Sponsor

ALCON ITALIA S.P.A.

Generic Drug Name

TRAVOPROST

Trial Indication(s)

Elevated intraocular pressure reduction in patient with ocular hypertension or open angle glaucoma

Protocol Number

IT-04-03

Protocol Title

Hypotonic efficacy and tolerability of Travoprost in patient with glaucoma or ocular hypertension, monotherapy or fixed association beta-blocking not controlled or intolerant

Clinical Trial Phase

Phase IV

Study Start/End Dates

FPFV: 10-January-2006
LPLV: 26-March-2007

Reason for Termination (if applicable)

The sponsor decided to interrupt the study at 129 patients instead of the 300 originally foreseen by the protocol due to the difficulties in patient's recruitment.

Study Design/Methodology

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

Centers

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Objectives

Primary 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. Age 20 - 80 years
3. Simple chronic glaucoma (including pigmentary glaucoma, pseudoexfoliation glaucoma) or ocular hypertension
4. Presence of perimeter defects compatible with glaucoma detected by Humphrey SITA 24-2 test
5. Therapy with beta-blockers used for at least one month in monotherapy or in fixed combination which show side effects, low compliance for the double daily administration and/or IOP $\geq$ 19 mmHg
6. Patients wearing contact lenses available 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. Patients not controlled under treatment with beta-blockers in fixed combination with prostaglandins
2. Secondary hypertension
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

129 subjects were enrolled in the study

Demographics

		Patients (N=126)
Age (years)	Average (DS)	64.65 (9.64)
	Min – Max	23 – 81
Sex	Male – N(%)	65 (51.59%)
	Female – N(%)	61 (48.41%)
Ethnicity	Caucasian – N(%)	125 (99.21%)
	Asian – N(%)	1 (0.79%)

Summary of Efficacy:

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

	Visit 1 - Baseline			**Visit 2 – 30 days**			**Visit 3 – 90 days**		
	10:00	**12:00**	**16:00**	**10:00**	**12:00**	**16:00**	**10:00**	**12:00**	**16:00**
N	122	122	121	122	122	122	116	115	115
Average	21.34	21.35	21.46	16.20	16.02	15.59	15.81	15.64	15.32
SD	3.11	3.15	2.98	2.89	2.92	2.76	2.61	2.66	2.58

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IOP (mmHg): descriptive statistics per visit of the 3 daily measures
Per-Protocol population

	Visit 1 - Baseline			Visit 2 – 30 days			Visit 3 – 90 days		
	10:00	**12:00**	**16:00**	**10:00**	**12:00**	**16:00**	**10:00**	**12:00**	**16:00**
N	111	111	111	111	111	111	111	110	110
Average	21.24	21.29	21.32	16.07	15.94	15.49	15.74	15.55	15.25
DS	2.74	2.53	2.44	2.59	2.66	2.40	2.60	2.65	2.59

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

LOCF	**Average**	**SD**	**Lim. inf. – Lim. sup.**		**p-value**
Baseline	21.38	2.79	20.88	21.88	
30 days	15.94	2.69	15.46	16.42	
90 days	15.73	2.81	15.23	16.24	
Delta – 30 days vs baseline	-5.44	2.64	-5.92	-4.97	<0.0001
Delta – 90 days vs baseline	-5.64	2.86	-6.16	-5.13	<0.0001
Delta % – 30 days vs baseline	-25.09	10.94	-27.05	-23.12	
Delta % – 90 days vs baseline	-25.98	11.96	-28.12	-23.83	

Average IOP (mmHg): descriptive statistics per visit and variation vs baseline
Per-Protocol population

	Average	**SD**	**Lim. inf. – Lim. sup.**		**p-value**
Baseline	21.28	2.25	20.86	21.71	
30 days	15.83	2.37	15.39	16.28	
90 days	15.52	2.44	15.06	15.98	
Delta – 30 days vs baseline	-5.45	2.69	-5.96	-4.94	<0.0001
Delta – 90 days vs baseline	-5.76	2.83	-6.30	-5.23	<0.0001
Delta % – 30 days vs baseline	-25.19	11.25	-27.31	-23.07	
Delta % – 90 days vs baseline	-26.63	11.81	-28.85	-24.41	

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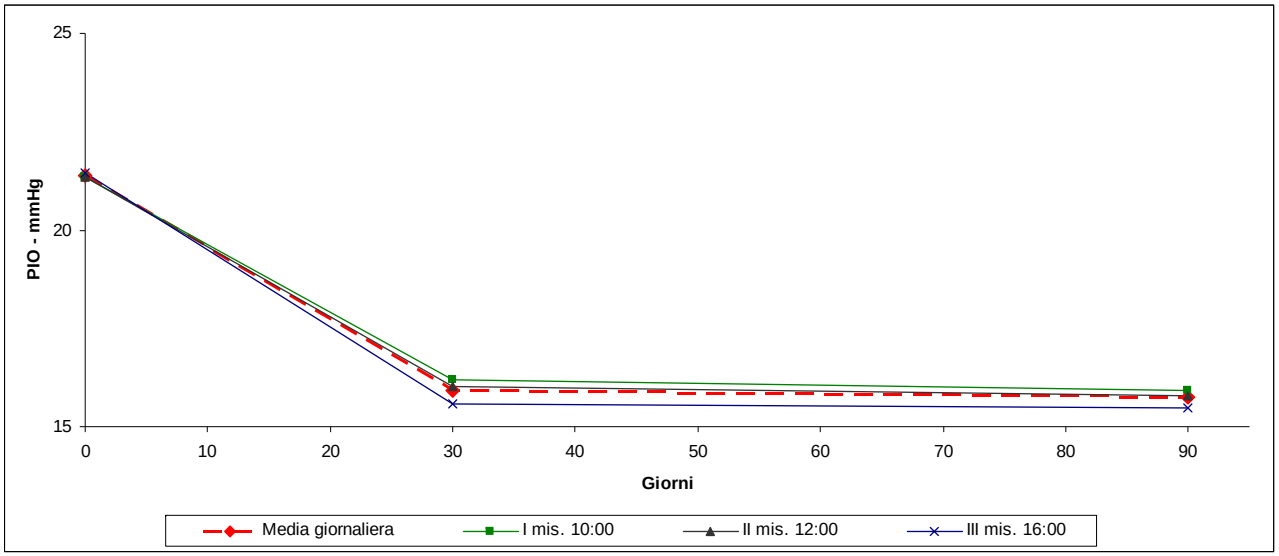
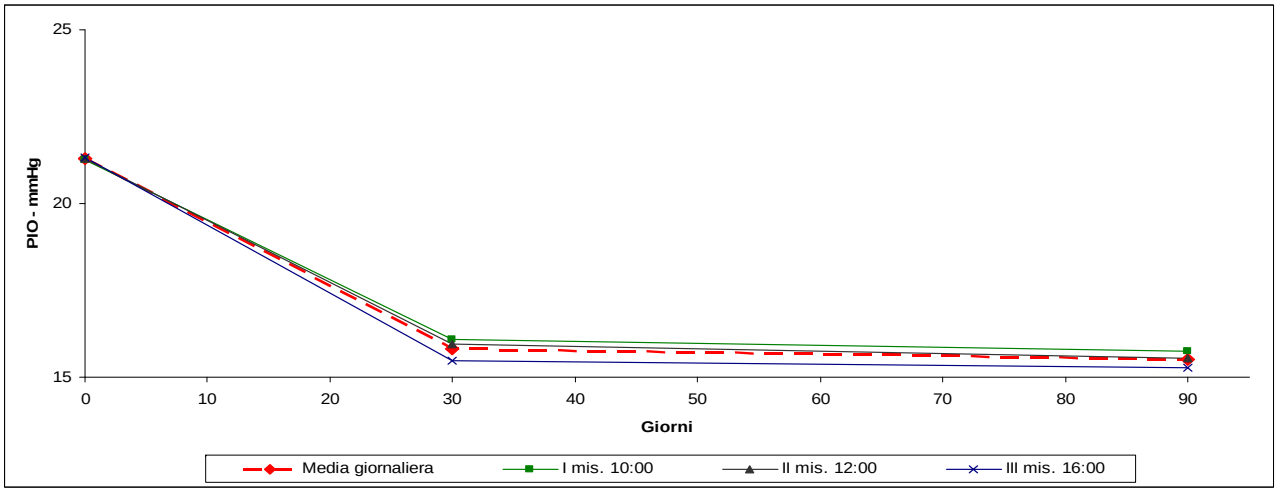
IOP – Intent-to-treat population



IOP – Per-Protocol population



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Summary of Safety:

Serious Adverse Events by System Organ Class

No serious adverse events were reported

Other Adverse Events by System Organ Class

Number of patients with adverse events per SOC and PT

Adverse event - MedDRA v8.1 **System Organ Class** **Preferred Term**	**Patients (N=126)**	
	N	**%**
Eye disorders	*16*	*12.70%*
Cataract	2	1.59%
Conjunctival hyperaemia	1	0.79%
Eye irritation	2	1.59%
Eye pruritus	1	0.79%
Foreign body sensation in eyes	2	1.59%
Lacrimation increased	4	3.17%
Ocular hyperaemia	9	7.14%
Vision blurred	2	1.59%
Visual disturbance	1	0.79%
Infections and infestations	1	*0.79%*
Conjunctivitis viral	1	0.79%
Nervous system disorders	1	*0.79%*
Syncope	1	0.79%
Respiratory, thoracic and mediastinal disorders	1	*0.79%*
Respiratory failure	1	0.79%
Skin and subcutaneous tissue disorders	2	*1.59%*
Hypertrichosis	1	0.79%
Pruritus	1	0.79%

Adverse event - MedDRA v8.1 System Organ Class Preferred Term	Patients (N=126)	
	N	%
Surgical and medical procedures	*1*	*0.79%*
Inguinal hernia repair	1	0.79%

Other Relevant Findings

There are no other relevant findings to disclose.

Date of Clinical Trial Report

11-September-2007