



## Clinical trial results:

### A PHASE 3 PROSPECTIVE, RANDOMIZED, DOUBLE-MASKED, 12-WEEK, PARALLEL GROUP STUDY EVALUATING THE EFFICACY AND SAFETY OF LATANOPROST AND TIMOLOL IN PAEDIATRIC SUBJECTS WITH GLAUCOMA.

#### Summary

EudraCT number	2007-004543-30
Trial protocol	GB DE ES IT SI BE PT FR CZ SK DK GR Outside EU/EEA
Global end of trial date	11 November 2009

#### Results information

Result version number	v2 (current)
This version publication date	30 July 2016
First version publication date	11 July 2015
Version creation reason	• Correction of full data set corrections required

#### Trial information

##### Trial identification

Sponsor protocol code	A6111137
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00716859
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 ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 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)	EMA-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	14 January 2010
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	11 November 2009
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To assess the relative effectiveness of latanoprost 0.005 percent (%) ophthalmic solution dosed once-daily and timolol 0.5% (or optionally 0.25% for subjects younger than 3 years old) dosed twice-daily in paediatric subjects less than or equal to ( $\leq$ ) 18 years of age who are diagnosed with paediatric glaucoma. Specifically, to demonstrate that latanoprost is not inferior to timolol within a non-inferiority margin of 3 millimeters of mercury (mmHg), with an option of switching to superiority, in the event that the lower limit of the 95% confidence interval (CI) for the treatment difference not only lies above the non-inferiority margin but also above zero.

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 subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 July 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Portugal: 12
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Serbia: 5
Country: Number of subjects enrolled	Slovakia: 12
Country: Number of subjects enrolled	Slovenia: 2
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Ukraine: 24
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Philippines: 10
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Czech Republic: 5

Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	India: 2
Worldwide total number of subjects	137
EEA total number of subjects	78

Notes:

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### 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)	23
Children (2-11 years)	66
Adolescents (12-17 years)	45
Adults (18-64 years)	3
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Randomization was stratified by age, diagnosis (congenital glaucoma [PCG] or non-congenital glaucoma [non-PCG], and intraocular pressure [IOP]) of the study eye at baseline.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Timolol

Arm description:

Timolol maleate ophthalmic solution was administered.

Arm type	Active comparator
Investigational medicinal product name	Timolol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

Subjects received 1 drop of Timolol 0.5% (or optionally 0.25% for subjects younger than 3 years old) at approximately 8 AM and again at approximately 8 PM.

<b>Arm title</b>	Latanoprost
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Arm description:

Latanoprost ophthalmic solution and vehicle was administered.

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

Dosage and administration details:

Subjects received 1 drop of vehicle daily at approximately 8 AM and 1 drop (latanoprost 0.005%) daily at approximately 8 PM.

<b>Number of subjects in period 1</b>	Timolol	Latanoprost
Started	69	68
Completed	61	64
Not completed	8	4
Consent withdrawn by subject	1	3
Lack of Efficacy	3	-
Adverse Event	4	1

## Baseline characteristics

### Reporting groups

Reporting group title	Timolol
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Reporting group description:

Timolol maleate ophthalmic solution was administered.

Reporting group title	Latanoprost
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Reporting group description:

Latanoprost ophthalmic solution and vehicle was administered.

Reporting group values	Timolol	Latanoprost	Total
Number of subjects	69	68	137
Age categorical			
Units: Subjects			
12 to 18 years	23	25	48
3 to less than (<) 12 years	29	26	55
0 to < 3 years	17	17	34
Gender categorical			
Units: Subjects			
Female	37	34	71
Male	32	34	66

## End points

### End points reporting groups

Reporting group title	Timolol
Reporting group description: Timolol maleate ophthalmic solution was administered.	
Reporting group title	Latanoprost
Reporting group description: Latanoprost ophthalmic solution and vehicle was administered.	

