Clinical trial results:
Safety and Pharmacokinetics of PATANASE® in Pediatric Patients 2 to < 6 Years of Age Who Have a History of Allergic Rhinitis

Summary

EudraCT number	2017-003970-16
Trial protocol	Outside EU/EEA
Global end of trial date	18 December 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-07-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	18 December 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2008
Global end of trial reached?	Yes
Global end of trial date	18 December 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 assess the safety and pharmacokinetic of Olopatadine Hydrochloride Nasal Spray 0.6% administered twice daily in pediatric patients 2 to < 6 years of age.

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	03 October 2008
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: 132
Worldwide total number of subjects	132
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)	132
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 9 study centers located in the US.

Pre-assignment

Screening details:

This reporting group includes all randomized and treated subjects (132).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Olo 0.6% 1 Spray

Arm description:

Olopatadine Hydrochloride Nasal Spray 0.6%, 1 spray in each nostril twice daily (BID) for 14 days, 1 single dose on Day 15

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

Dosage and administration details:

1 spray in each nostril BID for 14 days, 1 single dose on the 15th day

Arm title	Veh 1 Spray

Arm description:

Olopatadine Hydrochloride Nasal Spray Vehicle, 1 spray in each nostril BID for 15 days

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

Dosage and administration details:

1 spray in each nostril BID for 15 days

Number of subjects in period 1	Olo 0.6% 1 Spray	Veh 1 Spray
Started	66	66
Completed	63	63
Not completed	3	3
Reason not given	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Olo 0.6% 1 Spray
Reporting group description:	
Olopatadine Hydrochloride Nasal Spray 0.6%, 1 spray in each nostril twice daily (BID) for 14 days, 1 single dose on Day 15	
Reporting group title	Veh 1 Spray
Reporting group description:	
Olopatadine Hydrochloride Nasal Spray Vehicle, 1 spray in each nostril BID for 15 days	

Reporting group values	Olo 0.6% 1 Spray	Veh 1 Spray	Total
Number of subjects	66	66	132
Age categorical			
This analysis population includes all enrolled subjects who received at least one dose of study medication (Safety Analysis Set)			
Units: Subjects			
2 to <4 years	37	34	71
4 to <6 years	29	32	61
Gender categorical Units: Subjects			
Female	28	36	64
Male	38	30	68

End points

End points reporting groups

Reporting group title	Olo 0.6% 1 Spray
Reporting group description:	
Olopatadine Hydrochloride Nasal Spray 0.6%, 1 spray in each nostril twice daily (BID) for 14 days, 1 single dose on Day 15	
Reporting group title	Veh 1 Spray
Reporting group description:	
Olopatadine Hydrochloride Nasal Spray Vehicle, 1 spray in each nostril BID for 15 days	

Primary: Number of Serious Adverse Events (SAEs)

End point title	Number of Serious Adverse Events (SAEs)[1]
End point description:	
Adverse events were defined as any change (expected or unexpected) in a subject's nasal and/or medical health that occurred after initiation of study treatment.	
End point type	Primary
End point timeframe:	
Up through Day 15	

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: No formal statistical analysis was planned or conducted for this primary endpoint. Descriptive tables for adverse events were provided.

End point values	Olo 0.6% 1 Spray	Veh 1 Spray		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	66		
Units: number	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum plasma concentration (Cmax)

End point title	Maximum plasma concentration (Cmax)[2]
End point description:	
Plasma concentrations of olopatadine and its active metabolites [N-desmethyl olopatadine (M1), N-didesmethyl olopatadine (M2), and olopatadine N-oxide (M3)] were measured, and pharmacokinetic (PK) parameters for olopatadine and M1, M2, and M3 were estimated using a population PK model. There were no measurable plasma concentrations for M2. Mean systemic exposure parameters were based on post hoc individual parameter estimates.	
End point type	Secondary
End point timeframe:	
Up through Day 15	

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only subjects administered experimental drug were analyzed. Descriptive tables for pharmacokinetic parameters were provided.

End point values	Olo 0.6% 1 Spray			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: ng/mL				
arithmetic mean (standard deviation)				
Olopatadine	13.4 (± 4.60)			
M1	0.219 (± 0.078)			
M3	0.34 (± 0.152)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to attain Cmax from time of last dose (Tmax)

End point title	Time to attain Cmax from time of last dose (Tmax)[3]

End point description:

Plasma concentrations of olopatadine and its active metabolites, M1, M2, and M3 were measured, and PK parameters were estimated using a population PK model. There were no measurable plasma concentrations for M2. Mean systemic exposure parameters were based on post hoc individual parameter estimates.

End point type	Secondary

End point timeframe:

Up to Day 15

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only subjects administered experimental drug were analyzed. Descriptive tables for pharmacokinetic parameters were provided.

End point values	Olo 0.6% 1 Spray			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: hours				
arithmetic mean (standard deviation)				
Olopatadine	0.918 (± 0.293)			
M1	2.51 (± 0.245)			
M3	1.50 (± 0.224)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration - time curve (AUC0-12)

End point title	Area under the plasma concentration - time curve (AUC0-12)[4]

End point description:

Plasma concentrations of olopatadine and its active metabolites, M1, M2, and M3 were measured, and PK parameters were estimated using a population PK model. There were no measurable plasma concentrations for M2. Mean systemic exposure parameters were based on post hoc individual parameter estimates. AUC0-12 at steady state was determined as the ratio of dose to clearance of the analyte.

End point type	Secondary

End point timeframe:

Up to Day 15

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only subjects administered experimental drug were analyzed. Descriptive tables for pharmacokinetic parameters were provided.

End point values	Olo 0.6% 1 Spray			
Subject group type	Reporting group			
Number of subjects analysed	66			
Units: ng*h/mL				
arithmetic mean (standard deviation)				
Olopatadine	75.0 (± 26.4)			
M1	1.56 (± 0.54)			
M3	2.03 (± 0.917)			

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	11.0

Reporting groups

Reporting group title	Olo 0.6% 1 Spray

Reporting group description:

Olopatadine Hydrochloride Nasal Spray 0.6%, 1 spray in each nostril twice daily (BID) for 14 days, 1 single dose on the 15th day

Reporting group title	Veh 1 Spray

Reporting group description:

Olopatadine Hydrochloride Nasal Spray Vehicle, 1 spray in each nostril BID for 15 days

Serious adverse events	Olo 0.6% 1 Spray	Veh 1 Spray	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 66 (0.00%)	0 / 66 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Olo 0.6% 1 Spray	Veh 1 Spray	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 66 (22.73%)	14 / 66 (21.21%)	
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	0 / 66 (0.00%)	4 / 66 (6.06%)	
occurrences (all)	0	4	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	2 / 66 (3.03%)	6 / 66 (9.09%)	
occurrences (all)	2	7	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 66 (9.09%)	0 / 66 (0.00%)	
occurrences (all)	6	0	
Vomiting			
subjects affected / exposed	3 / 66 (4.55%)	4 / 66 (6.06%)	
occurrences (all)	3	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 66 (9.09%)	7 / 66 (10.61%)	
occurrences (all)	6	7	
Epistaxis			
subjects affected / exposed	4 / 66 (6.06%)	1 / 66 (1.52%)	
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