Eyelid Application of NCX 4251 for Treatment of Signs and Symptoms of Dry Eye Disease

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INTRODUCTION

NCX 4251 is a proprietary ophthalmic suspension of fluticasone propionate nanocrystals being developed by Nicox for the treatment of signs and symptoms of dry eye disease. NCX 4251 is delivered by topical application to the eyelids with the convenience of once daily (QD) administration.

Dry eye disease is a multifactorial inflammatory condition that affects a large segment of the adult population worldwide. Symptoms of dry eye disease include eye dryness and ocular discomfort, burning, itchiness, gritty feeling in the eyes, contact lens intolerance, and photophobia that impair the performance of common vision-related activities such as reading, driving, and performing activities involving video terminal displays. Dry eye disease is a chronic condition that frequently exacerbates spontaneously, or is triggered by physiological, environmental, or life-style conditions that require a safe and efficacious treatment with a fast onset of action to restore ocular surface protection and lubrication. The eyelid plays a key role in maintaining a healthy ocular surface. Inflammation of the eyelids and alteration of their physiological and protective functions is an important contributor to the manifestation of signs and symptoms of dry eye disease and blepharitis (including meibomian gland dysfunction).

METHODS

A total of 224 subjects with a documented history of blepharitis and exhibiting an acute exacerbation of blepharitis in both eyes (based on minimum scores for eyelid redness, eyelid debris and eyelid discomfort at the Screening and Baseline Visits) were randomized in a 1:1 ratio to NCX 4251 or placebo (vehicle of NCX 4251). Subjects performed daily lid scrubs with dilute baby shampoo and administered NCX 4251 or its vehicle directly to the eyelids and eyelid margins with an applicator once daily for 14 days, followed by an additional 14 days of lid scrubs only. Signs and symptoms of blepharitis and dry eye, as well as safety parameters were assessed. A post hoc analysis was performed on a subgroup of subjects (123 of the 224 subjects, 61 on placebo and 62 on NCX 4251) with baseline scores ≥2.0 on a scale of 0 (none) to 4 (severe) for inferior cornea fluorescein staining. The results of this post hoc analysis are reported here.

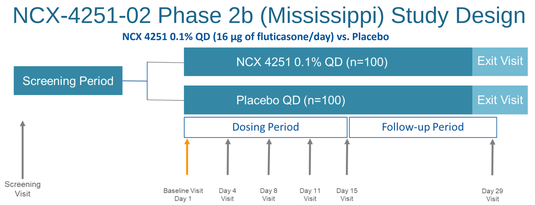
DEMOGRAPHICS AND DISPOSITION

		NCX 4251 (0.1%) QD N = 111	Placebo QD N = 113
Gender, n (%)	Female	75 (67.6%)	67 (59.3%)
	Male	36 (32.4%)	46 (40.7%)
Age, years (SD)		61.4 (13.75)	63.2 (14.31)
Race, n (%)			
White		84 (75.7%)	87 (77.0%)
American Indian or Alaska Native		0	0
Asian		1 (0.9%)	2 (1.8%)
Black or African American		26 (23.4%)	21 (18.6%)
Multi-Race		0	3 (2.7%)
Ethnicity, n (%)	Hispanic or Latino	5 (4.5%)	8 (7.1%)
	Not Hispanic or Latino	106 (95.5%)	105 (92.9%)
Completed the Study		109 (98.2%)	112 (99.1%)
Discontinued Prior to Study Completion		2 (1.8%)	1 (0.9%)
Reasons for Discontinuation	Lack of compliance	1	1
	Lost to follow up	1	0

PURPOSE

To describe a post hoc analysis of signs and symptoms of dry eye disease from a prospective, randomized, double-masked Phase 2b clinical trial (NCX-4251-02, 'Mississippi'; NCT04675242) that evaluated the safety and efficacy of NCX 4251 (fluticasone propionate ophthalmic suspension) 0.1% in subjects with mild to moderate signs and symptoms of dry eye and blepharitis.