### Primary: Reduction From Baseline in Mean IOP at Week 12, Last Observation Carried Forward (LOCF)

End point title	Reduction From Baseline in Mean IOP at Week 12, Last Observation Carried Forward (LOCF)
End point description: Calculated as Baseline IOP minus Week 12 IOP, LOCF. IOP measured using 1 of 3 methods: Goldmann applanation tonometry (preferred method, if feasible), Perkins tonometry, or TonoPen. IOP was measured twice and if the measurements were $\leq 2$ mmHg of each other, the mean of the 2 readings was recorded as the IOP at that time point. Otherwise, a third IOP measurement was taken and the median IOP recorded. Per Protocol (PP) Population: subjects with no major protocol violations who received at least 1 week of study medication and had at least Week 1 IOP measurements. LOCF.	
End point type	Primary
End point timeframe: Baseline, Week 12	

End point values	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: mmHg				
least squares mean (standard error)	5.72 ( $\pm$ 0.81)	7.18 ( $\pm$ 0.81)		

### Statistical analyses

Statistical analysis title	All groups
Statistical analysis description: Null hypothesis: latanoprost inferior to timolol (0.5 % optionally 0.25% for subjects younger than 3 years). Power calculation: assuming common standard deviation (7 mmHg), 110 subjects have 84% power to demonstrate latanoprost not inferior to timolol within 3 mmHg margin, assuming latanoprost has 1 mmHg reduction more than timolol in mean change from baseline IOP.	
Comparison groups	Timolol v Latanoprost

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
Parameter estimate	Mean difference (net)
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.81
upper limit	3.74

Notes:

[1] - If lower limit of 95% CI for treatment difference is above non-inferiority margin, then non-inferiority concluded. If lower limit of 95% CI for treatment difference is above non-inferiority margin and above zero, then superiority concluded. The difference and 95% CI of the difference in IOP reduction (Week 12) was computed from an analysis of covariance (ANCOVA) model with treatment and baseline diagnosis as factors and baseline IOP as covariate.

## Secondary: Reduction From Baseline in Mean IOP at Week 1

End point title	Reduction From Baseline in Mean IOP at Week 1
End point description:	
Calculated as Baseline IOP minus Week 1 IOP (observed). IOP measured using 1 of 3 methods: Goldmann applanation tonometry (preferred method, if feasible), Perkins tonometry, or TonoPen. IOP was measured twice and if the measurements were $\leq 2$ mmHg of each other, the mean of the 2 readings was recorded as the IOP at that time point. Otherwise, a third IOP measurement was taken and the median IOP recorded. Per protocol population was analysed.	
End point type	Secondary
End point timeframe:	
Baseline, Week 1	

End point values	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: mmHg				
least squares mean (standard error)	6.02 ( $\pm 0.83$ )	6.7 ( $\pm 0.84$ )		

## Statistical analyses

Statistical analysis title	All groups
Comparison groups	Timolol v Latanoprost
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	3.02



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**Secondary: Reduction From Baseline in Mean IOP at Week 4**

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End point title	Reduction From Baseline in Mean IOP at Week 4
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End point description:

Calculated as Baseline IOP minus Week 4 IOP (observed). IOP measured using 1 of 3 methods: Goldmann applanation tonometry (preferred method, if feasible), Perkins tonometry, or TonoPen. IOP was measured twice and if the measurements were  $\leq 2$  mmHg of each other, the mean of the 2 readings was recorded as the IOP at that time point. Otherwise, a third IOP measurement was taken and the median IOP recorded. Evaluable subjects in Per protocol population were analysed.

End point type	Secondary
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End point timeframe:

Baseline, Week 4

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End point values	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	49		
Units: mmHg				
least squares mean (standard error)	5.37 ( $\pm$ 0.94)	6.99 ( $\pm$ 0.92)		

**Statistical analyses**

<b>Statistical analysis title</b>	All groups
Comparison groups	Timolol v Latanoprost
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	4.25

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**Secondary: Reduction From Baseline in Mean IOP at Week 12 (Observed)**

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End point title	Reduction From Baseline in Mean IOP at Week 12 (Observed)
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End point description:

Calculated as Baseline IOP minus Week 12 IOP (observed). IOP measured using 1 of 3 methods: Goldmann applanation tonometry (preferred method, if feasible), Perkins tonometry, or TonoPen. IOP was measured twice and if the measurements were  $\leq 2$  mmHg of each other, the mean of the 2 readings was recorded as the IOP at that time point. Otherwise, a third IOP measurement was taken and the median IOP recorded. Evaluable subjects in Per protocol population were analysed.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	46		
Units: mmHg				
least squares mean (standard error)	6.96 ( $\pm$ 0.68)	7.75 ( $\pm$ 0.66)		

