Sponsor

Alcon Research, Ltd.

Generic Drug Name

Travoprost/timolol maleate

Trial Indications

Open-angle glaucoma or ocular hypertension

Protocol Number

C-09-007

Protocol Title

An Evaluation of Patient Reported Outcomes and Ocular Surface Health in Patients Using DuoTrav APS Eye Drops Solution Versus XALACOM® Eye Drops Solution

Clinical Trial Phase

Phase III

Study Start/End Dates

22 March 2010 / 13 May 2011

Reason for Termination

Not applicable

Study Design/Methodology

The design was parallel group, multicenter, double masked, randomized, active control.

C-09-007 was originally designed to use Ocular Surface Disease Index (OSDI) scores to evaluate DuoTrav APS and XALACOM in patients with open-angle glaucoma or ocular hypertension. The protocol was amended to use the National Eye Institute Visual Function Questionnaire (NEI VFQ-25) to assess changes in visual acuity that can occur due to the effects of preservative on the cornea.

Centers

Subjects were recruited from 39 investigational sites located in Argentina (4), Austria (1), Australia (4), Belgium (1), Brazil (6), France (6), Hungary (1), Italy (2), Israel (2), the Netherlands (1), Portugal (1), Taiwan (4), Thailand (3), and the United Kingdom (3).

Objectives

The primary objective was to understand differences in visual function-related patient-reported outcomes, between a non-benzalkonium chloride (BAK) medication (DuoTrav APS) and a BAK-preserved medication (XALACOM) as measured by the National Eye Institute Visual Function Questionnaire (NEI VFQ-25) in patients with open-angle glaucoma or ocular hypertension.

Test Product, Dose, and Mode of Administration

Test Product: DuoTrav APS (travoprost 40 micrograms/ml /timolol 5 mg/ml) Eye Drops, Solution
Dose: 1 drop in the study eye(s) once daily
Mode of Administration: Topical ocular

Reference Product: XALACOM (latanoprost 50 micrograms/ml /timolol 5 mg/ml) Eye Drops, Solution
Dose: 1 drop in the study eye(s) once daily
Mode of Administration: Topical ocular

Statistical Methods

The primary efficacy variable, mean NEI VFQ-25 composite (Visual Function) score at the end of the treatment period (Day 90), was summarized by treatment group. A two-sample t-test was used to test for differences between treatments in the mean scores.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

- Patients ≥ 18 years of age

- Must have a clinical diagnosis of open-angle glaucoma (with or without pseudoexfoliation or pigment dispersion component), or ocular hypertension in at least one eye.
- Must be willing and able to discontinue use of any topical ocular medication other than the study medication for the duration of the study.
- Must have had IOP controlled with mono-therapy using XALACOM for at least 1 continuous month prior to Visit 1.
- Women of childbearing potential must meet all specific conditions at Visit 1

Exclusion criteria:

- Any abnormality preventing reliable applanation tonometry in the study eye(s).
- Presence of any ocular pathology in either eye seen during the slit lamp or fundus exams that may preclude the safe administration of test article or safe participation in this study.
- Dry eye or KCS which has been, or is currently being, treated with the use of punctal plugs, punctal cautery, Restasis®, or topical ocular corticosteroids.
- Patients who have undergone keratorefractive ocular laser procedures, corneal surgery or surgery to the corneal surface, within 1 year prior to Visit1
- Any other ocular laser surgery in either eye within 3 months
- Patients who have undergone intraocular or extra-ocular surgery, in either eye, within 6 months prior to Visit 1.
- History of other progressive retinal or optic nerve disease.
- Severe central visual field loss in either eye based upon the clinical judgment of the investigator.
- Any history of, or current evidence of, infectious or inflammatory ocular conditions
- Ocular trauma within 6 months prior to Visit 1 in either eye, as determined by patient history and/or examination.
- History or evidence of corneal transplant or transplant variant procedures
- Patients with suspected or diagnosed Sjogren's syndrome.
- History of or current bronchial asthma, or severe chronic obstructive pulmonary disease
- History of or current severe, unstable or uncontrolled cardiovascular, hepatic, or renal disease.
- History of spontaneous or current hypoglycemia or uncontrolled diabetes.
- History of or current severe allergic rhinitis and bronchial hyper reactivity.

- Intolerance/hypersensitivity to any component of the medication
- Use of any systemic medications on a chronic basis that have not been on a stable dosing regimen for at least 30 days prior to Visit 1, or an anticipated change in dosing regimen of medications during the course of the study.
- Use of ocular medications other than XALACOM® within 7 days
- Use of corticosteroids within 30 days of Visit 1, or any anticipated use of corticosteroids during the course of the study.
- Use of contact lenses within 30 days of Visit 1. Concomitant use of contact lenses is also excluded for the duration of the study.

Participant Flow Table

	DuoTrav APS	XALACOM
Started	119	121
Safety Analysis Set	119	121
Intent-to-treat (ITT) Analysis Set	109	110
Completed	108	109
Discontinued	11	12
Reason for discontinued		
Adverse event	3	4
Lost to follow-up	1	0
Patient's decision unrelated to an adverse event	2	0

	DuoTrav APS	XALACOM
Noncompliance	1	1
Protocol violation	3	3
Reason not specified	1	4

Baseline Characteristics

Gender Demographic Statistics for ITT Population

Gender	DuoTrav APS	XALACOM
Male	49	46
Female	60	64

Categorical Age Demographic Statistics for ITT Population

Age	DuoTrav APS	XALACOM
<65	44	37
≥65	65	73

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Summary of Efficacy

Primary Outcome Measure

Descriptive Statistics for NEI VFQ-25 Composite Score by Treatment and Day

(ITT Data)

Day		DuoTrav APS	XALACOM	p-value*
Day 0 (Baseline)	N	109	110	0.465
	Mean	86.3	87.4	
	SD	11.9	10.6	
	(Min, Max)	(41, 100)	(50, 100)	
	95% CI	(84.1, 88.6)	(85.4, 89.4)	
Day 90 (Exit Visit)	N	108	109	0.194
	Mean	88.1	86.3	
	SD	9.7	11.3	
	(Min, Max)	(48, 100)	(51, 100)	
	95% CI	(86.3, 90.0)	(84.1, 88.4)	

SD = Standard Deviation
CI = Confidence Interval
*Two-sample t-test
VFQ-25 has 25 items with scores that range from 0 (worst possible score) to 100 (best possible score). VFQ-25 subscales are derived from the 25 items: general

vision, ocular pain, near activities, distance activities, social functioning, mental health, role difficulties, dependency, driving, color vision, and peripheral vision. Items within each subscale are averaged together to create the 12 subscale scores. VFQ-25 Composite Score is calculated by averaging ocular pain, near activities, distance activities, social functioning, mental health, role difficulties, dependency, driving, color vision, and peripheral vision subscale scores. VFQ-25 Composite Score ranges from 0 (worst possible score) to 100 (best possible score).

Secondary Outcome Measures

None reported.

Summary of Safety

Serious Adverse Events

Six participants had a serious adverse event: 3 in the DuoTrav APS group and 3 in the XALACOM group.

All Adverse Events by System Organ Class

	DuoTrav APS N = 119		**XALACOM N = 121**	
	N	%	N	%
RELATED				
Eye disorders				
Dry eye	4	3.4	2	1.7
Eye irritation	1	0.8	5	4.1
Ocular discomfort	1	0.8	2	1.7
Conjunctival hyperaemia	1	0.8	1	0.8

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	DuoTrav APS N = 119		XALACOM N = 121	
	N	%	N	%
Erythema of eyelid	1	0.8		
Eyelids pruritus	1	0.8		
Foreign body sensation in eyes	1	0.8		
Lacrimation increased	1	0.8		
Punctate keratitis	1	0.8		
Eye pruritus			2	1.7
Conjunctivitis			1	0.8
Skin and subcutaneous tissue disorders				
Skin discolouration			1	0.8
NOT RELATED				
Blood and lymphatic system disorders				
Anaemia			1	0.8
Ear and labyrinth disorders				

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	DuoTrav APS N = 119		XALACOM N = 121	
	N	%	N	%
Vertigo	1	0.8	1	0.8
Eye disorders				
Vision blurred	3	2.5	1	0.8
Dry eye	2	1.7	1	0.8
Eye discharge	2	1.7	1	0.8
Eye pain	2	1.7	1	0.8
Cataract	1	0.8	1	0.8
Eye irritation	1	0.8	1	0.8
Blepharitis	1	0.8		
Conjunctivitis	1	0.8		
Lacrimation increased	1	0.8		
Ocular hyperaemia	1	0.8		
Photophobia	1	0.8		

	DuoTrav APS N = 119		XALACOM N = 121	
	N	%	N	%
Visual acuity reduced	1	0.8		
Punctate keratitis			2	1.7
Abnormal sensation in eye			1	0.8
Eye swelling			1	0.8
Keratitis interstitial			1	0.8
Macular degeneration			1	0.8
Retinal degeneration			1	0.8
Gastrointestinal disorders				
Gastritis	1	0.8		
Haematochezia	1	0.8		
Diarrhoea			1	0.8
Gastritis erosive			1	0.8
Infections and infestations				

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	DuoTrav APS N = 119		XALACOM N = 121	
	N	%	N	%
Influenza	4	3.4	1	0.8
Cellulitis	1	0.8		
Sinusitis	1	0.8		
Nasopharyngitis			1	0.8
Urinary tract infection			1	0.8
Injury, poisoning and procedural complications				
Injury	1	0.8	1	0.8
Foreign body in eye			1	0.8
Musculoskeletal and connective tissue disorders				
Myalgia			1	0.8
Osteoarthritis			1	0.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Hepatic neoplasm	1	0.8		

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	DuoTrav APS N = 119		XALACOM N = 121	
	N	%	N	%
Nervous system disorders				
Headache	1	0.8	2	1.7
Psychiatric disorders				
Depression			1	0.8
Respiratory, thoracic and mediastinal disorders				
Cough	1	0.8		
Skin and subcutaneous tissue disorders				
Skin hyperpigmentation	1	0.8	1	0.8
Pruritus	1	0.8		
Surgical and medical procedures				
Aortic valve replacement			1	0.8
Vascular disorders				
Hypertension			1	0.8

Other Relevant Findings

No other relevant findings to disclose.

Date of Clinical Trial Report

10-May-2012