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 standard deviation	 36.7 ± 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 standard deviation	 4.3 ± 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 standard deviation	 4.0 ± 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

No statistical analyses for this end point

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