## Statistical analyses

Statistical analysis title	All groups
Comparison groups	Timolol v Latanoprost
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.67

## Secondary: Mean IOP at Baseline

End point title	Mean IOP at Baseline
End point description:	IOP measured using 1 of 3 methods: Goldmann applanation tonometry (preferred method, if feasible), Perkins tonometry, or TonoPen. IOP was measured twice and if the measurements were $\leq 2$ mmHg of each other, the mean of the 2 readings was recorded as the IOP at that time point. Otherwise, a third IOP measurement was taken and the median IOP recorded. Per protocol population was analysed.
End point type	Secondary
End point timeframe:	
Baseline	

End point values	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: mmHg				
arithmetic mean (standard deviation)	27.8 ( $\pm$ 6.18)	27.3 ( $\pm$ 5.46)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean IOP at Week 1

End point title	Mean IOP at Week 1
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End point description:

IOP measured using 1 of 3 methods: Goldmann applanation tonometry (preferred method, if feasible), Perkins tonometry, or TonoPen. IOP was measured twice and if the measurements were  $\leq 2$  mmHg of each other, the mean of the 2 readings was recorded as the IOP at that time point. Otherwise, a third IOP measurement was taken and the median IOP recorded. Per protocol population was analysed.

End point type	Secondary
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End point timeframe:

Week 1

End point values	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: mmHg				
arithmetic mean (standard deviation)	21.7 ( $\pm$ 7.99)	20.6 ( $\pm$ 6.38)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean IOP at Week 4

End point title	Mean IOP at Week 4
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End point description:

IOP measured using 1 of 3 methods: Goldmann applanation tonometry (preferred method, if feasible), Perkins tonometry, or TonoPen. IOP was measured twice and if the measurements were  $\leq 2$  mmHg of each other, the mean of the 2 readings was recorded as the IOP at that time point. Otherwise, a third IOP measurement was taken and the median IOP recorded. Evaluable subjects in per protocol population were analysed.

End point type	Secondary
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End point timeframe:

Week 4

End point values	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	49		
Units: mmHg				
arithmetic mean (standard deviation)	21.5 (± 7.49)	20.1 (± 6.82)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean IOP at Week 12

End point title	Mean IOP at Week 12
End point description: IOP measured using 1 of 3 methods: Goldmann applanation tonometry (preferred method, if feasible), Perkins tonometry, or TonoPen. IOP was measured twice and if the measurements were $\leq 2$ mmHg of each other, the mean of the 2 readings was recorded as the IOP at that time point. Otherwise, a third IOP measurement was taken and the median IOP recorded. Evaluable subjects in per protocol population.	
End point type	Secondary
End point timeframe: Week 12	

End point values	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	46		
Units: mmHg				
arithmetic mean (standard deviation)	19.8 (± 3.5)	19.2 (± 5.87)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Greater Than or Equal to ( $\geq$ ) 15% IOP Reduction From Baseline at Both Weeks 4 and 12

End point title	Percentage of Subjects With Greater Than or Equal to ( $\geq$ ) 15% IOP Reduction From Baseline at Both Weeks 4 and 12
End point description: Subjects with $\geq 15\%$ IOP reduction from baseline at both Week 4 and Week 12. Calculated as (post baseline IOP minus baseline IOP) divided by IOP, multiplied by 100%. IOP measured using 1 of 3 methods: Goldmann applanation tonometry (preferred method, if feasible), Perkins tonometry, or TonoPen. IOP was measured twice and if the measurements were $\leq 2$ mmHg of each other, the mean of the 2 readings was recorded as the IOP at that time point. Otherwise, a third IOP measurement was taken and the median IOP recorded. Evaluable subjects in Per protocol population were analysed.	
End point type	Secondary
End point timeframe: Baseline, Week 4, Week 12	

<b>End point values</b>	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: percentage of subjects				
number (confidence interval 95%)	52 (38 to 66)	60 (46 to 74)		

## Statistical analyses

<b>Statistical analysis title</b>	All groups
Statistical analysis description: P-value from a Cochran-Mantel-Haenszel chi-square test stratified by baseline diagnosis (PCG vs non-PCG).	
Comparison groups	Timolol v Latanoprost
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3315
Method	Cochran-Mantel-Haenszel

## Secondary: Percentage of Subjects Discontinuing Therapy Due to a Drug-related Adverse Experience

<b>End point title</b>	Percentage of Subjects Discontinuing Therapy Due to a Drug-related Adverse Experience
End point description: An investigator's causality assessment was the determination of whether there existed a reasonable possibility that the investigational product caused or contributed to an adverse event (AE). If the investigator did not know whether or not investigational product caused the event, then the event was handled as "related to investigational product" for reporting purposes. Intent to treat (ITT) population: all subjects who were randomized into the study and received at least 1 dose of study medication.	
End point type	Secondary
End point timeframe: Baseline through Week 12	

<b>End point values</b>	Timolol	Latanoprost		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	68		
Units: percentage of subjects				
number (not applicable)	1.4	0		

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to 30 days after last study treatment administration

Adverse event reporting additional description:

Same event may appear as AE and SAE. However, what is presented are distinct events. An event may be categorized as serious in 1 subject and non serious in another, or 1 subject may have experienced both serious, non serious event during study. EU BR specific AE tables were generated separately as per EU format using the latest coding dictionary.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

### Reporting groups

Reporting group title	Timolol
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Reporting group description:

Timolol maleate ophthalmic solution; 1 drop of timolol 0.5% (or optionally 0.25% for subjects younger than 3 years old) at approximately 8 AM and again at approximately 8 PM .

Reporting group title	Latanoprost
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Reporting group description:

Latanoprost ophthalmic solution and vehicle; 1 drop of vehicle daily at approximately 8 AM and 1 drop (latanoprost 0.005%) daily at approximately 8 PM.

Serious adverse events	Timolol	Latanoprost	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 69 (10.14%)	2 / 68 (2.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Congenital, familial and genetic disorders			
Developmental glaucoma			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Trabeculectomy			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			

subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal perforation			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye haemorrhage			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lens dislocation			
subjects affected / exposed	0 / 69 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			



subjects affected / exposed	0 / 69 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 69 (0.00%)	1 / 68 (1.47%)	
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: 2 %

<b>Non-serious adverse events</b>	Timolol	Latanoprost	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 69 (30.43%)	15 / 68 (22.06%)	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 69 (5.80%)	2 / 68 (2.94%)	
occurrences (all)	5	2	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 69 (2.90%)	2 / 68 (2.94%)	
occurrences (all)	2	2	
Therapeutic response changed			
subjects affected / exposed	0 / 69 (0.00%)	2 / 68 (2.94%)	
occurrences (all)	0	3	
Eye disorders			

Conjunctival disorder subjects affected / exposed occurrences (all)	2 / 69 (2.90%) 2	0 / 68 (0.00%) 0	
Conjunctival hyperaemia subjects affected / exposed occurrences (all)	6 / 69 (8.70%) 7	3 / 68 (4.41%) 4	
Corneal oedema subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	2 / 68 (2.94%) 2	
Visual acuity reduced subjects affected / exposed occurrences (all)	2 / 69 (2.90%) 3	0 / 68 (0.00%) 0	
Infections and infestations			
Influenza subjects affected / exposed occurrences (all)	4 / 69 (5.80%) 5	0 / 68 (0.00%) 0	
Nasopharyngitis subjects affected / exposed occurrences (all)	5 / 69 (7.25%) 5	4 / 68 (5.88%) 4	
Rhinitis subjects affected / exposed occurrences (all)	1 / 69 (1.45%) 1	2 / 68 (2.94%) 2	
Viral infection subjects affected / exposed occurrences (all)	2 / 69 (2.90%) 2	1 / 68 (1.47%) 1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 October 2007	1) Removal of the follow-up visit 1 week after end of treatment was made. 2) Confirmation that discontinuation of any topical or systemic ocular hypotensive medications should be completed at least 24 hours before the Baseline visit was made.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported