Clinical trial results:
A 3 Month, Multicenter, Double-Masked Safety and Efficacy Study of Travoprost Ophthalmic Solution, 0.004% Compared to Timolol (0.5% or 0.25%) in Pediatric Glaucoma Patients

Summary

EudraCT number	2012-001324-34
Trial protocol	BE GB PL DE PT NL ES
Global end of trial date	25 March 2014

Results information

Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	C-12-008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01664039
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alcon Research, Ltd.
Sponsor organisation address	6201 S. Freeway, Fort Worth, Texas, United States, 76134
Public contact	Head, Pharma, GCRA, Alcon Research, Ltd. , +1 888-451-3937, alcon.medinfo@alcon.com
Scientific contact	Head, Pharma, GCRA, Alcon Research, Ltd., +1 888-451-3937, alcon.medinfo@alcon.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001271-PIP01-12
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 March 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 March 2014
Global end of trial reached?	Yes
Global end of trial date	25 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to demonstrate that the IOP-lowering efficacy of Travoprost Ophthalmic Solution, 0.004% (preserved with POLYQUAD) is noninferior to Timolol Ophthalmic Solution (0.5% or 0.25%) in pediatric glaucoma patients.

Protection of trial subjects:

Prior to the start of the study, the study protocol, the informed consent and assent documents, patient instruction sheets, the Investigator's Brochure, as well as any advertising materials used to recruit patients were submitted to institutional review boards (IRBs) and independent ethics committees (IECs). The IRB/IECs reviewed all documents and approved required documents; copies of the approval letters were provided to Alcon. Consistent with both the IRB/IEC's requirements and all applicable regulations, the Investigators periodically provided study updates to the IRB/IEC. A patient or parent/legal guardian (if necessary, a legally authorized representative) provided informed consent, and children signed an approved assent form when appropriate. This study was conducted in accordance with Good Clinical Practices (GCP) and the ethical principles that have their origins in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 September 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United States: 67
Country: Number of subjects enrolled	Colombia: 35
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Saudi Arabia: 3
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Romania: 15
Country: Number of subjects enrolled	Philippines: 10
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	United Kingdom: 4

Worldwide total number of subjects	152
EEA total number of subjects	31

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	10
Children (2-11 years)	85
Adolescents (12-17 years)	57
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients in this study were enrolled across 38 investigational centers in the United States, Germany, Singapore, United Kingdom, Taiwan, Philippines, Spain, Saudi Arabia, Columbia, France, Portugal, Belgium, Poland, Romania, Puerto Rico, and Mexico.

Pre-assignment

Screening details:

Of the 184 enrolled, 32 participants were exited as screen failures prior to randomization. This reporting group includes all randomized participants (152).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Travoprost

Arm description:

1 drop administered in each eye in the evening with Travoprost vehicle in the morning for 3 months

Arm type	Experimental
Investigational medicinal product name	Travoprost 40 µg/mL Eye Drops, Solution preserved with POLYQUAD (PQ)
Investigational medicinal product code	
Other name	Travoprost PQ
Pharmaceutical forms	Eye drops
Routes of administration	Topical use

Dosage and administration details:

Travoprost 40 µg/mL Eye Drops, solution preserved with POLYQUAD, 1 drop instilled in each eye, once daily in the evening for 3 months

Arm title	Timolol

Arm description:

1 drop administered in each eye twice daily (once in the morning and once in the evening) for 3 months

Arm type	Active comparator
Investigational medicinal product name	Timolol eye drops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Topical use

Dosage and administration details:

One drop instilled in each eye, twice daily (morning and evening)

Number of subjects in period 1	Travoprost	Timolol
Started	77	75
Completed	71	74
Not completed	6	1
Treatment failure	5	1
Inadequate IOP control	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Travoprost
Reporting group description:	
1 drop administered in each eye in the evening with Travoprost vehicle in the morning for 3 months	
Reporting group title	Timolol
Reporting group description:	
1 drop administered in each eye twice daily (once in the morning and once in the evening) for 3 months	

Reporting group values	Travoprost	Timolol	Total
Number of subjects	77	75	152
Age categorical			
Units: Subjects			
2 months to <3 years	10	6	16
3 to <12 years	40	39	79
12 to <18 years	27	30	57
Age continuous			
Units: years			
arithmetic mean	9.2	10	
standard deviation	± 4.8	± 4.58	-
Gender categorical			
This analysis population includes all patients who received study drug and completed at least 1 scheduled on-therapy visit.			
Units: Subjects			
Female	40	40	80
Male	37	35	72

End points

End points reporting groups

Reporting group title	Travoprost
Reporting group description:	
1 drop administered in each eye in the evening with Travoprost vehicle in the morning for 3 months	
Reporting group title	Timolol
Reporting group description:	
1 drop administered in each eye twice daily (once in the morning and once in the evening) for 3 months	

Primary: Mean Change from Baseline in IOP at Month 3

End point title	Mean Change from Baseline in IOP at Month 3
End point description:	
IOP (fluid pressure inside the eye) was assessed using a calibrated tonometer and measured in millimeters of mercury (mmHg). A higher IOP can be a greater risk factor for developing glaucoma or glaucoma progression (leading to optic nerve damage). One eye from each participant was chosen as the study eye and only the study eye was used for analysis.	
End point type	Primary
End point timeframe:	
Baseline (Day 0), Month 3	

End point values	Travoprost	Timolol		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71[1]	74[2]		
Units: mmHg				
arithmetic mean (standard error)	-5.4 (± 0.98)	-5.3 (± 0.93)		

Notes:

[1] - Observed cases only.

[2] - Observed cases only.

Statistical analyses

Statistical analysis title	Comparison of Mean IOP Change from Base at Month 3
Statistical analysis description:	
Treatment differences in mean IOP change from baseline were examined with a pairwise test at the Month 3 visit. The pairwise test was based on the least squares means derived from a repeated measures analysis of variance with treatment, visit, primary diagnosis and baseline IOP strata (<27, 27-31, or >31 mmHg) in the model. Non-inferiority of Travoprost 0.004% PQ to Timolol was established if the upper limit of the 95% CI for the difference between treatment groups was less than 3.0 mmHg	
Comparison groups	Travoprost v Timolol
Number of subjects included in analysis	145
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.1

Confidence interval	
level	Other: 0.05 %
sides	2-sided
lower limit	-1.5
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.72

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected for the duration of the study (1 year, 6 months). An AE was defined as any untoward medical occurrence in a patient who is administered a study medication, regardless of causal relationship with the medication.

Adverse event reporting additional description:

All AEs were obtained as solicited comments from patients and as observations by the study Investigator as outlined in the study protocol. This analysis population includes all randomized participants.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Travoprost

Reporting group description:

All participants who received travoprost with vehicle

Reporting group title	Timolol

Reporting group description:

All participants who received timolol

Serious adverse events	Travoprost	Timolol	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 77 (0.00%)	2 / 75 (2.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Keratitis bacterial			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Travoprost	Timolol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 77 (28.57%)	6 / 75 (8.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 77 (6.49%)	2 / 75 (2.67%)	
occurrences (all)	7	3	
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	15 / 77 (19.48%)	3 / 75 (4.00%)	
occurrences (all)	18	3	
Growth of eyelashes			
subjects affected / exposed	5 / 77 (6.49%)	0 / 75 (0.00%)	
occurrences (all)	5	0	
Conjunctival hyperaemia			
subjects affected / exposed	4 / 77 (5.19%)	1 / 75 (1.33%)	
occurrences (all)	4	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported