Sponsor

ALCON ITALIA S.P.A.

Generic Drug Name

TRAVOPROST

Trial Indication(s)

Reducing high pressure in patient with ocular hypertension or open-angle glaucoma

Protocol Number

IT-04-01

Protocol Title

Hypotonic efficacy and tolerability of Travoprost in patient with open angle primary glaucoma and/or ocular hypertension, not controlled with dorzolamide + timolol treatment in fixed association, or intolerant to it

Clinical Trial Phase

Phase IV

Study Start/End Dates

FPFV: 1-August-2005

LPLV: 26-March-2007

Reason for Termination (if applicable)

The sponsor decided to interrupt the study at 59 patients instead of the 80 originally foreseen by the protocol due to the difficulties in patient recruitment.

Study Design/Methodology

This was a Phase IV, multicenter, non-controlled, single group study

Centers

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Objective

The primary objective of this study was to confirm efficacy of Travoprost on intraocular pressure (IOP) by evaluation of the variation versus base level 3 months after beginning of the therapy

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

Travoprost 40 micrograms/ml eye drops solution

1 drop of Travoprost in the eye every night for 3 months

Statistical Methods

Usual descriptive statistical analysis

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

1. Written informed consent
2. Males and female age $\geq$ 30 years
3. IOP not adequately controlled by treatment with dorzolamide + timolol fixed combination ($\geq$ 19 mmHg) or intolerance to the combination
4. Diagnosis of open angle primary glaucoma (MD $\leq$ 10 dB) or intraocular pressure (IOP $\geq$ 19 mmHg), never treated with prostaglandin analogues
5. Visual acuity (best corrected) $\geq$ 20/200
6. Patients wearing contact lenses need to remove the lenses prior to the instillation of the drug and not wear them for the following 15 minutes
7. Possibility to adhere to the treatment and to the protocol

Exclusion criteria:

1. Secondary hypertension
2. Diagnosis of open angle primary glaucoma with MD > 10 dB
3. Previous surgeries on the eye, included cataract surgery, during 3 months prior to the beginning of the study

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4. Trabeculoplasty with argon laser during 3 months prior to the beginning of the study
5. Hypersensitivity to the product in study
6. Patients with positive anamnesis for keratitis herpetica, uveitis, chronic ocular inflammation or corneal ulcer to both eyes
7. Positive anamnesis for the presence of other ocular abnormalities or for symptoms that, according to the investigator, could prevent the patient's participation to the study
8. Variation of the therapy with medicine potentially interfering with IOP (sympathomimetic, alfa and beta adrenergic blockers, alfa agonists, calcium channel blockers, ACE-inhibitors) during 30 days prior to the beginning of the study or during the study
9. Pregnant women, lactating women or potentially fertile women not using adequate contraceptive methods.
10. Participation to a clinical study during the previous month

Subject disposition

59 subjects were enrolled in the study

Demographics

		Patients (N=58)
Age (years)	Average (SD)	66.93 (9.59)
	Min – Max	34 – 85
Sex	Male – N(%)	26 (44.83%)
	Female – N(%)	32 (55.17%)
Etnicity	Caucasian – N(%)	58 (100.00%)

Summary of Efficacy:

IOP* (mmHg): descriptive statistics per visit of the 3 daily measures
Intent-to-treat population

	Visit 1 - Baseline			**Visit 2 – 45 days**			**Visit 3 – 90 days**		
	10:00	**12:00**	**16:00**	**10:00**	**12:00**	**16:00**	**10:00**	**12:00**	**16:00**
N	57	57	57	57	57	57	57	57	57
Average	21.01	20.74	19.90	18.29	18.17	17.54	18.22	17.97	17.30
SD	2.32	2.20	2.42	2.40	2.45	2.31	2.53	2.22	2.14

