## Sponsor

Alcon Research, Ltd.

## Generic Drug Name

Brinzolamide 10 mg/ml + Timolol 5 mg/ml Eye Drops, Suspension

## Trial Indication(s)

Open-angle glaucoma or ocular hypertension

## Protocol Number

C-05-10

## Protocol Title

Comparison of Safety and Efficacy of Brinzolamide/Timolol Fixed Combination vs COSOPT® in Patients with Open-Angle Glaucoma or Ocular Hypertension

## Clinical Trial Phase

Phase 3

## Study Start/End Dates

October 24, 2005 to August 30, 2007

## Reason for Termination (if applicable)

Not Applicable

## Study Design/Methodology

This was a multi-center, randomized, parallel group, double-masked, active controlled trial.

## Centers

Subjects were recruited from 45 investigational sites located in Australia (5), Belgium (2), France (2), Italy (1), Latvia (2), Lithuania (1), Singapore (2), Sweden (1), Taiwan (1), United Kingdom (2), and the United States (26).

## Objectives

The primary objective of this study was to compare the safety and IOP-lowering efficacy of Brinzolamide 10 mg/ml + Timolol 5 mg/ml Eye Drops, Suspension to COSOPT in patients with open-angle glaucoma or ocular hypertension.

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

**Test Product:** Brinzolamide 10 mg/ml + Timolol 5 mg/ml Eye Drops, Suspension
Dose: One drop in the study eye(s) twice-daily at 8:00 AM and at 8:00 PM
Mode of Administration: Topical ocular

**Reference Product:** COSOPT (Dorzolamide 20 mg/ml + Timolol 5 mg/ml Eye Drops, Solution)
Dose: One drop in the study eye(s) twice-daily at 8:00 AM and at 8:00 PM
Mode of Administration: Topical ocular

## Statistical Methods

The primary analysis involved comparisons of Brinzolamide 10 mg/ml + Timolol 5 mg/ml Eye Drops, Suspension versus COSOPT at each time point at the Month 6 visit. Primary inference for the test of non-inferiority was based on the per protocol data set.

## Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

- 18 years of age or older
- Diagnosis of open-angle glaucoma or ocular hypertension
- Other protocol-defined inclusion criteria may apply

Exclusion criteria:

- Under 18

- Pregnant
- Other protocol-defined exclusion criteria may apply

## Participant Flow Table

**Patient Status**
**(All Patients Enrolled)**

| | Brinzolamide/Timolol | COSOPT | Total |
|---|---|---|---|
| | N | N | N |
| Started | 220 | 217 | 437 |
| Completed | 204 | 189 | 393 |
| Discontinued | 16 | 28 | 44 |
| *Reasons for Discontinuation* | | | |
| Inadequate control of IOP | 5 | 5 | 10 |
| Adverse Event | 8 | 13 | 21 |
| Decision Unrelated to an Adverse Event | 1 | 2 | 3 |
| Lost to Follow-Up | 2 | 2 | 4 |
| Non-Compliance | 0 | 1 | 1 |
| Other | 0 | 5 | 5 |

Brinzolamide/Timolol = Brinzolamide 10 mg/ml + Timolol 5 mg/ml Eye Drops, Suspension
COSOPT = Dorzolamide 20 mg/ml + Timolol 5 mg/ml Eye Drops, Solution

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## Baseline Characteristics

**Demographic Statistics by Treatment Group (Per Protocol Data)**

| | Total | | Brinzolamide/Timolol | | COSOPT | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| Total | 419 | 100.0 | 218 | 100.0 | 201 | 100.0 |
| **Age (years)** | | | | | | |
| 18 to 64 | 192 | 45.8 | 91 | 41.7 | 101 | 50.2 |
| 65 to 74 | 152 | 67.0 | 82 | 64.6 | 70 | 70.0 |
| 75 to 84 | 68 | 30.0 | 42 | 33.1 | 26 | 26.0 |
| 85 to 95 | 7 | 3.1 | 3 | 2.4 | 4 | 4.0 |
| **Sex** | | | | | | |
| Male | 174 | 41.5 | 95 | 43.6 | 79 | 39.3 |
| Female | 245 | 58.5 | 123 | 56.4 | 122 | 60.7 |

Brinzolamide/Timolol = Brinzolamide 10 mg/ml + Timolol 5 mg/ml Eye Drops, Suspension
COSOPT = Dorzolamide 20 mg/ml / Timolol 5 mg/ml Eye Drops, Solution

## Summary of Efficacy

## Primary Outcome Measure

**Comparison of Mean IOP (mmHg)**
**(Per Protocol Data)**
**Brinzolamide/Timolol versus COSOPT**

| | | Brinzolamide/Timolol | | COSOPT | | Difference | P-value | Upper 95% CI | Lower 95% CI |
|---|---|---|---|---|---|---|---|---|---|
| | | Mean | N | Mean | N | | | | |
| Month 6 | 8AM | 18.5 | 205 | 18.9 | 181 | -0.5 | 0.2235 | 0.3 | -1.2 |
| | 10AM | 17.1 | 204 | 17.2 | 181 | -0.1 | 0.7512 | 0.6 | -0.8 |
| | 4PM | 17.3 | 200 | 17.2 | 180 | 0.1 | 0.7014 | 0.9 | -0.6 |

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CI=Confidence Interval
Estimates based on least squares means using repeated measures analysis of variance
P-values and confidence intervals were based on repeated measures analysis of variance.

## Secondary Outcome Measures

None reported.

## Summary of Safety

## Serious Adverse Events

| Serious Adverse Event | Brinzolamide/ Timolol Affected (2)/ At Risk (220) | COSOPT Affected (1)/ At Risk (217) | Fatal? | Attributable to study drug? |
|---|---|---|---|---|
| Renal cell carcinoma | 1 | 0 | Yes | No |
| Death from unknown cause | 1 | 0 | Yes | No |

| | | | | |
|---|---|---|---|---|
| Serious adverse drug reaction | 0 | 1 | No | Yes |

## Other Adverse Events by System Organ Class

**All Adverse Drug Reactions**
**(Overall Safety Population)**

| Coded Adverse Event | Brinzolamide/ Timolol (N=220) | | COSOPT (N =217) | |
|---|---|---|---|---|
| | N | % | N | % |
| Immune System disorders | | | | |
| Hypersensitivity | 0 | 0.0 | 2 | 0.9 |
| Psychiatric disorders | | | | |
| Insomnia | 1 | 0.5 | 0 | 0.0 |
| Nervous system disorders | | | | |
| Dysgeusia | 7 | 3.2 | 6 | 2.8 |
| Headache | 0 | 0.0 | 2 | 0.9 |
| Eye disorders | | | | |
| Blurred vision | 8 | 3.6 | 1 | 0.5 |
| Eye irritation | 6 | 2.7 | 23 | 10.6 |

| | | | | |
|---|---|---|---|---|
| Eye pain | 6 | 2.7 | 14 | 6.5 |
| Foreign body sensation in eyes | 3 | 1.4 | 1 | 0.5 |
| Eye discharge | 2 | 0.9 | 0 | 0.0 |
| Ocular hyperaemia | 1 | 0.5 | 3 | 1.4 |
| Blepharitis | 1 | 0.5 | 1 | 0.5 |
| Blepharitis allergic | 1 | 0.5 | 1 | 0.5 |
| Eye pruritus | 1 | 0.5 | 1 | 0.5 |
| Eyelid margin crusting | 1 | 0.5 | 1 | 0.5 |
| Abnormal sensation in eye | 1 | 0.5 | 0 | 0.0 |
| Anterior chamber flare | 1 | 0.5 | 0 | 0.0 |
| Asthenopia | 1 | 0.5 | 0 | 0.0 |
| Conjunctival hyperaemia | 1 | 0.5 | 0 | 0.0 |
| Conjunctivitis allergic | 1 | 0.5 | 0 | 0.0 |
| Corneal erosion | 1 | 0.5 | 0 | 0.0 |
| Dry eye | 1 | 0.5 | 0 | 0.0 |

| | | | | |
|---|---|---|---|---|
| Erythema of eyelid | 1 | 0.5 | 0 | 0.0 |
| Eyelids pruritus | 1 | 0.5 | 0 | 0.0 |
| Conjunctival follicles | 0 | 0.0 | 1 | 0.5 |
| Lacrimation increased | 0 | 0.0 | 1 | 0.5 |
| Photophobia | 0 | 0.0 | 1 | 0.5 |
| Cardiac disorders | | | | |
| Bradycardia | 0 | 0.0 | 1 | 0.5 |
| Respiratory, thoracic, and mediastinal disorders | | | | |
| Cough | 1 | 0.5 | 0 | 0.0 |
| Rhinorrhoea | 1 | 0.5 | 0 | 0.0 |
| Orthopnoea | 0 | 0.0 | 1 | 0.5 |
| Skin and subcutaneous tissue disorders | | | | |
| Hair disorder | 1 | 0.5 | 0 | 0.0 |
| Lichen planus | 1 | 0.5 | 0 | 0.0 |
| Investigations | | | | |

| | | | | |
|---|---|---|---|---|
| Heart rate decreased | 0 | 0.0 | 2 | 0.9 |
| Blood pressure decreased | 0 | 0.0 | 1 | 0.5 |
| Corneal staining | 0 | 0.0 | 1 | 0.5 |

Coded Adverse Event = MedDRA Preferred Term (version 10.0) presented by System Organ Class.
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## Other Relevant Findings

No other relevant findings to disclose.

## Date of Clinical Trial Report

20 November 2007