Clinical trial results:
A PHASE 1, OPEN-LABEL STUDY OF LATANOPROST ACID PLASMA CONCENTRATIONS IN PEDIATRIC AND ADULT GLAUCOMA SUBJECTS TREATED WITH LATANOPROST 0.005%

Summary

EudraCT number	2008-000844-15
Trial protocol	GB ES PT DK PL IT GR Outside EU/EEA
Global end of trial date	26 March 2009

Results information

Result version number	v1 (current)
This version publication date	13 June 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	A6111139

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00638742
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000011-PIP01-07
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	23 September 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 March 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the steady-state systemic plasma concentrations of latanoprost acid following administration of latanoprost 0.005 percent (%) (1.5 microgram[mcg]) in pediatric and adult subjects with glaucoma or ocular hypertension.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 May 2008
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	Portugal: 3
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	United States: 31
Country: Number of subjects enrolled	South Africa: 3
Worldwide total number of subjects	47
EEA total number of subjects	13

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)	7
Children (2-11 years)	11

Adolescents (12-17 years)	7
Adults (18-64 years)	12
From 65 to 84 years	8
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted at 12 centers in 6 countries between 19 May 2008 to 26 March 2009.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Latanoprost (0 to less than [<] 3 Years)

Arm description:

Subjects aged less than 3 years received latanoprost 0.005% in either one or both eyes.

Arm type	Experimental
Investigational medicinal product name	Latanoprost
Investigational medicinal product code	
Other name	Xalatan
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

One drop (1.5 mcg) of 0.005% latanoprost daily in either one or both eyes for at least 2 weeks.

Arm title	Latanoprost (3 to < 12 years)

Arm description:

Subjects aged 3 to < 12 years received latanoprost 0.005% in either one or both eyes.

Arm type	Experimental
Investigational medicinal product name	Latanoprost
Investigational medicinal product code	
Other name	Xalatan
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

One drop (1.5 mcg) of 0.005% latanoprost daily in either one or both eyes for at least 2 weeks.

Arm title	Latanoprost (12 to < 18 years)

Arm description:

Subjects aged from 12 to < 18 years recieved latanoprost 0.005% daily in either one or both eyes.

Arm type	Experimental
Investigational medicinal product name	Latanoprost
Investigational medicinal product code	
Other name	Xalatan
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

One drop (1.5 mcg) of 0.005% latanoprost daily in either one or both eyes for at least 2 weeks.

Arm title	Latanoprost (greater than or equal to [≥] 18 years)

Arm description:

Subjects aged ≥ 18 years recieved latanoprost 0.005% daily in either one or both eyes.

Arm type	Experimental
Investigational medicinal product name	Latanoprost
Investigational medicinal product code	
Other name	Xalatan
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

One drop (1.5 mcg) of 0.005% latanoprost daily in either one or both eyes for at least 2 weeks.

Number of subjects in period 1	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)
Started	8	10	7
Completed	7	10	7
Not completed	1	0	0
Protocol Violation	1	-	-

Number of subjects in period 1	Latanoprost (greater than or equal to [≥] 18 years)
Started	22
Completed	22
Not completed	0
Protocol Violation	-

Baseline characteristics

Reporting groups	
Reporting group title	Latanoprost (0 to less than [<] 3 Years)
Reporting group description:	
Subjects aged less than 3 years received latanoprost 0.005% in either one or both eyes.	
Reporting group title	Latanoprost (3 to < 12 years)
Reporting group description:	
Subjects aged 3 to < 12 years received latanoprost 0.005% in either one or both eyes.	
Reporting group title	Latanoprost (12 to < 18 years)
Reporting group description:	
Subjects aged from 12 to < 18 years recieved latanoprost 0.005% daily in either one or both eyes.	
Reporting group title	Latanoprost (greater than or equal to [≥] 18 years)
Reporting group description:	
Subjects aged ≥ 18 years recieved latanoprost 0.005% daily in either one or both eyes.	