*IOP: mean value of the 3 measurements made at each time

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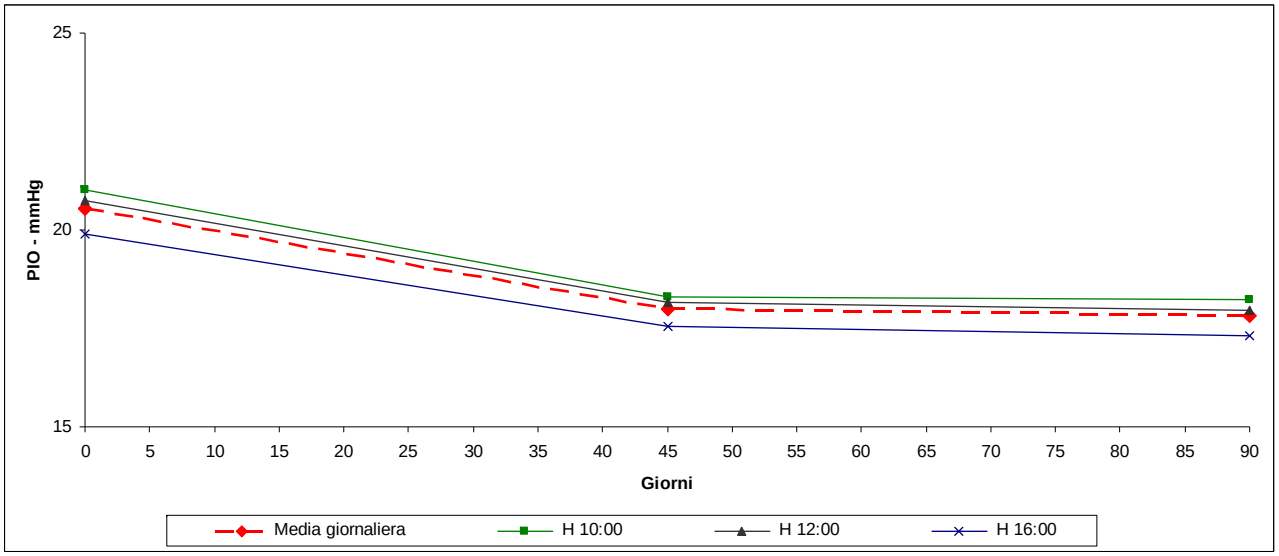
Average IOP (mmHg): descriptive statistics per visit and variation with respect to the baseline
Intent-to-treat population

	Average	SD	Lim. inf. – Lim. sup.		p-value
Baseline	20.55	2.06			
45 days	18.00	2.23			
90 days	17.83	2.15			
Delta – 45 days vs baseline	-2.55	2.51	-3.22	-1.89	<.0001
Delta – 90 days vs baseline	-2.72	2.64			<.0001
Delta % – 45 days vs baseline	-11.89	11.63			
Delta % – 90 days vs baseline	-12.63	12.17			

IOP variation – Popolazione
Intent-to-treat population



Summary of Safety:

The drug did not cause alterations of the visual acuity levels. No alterations detected by lamp test and ophthalmoscopic examination.

Serious Adverse Events by System Organ Class

One Serious Adverse Event was reported (laryngeal cancer) and believed not to be correlated to the drug under study.

Other Adverse Events by System Organ Class

Number of patients with adverse events per SOC e PT – Safety population

Adverse event - MedDRA v8.1 **System Organ Class** **Preferred Term**	**Patient (N=58)**	
	N	**%**
Cardiac disorders	1	1.72%
Extrasystoles	1	1.72%
Ear and labyrinth disorders	1	1.72%
Vertigo	1	1.72%
Eye disorders	6	10.34%
Conjunctival haemorrhage	1	1.72%
Conjunctival hyperaemia	2	3.45%
Conjunctivitis	1	1.72%
Eye pruritus	2	3.45%
Ocular hyperaemia	1	1.72%
Visual acuity reduced	1	1.72%
Gastrointestinal disorders	1	1.72%
Dyspepsia	1	1.72%
Infections and infestations	1	1.72%
Gastroenteritis	1	1.72%
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	1.72%

Adverse event - MedDRA v8.1 System Organ Class Preferred Term	Patient (N=58)	
	N	%
Laryngeal cancer	1	1.72%
Psychiatric disorders	1	1.72%
Insomnia	1	1.72%
Reproductive system and breast disorders	1	1.72%
Benign prostatic hyperplasia	1	1.72%

Other Relevant Findings

There are no other relevant findings to disclose.

Date of Clinical Trial Report

1-October-2007