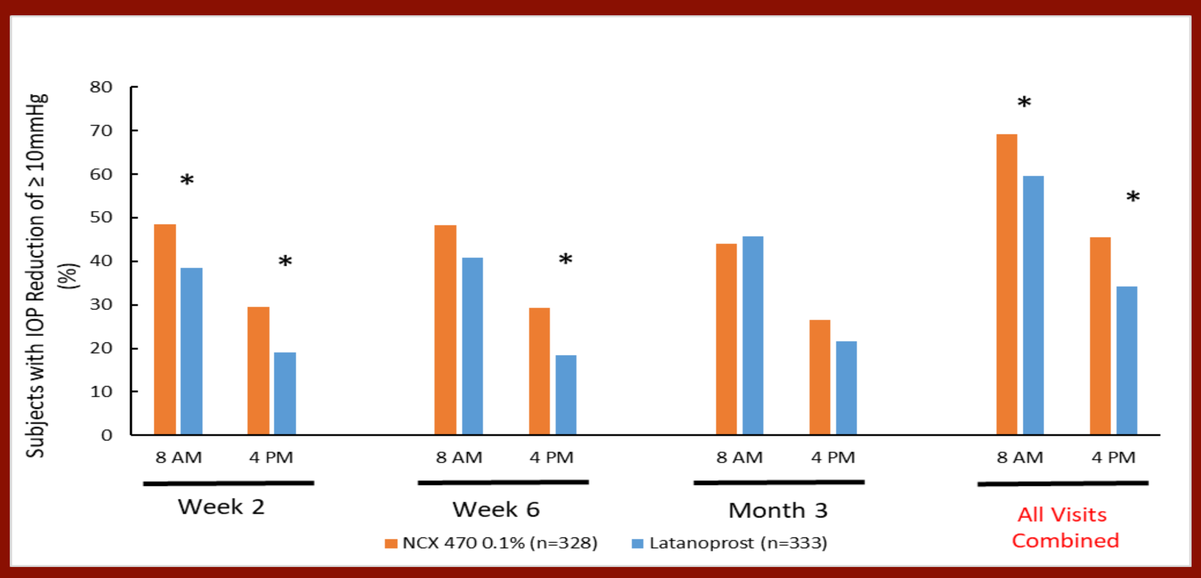
RESULTS

In this phase 3 clinical trial, 328 subjects were randomized to NCX 470 0.1% and 333 to latanoprost 0.005%. NCX 470 met the primary efficacy endpoint of non-inferiority to latanoprost at all 9 of 9 timepoints. When evaluating the proportion of subjects demonstrating a 10 mmHg or more reduction from baseline, NCX 470 demonstrated a statistically greater proportion when Week 2, Week 6, and Month 3 visits are combined ranging from 69% to 46% in the NCX 470 group compared to 60% to 34% in the latanoprost group. NCX 470 was safe and well tolerated; the most common adverse event (AE) was ocular hyperemia in 11.9% of the NCX 470 subjects vs. 3.3% of latanoprost subjects.

There were no ocular serious AEs and no treatment related non-ocular serious AEs.

Proportion of Subjects Achieving Time-Matched IOP Reduction from Baseline of ≥ 10 mmHg

(Observed Data from 8AM and 4PM) Intent-to-Treat Population)



Subject Demographics (ITT Population)	NCX 470 0.1% (N=328)	Latanoprost 0.005% (N=333)
Age (years)		
n	328	333
Mean (SD)	63.6 (10.12)	62.7 (11.73)
Age Categories (years), n (%)		
>= 18 to < 65	168 (51.2%)	174 (52.3%)
>= 65	160 (48.8%)	159 (47.7%)
>= 75	40 (12.2%)	46 (13.8%)
Sex, n (%)		
Male	128 (39.0%)	145 (43.5%)
Female	200 (61.0%)	188 (56.5%)
Race, n (%)		
Black or African American	110 (33.5%)	109 (32.7%)
White	212 (64.6%)	216 (64.9%)
Other	6 (1.8%)	8 (2.4%)
Ethnicity, n (%)		
Hispanic or Latino	59 (18.0%)	67 (20.1%)
Not Hispanic or Latino	267 (81.4%)	265 (79.6%)
Not Reported	2 (0.6%)	1 (0.3%)
Baseline IOP (mmHg)		
8AM - Mean (SD)	28.28 (2.000)	28.22 (2.011)
4PM - Mean (SD)	25.52 (2.455)	25.40 (2.422)

Note: Age is calculated using the following equation: Age=(Informed Consent Date-Date of Birth)/365.25

		NCX 470 0.1% (n=328) %	Latanoprost (n=333) %	p-value
Week 2	8 AM	48.50	38.40	0.0114
	4 PM	29.40	19.10	0.0024
Week 6	8 AM	48.30	40.90	0.0667
	4 PM	29.30	18.50	0.0015
Month 3	8 AM	43.90	45.70	0.6891
	4 PM	26.50	21.60	0.1617
Combined All Visits	8 AM	69.10	59.60	0.0114
	4 PM	45.60	34.30	0.0038

CONCLUSIONS

The study met its primary endpoint of demonstrating non-inferiority to latanoprost at all timepoints. A statistically greater proportion of subjects dosed with NCX 470 demonstrated at least a 10 mmHg reduction from baseline, compared to latanoprost. NCX 470 was well tolerated with only 4.3% of subjects in the NCX 470 arm vs 5.1% in the latanoprost arm discontinuing the trial. The most common adverse event was ocular hyperemia.

In the large phase 3 Mont Blanc trial, NCX 470 achieved its primary efficacy endpoint of non-inferiority to latanoprost and may provide ≥ 10 mmHg of IOP reduction more frequently than latanoprost. NCX 470 was safe and well tolerated and may provide an additional treatment option for glaucoma patients.

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