NCX 470, a Nitric Oxide Donating Bimatoprost, Demonstrates Non-inferiority to Latanoprost in Phase 3 Mont Blanc Clinical Trial

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Purpose: 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.

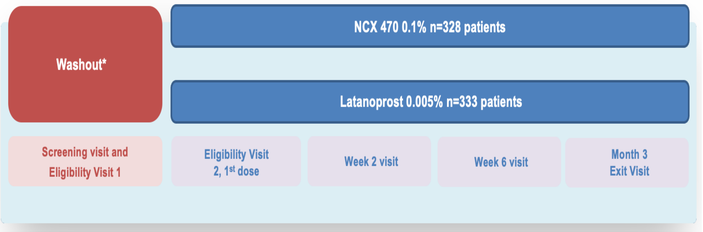
Methods: The trial was a randomized, double-masked, multi-center, parallel group trial with an initial adaptive dose selection phase in which the higher dose, NCX 470 0.1%, was chosen for further evaluation.

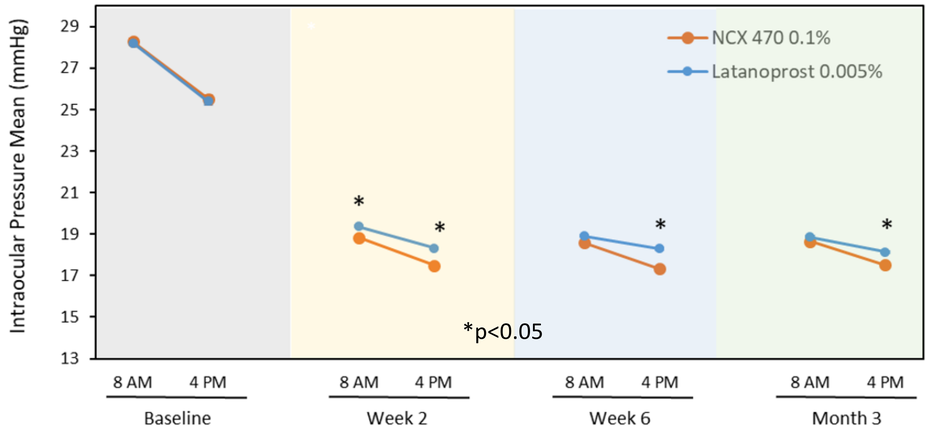
Medications were dosed once daily in the evening for 3 months.

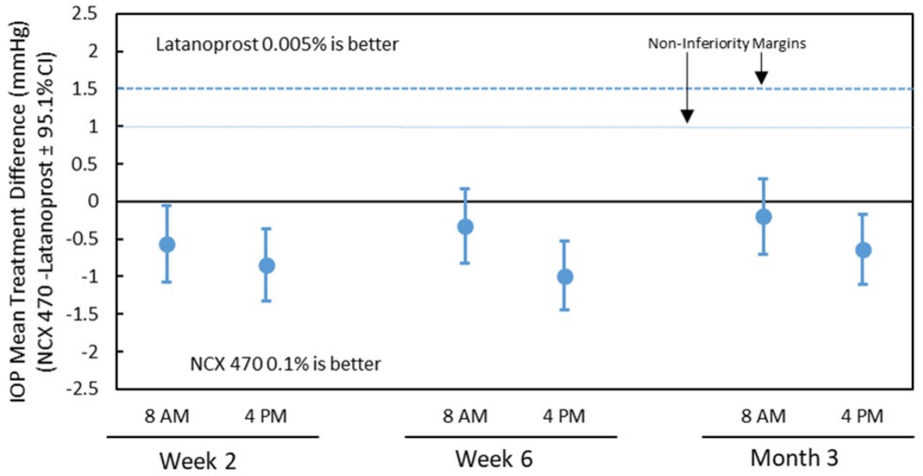
Evaluated at 8AM and 4PM at week 2, week 6 and month 3.

Efficacy was based on mean IOP reduction from baseline at the 8AM and 4PM timepoints at week 2, week 6 and month 3.

The primary efficacy objective was to demonstrate non-inferiority, and the secondary objective was to demonstrate superiority to latanoprost.







Baseline Characteristics, Demographics and Disposition

	NCX 470 0.1% N = 328	Latanoprost 0.005% N = 333
Mean Diurnal Baseline (8am+4pm) IOP, mmHg, Study Eye (SD)	26.90 (2.04)	26.81 (2.02)
Gender, n (%)		
Female	200 (61.0%)	188 (56.5%)
Male	128 (39.0%)	145 (43.5%)
Age, Years (SD)	63.6 (10.12)	62.7 (11.73)
Discontinued Prior to Study Completion	14 (4.3%)	17 (5.1%)
Reasons for Discontinuation		
Adverse Event	8 (57.1%)	6 (35.3%)
Lost to Follow-up	1 (7.1%)	4 (23.5%)
Physician Decision	0	0
Sponsor or IRB Decision	1 (7.1%)	2 (11.8%)
Protocol Violation	0	1 (5.9%)
Withdrawal by Subject	3 (21.4%)	3 (17.6%)
IOP greater than 36 mmHg	0	0
Other	1 (7.1%)	1 (5.9%)

Adverse Events

	NCX 470 0.1% N = 327 n (%)	Latanoprost 0.005% N = 330 n (%)
Eye Disorders		
Ocular hyperemia	39 (11.9%)	11 (3.3%)
Conjunctival hyperemia	36 (11.0%)	7 (2.1%)
Eye pruritus	17 (5.2%)	6 (1.8%)
Eye irritation	8 (2.4%)	4 (1.2%)
Punctate keratitis	8 (2.4%)	6 (1.8%)
Dry eye	5 (1.5%)	4 (1.2%)
Eye pain	4 (1.2%)	4 (1.2%)
Growth of eyelashes	5 (1.5%)	0
Eyelids pruritus	4 (1.2%)	0
General Disorders and Administration Site Conditions		
Instillation site pain	20 (6.1%)	8 (2.4%)

Results: NCX 470 met the primary efficacy endpoint of non-inferiority to latanoprost. The IOP-lowering from baseline ranged from 8.0 to 9.7 mmHg for NCX 470 and 7.1 to 9.4 mmHg for latanoprost.

IOP reductions for NCX 470 were numerically greater than those for latanoprost at all 6 timepoints, and statistically significant ($p<0.049$) at 4 of the 6 timepoints. The secondary superiority endpoint required statistically significant results at all 6 time points, and this was not achieved.

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.

Conclusion:

NCX 470 0.1% demonstrated non-inferiority to latanoprost for reduction from baseline in time-matched IOP. While NCX 470 was statistically superior to latanoprost at 4 of 6 timepoints, it did not meet the secondary study endpoint of superiority over latanoprost at all 6 timepoints.

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.