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Sponsor

Alcon Research, Ltd.

Generic Drug Name

Travoprost/timolol maleate fixed combination

Trial Indication(s)

Ocular Hypertension and Primary Open-Angle Glaucoma

Protocol Number

CMS-06-12

Protocol Title

Safety and Efficacy of Switching to the Travoprost/Timolol Maleate Fixed Combination (DuoTrav®) from prior Mono- or Two-drug Therapy in Germany

Clinical Trial Phase

Phase IV

Study Start/End Dates

31-August-2007 / 17-December-2008

Reason for Termination (if applicable)

Not Applicable

Study Design/Methodology

This was a prospective, open-label, observational cohort study.

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Centers

Subjects were recruited from 22 investigational sites located in Germany.

Objectives

The primary objective was to assess the safety and efficacy of switching to Travoprost/Timolol Maleate Fixed Combination (TTFC) from other mono- or two-drug (fixed or unfixed combinations) therapies.

Test Product (s), Dose(s), and Mode(s) of Administration

Test Product: Travoprost 0.004% / timolol maleate 0.5% fixed combination (TTFC)
Dose: One drop in study eye(s) once daily in the evening (at 8:00 PM) for 12 weeks
Mode of Administration: Topical ocular

Statistical Methods

The primary efficacy variable, the change in intraocular pressure between travoprost and TTFC, was analyzed by a paired t test within a one-way ANOVA test. The patient's participation in the trial was considered a success if they adequately tolerated study therapy and demonstrated a further reduction in intraocular pressure (≥ 1 mm Hg) from Visit 1.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

- Meets protocol-specified criteria for qualification and contraception
- Voluntarily consents to participate and provides written informed consent prior to any protocol-specific procedures

Exclusion criteria:

- Use of medications outside protocol-specified parameters
- Signs, symptoms or history of any condition that, per protocol or in the opinion of the investigator, might compromise:
  1. the safety or well-being of the participant or study staff
  2. the safety or well-being of the participant's offspring (such as through or breast-feeding)
  3. the analysis of results

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Participant Flow Table

	Overall Participants
Started	522
Intent-to-treat (ITT) Analysis Set	522
Per Protocol (PP) Analysis Set	474
Completed	474
Discontinued	48
Reason for discontinued	
Lack of efficacy	1
Adverse event	19
Lost to follow-up	1
Non-compliance	2
Withdrawal of consent	6
Protocol deviation	20

Baseline Characteristics

Gender Demographic Statistics for ITT Population

Gender	Overall participants
Male	204
Female	318

Categorical Age Demographic Statistics for ITT Population

Age	Overall participants
≤55	70
56-65	123
66-75	196
≥76	133

Summary of Efficacy

Significant decreases in intraocular pressure were observed for all prior treatments. Intraocular pressure decreased between Day 0 and Week 4 visits; there was also a slight decrease between Week 4 and Month 3 visits. Overall, 485 (92.9%) subjects were considered a treatment success after they switched to DuoTrav.

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Primary Outcome Result(s)

Change in Intraocular Pressure from Baseline for Participants with Prior Travoprost Therapy
Time Frame: Baseline to Visit 3 (12 weeks)

Units: mmHg

	N	Baseline Mean (SD)	Visit 3 Mean (SD)	Change from baseline at Visit 3	P-value
Intent to Treat Population	51	22.1 (2.36)	16.2 (2.52)	5.9 (2.73)	<0.001
Per Protocol Population	45	22.1 (2.48)	15.8 (2.30)	6.3 (2.52)	<0.001

Secondary Outcome Result(s)

None reported.

Summary of Safety

Among the ITT population, there were 93 (17.8%) subjects with at least one adverse event. Of those, 15 (2.9%) were severe; the remaining 78 were either mild or moderate. The most frequently experienced adverse event was ocular hyperemia, with 37 (7.0%) instances.

Safety Results

Serious Adverse Events

	N=522
SAE Description	N
Kidney stones	1
Dizziness leading to hospitalization	1
Fractured arm	1

Other Adverse Events

	N=522
AE Description	N
Ocular hyperemia	21
Conjunctival hyperemia	16
Ocular itching	13
Ocular burning	12
Decreased visual acuity	6

Burning	5
Headache	5
Watering eyes	5
Conjunctivitis	4
Ocular pain	4
Burning on instillation	3
Foreign body sensation	3
Insomnia	3
Ocular dryness	3
Photosensitivity	3
Vertigo	3
Lid redness	2
Ocular irritation	2
Shortness of breath	2
Skin lesion	2
Systemic hypertension	2

Anxiety climbing stairs	1
Blepharitis	1
Bradycardia	1
Cardiac palpitations	1
Cataract	1
Chalazion	1
Change in blood pressure	1
Conjunctival hyperemia	1
Conjunctival inflammation	1
Cough	1
Dry neck	1
Fatigue	1
Feeling hot	1
Feeling of pressure around heart	1
Gastritis	1
Heart Palpitations	1

Herpes – lip	1
Inferior periocular hyperpigmentation	1
Joint pain	1
Knee pain (left)	1
Lower lid redness	1
Lump in throat	1
Nausea after dosing	1
Numb fingertips	1
Ocular discharge	1
Ocular discomfort after dosing	1
Ocular dryness (in A.M.)	1
Ocular fatigue	1
Ocular pressure	1
Petichiae on head and forehead	1
Reduction in visual acuity	1
Scratchy eyes (in A.M.)	1

Swollen eyelids	1
Systemic itching	1
Taste alteration	1
Taste alteration (after dosing)	1
Unexplained weakness while visiting Dentist	1

Other Relevant Findings

There are no other relevant findings to disclose.

Date of Clinical Trial Report

22-December-2009