



Clinical trial results:

An Open-label, Long-term Study, with AL-4943A Ophthalmic Solution, 0.2% in Patients with Allergic Conjunctivitis

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-003953-41 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 23 May 2010 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 04 January 2018 |
| First version publication date | 04 January 2018 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | C-09-050 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01037179 |
| 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 | Ophthalmology Unit, Novartis Pharmaceuticals, +44 01276 6673 3391, dennis.wong@novartis.com |
| Scientific contact | Ophthalmology Unit, Novartis Pharmaceuticals, +44 01276 6673 3391, dennis.wong@novartis.com |

Notes:

Paediatric regulatory details

| | |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| 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 May 2010 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 23 May 2010 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 May 2010 |
| 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 safety and efficacy of long-term use of AL-4943A Ophthalmic Solution, 0.2% in patients with allergic conjunctivitis.

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 | 17 February 2010 |
| 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 | Japan: 110 |
| Worldwide total number of subjects | 110 |
| EEA total number of subjects | 0 |

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) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 10 |

| | |
|----------------------|-----|
| Adults (18-64 years) | 100 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 1 study center located in Japan.

Pre-assignment

Screening details:

This reporting group includes all enrolled and treated subjects.

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 | AL-4943A 0.2% |
|------------------|---------------|

Arm description:

AL-4943A 0.2% ophthalmic solution, 2 drops in each eye, twice daily (morning and evening) for 10 weeks

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | AL-4943A 0.2% ophthalmic solution |
| Investigational medicinal product code | |
| Other name | Pataday™ |
| Pharmaceutical forms | Eye drops, solution |
| Routes of administration | Ophthalmic use |

Dosage and administration details:

Two drops in each eye, twice daily (morning and evening) for 10 weeks

| | |
|---------------------------------------|---------------|
| Number of subjects in period 1 | AL-4943A 0.2% |
| Started | 110 |
| Completed | 109 |
| Not completed | 1 |
| Subject withdrawal | 1 |

Baseline characteristics

Reporting groups

| | |
|--|---------------|
| Reporting group title | AL-4943A 0.2% |
| Reporting group description: AL-4943A 0.2% ophthalmic solution, 2 drops in each eye, twice daily (morning and evening) for 10 weeks | |

| Reporting group values | AL-4943A 0.2% | Total | |
|------------------------|---------------|-------|--|
| Number of subjects | 110 | 110 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--|--------|----|--|
| Age continuous | | | |
| This analysis population includes all subjects who received study medication and completed at least one on-therapy study visit (Intent-to-Treat Analysis Set). | | | |
| Units: years | | | |
| arithmetic mean | 36.7 | | |
| standard deviation | ± 10.3 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 66 | 66 | |
| Male | 44 | 44 | |
| Itching Score | | | |
| Ocular itching was assessed by the subject and graded on a 6-unit scale, where 0="did not occur" and 5="virtually all the time over the past three days". Intent-to-Treat Analysis Set. | | | |
| Units: units on a scale | | | |
| arithmetic mean | 4.3 | | |
| standard deviation | ± 0.6 | - | |
| Total Hyperemia Score | | | |
| Ocular hyperemia (visible eye redness) was assessed by the investigator. Total hyperemia score was defined as the sum of palpebral and bulbar conjunctival hyperemia scores. Each hyperemia was measured on 6-unit scale, where 0=none and 5=severe redness. Intent-to-Treat Analysis Set. | | | |
| Units: units on a scale | | | |
| arithmetic mean | 4.0 | | |
| standard deviation | ± 1.2 | - | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | AL-4943A 0.2% |
| Reporting group description: AL-4943A 0.2% ophthalmic solution, 2 drops in each eye, twice daily (morning and evening) for 10 weeks | |
| Subject analysis set title | Baseline |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Intent-to-Treat Analysis Set at Baseline | |
| Subject analysis set title | Week 2 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Intent-to-Treat Analysis Set at Week 2 | |
| Subject analysis set title | Week 4 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Intent-to-Treat Analysis Set at Week 4 | |
| Subject analysis set title | Week 6 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Intent-to-Treat Analysis Set at Week 6 | |
| Subject analysis set title | Week 8 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Intent-to-Treat Analysis Set at Week 8 | |
| Subject analysis set title | Week 10 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Intent-to-Treat Analysis Set at Week 10 | |

Primary: Mean Change from Baseline (BL) in Itching Score by Visit

| | |
|---|---|
| End point title | Mean Change from Baseline (BL) in Itching Score by Visit ^[1] |
| End point description: Ocular itching was assessed by the subject and graded on a 6-unit scale, where 0="did not occur" and 5="virtually all the time over the past three days". Average scores from the subject's two eyes were used. A more negative change indicates improvement. Intent-To-Treat, with missing data imputed using Last Observation Carried Forward (LOCF). | |
| End point type | Primary |
| End point timeframe: Baseline, Week 2, Week 4, Week 6, Week 8, Week 10 | |

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: This was a one-arm descriptive study; no hypothesis testing was performed. Descriptive statistics were provided. Comparisons for each week vs baseline were presented.

| | | | | |
|--------------------------------------|------------------|--|--|--|
| End point values | AL-4943A 0.2% | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 110 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 2 | -1.2 (± 1.2) | | | |
| Week 4 | -1.5 (± 1.4) | | | |
| Week 6 | -1.8 (± 1.5) | | | |
| Week 8 | -2.2 (± 1.6) | | | |
| Week 10 | -2.4 (± 1.7) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change from BL in Total Hyperemia Score by Visit

| | |
|-----------------|--|
| End point title | Mean Change from BL in Total Hyperemia Score by Visit ^[2] |
|-----------------|--|

End point description:

Ocular hyperemia (visible eye redness) was assessed by the investigator. Total hyperemia score was defined as the sum of palpebral and bulbar conjunctival hyperemia scores. Each hyperemia was measured on 6-unit scale, where 0=none and 5=severe redness. Average scores from the subject's both eyes were used. A more negative change indicates improvement. Intent-to-Treat, with missing values imputed using LOCF.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Week 2, Week 4, Week 6, Week 8, Week 10

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: This was a one-arm descriptive study; no hypothesis testing was performed. Descriptive statistics were provided.

| | | | | |
|--------------------------------------|------------------|--|--|--|
| End point values | AL-4943A 0.2% | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 110 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 2 | -0.9 (± 1.2) | | | |
| Week 4 | -1.5 (± 1.3) | | | |
| Week 6 | -2.1 (± 1.3) | | | |
| Week 8 | -2.7 (± 1.3) | | | |
| Week 10 | -3.2 (± 1.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Subjective Symptoms (except ocular itching)

| | |
|-----------------|---|
| End point title | Subjective Symptoms (except ocular itching) |
|-----------------|---|

End point description:

Subjective symptoms were measured on 4-unit scale (Photophobia: 0=Not glaring to 3=Too glaring to open the eyes in a light place; Lacrimation: 0=Does not weigh on mind to 3=Tearful so that tears flow down the cheek; Eye Discharge: 0=Does not weigh on mind to 3=So much as to glue the eyelids shut on awaking in the morning; Foreign Body Sensation: 0=Does not weigh on mind to 3=Always feels gritty so that the eyes cannot be kept open; and Eye Pain: 0=Painless to 3=Too painful to open the eyes). Average scores from the subject's both eyes were used. Intent-To-Treat, with missing data imputed using LOCF. Descriptive statistics are presented.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 2, Week 4, Week 6, Week 8, Week 10

| End point values | Baseline | Week 2 | Week 4 | Week 6 |
|--------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 110 | 110 | 110 | 110 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Photophobia | 0.2 (± 0.5) | 0.1 (± 0.3) | 0.1 (± 0.3) | 0.1 (± 0.3) |
| Lacrimation Score | 0.8 (± 0.8) | 0.5 (± 0.7) | 0.4 (± 0.6) | 0.3 (± 0.5) |
| Eye Discharge Score | 0.6 (± 0.8) | 0.5 (± 0.6) | 0.3 (± 0.5) | 0.2 (± 0.5) |
| Foreign Body Sensation Score | 0.8 (± 0.6) | 0.4 (± 0.6) | 0.3 (± 0.5) | 0.2 (± 0.5) |
| Eye Pain Score | 0.2 (± 0.4) | 0.1 (± 0.4) | 0.1 (± 0.3) | 0.1 (± 0.2) |

| End point values | Week 8 | Week 10 | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 110 | 110 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Photophobia | 0.1 (± 0.3) | 0.0 (± 0.2) | | |
| Lacrimation Score | 0.2 (± 0.5) | 0.1 (± 0.4) | | |
| Eye Discharge Score | 0.2 (± 0.5) | 0.1 (± 0.4) | | |
| Foreign Body Sensation Score | 0.2 (± 0.4) | 0.1 (± 0.3) | | |
| Eye Pain Score | 0.0 (± 0.2) | 0.0 (± 0.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Findings

| | |
|-----------------|--------------------|
| End point title | Objective Findings |
|-----------------|--------------------|

End point description:

Palpebral conjunctiva hyperemia and bulbar conjunctiva hyperemia were measured on a 6-unit scale, where 0=none/minimum redness and 5=maximum redness. Other objective findings were measured on

a 4-unit scale (Swelling: 0=none to 3=Diffuse swelling of eyelid with opacity; Follicles: 0=none to 3=20 or more follicles, Papilla: 0=none to 3=0.6 or more of diameter; Megalopapilla: 0=none to 3=Papilla of upper palpebral conjunctiva is bulging in the range of 1/2 or more; Edema: 0=none to 3=Alveolar edema; Trantas' dots: 0=none to 3=9 dots or more; Circumference Swelling: 0=none to 3=Range is more than 2/3 of circumference; Corneal Epithelium: 0=none to 3=Shield ulcer or epithelial erosion). Average scores from the individual's both eyes were used. Intent-To-Treat, with missing data imputed using LOCF. Descriptive statistics are presented.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 2, Week 4, Week 6, Week 8, Week 10 | |

| End point values | Baseline | Week 2 | Week 4 | Week 6 |
|--------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 110 | 110 | 110 | 110 |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Palpebral conjunctiva hyperemia | 2.4 (± 0.6) | 1.8 (± 0.7) | 1.6 (± 0.7) | 1.3 (± 0.8) |
| Swelling | 1.2 (± 0.5) | 1.1 (± 0.6) | 1.0 (± 0.5) | 0.9 (± 0.6) |
| Follicles | 0.9 (± 0.7) | 1.0 (± 0.9) | 0.9 (± 0.7) | 0.7 (± 0.6) |
| Papilla | 0.6 (± 0.7) | 0.4 (± 0.5) | 0.4 (± 0.5) | 0.3 (± 0.4) |
| Megalopapilla | 0.0 (± 0.0) | 0.0 (± 0.0) | 0.0 (± 0.0) | 0.0 (± 0.0) |
| Bulbar conjunctiva hyperemia | 1.6 (± 0.8) | 1.2 (± 0.6) | 0.9 (± 0.6) | 0.6 (± 0.7) |
| Edema | 0.9 (± 0.6) | 0.7 (± 0.5) | 0.7 (± 0.5) | 0.6 (± 0.5) |
| Trantas' dots | 0.0 (± 0.0) | 0.0 (± 0.0) | 0.0 (± 0.0) | 0.0 (± 0.0) |
| Circumference swelling | 0.0 (± 0.0) | 0.0 (± 0.0) | 0.0 (± 0.0) | 0.0 (± 0.0) |
| Corneal Epithelium | 0.0 (± 0.0) | 0.0 (± 0.0) | 0.0 (± 0.0) | 0.0 (± 0.0) |

| End point values | Week 8 | Week 10 | | |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 110 | 110 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Palpebral conjunctiva hyperemia | 0.9 (± 0.7) | 0.6 (± 0.7) | | |
| Swelling | 0.6 (± 0.5) | 0.5 (± 0.5) | | |
| Follicles | 0.6 (± 0.6) | 0.4 (± 0.5) | | |
| Papilla | 0.3 (± 0.4) | 0.2 (± 0.4) | | |
| Megalopapilla | 0.0 (± 0.0) | 0.0 (± 0.0) | | |
| Bulbar conjunctiva hyperemia | 0.4 (± 0.5) | 0.2 (± 0.4) | | |
| Edema | 0.4 (± 0.5) | 0.2 (± 0.4) | | |
| Trantas' dots | 0.0 (± 0.0) | 0.0 (± 0.0) | | |
| Circumference swelling | 0.0 (± 0.0) | 0.0 (± 0.0) | | |
| Corneal Epithelium | 0.0 (± 0.0) | 0.0 (± 0.0) | | |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Only total subjects affected by non-serious AEs that occur at >5% are reported. This analysis population includes all subjects who received study medication (Safety Analysis Set).

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

Dictionary used

| | |
|-----------------|----------|
| Dictionary name | MedDRA/J |
|-----------------|----------|

| | |
|--------------------|------|
| Dictionary version | 13.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | AL-4943A 0.2% |
|-----------------------|---------------|

Reporting group description:

AL-4943A 0.2% ophthalmic solution, 2 drops in each eye, twice daily (morning and evening) for 10 weeks

| Serious adverse events | AL-4943A 0.2% | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 110 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | AL-4943A 0.2% | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 74 / 110 (67.27%) | | |
| Eye disorders | | | |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 74 / 110 (67.27%) | | |
| occurrences (all) | 98 | | |

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