Clinical trial results:
Safety and Efficacy of Olopatadine HCl Nasal Spray in 6-11 Year Old Patients

Summary

EudraCT number	2017-003856-22
Trial protocol	Outside EU/EEA
Global end of trial date	24 November 2008

Results information

Result version number	v1 (current)
This version publication date	02 February 2018
First version publication date	02 February 2018

Trial information

Trial identification

Sponsor protocol code	C-07-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00578929
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	24 November 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 November 2008
Global end of trial reached?	Yes
Global end of trial date	24 November 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 compare Olopatadine Hydrochloride (HCl) Nasal Spray 0.6% and Olopatadine HCl Nasal Spray Vehicle when given twice daily (BID) for the treatment of Seasonal Allergic Rhinitis (SAR) for a 2-week period.

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	28 September 2007
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	United States: 1188
Worldwide total number of subjects	1188
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)	1188
Adolescents (12-17 years)	0

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

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 173 study centers in the United States.

Pre-assignment

Screening details:

A total of 2388 subjects were screened for possible study participation and given Olopatadine HCl Nasal Spray Vehicle as run-in treatment. Of these, 1200 subjects were screen failures and not enrolled into the study. The remaining 1188 subjects were enrolled into the randomized treatment period. This reporting group includes all treated subjects.

Period 1

Period 1 title	Treatment (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% 1 Spray

Arm description:

Olopatadine HCl Nasal Spray 0.6%, 1 spray per nostril BID

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

Dosage and administration details:

Olopatadine HCl Nasal Spray 0.6%, 1 spray per nostril BID

Arm title	Olo 0.6% 2 Sprays

Arm description:

Olopatadine HCl Nasal Spray 0.6%, 2 sprays per nostril BID

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

Dosage and administration details:

Olopatadine HCl Nasal Spray 0.6%, 2 sprays per nostril BID

Arm title	Veh 1 Spray

Arm description:

Olopatadine HCl Nasal Spray Vehicle, 1 spray per nostril BID

Arm type	Active comparator

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

Dosage and administration details:

Olopatadine HCl Nasal Spray Vehicle, 1 or 2 sprays per nostril BID

Arm title	Veh 2 sprays

Arm description:

Olopatadine HCl Nasal Spray Vehicle, 2 sprays per nostril BID

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

Dosage and administration details:

Olopatadine HCl Nasal Spray Vehicle, 1 or 2 sprays per nostril BID

Number of subjects in period 1	Olo 0.6% 1 Spray	Olo 0.6% 2 Sprays	Veh 1 Spray
Started	298	296	297
Completed	281	288	283
Not completed	17	8	14
Reason not given	3	-	-
Adverse event, non-fatal	7	5	4
Protocol violation	1	-	3
Treatment Failure	3	2	4
Decision unrelated to an AE	1	-	2
Lost to follow-up	2	1	1

Number of subjects in period 1	Veh 2 sprays
Started	297
Completed	283
Not completed	14
Reason not given	1
Adverse event, non-fatal	4
Protocol violation	-
Treatment Failure	8
Decision unrelated to an AE	1
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Olo 0.6% 1 Spray
Reporting group description:	
Olopatadine HCl Nasal Spray 0.6%, 1 spray per nostril BID	
Reporting group title	Olo 0.6% 2 Sprays
Reporting group description:	
Olopatadine HCl Nasal Spray 0.6%, 2 sprays per nostril BID	
Reporting group title	Veh 1 Spray
Reporting group description:	
Olopatadine HCl Nasal Spray Vehicle, 1 spray per nostril BID	
Reporting group title	Veh 2 sprays
Reporting group description:	
Olopatadine HCl Nasal Spray Vehicle, 2 sprays per nostril BID	

Reporting group values	Olo 0.6% 1 Spray	Olo 0.6% 2 Sprays	Veh 1 Spray
Number of subjects	298	296	297
Age categorical Units: Subjects			
6 to 8 years	121	121	121
9 to 11 years	177	175	176
Gender categorical Units: Subjects			
Female	130	122	125
Male	168	174	172
Total Reflective Nasal Symptom Score (rTNSS)			
Nasal symptoms scores (runny nose, stuffy nose, itchy nose, and sneezing) were evaluated twice daily while on study therapy via subject diary and rated on a 4-unit scale, where 0=none, 1=mild, 2=moderate, and 3=severe. Baseline rTNSS was the average of the AM and PM reflective severity scores for the sum of the individual severity scores averaged across 3 qualifying diary days.			
Units: units on a scale			
arithmetic mean	8.99	9.16	9.11
standard deviation	± 1.757	± 1.598	± 1.686
Total Reflective Ocular Symptom Score (TOSS)			
Ocular symptoms (itchy eyes and watery eyes) were evaluated twice daily while on study therapy via a subject diary and rated on a 4-unit scale, where 0=none, 1=mild, 2=moderate, and 3=severe. Baseline reflective TOSS was the average of the AM and PM reflective severity scores for the sum of the individual severity scores averaged across 3 qualifying diary days.			
Units: units on a scale			
arithmetic mean	3.46	3.59	3.53
standard deviation	± 1.565	± 1.489	± 1.56

Reporting group values	Veh 2 sprays	Total	
Number of subjects	297	1188	
Age categorical Units: Subjects			
6 to 8 years	122	485	
9 to 11 years	175	703	

Gender categorical Units: Subjects			
Female	124	501	
Male	173	687	
Total Reflective Nasal Symptom Score (rTNSS)			
Nasal symptoms scores (runny nose, stuffy nose, itchy nose, and sneezing) were evaluated twice daily while on study therapy via subject diary and rated on a 4-unit scale, where 0=none, 1=mild, 2=moderate, and 3=severe. Baseline rTNSS was the average of the AM and PM reflective severity scores for the sum of the individual severity scores averaged across 3 qualifying diary days.			
Units: units on a scale			
arithmetic mean	8.85		
standard deviation	± 1.785	-	
Total Reflective Ocular Symptom Score (TOSS)			
Ocular symptoms (itchy eyes and watery eyes) were evaluated twice daily while on study therapy via a subject diary and rated on a 4-unit scale, where 0=none, 1=mild, 2=moderate, and 3=severe. Baseline reflective TOSS was the average of the AM and PM reflective severity scores for the sum of the individual severity scores averaged across 3 qualifying diary days.			
Units: units on a scale			
arithmetic mean	3.29		
standard deviation	± 1.662	-	

End points

End points reporting groups

Reporting group title	Olo 0.6% 1 Spray
Reporting group description:	
Olopatadine HCl Nasal Spray 0.6%, 1 spray per nostril BID	
Reporting group title	Olo 0.6% 2 Sprays
Reporting group description:	
Olopatadine HCl Nasal Spray 0.6%, 2 sprays per nostril BID	
Reporting group title	Veh 1 Spray
Reporting group description:	
Olopatadine HCl Nasal Spray Vehicle, 1 spray per nostril BID	
Reporting group title	Veh 2 sprays
Reporting group description:	
Olopatadine HCl Nasal Spray Vehicle, 2 sprays per nostril BID	
Subject analysis set title	Olo 0.6% 1 spray
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This analysis population includes all subjects who received study medication and had at least 1 on-therapy visit (Intent-to-Treat (ITT) Analysis Set).	
Subject analysis set title	Veh 1 spray
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Intent-to-Treat, with non-missing data at both visits and nonzero baseline data	
Subject analysis set title	Olo 0.6% 2 sprays
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Intent-to-Treat, with non-missing data at both visits and nonzero baseline data	
Subject analysis set title	Veh 2 sprays
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Intent-to-Treat, with non-missing data at both visits and nonzero baseline data	
Subject analysis set title	Olo 0.6% 1 spray
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Intent-to-treat, with non-missing data at both visits and nonzero baseline data	
Subject analysis set title	Veh 1 spray
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Intent-to-treat, with non-missing data at both visits and nonzero baseline data	
Subject analysis set title	Olo 0.6% 2 sprays
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Intent-to-Treat, with non-missing data at both visits and nonzero baseline data	
Subject analysis set title	Veh 2 sprays
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Intent-to-Treat, with non-missing data at both visits and nonzero baseline data	

Primary: Percent Change from Baseline in rTNSS

End point title	Percent Change from Baseline in rTNSS

End point description:

The rTNSS was defined as the average of the AM and PM reflective (how the subject felt for the last 12 hours) severity scores for the sum of assessments of runny nose, stuffy nose, itchy nose, and sneezing, averaged across the first 14 complete days of the randomized treatment phase. Symptoms were evaluated twice daily while on study therapy via a subject telephone diary and rated on a 4-unit scale, where 0=none, 1=mild, 2=moderate, and 3=severe. A more negative change number indicates improvement, namely lessening of the symptom.

End point type	Primary

End point timeframe:

Baseline, up through first 14 complete days of treatment

End point values	Olo 0.6% 1 spray	Veh 1 spray	Olo 0.6% 2 sprays	Veh 2 sprays
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	294	294	293	293
Units: units on a scale				
arithmetic mean (standard deviation)	-24.69 (± 25.475)	-17.91 (± 24.125)	-26.46 (± 24.897)	-20.82 (± 24.394)

Statistical analyses

Statistical analysis title	Percent Change from Baseline in rTNSS
Comparison groups	Olo 0.6% 2 sprays v Veh 2 sprays
Number of subjects included in analysis	586
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	ANCOVA

Statistical analysis title	Percent Change from Baseline in rTNSS
Comparison groups	Olo 0.6% 1 spray v Veh 1 spray
Number of subjects included in analysis	588
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007
Method	ANCOVA

Secondary: Percent Change from Baseline in rTOSS

End point title	Percent Change from Baseline in rTOSS

End point description:

The rTOSS was defined as the average of the AM and PM reflective severity scores for the sum of the

assessments of ocular symptoms (itchy and watery eyes), averaged across 14 days. Symptoms were evaluated twice daily while on study therapy via a subject telephone diary and rated on a 4-unit scale, where 0=none, 1=mild, 2=moderate, and 3=severe. A more negative change number indicates improvement, namely lessening of the symptom.

End point type	Secondary

End point timeframe:

Baseline, up through first 14 complete days of treatment

End point values	Olo 0.6% 1 spray	Veh 1 spray	Olo 0.6% 2 sprays	Veh 2 sprays
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	287	288	289	283
Units: units on a scale				
arithmetic mean (standard deviation)	-24.45 (± 59.073)	-6.06 (± 108.653)	-26.34 (± 41.552)	-8.20 (± 71.537)

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	10.0

Reporting groups

Reporting group title	Olo 0.6% 1 Spray

Reporting group description:

Olopatadine HCl Nasal Spray 0.6%, 1 spray per nostril BID

Reporting group title	Olo 0.6% 2 Sprays

Reporting group description:

Olopatadine HCl Nasal Spray 0.6%, 2 sprays per nostril BID

Reporting group title	Veh 1 Spray

Reporting group description:

Olopatadine HCl Nasal Spray Vehicle, 1 spray per nostril BID

Reporting group title	Veh 2 sprays

Reporting group description:

Olopatadine HCl Nasal Spray Vehicle, 2 sprays per nostril BID

Serious adverse events	Olo 0.6% 1 Spray	Olo 0.6% 2 Sprays	Veh 1 Spray
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 298 (0.00%)	0 / 296 (0.00%)	0 / 297 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Veh 2 sprays		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 297 (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	Olo 0.6% 1 Spray	Olo 0.6% 2 Sprays	Veh 1 Spray
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 298 (9.73%)	26 / 296 (8.78%)	21 / 297 (7.07%)
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 298 (4.36%)	9 / 296 (3.04%)	11 / 297 (3.70%)
occurrences (all)	16	9	11
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	17 / 298 (5.70%)	18 / 296 (6.08%)	11 / 297 (3.70%)
occurrences (all)	19	22	15

Non-serious adverse events	Veh 2 sprays		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 297 (10.10%)		
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 297 (5.39%)		
occurrences (all)	16		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	16 / 297 (5.39%)		
occurrences (all)	22		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2008	Statistical analysis section revised to incorporate an analysis of covariance with randomization stratification factor and baseline TNSS as covariates, as instructed by Health Authority.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported