Clinical trial results:
Safety Study of Olopatadine Nasal Spray
Summary

EudraCT number	2017-003846-26
Trial protocol	Outside EU/EEA
Global end of trial date	28 January 2008

Results information

Result version number	v1 (current)
This version publication date	25 January 2018
First version publication date	25 January 2018

Trial information

Trial identification

Sponsor protocol code	C-05-69

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00578331
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 0127666733391, dennis.wong@novartis.com
Scientific contact	Ophthalmology Unit, Novartis Pharmaceuticals, +44 0127666733391, 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	28 January 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2008
Global end of trial reached?	Yes
Global end of trial date	28 January 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to describe and compare the safety and efficacy of Olopatadine HCl Nasal Spray 0.6% versus Vehicle when given as two sprays per nostril twice daily (BID) for up to 12 months in subjects with perennial allergic rhinitis (PAR).

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	06 December 2006
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	United States: 890
Worldwide total number of subjects	890
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)	99

Adults (18-64 years)	771
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 80 study centers located in the US.

Pre-assignment

Screening details:

This reporting group includes all randomized and treated subjects (890).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Olo 0.6%

Arm description:

Olopatadine HCl 0.6% Nasal Spray, 2 sprays/nostril twice-daily for up to 12 months

Arm type	Experimental
Investigational medicinal product name	Olopatadine HCl 0.6% Nasal Spray
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

2 sprays/nostril twice-daily

Arm title	Vehicle

Arm description:

Olopatadine Vehicle Placebo Nasal Spray, 2 sprays/nostril twice-daily for up to 12 months

Arm type	Placebo
Investigational medicinal product name	Olopatadine Vehicle Nasal Spray
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

2 sprays/nostril twice-daily

Number of subjects in period 1	Olo 0.6%	Vehicle
Started	445	445
Completed	320	329
Not completed	125	116
Adverse event, non-fatal	30	24

Treatment Failure	24	16
Decision Unrelated to an Adverse Event	28	27
Protocol Violation	9	7
Lost to follow-up	20	29
Other - Reason not given	14	13

Baseline characteristics

Reporting groups	
Reporting group title	Olo 0.6%
Reporting group description:	
Olopatadine HCl 0.6% Nasal Spray, 2 sprays/nostril twice-daily for up to 12 months	
Reporting group title	Vehicle
Reporting group description:	
Olopatadine Vehicle Placebo Nasal Spray, 2 sprays/nostril twice-daily for up to 12 months	

Reporting group values	Olo 0.6%	Vehicle	Total
Number of subjects	445	445	890
Age categorical Units: Subjects			
Adolescents (12-17 years)	46	53	99
Adults (18-64 years)	388	383	771
≥ 65 years	11	9	20
Gender categorical Units: Subjects			
Female	282	296	578
Male	163	149	312

End points

End points reporting groups	
Reporting group title	Olo 0.6%
Reporting group description:	
Olopatadine HCl 0.6% Nasal Spray, 2 sprays/nostril twice-daily for up to 12 months	
Reporting group title	Vehicle
Reporting group description:	
Olopatadine Vehicle Placebo Nasal Spray, 2 sprays/nostril twice-daily for up to 12 months	

Primary: Mean Patient-Rated Relief Assessment at Day 30 by Treatment Group	
End point title	Mean Patient-Rated Relief Assessment at Day 30 by Treatment Group
End point description:	
At each post-treatment visit, subjects answered the symptom relief question: "I would rate the study medication's effectiveness for relieving my allergy symptoms since my last visit as:" on a 4-point scale, where 1=Complete Relief, 2=Moderate Relief, 3=Mild Relief, and 4=No Relief. This analysis population includes all subjects who received drug and had at least one on-therapy visit (Intent-to-Treat Analysis Set), with non-missing data.	
End point type	Primary
End point timeframe:	
Day 30	

End point values	Olo 0.6%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	431	430		
Units: units on a scale				
arithmetic mean (standard deviation)	2.5 (± 0.9)	2.7 (± 0.9)		

Statistical analyses

Statistical analysis title	Response to Subject-Rated Relief Assessment
Comparison groups	Olo 0.6% v Vehicle
Number of subjects included in analysis	861
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0011
Method	t-test, 2-sided

Secondary: Average number of days rescue medication was used	
End point title	Average number of days rescue medication was used

End point description:

Use of rescue medication (pseudoephedrine) was recorded by the subject in a dosing diary.

End point type	Secondary

End point timeframe:

Up through Month 12

End point values	Olo 0.6%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	439[1]	439[2]		
Units: days				
arithmetic mean (standard deviation)	11.8 (± 26.6)	10.2 (± 22.4)		

Notes:

[1] - Intent-to-treat with non-missing data

[2] - Intent-to-treat with non-missing data

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Patient-Rated Relief Assessment for Months 1 to 12 by Treatment Group

End point title	Mean Patient-Rated Relief Assessment for Months 1 to 12 by Treatment Group

End point description:

At each post-treatment visit, subjects answered the symptom relief question: "I would rate the study medication's effectiveness for relieving my allergy symptoms since my last visit as:" on a 4-point scale, where 1=Complete Relief, 2=Moderate Relief, 3=Mild Relief, and 4=No Relief. Ratings were averaged over the entire study. Intent-to-Treat with non-missing response.

End point type	Secondary

End point timeframe:

Up through Month 12

End point values	Olo 0.6%	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	438	437		
Units: units on a scale				
arithmetic mean (standard deviation)	2.5 (± 0.8)	2.6 (± 0.9)		

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.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Olo 0.6%

Reporting group description:

Olopatadine HCl 0.6% Nasal Spray, 2 sprays/nostril twice-daily for up to 12 months

Reporting group title	Vehicle

Reporting group description:

Olopatadine Vehicle Placebo Nasal Spray, 2 sprays/nostril twice-daily for up to 12 months

Serious adverse events	Olo 0.6%	Vehicle	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 445 (3.37%)	15 / 445 (3.37%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	1 / 445 (0.22%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid neoplasm			
subjects affected / exposed	1 / 445 (0.22%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	1 / 445 (0.22%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injury			
subjects affected / exposed	2 / 445 (0.45%)	3 / 445 (0.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Post procedural complication			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hip dysplasia			
subjects affected / exposed	1 / 445 (0.22%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral embolism			
subjects affected / exposed	1 / 445 (0.22%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cholecystectomy			
subjects affected / exposed	1 / 445 (0.22%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hysterectomy			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc operation			

subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint surgery			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	1 / 445 (0.22%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroidectomy			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
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			
Hyperemesis gravidarum			
subjects affected / exposed	1 / 445 (0.22%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Faecaloma			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hiatus hernia			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 445 (0.22%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Genital prolapse			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 445 (0.00%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 445 (0.22%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 445 (0.67%)	0 / 445 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 445 (0.22%)	1 / 445 (0.22%)	
occurrences causally related to treatment / all	0 / 1	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	Olo 0.6%	Vehicle	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	309 / 445 (69.44%)	319 / 445 (71.69%)	
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	31 / 445 (6.97%)	49 / 445 (11.01%)	
occurrences (all)	34	61	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	29 / 445 (6.52%)	3 / 445 (0.67%)	
occurrences (all)	30	3	
Headache			
subjects affected / exposed	57 / 445 (12.81%)	56 / 445 (12.58%)	
occurrences (all)	123	110	
Sinus headache			
subjects affected / exposed	15 / 445 (3.37%)	23 / 445 (5.17%)	
occurrences (all)	21	42	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	28 / 445 (6.29%)	29 / 445 (6.52%)	
occurrences (all)	44	62	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	29 / 445 (6.52%)	24 / 445 (5.39%)	
occurrences (all)	36	33	
Cough			
subjects affected / exposed	23 / 445 (5.17%)	23 / 445 (5.17%)	
occurrences (all)	32	29	
Epistaxis			
subjects affected / exposed	111 / 445 (24.94%)	126 / 445 (28.31%)	
occurrences (all)	189	212	
Nasal ulcer			
subjects affected / exposed	46 / 445 (10.34%)	38 / 445 (8.54%)	
occurrences (all)	62	52	

Pharyngolaryngeal pain			
subjects affected / exposed	21 / 445 (4.72%)	26 / 445 (5.84%)	
occurrences (all)	24	29	
Rhinitis allergic			
subjects affected / exposed	46 / 445 (10.34%)	65 / 445 (14.61%)	
occurrences (all)	97	148	
Infections and infestations			
Bronchitis			
subjects affected / exposed	23 / 445 (5.17%)	19 / 445 (4.27%)	
occurrences (all)	25	21	
Nasopharyngitis			
subjects affected / exposed	72 / 445 (16.18%)	67 / 445 (15.06%)	
occurrences (all)	98	90	
Rhinitis			
subjects affected / exposed	87 / 445 (19.55%)	73 / 445 (16.40%)	
occurrences (all)	126	108	
Sinusitis			
subjects affected / exposed	66 / 445 (14.83%)	58 / 445 (13.03%)	
occurrences (all)	96	72	
Upper respiratory tract infection			
subjects affected / exposed	73 / 445 (16.40%)	75 / 445 (16.85%)	
occurrences (all)	97	102	

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