Clinical trial results:
Safety of PATANASE® Nasal Spray in Patients With Perennial Allergic Rhinitis

Summary

EudraCT number	2017-002726-20
Trial protocol	Outside EU/EEA
Global end of trial date	04 January 2011

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-08-32

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00789555
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alcon Research
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	04 January 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 January 2011
Global end of trial reached?	Yes
Global end of trial date	04 January 2011
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 local nasal adverse effects, as well as systemic effects, of PATANASE nasal spray when compared with Patanase Vehicle, pH 3.7 and Patanase Vehicle, pH 7.0 in patients 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	19 November 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: 1260
Worldwide total number of subjects	1260
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)	146

Adults (18-64 years)	1086
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited and enrolled from 69 US study centers.

Pre-assignment

Screening details:

234 subjects were enrolled under protocol Version 1.0, then exited due to a revision in the study plan. A new cohort of 1026 subjects was enrolled in protocol Version 2.0, for a total enrollment of 1260 subjects.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	PATANASE

Arm description:

Two sprays in each nostril twice a day for up to 12 months

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

Dosage and administration details:

Olopatadine hydrochloride 0.6% nasal spray (PATANASE)
Two sprays in each nostril twice a day (morning and evening) for up to 12 months

Arm title	Patanase Vehicle, pH 3.7

Arm description:

Olopatadine nasal spray vehicle, pH 3.7, two sprays in each nostril twice a day (morning and evening) for up to 12 months

Arm type	Placebo Comparator
Investigational medicinal product name	Olopatadine nasal spray vehicle, pH 3.7
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Two sprays in each nostril twice a day (morning and evening) for up to 12 months

Arm title	Patanase Vehicle, pH 7.0

Arm description:

Olopatadine nasal spray vehicle, pH 7.0, two sprays in each nostril twice a day (morning and evening) for up to 12 months

Arm type	Placebo Comparator

Investigational medicinal product name	Olopatadine nasal spray vehicle, pH 7.0
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

Two sprays in each nostril twice a day (morning and evening) for up to 12 months

Number of subjects in period 1	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0
Started	421	417	422
Completed	262	278	263
Not completed	159	139	159
Treatment failure	11	8	12
Protocol Amendment	78	76	80
Adverse event, non-fatal	17	7	10
Patient decision unnrelated to adv event	38	29	26
Protocol Violation	6	9	13
Lost to follow-up	9	10	18

Baseline characteristics

Reporting groups	
Reporting group title	PATANASE
Reporting group description:	
Two sprays in each nostril twice a day for up to 12 months	
Reporting group title	Patanase Vehicle, pH 3.7
Reporting group description:	
Olopatadine nasal spray vehicle, pH 3.7, two sprays in each nostril twice a day (morning and evening) for up to 12 months	
Reporting group title	Patanase Vehicle, pH 7.0
Reporting group description:	
Olopatadine nasal spray vehicle, pH 7.0, two sprays in each nostril twice a day (morning and evening) for up to 12 months	

Reporting group values	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0
Number of subjects	421	417	422
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	36.8	36.2	38.3
standard deviation	± 14.5	± 14.2	± 14.6
Gender categorical Units: Subjects			
Female	251	260	278
Male	170	157	144

Reporting group values	Total		
Number of subjects	1260		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	789		
Male	471		

End points

End points reporting groups

Reporting group title	PATANASE
Reporting group description:	
Two sprays in each nostril twice a day for up to 12 months	
Reporting group title	Patanase Vehicle, pH 3.7
Reporting group description:	
Olopatadine nasal spray vehicle, pH 3.7, two sprays in each nostril twice a day (morning and evening) for up to 12 months	
Reporting group title	Patanase Vehicle, pH 7.0
Reporting group description:	
Olopatadine nasal spray vehicle, pH 7.0, two sprays in each nostril twice a day (morning and evening) for up to 12 months	

Primary: Percentage of Subjects With Clinically Relevant Change From Baseline (Day 0) in Nasal Examination Parameters to Exit (Month 12 or Sooner)

End point title	Percentage of Subjects With Clinically Relevant Change From Baseline (Day 0) in Nasal Examination Parameters to Exit (Month 12 or Sooner)
End point description:	
Percentage of subjects with clinically relevant change from baseline in protocol-specific safety parameters to time of exit, based on the assessment of the investigator, regardless of causality (related or not related) to test article. This analysis population includes all subjects who received study drug (Safety Analysis Set), minus any missing data.	
End point type	Primary
End point timeframe:	
Baseline (Day 0), Exit (Month 12 or sooner)	

End point values	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	386	386	381	
Units: Percentage of subjects				
number (not applicable)				
Anatomic Abnormalities	0.8	1.3	0.3	
Bleeding	0.8	1.0	2.6	
Infection	0.3	1.0	0.0	
Possible Ulcerations	0.5	0.5	1.6	

Statistical analyses

Statistical analysis title	Clinically relevant change: Anatomic Abnormalities
Comparison groups	PATANASE v Patanase Vehicle, pH 3.7

Number of subjects included in analysis	772
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.7251
Method	Chi-squared

Notes:

[1] - Chi-squared test of independence

Statistical analysis title	Clinically relevant change: Anatomic Abnormalities
Comparison groups	PATANASE v Patanase Vehicle, pH 7.0
Number of subjects included in analysis	767
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.6241
Method	Fisher exact

Notes:

[2] - Fisher's Exact test

Statistical analysis title	Clinically relevant change: Bleeding
Comparison groups	PATANASE v Patanase Vehicle, pH 3.7
Number of subjects included in analysis	772
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 1
Method	Chi-squared

Notes:

[3] - Chi-squared test of independence

Statistical analysis title	Clinically relevant change: Bleeding
Comparison groups	PATANASE v Patanase Vehicle, pH 7.0
Number of subjects included in analysis	767
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.0475
Method	Fisher exact

Notes:

[4] - Fisher's Exact test

Statistical analysis title	Clinically relevant change: Infection
Comparison groups	PATANASE v Patanase Vehicle, pH 3.7
Number of subjects included in analysis	772
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.3734
Method	Chi-squared

Notes:

[5] - Chi-squared test of Independence

Statistical analysis title	Clinically relevant change: Infection
Comparison groups	PATANASE v Patanase Vehicle, pH 7.0
Number of subjects included in analysis	767
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 1
Method	Fisher exact

Notes:

[6] - Fisher's Exact test

Statistical analysis title	Clinically relevant change: Possible ulcerations
Comparison groups	PATANASE v Patanase Vehicle, pH 3.7
Number of subjects included in analysis	772
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 1
Method	Fisher exact

Notes:

[7] - Fisher's Exact test

Statistical analysis title	Clinically relevant change: Possible ul...
Comparison groups	PATANASE v Patanase Vehicle, pH 7.0
Number of subjects included in analysis	767
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 0.1749
Method	Chi-squared

Notes:

[8] - Chi-squared test of independence

Primary: Self-Rated Relief Assessment at Day 30

End point title	Self-Rated Relief Assessment at Day 30

End point description:

Relief assessment as rated by the subject on a 4-point scale, where 1=complete relief and 4=no relief. The subject answered the following question: "I would rate the study medication's effectiveness for relieving my allergy symptoms since my last visit as: (1) Complete Relief; (2) Moderate Relief; (3) Mild Relief; (4) No Relief." This analysis population includes all subjects enrolled under protocol Version 2.0 who received study drug and attended at least one on-therapy study visit (ITT). The LOCF (last observation carried forward method) was used to impute missing data.

End point type	Primary

End point timeframe:

Day 30

End point values	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	328	331	330	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Self-Rated Relief Assessment at Day 30	2.4 (± 0.9)	2.7 (± 1.0)	2.7 (± 0.9)	

Statistical analyses

Statistical analysis title	Mean response in Self-rated Relief Assessment
Comparison groups	Patanase Vehicle, pH 3.7 v PATANASE
Number of subjects included in analysis	659
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	t-test, 2-sided

Secondary: Percentage of Subjects With Change From Baseline (Day 0) in Pulse Rate Beats Per Minute (BPM) to Exit (Month 12 or Sooner)

End point title	Percentage of Subjects With Change From Baseline (Day 0) in Pulse Rate Beats Per Minute (BPM) to Exit (Month 12 or Sooner)

End point description:

Percentage of subjects with change from baseline in pulse measurement to time of exit, as recorded based on a full 60-second count after the patient rested for five minutes. Safety analysis set, minus any missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 0), Exit (Month 12 or sooner)

End point values	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	416	414	418	
Units: Percentage of subjects				
number (not applicable)				
Decrease greater than 30 BPM	0.0	0.0	0.0	
Decrease 21-30 BPM	0.7	1.2	0.5	
Decrease 11-20 BPM	7.5	9.2	6.2	
Decrease 1-10 BPM	27.2	30.4	34.7	
No Change	7.5	6.5	7.9	
Increase 1-10 BPM	38.7	38.9	39.7	
Increase 11-20 BPM	16.8	9.9	8.9	
Increase 21-30 BPM	1.4	3.6	1.4	
Increase greater than 30 BPM	0.2	0.2	0.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Change From Baseline (Day 0) in Blood Pressure (Systolic) to Exit (Month 12 or Sooner)

End point title	Percentage of Subjects With Change From Baseline (Day 0) in Blood Pressure (Systolic) to Exit (Month 12 or Sooner)

End point description:

Percentage of subjects with change from baseline in systolic blood pressure to time of exit, as obtained in a sitting position after the subject rested for five minutes. Two measurements, separated by two minutes, were obtained, from which the average systolic pressure was derived. If the first two readings differed by more than 5 millimeters of mercury (mmHg), a third reading was taken two minutes later and all three were used to determine the average. The first appearance of sound (phase 1) was used to define systolic blood pressure. Safety analysis set, minus any missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 0), Exit (Month 12 or sooner)

End point values	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	416	413	418	
Units: Percentage of subjects				
number (not applicable)				
Decrease greater than 30 mmHg	0.5	1.2	0.5	
Decrease 21-30 mmHg	1.0	2.4	2.4	
Decrease 11-20 mmHg	11.8	9.2	10.0	
Decrease 1-10 mmHg	35.3	36.3	35.4	
No change	4.6	5.3	5.3	
Increase 1-10 mmHg	35.1	33.4	34.4	
Increase 11-20 mmHg	10.6	10.2	10.5	
Increase 21-30 mmHg	1.2	1.9	1.2	
Increase greater than 30 mmHg	0.0	0.0	0.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Change From Baseline (Day 0) in Blood Pressure (Diastolic) to Exit (Month 12 or Sooner)

End point title	Percentage of Subjects With Change From Baseline (Day 0) in

	Blood Pressure (Diastolic) to Exit (Month 12 or Sooner)

End point description:

Percentage of subjects with change from baseline in diastolic blood pressure to time of exit, as obtained in a sitting position after the subject rested for five minutes. Two measurements, separated by two minutes, were obtained, from which the average systolic pressure was derived. If the first two readings differed by more than 5 millimeters of mercury (mmHg), a third reading was taken two minutes later and all three were used to determine the average. The disappearance of sound (phase 5) was used to define diastolic blood pressure. Safety analysis set, minus any missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 0), Exit (Month 12 or sooner)

End point values	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	416	413	418	
Units: Percentage of subjects				
number (not applicable)				
Decrease greater than 30 mmHg	0.0	0.2	0.2	
Decrease 21-30 mmHg	0.7	1.0	0.5	
Decrease 11-20 mmHg	8.7	13.6	11.5	
Decrease 1-10 mmHg	44.5	38.7	42.6	
No change	7.5	6.1	6.5	
Increase 1-10 mmHg	33.2	33.4	33.7	
Increase 11-20 mmHg	5.3	6.5	5.0	
Increase 21-30 mmHg	0.2	0.5	0.0	
Increase greater than 30 mmHg	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinically Relevant Change From Baseline (Day 0) in Physical Examination Parameters to Exit (Month 12 or Sooner)

End point title	Percentage of Subjects With Clinically Relevant Change From Baseline (Day 0) in Physical Examination Parameters to Exit (Month 12 or Sooner)

End point description:

Percentage of subjects with clinically relevant change from baseline in protocol-specific safety parameters to time of exit, based on the assessment of the investigator, regardless of causality (related or not related) to test article. Safety analysis set, minus any missing data.

End point type	Secondary

End point timeframe:

Baseline (Day 0), Exit (Month 12 or sooner)

End point values	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	404	403	392	
Units: Percentage of subjects				
number (not applicable)				
Head/EENT	5.2	4.2	4.6	
Neck	0.0	0.7	0.0	
Cardiovascular	0.0	0.5	0.3	
Pulmonary	0.7	0.2	0.3	
Abdomen	0.0	0.0	0.3	
Skin and Extremities	1.2	0.5	1.3	
Neurological	0.7	0.0	0.0	
Lymph Nodes	0.0	0.2	0.0	
Musculoskeletal	0.0	0.5	0.5	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected for the duration of the study: 2 years, 1 month, 16 days. Adverse events were defined as any untoward (unfavorable and unintended) medical occurrence in a subject administered a test article.

Adverse event reporting additional description:

Adverse events were collected after the first dose of study medication at Visit 1 and during each monthly on-therapy study visit through Visit 13 (or Early Exit). Safety Analysis Set was used for analysis. Only total subjects affected by non-serious AEs that occur at >5% are reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	PATANASE

Reporting group description:

Two sprays in each nostril twice a day for up to 12 months

Reporting group title	Patanase Vehicle, pH 3.7

Reporting group description:

Two sprays in each nostril twice a day for up to 12 months

Reporting group title	Patanase Vehicle, pH 7.0

Reporting group description:

Two sprays in each nostril twice a day for up to 12 months

Serious adverse events	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 421 (1.90%)	7 / 417 (1.68%)	14 / 422 (3.32%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Cystostomy closure			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Internal fixation of fracture			

subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fusion surgery			
subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 421 (0.00%)	1 / 417 (0.24%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menometrorrhagia			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menstruation irregular			
subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			

subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	0 / 421 (0.00%)	1 / 417 (0.24%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	1 / 421 (0.24%)	1 / 417 (0.24%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cervicobrachial syndrome			

subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Impaired gastric emptying			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intravertebral disc protrusion			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw disorder			
subjects affected / exposed	0 / 421 (0.00%)	1 / 417 (0.24%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 421 (0.00%)	1 / 417 (0.24%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 421 (0.00%)	1 / 417 (0.24%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster oticus			
subjects affected / exposed	0 / 421 (0.00%)	0 / 417 (0.00%)	1 / 422 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	0 / 421 (0.00%)	1 / 417 (0.24%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sialoadenitis			
subjects affected / exposed	1 / 421 (0.24%)	0 / 417 (0.00%)	0 / 422 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	PATANASE	Patanase Vehicle, pH 3.7	Patanase Vehicle, pH 7.0
Total subjects affected by non-serious adverse events			
subjects affected / exposed	220 / 421 (52.26%)	213 / 417 (51.08%)	214 / 422 (50.71%)
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	31 / 421 (7.36%)	28 / 417 (6.71%)	37 / 422 (8.77%)
occurrences (all)	41	34	57
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 421 (5.70%)	27 / 417 (6.47%)	25 / 422 (5.92%)
occurrences (all)	32	38	38
Respiratory, thoracic and mediastinal disorders			

Epistaxis			
subjects affected / exposed	92 / 421 (21.85%)	76 / 417 (18.23%)	85 / 422 (20.14%)
occurrences (all)	159	117	136
Nasal ulcer			
subjects affected / exposed	31 / 421 (7.36%)	27 / 417 (6.47%)	35 / 422 (8.29%)
occurrences (all)	38	39	46
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	50 / 421 (11.88%)	51 / 417 (12.23%)	48 / 422 (11.37%)
occurrences (all)	70	81	66
Rhinitis			
subjects affected / exposed	51 / 421 (12.11%)	59 / 417 (14.15%)	61 / 422 (14.45%)
occurrences (all)	81	94	100
Sinusitis			
subjects affected / exposed	55 / 421 (13.06%)	48 / 417 (11.51%)	49 / 422 (11.61%)
occurrences (all)	71	59	62
Upper respiratory tract infection			
subjects affected / exposed	36 / 421 (8.55%)	52 / 417 (12.47%)	45 / 422 (10.66%)
occurrences (all)	43	64	49

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 June 2009	This study was amended following comments received from the Health Authority. At the time of the amendment's implementation, 234 patients were enrolled in the study. Because the amendment substantially revised the study plan, the analysis variables, and the entry criteria, all of the active patients at the time the amendment was implemented were discontinued and an entirely new cohort of patients was subsequently enrolled.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported