Sponsor

Alcon Research, Ltd.

Generic Drug Name

Brinzolamide/timolol maleate fixed combination (BTFC)

Trial Indication(s)

Open-angle glaucoma
Ocular hypertension

Protocol Number

SMA-08-22

Protocol Title

The Efficacy and Safety of Adding the Brinzolamide/Timolol Maleate Fixed Combination to Prostaglandin Monotherapy

Clinical Trial Phase

Phase IV

Study Start/End Dates

10 July 2009 to 27 August 2010

Reason for Termination (if applicable)

Not applicable

Study Design/Methodology

This was a prospective, open-label, historical-controlled study of the efficacy and safety of adding BTFC to an existing prostaglandin monotherapy regimen for the reduction of intraocular pressure (IOP) in adult patients with open-angle glaucoma or ocular hypertension for whom monotherapy provided insufficient IOP reduction.

Centers

Subjects were recruited from 5 investigational sites located in Germany.

Objectives

The primary objective of this study was to assess the safety and efficacy of adding BTFC to prostaglandin monotherapy

Test Product, Dose, and Mode of Administration

Test product: Brinzolamide/timolol maleate fixed combination
Dose: 1 drop in the study eye(s) instilled 2 times daily
Mode of administration: Topical ocular

Statistical Methods

The efficacy results were based upon the intent to treat (ITT) population which included all participants enrolled in the study. The differences in IOP between Visit 1 and Visit 3 in the overall patient population (primary endpoint) and within the subgroups by diagnosis, prostaglandin brand, and prescribed dosing regimen (secondary endpoints) were analyzed using paired *t*-tests within 1-way analysis of variance (ANOVA) models.

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 breast-feeding)
  3. the analysis of results

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Participant Flow Table

Disposition of Patients

	N = 47 n (%)
Informed consent	47 (100.0%)
PP population	47 (100.0%)
ITT population	47 (100.0%)
Safety population	47 (100.0%)
Inclusion criteria (all true)	47 (100.0%)
Exclusion criteria (all false)	47 (100.0%)
Withdrawals (Lost to follow up)	0 (0.0%)

All participants completed the study.

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Baseline Characteristics

Demographics (ITT)

		N = 47 n (%)
Gender	Female	31 (66.0)
	Male	16 (34.0)
Race of Patient	Caucasian	47 (100.0)
Age (years)	≤ 55	8 (17.0)
	56-65	15 (31.9)
	66-75	16 (34.0)
	≥ 76	8 (17.0)

Summary of Efficacy

In this study, 47 patients were enrolled and completed the study. All 47 patients were evaluated for efficacy within the ITT analysis set and for safety within the safety analysis set. The mean IOP decreased significantly, from 22.1 mmHg at Visit 1 to 16.7 mmHg at Visit 3 ($P<0.001$), resulting in an additional 24.4% reduction in IOP from baseline after the addition of BTFC to prostaglandin monotherapy.

Primary Outcome Result

Change in Intraocular Pressure from Visit 1 to Visit 3
Time Frame: Visit 1 to Visit 3
Units: mmHg

Intraocular Pressure (Both Eyes) by Visit (ITT)

	Visit 1 (Day 0)	Visit 2 (Week 4)	Visit 3 (Week 12/Early Exit)	*P* value[a]
N	47	47	47	
Mean (SD)	22.1 (2.0)	16.7 (2.7)	16.7 (2.6)	< .001
Median	22.0	17.5	17.0	
(Q1, Q3)	(21.0, 23.0)	(14.5, 18.5)	(15.0, 19.0)	
(Min, Max)	(14.5, 26.5)	(11.0, 22.5)	(11.5, 21.5)	
SE	0.3	0.4	0.4	
95% CI	(21.5, 22.7)	(15.9, 17.5)	(15.9, 17.5)	

Secondary Outcome Result(s)

None reported.

Summary of Safety

Six patients reported a total of 17 adverse events (AEs). Of these, 1 patient experienced a serious AE (gastroenteropathy); the investigator judged this event as not related to study medication. None of the AEs resulted in patient discontinuation from the study.

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Safety Results

All Adverse Events by System Organ Class

Adverse Events by Diagnosis

Diagnosis	Verbatim Description of Adverse Event	N = 47	
		Number of Events (%)	Number of Patients (%)
Any		17 (100.0)	6 (12.8)
Primary open-angle glaucoma	Any	15 (88.2)	5 (10.6)
	bitter taste	3 (17.6)	3 (6.4)
	blurred vision	2 (11.8)	2 (4.3)
	burning	2 (11.8)	2 (4.3)
	burning eyes	1 (5.9)	1 (2.1)
	conjunctiva hyperemia	1 (5.9)	1 (2.1)
	conjunctiva: hyperemia	1 (5.9)	1 (2.1)
	dry eye feeling	1 (5.9)	1 (2.1)
	gastroenteropathy	1 (5.9)	1 (2.1)
	glued eyes	1 (5.9)	1 (2.1)
	headache, hot flash, vertigo, anxiety state, subjective dyspnoe	1 (5.9)	1 (2.1)
	rash under the eye	1 (5.9)	1 (2.1)
Ocular hypertension	Any	2 (11.8)	1 (2.1)
	beginning chalazion upper lid	1 (5.9)	1 (2.1)
	Helicobacter pylori infection	1 (5.9)	1 (2.1)

Other Relevant Findings

There are no other relevant findings to disclose.

Date of Clinical Trial Report

27 September 2011