Reporting group values	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)
Number of subjects	8	10	7
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	1.3	8.7	13.6
standard deviation	± 0.7	± 1.9	± 1.4
Gender categorical			
Units: Subjects			
Female	1	7	3
Male	7	3	4

Reporting group values	Latanoprost (greater than or equal to [≥] 18 years)	Total	
Number of subjects	22	47	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	62.8		
standard deviation	± 13.9	-	
Gender categorical			
Units: Subjects			
Female	12	23	
Male	10	24	

End points

End points reporting groups

Reporting group title	Latanoprost (0 to less than [<] 3 Years)
Reporting group description:	
Subjects aged less than 3 years received latanoprost 0.005% in either one or both eyes.	
Reporting group title	Latanoprost (3 to < 12 years)
Reporting group description:	
Subjects aged 3 to < 12 years received latanoprost 0.005% in either one or both eyes.	
Reporting group title	Latanoprost (12 to < 18 years)
Reporting group description:	
Subjects aged from 12 to < 18 years recieved latanoprost 0.005% daily in either one or both eyes.	
Reporting group title	Latanoprost (greater than or equal to [≥] 18 years)
Reporting group description:	
Subjects aged ≥ 18 years recieved latanoprost 0.005% daily in either one or both eyes.	

Primary: Maximum Observed Plasma Concentration (Cmax)

End point title	Maximum Observed Plasma Concentration (Cmax)[1]
End point description:	
Subjects analysed for the endpoint are those included in the Evaluable Pharmacokinetic Analysis set. Evaluable PK analyis set included all enrolled subjects who were treated, had at least 1 quantifiable concentration and without major protocol deviation.	
End point type	Primary
End point timeframe:	
pre-dose, 5, 15, 30, 60 minutes post-dose	

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: Only descriptive data was planned for this endpoint.

End point values	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)	Latanoprost (greater than or equal to [≥] 18 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	6	17
Units: picogram/milliliter				
arithmetic mean (standard deviation)	140.41 (± 63.941)	67.51 (± 54.612)	24.32 (± 15.752)	29.19 (± 12.635)

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Maximum Observed Plasma Concentration (Tmax)

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax)[2]

End point description:

Subjects analysed for the endpoint are those included in the Evaluable Pharmacokinetic Analysis set. Evaluable PK analyis set included all enrolled subjects who were treated, had at least 1 quantifiable concentration and without major protocol deviation.

End point type	Primary

End point timeframe:

pre-dose, 5, 15, 30, 60 minutes post-dose

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: Only descriptive data was planned for this endpoint.

End point values	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)	Latanoprost (greater than or equal to [≥] 18 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	6	17
Units: minutes				
median (full range (min-max))	5 (5 to 15)	5 (5 to 5)	5 (5 to 5)	5 (4 to 18)

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Elimination Half-Life (t1/2)

End point title	Plasma Elimination Half-Life (t1/2)[3]

End point description:

Plasma decay half-life is the time calculated for the plasma concentration to decrease by one half. Subjects analysed for the endpoint are those included in the Evaluable Pharmacokinetic Analysis set. Evaluable PK analyis set included all enrolled subjects who were treated, had at least 1 quantifiable concentration and without major protocol deviation.

End point type	Primary

End point timeframe:

Pre-dose, 5, 15, 30, 60 minutes post-dose

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: Only descriptive data was planned for this endpoint.

End point values	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)	Latanoprost (greater than or equal to [≥] 18 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[4]	5[5]	0[6]	4[7]
Units: minutes				
arithmetic mean (standard deviation)	20.058 (± 4.7892)	11.993 (± 3.4536)	()	20.511 (± 7.1454)

Notes:

[4] - Number of subjects analysed for this endpoint.

[5] - Number of subjects analysed for this endpoint.

[6] - None of the subjects had sufficient data to characterize the terminal elimination phase.

[7] - Number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Primary: Systemic Clearance (CL/F)

End point title	Systemic Clearance (CL/F)[8]

End point description:

Clearance of a drug is a measure of the rate at which a drug is removed from the body. Evaluable Pharmacokinetic Analysis Set include all enrolled subjects who are treated, have at least 1 quantifiable concentration and without major protocol deviation.

End point type	Primary

End point timeframe:

Pre-dose, 5, 15, 30, 60 minutes post-dose

Notes:

[8] - 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: Only descriptive data was planned for this endpoint.

End point values	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)	Latanoprost (greater than or equal to [≥] 18 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[9]	5[10]	0[11]	3[12]
Units: milliliter/minutes (mL/min)				
arithmetic mean (standard deviation)	730 (± 298.98)	2093.9 (± 965.05)	()	2168.9 (± 530.1)

Notes:

[9] - Number of subjects analysed for this endpoint.

[10] - Number of subjects analysed for this endpoint.

[11] - None of the subjects had sufficient data to characterize the terminal elimination phase.

[12] - Number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution ((Vz/F)

End point title	Apparent Volume of Distribution ((Vz/F)[13]

End point description:

Volume of distribution is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired blood concentration of a drug. Subjects analysed for the endpoint are those included in the Evaluable Pharmacokinetic Analysis set. Evaluable PK analyis set included all enrolled subjects who were treated, had at least 1 quantifiable concentration and without major protocol deviation.

End point type	Primary

End point timeframe:

Pre-dose, 5, 15, 30, 60 mintues post-dose

Notes:

[13] - 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: Only descriptive data was planned for this endpoint.

End point values	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)	Latanoprost (greater than or equal to [≥] 18 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[14]	5[15]	0[16]	3[17]
Units: liter				
arithmetic mean (standard deviation)	22.26 (± 14.927)	39.84 (± 29.258)	()	52.32 (± 6.328)

Notes:

[14] - Number of subjects analysed for this endpoint.

[15] - Number of subjects analysed for this endpoint.

[16] - None of the subjects had sufficient data to characterize the terminal elimination phase.

[17] - Number of subjects analysed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events Related to Systemic Exposure of Latanoprost

End point title	Number of Participants With Adverse Events Related to Systemic Exposure of Latanoprost

End point description:

An adverse event is any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. Safety Analysis Set: All subjects who receive at least 1 dose of study medication.

End point type	Secondary

End point timeframe:

Baseline up to 28 days after last dose of study drug.

End point values	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)	Latanoprost (greater than or equal to [≥] 18 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	10	7	22
Units: subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Baseline up to 28 days after last dose of study drug.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups	
Reporting group title	Latanoprost (0 to less than [<] 3 Years)
Reporting group description: Subjects with age less than 3 years recieved Latanoprost 0.005% daily in either one or both eyes.	
Reporting group title	Latanoprost (3 to < 12 years)
Reporting group description: Subjects with age from 3 to < 12 years recieved latanoprost 0.005% daily in either one or both eyes.	
Reporting group title	Latanoprost (12 to < 18 years)
Reporting group description: Subjects from 12 to < 18 years of age recieved latanoprost 0.005% daily in either one or both eyes.	
Reporting group title	Latanoprost (greater than or equal to [≥]18 years
Reporting group description: Subjects with age ≥ 18 years recieved latanoprost 0.005% daily in either one or both eyes.	

Serious adverse events	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Latanoprost (greater than or equal to [≥]18 years		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Latanoprost (0 to less than [<] 3 Years)	Latanoprost (3 to < 12 years)	Latanoprost (12 to < 18 years)
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 8 (0.00%)	0 / 10 (0.00%)	0 / 7 (0.00%)

Non-serious adverse events	Latanoprost (greater than or equal to [≥]18 years		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 22 (0.00%)		

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 were reported during the study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2008	1. Total blood sampling volume for adult patients ≥18 years of age changed from 32 mL to approximately 64 mL. 2. Clinical laboratory, blood pressure, and pulse rate abnormalities of potential clinical concern were evaluated in addition to other evaluations. 3. Females of childbearing potential (post-menarchal females) must have a negative urine pregnancy test at screening or on the study day (prior to dosing). 4. Sampling was not acceptable method of blood collection for either the safety labs or pharmacokinetic samples due to the risk of hemolysis, heel or scalp. 5. Results of the pharmacokinetic data from the older pediatric group (12 to <18 years old) were examined before proceeding to the 2nd age group (3 to <12 years olds) and were re-evaluated before enrolling the youngest age group (0 to <3 years).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported