Clinical trial results:
An Open-Label, Pharmacokinetic and Safety Study of Travoprost Ophthalmic Solution, 0.004% in Pediatric Glaucoma or Ocular Hypertension Patients

Summary

EudraCT number	2012-001640-22
Trial protocol	GB BE ES FR
Global end of trial date	10 July 2013

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-12-009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01658839
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alcon Research, Ltd.
Sponsor organisation address	6201 South Freeway, Fort Worth, Texas, United States, 76134
Public contact	Head, Pharma, GCRA, Alcon Research, Ltd. , +1 8884513937, alcon.medinfo@alcon.com
Scientific contact	Head, Pharma, GCRA, Alcon Research, Ltd., +1 8884513937, 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	10 July 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 July 2013
Global end of trial reached?	Yes
Global end of trial date	10 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to assess the safety and describe the steady-state plasma pharmacokinetic (PK) profiles of Travoprost ophthalmic solution, 0.004% following a once daily administration for 7 days in pediatric glaucoma or ocular hypertension patients.

Protection of trial subjects:

This study was performed in compliance with the ethical principles of the Declaration of Helsinki and Good Clinical Practice (GCP). A parent/legal guardian (if necessary, a legally authorized representative) provided informed consent, and the child signed an approved assent form when applicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 January 2013
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	Spain: 1
Country: Number of subjects enrolled	United States: 21
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Saudi Arabia: 2
Worldwide total number of subjects	25
EEA total number of subjects	2

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)	4
Children (2-11 years)	9
Adolescents (12-17 years)	12
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 4 investigational centers located in the US, 1 located in France, 1 located in Spain, and 1 located in Saudi Arabia.

Pre-assignment

Screening details:

This reporting group includes all enrolled participants (25).

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Travoprost

Arm description:

Travoprost ophthalmic solution, 0.004%, one drop administered topically in the inferior cul-de-sac of the eye each morning at 9 AM (± 60 minutes) for 7 days

Arm type	Experimental
Investigational medicinal product name	Travatan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Topical use

Dosage and administration details:

One drop administered topically in the inferior cul-de-sac of the eye each morning at 9 AM (± 60 minutes) for 7 days

Number of subjects in period 1	Travoprost
Started	25
Completed	25

Baseline characteristics

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	25	25	
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	4	4	
Children (2-11 years)	9	9	
Adolescents (12-17 years)	12	12	
Age continuous Units: years			
arithmetic mean	9.9		
standard deviation	± 5	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	13	13	

End points

End points reporting groups

Reporting group title	Travoprost

Reporting group description:

Travoprost ophthalmic solution, 0.004%, one drop administered topically in the inferior cul-de-sac of the eye each morning at 9 AM (± 60 minutes) for 7 days

Primary: Maximum Observed Travoprost Free Acid Plasma Concentration (Cmax)

End point title	Maximum Observed Travoprost Free Acid Plasma Concentration (Cmax)[1]

End point description:

Travoprost free acid plasma concentrations at each collection time point (predose, 10, 20, 40, 80 minutes postdose) were quantitated using a high performance liquid chromatography/tandem mass spectrometry method (HPLC/MS/MS). Cmax was calculated for each participant with at least 1 quantifiable time point. Here, n=all participants who received at least 2 doses of the study drug, satisfied protocol required criteria relevant to the assessments of PK parameters, had at least 1 postdose blood draw, and for whom adequate PK data were collected (without collection or analytical deviations that would affect the integrity of the data).

End point type	Primary

End point timeframe:

Day 7, Up to 80 minutes postdose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm study; no control data. No hypothesis testing done. Summaries provided using descriptive statistics.

End point values	Travoprost			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: ng/mL				
arithmetic mean (standard deviation)				
Overall (n=11)	0.0256 (± 0.0158)			
2 mo to < 3 years (n=2)	0.0471 (± 0.0105)			
3 to <12 years (n=6)	0.0258 (± 0.0128)			
12 to <18 years (n=3)	0.0109 (± 0.000046)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Cmax (Tmax)

End point title	Time to Reach Cmax (Tmax)[2]

End point description:

Analyte plasma concentrations at each collection time point (predose, 10, 20, 40, 80 minutes postdose)

were quantitated using a high performance liquid chromatography/tandem mass spectrometry method (HPLC/MS/MS). Tmax was calculated for each participant with at least 1 quantifiable time point. Here, n=all participants who received at least 2 doses of the study drug, satisfied protocol required criteria relevant to the assessments of PK parameters, had at least 1 postdose blood draw, and for whom adequate PK data were collected (without collection or analytical deviations that would affect the integrity of the data).

End point type	Primary

End point timeframe:

Day 7, Up to 80 minutes postdose

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm study; no control data. No hypothesis testing done. Summaries provided using descriptive statistics.

End point values	Travoprost			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: hours				
arithmetic mean (standard deviation)				
Overall (n=11)	0.25 (± 0.15)			
2 mo to <3 years (n=2)	0.26 (± 0.11)			
3 to <12 years (n=6)	0.17 (± 0)			
12 to <18 years (n=3)	0.39 (± 0.26)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to last measurable concentration (Tlast)

End point title	Time to last measurable concentration (Tlast)[3]

End point description:

Analyte plasma concentrations at each collection time point (predose, 10, 20, 40, 80 minutes postdose) were quantitated using a high performance liquid chromatography/tandem mass spectrometry method (HPLC/MS/MS). Tlast was calculated for each participant with at least 1 quantifiable time point. Here, n=all participants who received at least 2 doses of the study drug, satisfied protocol required criteria relevant to the assessments of PK parameters, had at least 1 postdose blood draw, and for whom adequate PK data were collected (without collection or analytical deviations that would affect the integrity of the data).

End point type	Primary

End point timeframe:

Day 7, Up to 80 minutes postdose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm study; no control data. No hypothesis testing done. Summaries provided using descriptive statistics.

End point values	Travoprost			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: hours				
arithmetic mean (standard deviation)				
Overall (n=11)	0.42 (± 0.35)			
2 mo to <3 years (n=2)	0.34 (± 0.01)			
3 to <12 years (n=6)	0.46 (± 0.47)			
12 to <18 years (n=3)	0.39 (± 0.26)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the analyte plasma concentration-time curve to the last quantifiable sampling time point [AUC(0-tlast)]

End point title	Area under the analyte plasma concentration-time curve to the last quantifiable sampling time point [AUC(0-tlast)][4]

End point description:

Analyte plasma concentrations at each collection time point (predose, 10, 20, 40, 80 minutes postdose) were quantitated using a high performance liquid chromatography/tandem mass spectrometry method (HPLC/MS/MS). AUC(0-tlast) was calculated for each participant with at least 2 quantifiable time points. Here, n=all participants who received at least 2 doses of the study drug, satisfied protocol required criteria relevant to the assessments of PK parameters, had at least 1 postdose blood draw, and for whom adequate PK data were collected (without collection or analytical deviations that would affect the integrity of the data).

End point type	Primary

End point timeframe:

Day 7, Up to 80 minutes postdose

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm study; no control data. No hypothesis testing done.Summaries provided using descriptive statistics.

End point values	Travoprost			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng*hr/mL				
arithmetic mean (standard deviation)				
Overall (n=6)	0.0116 (± 0.0099)			
2 mo to <3 years (n=2)	0.0101 (± 0.0014)			
3 to <12 years (n=4)	0.0123 (± 0.0127)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Analyte Plasma Concentration-time Curve Over the Dosing Interval (Inf)[AUC(0-∞)]

End point title	Area Under the Analyte Plasma Concentration-time Curve Over the Dosing Interval (Inf)[AUC(0-∞)][5]

End point description:

Analyte plasma concentrations at each collection time point (predose, 10, 20, 40, 80 minutes postdose) were quantitated using a high performance liquid chromatography/tandem mass spectrometry method (HPLC/MS/MS). AUC(0-∞) was calculated for each participant with at least 3 quantifiable time points. Here, n=all participants who received at least 2 doses of the study drug, satisfied protocol required criteria relevant to the assessments of PK parameters, had at least 1 postdose blood draw, and for whom adequate PK data were collected (without collection or analytical deviations that would affect the integrity of the data). 99999=standard deviation was not estimated.

End point type	Primary

End point timeframe:

Day 7, Up to 80 minutes postdose

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm study; no control data. No hypothesis testing done. Summaries provided using descriptive statistics.

End point values	Travoprost			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: ng*hr/mL				
arithmetic mean (standard deviation)				
Overall (n=1) 3 to <12 years (n=1)	0.0389 (± 99999) 0.0389 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Primary: Half-life (t½)

End point title	Half-life (t½)[6]

End point description:

Analyte plasma concentrations at each collection time point (predose, 10, 20, 40, 80 minutes postdose) were quantitated using a high performance liquid chromatography/tandem mass spectrometry method (HPLC/MS/MS). T½ was calculated for each participant with at least 3 quantifiable time points. Here, n=all participants who received at least 2 doses of the study drug, satisfied protocol required criteria relevant to the assessments of PK parameters, had at least 1 postdose blood draw, and for whom adequate PK data were collected (without collection or analytical deviations that would affect the integrity of the data). 99999=standard deviation was not estimated.

End point type	Primary

End point timeframe:

Day 7, Up to 80 minutes postdose

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm study; no control data. No hypothesis testing done. Summaries provided using

descriptive statistics.

End point values	Travoprost			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: hours				
arithmetic mean (standard deviation)				
Overall (n=1)	0.53 (± 99999)			
3 to <12 years (n=1)	0.53 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events (AEs) were collected for the duration of the study (6 months). This analysis group includes all participants who received study drug.

Adverse event reporting additional description:

An AE is defined as any untoward medical occurrence in a participant who is administered a study medication, regardless of whether or not the event has a causal relationship with the medication. Reports of AEs were obtained as solicited comments from the study participants and as observations by the study Investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Travoprost

Reporting group description:

Travoprost ophthalmic solution, 0.004% (new formulation), one drop administered topically in the inferior cul-de-sac of the eye each morning at 9 AM (± 60 minutes) for 7 days

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No non-serious adverse events occurred above the reporting threshold.

Serious adverse events	Travoprost		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 25 (4.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Trabeculectomy			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Travoprost		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)		

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