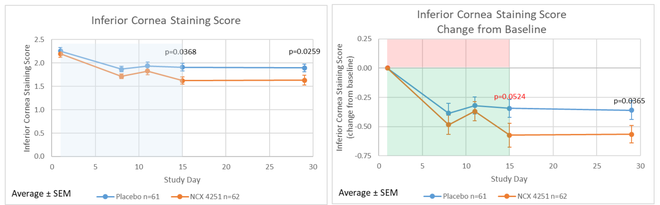
STUDY DESIGN



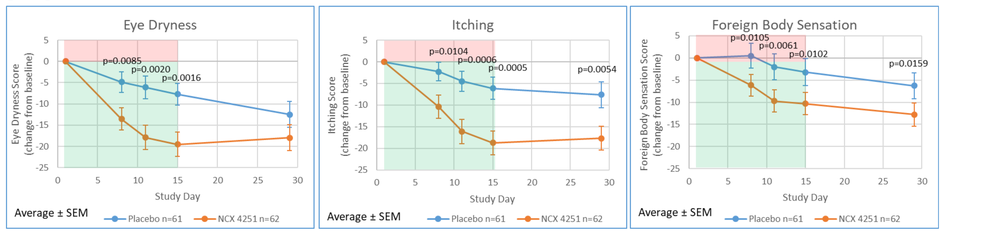
RESULTS

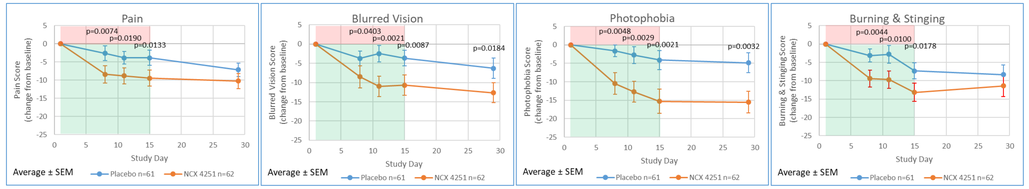
Sign

Inferior Cornea Fluorescein Staining



Symptoms*





* Symptom scores were evaluated using a Visual Analog Scale (VAS) where 0 corresponds to "no discomfort" and 100 corresponds to "maximal discomfort."

Change from Baseline at Day 15 in Symptom VAS Scores

Symptom	Treatment Effect NCX 4251 - Placebo	95% CI	p-value[1]
Eye Dryness	-12.3	(-19.8, -4.7)	**0.0016**
Itching*	-13.0	(-20.2, -5.8)	**0.0005**
Foreign Body Sensation*	-9.8	(-17.2, -2.4)	**0.0102**
Pain	-7.4	(-13.2, -1.6)	**0.0133**
Blurred Vision*	-8.6	(-15.0, -2.2)	**0.0087**
Photophobia*	-12.0	(-19.5, -4.5)	**0.0021**
Burning and Stinging	-7.6	(-13.9, -1.3)	**0.0178**

* = For these symptoms, statistically significant effect of NCX 4251 was also observed at Day 29 (two weeks after the end of treatment)
1 = p-value for treatment effect in ANCOVA using baseline VAS as a covariate

Safety

NCX 4251 was safe and well tolerated

- Only 3 subjects (out of 224) discontinued the study, ***none*** due to an AE
- Most AEs were mild in severity
- No elevations in IOP of 10 mmHg or higher were observed in the NCX 4251 treatment arm
- No treatment-related systemic effects were observed

Treatment-Emergent Adverse Events

	NCX 4251 0.1% QD (N=111)		Placebo QD (N=113)	
System Organ Class (SOC) Preferred Term (PT)	Events, n	Subjects, n (%)	Events, n	Subjects, n (%)
Eye Disorders				
Visual Acuity Reduced	1	1 (0.9%)	2	2 (1.8%)
Eye Pruritus	1	1 (0.9%)	1	1 (0.9%)
Vitreous Detachment	1	1 (0.9%)	1	1 (0.9%)
Conjunctival Haemorrhage	0	0	1	1 (0.9%)
Conjunctival Hyperaemia	2	1 (0.9%)	0	0
Eyelid Irritation	0	0	1	1 (0.9%)
Eyelids Pruritus	1	1 (0.9%)	0	0
Vision Blurred	0	0	1	1 (0.9%)
General Disorders and Administration Site Conditions				
Instillation Site Pain	1	1 (0.9%)	5	5 (4.4%)
Instillation Site Oedema	0	0	1	1 (0.9%)

CONCLUSIONS

NCX 4251 Ophthalmic Suspension, 0.1% was safe and well tolerated. Once daily eyelid administration of NCX 4251 for 14 days produced statistically significant improvements vs. placebo in all dry eye symptoms evaluated in this study at all time points during drug administration. For some symptoms significant improvements persisted for up to 14 days after treatment. Improvement of inferior cornea staining approached statistical significance (p=0.0524) vs placebo. NCX 4251 could prove useful for exacerbation or flares of dry eye and as a bridge for slow onset chronic treatments, and warrants further clinical investigation.

Commercial Relationships Disclosure:
G. Foulks, University of Louisville (C); A. C. Kothe, Silver Pharma Consulting (C);
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