



Clinical trial results:

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

Summary

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

Results information

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

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | C-12-008 |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

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

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

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

Notes:

Subjects enrolled per age group

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

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Travoprost |

Arm description:

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

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

Dosage and administration details:

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

| | |
|------------------|---------|
| Arm title | Timolol |
|------------------|---------|

Arm description:

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

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

Dosage and administration details:

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

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

Baseline characteristics

Reporting groups

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

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

End points

End points reporting groups

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

Primary: Mean Change from Baseline in IOP at Month 3

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

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

Notes:

[1] - Observed cases only.

[2] - Observed cases only.

Statistical analyses

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

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

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 15.0 |

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Travoprost |
|-----------------------|------------|

Reporting group description:

All participants who received travoprost with vehicle

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

Reporting group description:

All participants who received timolol

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported