



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 | v1 |
| This version publication date | 30 May 2016 |
| First version publication date | 11 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | A6111137 |
|-----------------------|----------|

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:

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 |
| Arm title | 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.

| | |
|------------------|-------------|
| Arm title | Latanoprost |
|------------------|-------------|

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.

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| Consent withdrawn by subject | 1 | 3 |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

Baseline characteristics

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.

| 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 ≤ 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 ^[1] |
| 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 ≤ 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 (± 0.83) | 6.7 (± 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 |

Secondary: Reduction From Baseline in Mean IOP at Week 4

| | |
|-----------------|---|
| End point title | Reduction From Baseline in Mean IOP at Week 4 |
|-----------------|---|

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 ≤ 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

| 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

| | |
|---|-----------------------|
| Statistical analysis title | 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 |

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

| | |
|-----------------|---|
| End point title | Reduction From Baseline in Mean IOP at Week 12 (Observed) |
|-----------------|---|

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 ≤ 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 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 ≤ 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 |
|-----------------|--------------------|

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 ≤ 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:

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 |
|-----------------|--------------------|

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 ≤ 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:

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 ≤ 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 ≤ 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 | |

| End point values | 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

| Statistical analysis title | 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

| End point title | 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 | |

| End point values | 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

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 |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Latanoprost |
|-----------------------|-------------|

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.

| | |
|-----------------------|---------|
| Reporting group title | Timolol |
|-----------------------|---------|

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 .

| Serious adverse events | Latanoprost | Timolol | |
|---|----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 68 (2.94%) | 7 / 69 (10.14%) | |
| 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 | 0 / 68 (0.00%) | 1 / 69 (1.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Trabeculectomy | | | |
| subjects affected / exposed | 0 / 68 (0.00%) | 1 / 69 (1.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |

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

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

Frequency threshold for reporting non-serious adverse events: 2 %

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

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

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:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported