Clinical trial results:
A Multicenter, Randomized, Placebo-controlled Study of SBC-102 in Patients with Lysosomal Acid Lipase Deficiency (ARISE [Acid Lipase Replacement Investigating Safety and Efficacy])

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2011-002750-31
Trial protocol	DE GB IT ES CZ PL GR HR FR
Global end of trial date	

Results information

Result version number	v2
This version publication date	20 July 2016
First version publication date	06 August 2015
Version creation reason	• Correction of full data set Corrections are made in line with posting of the results of this trial to clinicaltrials.gov

Trial information

Trial identification

Sponsor protocol code	LAL-CL02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01757184
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals
Sponsor organisation address	352 Knotter Drive, Cheshire, United States, CT 06410
Public contact	Raquel Cerezo, Clinical Project Lead, Alexion Pharmaceuticals, +1 7814302475, CerezoR@alxn.com
Scientific contact	Mark Friedman, Medical Director, Alexion Pharmaceuticals, +1 7814302497, mark.friedman@alxn.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001331-PIP01-12
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?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	04 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2014
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate efficacy of sebelipase alfa relative to placebo, based on normalisation of alanine aminotransferase (ALT) in patients with Lysosomal Acid Lipase (LAL) Deficiency.

Protection of trial subjects:

Subjects have the right to withdraw from the study at any time for any reason without prejudice to further treatment. The investigator and Sponsor also have the right to withdraw subjects from the study at any time. Specific reasons for discontinuation may include, but are not restricted to, the following:
- intercurrent illness
- medical-significant AEs, including AEs requiring emergency unblinding
- pregnancy
- protocol deviation or non-compliance
- termination of the study by the sponsor

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 January 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	30 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Croatia: 1
Country: Number of subjects enrolled	Czech Republic: 5
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Turkey: 4

Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	66
EEA total number of subjects	31

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)	24
Adolescents (12-17 years)	23
Adults (18-64 years)	19
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 55 study centers located in 17 countries were initiated in this study including 49 during recruitment and 6 after to allow transfer of subjects for local treatment. Subjects were screened at 41 of 55 study centers in all countries except Greece.

Pre-assignment

Screening details:

To assess eligibility, subjects were screened for a period of up to 6 weeks prior to enrollment in the study. A total of 86 subjects were screened. Six of these subjects underwent re-screening (of which 2 were eligible for the study). In total, 66 subjects were eligible for the study and 20 subjects were screen failures.

Period 1

Period 1 title	Double-blind followed by Open-Label (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-blind Sebelipase Alfa

Arm description:

Double-blind period: IV infusions

Arm type	Experimental
Investigational medicinal product name	Sebelipase alfa
Investigational medicinal product code	SBC-102
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Every other week IV infusions of SBC-102 at a dose of 1 mg/kg

Arm title	Double-blind Placebo

Arm description:

Double-blind period: IV infusions

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Every other week infusions of placebo

Number of subjects in period 1	Double-blind Sebelipase Alfa	Double-blind Placebo
Started	36	30
Completed	35	30
Not completed	1	0
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Double-blind Sebelipase Alfa
Reporting group description: Double-blind period: IV infusions	
Reporting group title	Double-blind Placebo
Reporting group description: Double-blind period: IV infusions	

Reporting group values	Double-blind Sebelipase Alfa	Double-blind Placebo	Total
Number of subjects	36	30	66
Age categorical Units: Subjects			
Children (2-11 years)	14	10	24
Adolescents (12-17 years)	9	14	23
Adults (18-64 years)	13	6	19
Age continuous Units: years			
arithmetic mean	16.9	15.2	
standard deviation	± 11.6	± 10.2	-
Gender categorical Units: Subjects			
Female	18	15	33
Male	18	15	33
Ethnicity Units: Subjects			
Hispanic or Latino	6	4	10
Not Hispanic or Latino	30	26	56
Race Units: Subjects			
Asian	1	0	1
Japanese	2	0	2
Black or African American	1	0	1
White	27	28	55
Other	5	2	7

Subject analysis sets	
Subject analysis set title	FAS
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The FAS comprised subjects in the Consented Set who, in addition, were randomised and received at least 1 dose of sebelipase alfa or placebo. The FAS was a modified intention-to-treat (ITT) dataset.	
Subject analysis set title	Consented Set
Subject analysis set type	Intention-to-treat
Subject analysis set description: The Consented Subject Set (Consented Set) was comprised of all subjects who signed informed consent.	
Subject analysis set title	Per Protocol Set

Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol Set (PP Set) comprised subjects in the FAS who, in addition, (1) received at least 9 complete infusions of study drug during the double-blind treatment period; (2) had measurements of ALT at both baseline and Week 20; (3) had Week 20 assessments within 12 to 21 days of the preceding (Week 18) infusion; (4) did not change their LLM; and (5) did not have any other major protocol deviation that would affect interpretation of results for serum transaminases or serum lipids.

Subject analysis set title	Extension Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Extension Analysis Set (EAS), comprised of subjects in the Consented Set who, in addition, were randomised to treatment and received at least 1 dose (or any portion of a dose) of sebelipase alfa. For subjects who were originally randomised to sebelipase alfa and received at least 1 dose of sebelipase alfa (SA/SA), all assessments from both the double-blind and the open-label period were included in the EAS. This included subjects who were dosed in the double-blind phase with sebelipase alfa, but did not initiate open-label sebelipase alfa. For subjects who were originally randomised to placebo and received at least 1 dose of sebelipase alfa in the open-label period (PBO/SA), only assessments from the open-label period were included in the EAS.

Reporting group values	FAS	Consented Set	Per Protocol Set
Number of subjects	66	66	63
Age categorical Units: Subjects			
Children (2-11 years)	24	24	23
Adolescents (12-17 years)	23	23	22
Adults (18-64 years)	19	19	18
Age continuous Units: years			
arithmetic mean	16.1	16.1	16.3
standard deviation	± 10.9	± 10.9	± 11.1
Gender categorical Units: Subjects			
Female	33	33	33
Male	33	33	30
Ethnicity Units: Subjects			
Hispanic or Latino	10	10	9
Not Hispanic or Latino	56	56	54
Race Units: Subjects			
Asian	1	1	1
Japanese	2	2	1
Black or African American	1	1	1
White	55	55	53
Other	7	7	7

Reporting group values	Extension Analysis Set		
Number of subjects	66		
Age categorical Units: Subjects			
Children (2-11 years)	24		
Adolescents (12-17 years)	23		
Adults (18-64 years)	19		

Age continuous Units: years			
arithmetic mean	16.1		
standard deviation	± 10.9		
Gender categorical Units: Subjects			
Female	33		
Male	33		
Ethnicity Units: Subjects			
Hispanic or Latino	10		
Not Hispanic or Latino	56		
Race Units: Subjects			
Asian	1		
Japanese	2		
Black or African American	1		
White	55		
Other	7		

End points

End points reporting groups

Reporting group title	Double-blind Sebelipase Alfa
Reporting group description: Double-blind period: IV infusions	
Reporting group title	Double-blind Placebo
Reporting group description: Double-blind period: IV infusions	
Subject analysis set title	FAS
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: The FAS comprised subjects in the Consented Set who, in addition, were randomised and received at least 1 dose of sebelipase alfa or placebo. The FAS was a modified intention-to-treat (ITT) dataset.	
Subject analysis set title	Consented Set
Subject analysis set type	Intention-to-treat
Subject analysis set description: The Consented Subject Set (Consented Set) was comprised of all subjects who signed informed consent.	
Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description: The Per Protocol Set (PP Set) comprised subjects in the FAS who, in addition, (1) received at least 9 complete infusions of study drug during the double-blind treatment period; (2) had measurements of ALT at both baseline and Week 20; (3) had Week 20 assessments within 12 to 21 days of the preceding (Week 18) infusion; (4) did not change their LLM; and (5) did not have any other major protocol deviation that would affect interpretation of results for serum transaminases or serum lipids.	
Subject analysis set title	Extension Analysis Set
Subject analysis set type	Sub-group analysis
Subject analysis set description: Extension Analysis Set (EAS), comprised of subjects in the Consented Set who, in addition, were randomised to treatment and received at least 1 dose (or any portion of a dose) of sebelipase alfa. For subjects who were originally randomised to sebelipase alfa and received at least 1 dose of sebelipase alfa (SA/SA), all assessments from both the double-blind and the open-label period were included in the EAS. This included subjects who were dosed in the double-blind phase with sebelipase alfa, but did not initiate open-label sebelipase alfa. For subjects who were originally randomised to placebo and received at least 1 dose of sebelipase alfa in the open-label period (PBO/SA), only assessments from the open-label period were included in the EAS.	

Primary: ALT normalisation

End point title	ALT normalisation
End point description: The primary efficacy endpoint was the proportion of subjects who achieved ALT (alanine aminotransferase) normalisation (i.e., ALT below the age-and gender-specific ULN provided by the central laboratory performing this assay) at the end of the double-blind treatment period (i.e. the last double-blind assessment), relative to placebo.	
End point type	Primary
End point timeframe: At the end of double-blind period (week 20)	

End point values	Double-blind Sebelipase Alfa	Double-blind Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	30		
Units: number of subjects with normalized ALT	11	2		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Double-blind Sebelipase Alfa v Double-blind Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0271
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: LDL-c Reduction

End point title	LDL-c Reduction
End point description:	
Relative reduction (percentage change from baseline) in LDL-c at the end of the double-blind period	
End point type	Secondary
End point timeframe:	
At end of double-blind period (week 20)	

End point values	Double-blind Sebelipase Alfa	Double-blind Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	30		
Units: mean percent reduction				
arithmetic mean (standard deviation)	-28.42 (± 22.304)	-6.25 (± 13.015)		

Statistical analyses

Statistical analysis title	Secondary efficacy endpoint
Comparison groups	Double-blind Sebelipase Alfa v Double-blind Placebo

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Risk difference (RD)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: non-HDL-c Reduction

End point title	non-HDL-c Reduction

End point description:

Relative reduction (percentage change from baseline) in non-high-density lipoprotein-cholesterol (non-HDL-c) at the end of the double-blind period

End point type	Secondary

End point timeframe:

At the end of the double-blind period (week 20)

End point values	Double-blind Sebelipase Alfa	Double-blind Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	30		
Units: Percent reduction				
arithmetic mean (standard deviation)	-27.97 (± 18.612)	-6.94 (± 10.922)		

Statistical analyses

Statistical analysis title	Secondary efficacy endpoint
Comparison groups	Double-blind Sebelipase Alfa v Double-blind Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Risk difference (RD)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: Triglycerides Reduction

End point title	Triglycerides Reduction
End point description:	
Relative reduction (percentage change from baseline) in triglycerides (TG) at the end of the double-blind period	
End point type	Secondary
End point timeframe:	
At the end of double-blind period (week 20)	

End point values	Double-blind Sebelipase Alfa	Double-blind Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	30		
Units: percent decrease from baseline				
arithmetic mean (standard deviation)	-25.45 (± 29.411)	-11.14 (± 28.827)		

Statistical analyses

Statistical analysis title	Secondary efficacy endpoint
Comparison groups	Double-blind Sebelipase Alfa v Double-blind Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0375
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Risk difference (RD)
Confidence interval	
level	95 %
sides	2-sided

Secondary: HDL-c Increase

End point title	HDL-c Increase
End point description:	
Relative increase (percentage change from baseline) in high-density lipoprotein-cholesterol (HDL-c) at the end of the double-blind period	
End point type	Secondary
End point timeframe:	
At the end of the double-blind period (week 20)	

End point values	Double-blind Sebelipase Alfa	Double-blind Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	30		
Units: percent increase from baseline				
arithmetic mean (standard deviation)	19.57 (± 16.833)	-0.29 (± 12.36)		

Statistical analyses

Statistical analysis title	Secondary efficacy endpoint
Comparison groups	Double-blind Sebelipase Alfa v Double-blind Placebo
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Risk difference (RD)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: Liver Fat Content Reduction

End point title	Liver Fat Content Reduction

End point description:

Decrease in liver fat content, as assessed by magnetic resonance imaging (MRI) (in the subset of subjects for whom imaging was performed)

End point type	Secondary

End point timeframe:

At end of the double-blind period (week 20)

End point values	Double-blind Sebelipase Alfa	Double-blind Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	25		
Units: percent decrease from baseline				
arithmetic mean (standard deviation)	-31.98 (± 26.763)	-4.21 (± 15.559)		

Statistical analyses

Statistical analysis title	Secondary efficacy endpoint
Comparison groups	Double-blind Sebelipase Alfa v Double-blind Placebo
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Risk difference (RD)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: Liver Histology Improvement	
End point title	Liver Histology Improvement
End point description:	
Improvement in hepatic histology (in the subset of subjects for whom liver biopsy was performed, as determined by blinded central review)	
End point type	Secondary
End point timeframe:	
At the end of double-blind period (week 20)	

End point values	Double-blind Sebelipase Alfa	Double-blind Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	10		
Units: # subjects with improved liver histology	10	4		

Statistical analyses

Statistical analysis title	Secondary efficacy endpoint
Comparison groups	Double-blind Sebelipase Alfa v Double-blind Placebo

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4216
Method	Fisher exact
Confidence interval	
level	95 %
sides	2-sided

Secondary: Liver Volume Reduction

End point title	Liver Volume Reduction

End point description:

Relative reduction (percentage change from baseline) in liver volume, as assessed by magnetic resonance imaging, in the subset of subjects for whom imaging was performed.

End point type	Secondary

End point timeframe:

At the end of the double-blind period (week 20)

End point values	Double-blind Sebelipase Alfa	Double-blind Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	27		
Units: percent from baseline				
arithmetic mean (standard deviation)	-10.28 (± 10.51)	-2.66 (± 10.107)		

Statistical analyses

Statistical analysis title	Secondary efficacy endpoint
Comparison groups	Double-blind Sebelipase Alfa v Double-blind Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0068
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Risk difference (RD)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: AST Normalisation

End point title	AST Normalisation

End point description:

The proportion of subjects with an abnormal baseline aspartate aminotransferase (AST; i.e., > ULN) who achieved AST normalisation, based on age- and gender-specific normal ranges provided by the central laboratory performing this assay

End point type	Secondary

End point timeframe:

At end of double-blind period (week 20)

End point values	Double-blind Sebelipase Alfa	Double-blind Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	29		
Units: participants	15	1		

Statistical analyses

Statistical analysis title	Secondary efficacy endpoint
Comparison groups	Double-blind Sebelipase Alfa v Double-blind Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	Fisher exact
Confidence interval	
level	95 %
sides	2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 20 week double-blind treatment period	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1
Reporting groups	
Reporting group title	Sebelipase Alfa group
Reporting group description: Subjects receiving receive sebelipase alfa 1 mg/kg via IV infusion qow	
Reporting group title	Placebo group
Reporting group description: Subjects received matched placebo via IV infusion qow.	

Serious adverse events	Sebelipase Alfa group	Placebo group	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 36 (5.56%)	1 / 30 (3.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Road traffic accident			
subjects affected / exposed	0 / 36 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Infusion related reaction			
subjects affected / exposed	1 / 36 (2.78%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Gastroenteritis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Sebelipase Alfa group	Placebo group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 36 (86.11%)	28 / 30 (93.33%)	
Investigations			
Body temperature increased			
subjects affected / exposed	2 / 36 (5.56%)	1 / 30 (3.33%)	
occurrences (all)	4	1	
Injury, poisoning and procedural complications			
Procedural pain	Additional description: Procedural pain after liver biopsy unrelated to study drug		
subjects affected / exposed	1 / 36 (2.78%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 36 (27.78%)	6 / 30 (20.00%)	
occurrences (all)	17	7	
Syncope			
subjects affected / exposed	2 / 36 (5.56%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 36 (19.44%)	6 / 30 (20.00%)	
occurrences (all)	7	6	
Asthenia			
subjects affected / exposed	3 / 36 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	3	1	

Fatigue			
subjects affected / exposed	0 / 36 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Vaccination site pain			
subjects affected / exposed	0 / 36 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 36 (16.67%)	5 / 30 (16.67%)	
occurrences (all)	6	6	
Abdominal pain			
subjects affected / exposed	3 / 36 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	4	1	
Constipation			
subjects affected / exposed	3 / 36 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
Nausea			
subjects affected / exposed	3 / 36 (8.33%)	2 / 30 (6.67%)	
occurrences (all)	3	2	
Vomiting			
subjects affected / exposed	3 / 36 (8.33%)	3 / 30 (10.00%)	
occurrences (all)	4	6	
Abdominal pain upper			
subjects affected / exposed	2 / 36 (5.56%)	2 / 30 (6.67%)	
occurrences (all)	3	2	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	6 / 36 (16.67%)	1 / 30 (3.33%)	
occurrences (all)	8	1	
Epistaxis			
subjects affected / exposed	4 / 36 (11.11%)	6 / 30 (20.00%)	
occurrences (all)	8	7	
Cough			
subjects affected / exposed	3 / 36 (8.33%)	3 / 30 (10.00%)	
occurrences (all)	3	4	
Rhinorrhoea			

subjects affected / exposed	2 / 36 (5.56%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 36 (2.78%)	3 / 30 (10.00%)	
occurrences (all)	3	4	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 36 (5.56%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	6 / 36 (16.67%)	6 / 30 (20.00%)	
occurrences (all)	8	7	
Nasopharyngitis			
subjects affected / exposed	4 / 36 (11.11%)	3 / 30 (10.00%)	
occurrences (all)	4	3	
Sinusitis	Additional description: Non-serious sinusitis unrelated to study drug		
subjects affected / exposed	2 / 36 (5.56%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	2 / 36 (5.56%)	3 / 30 (10.00%)	
occurrences (all)	2	3	
Tonsillitis			
subjects affected / exposed	2 / 36 (5.56%)	4 / 30 (13.33%)	
occurrences (all)	2	4	
Pharyngitis			
subjects affected / exposed	0 / 36 (0.00%)	5 / 30 (16.67%)	
occurrences (all)	0	5	
Respiratory tract infection viral			
subjects affected / exposed	0 / 36 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	

Varicella subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	3 / 30 (10.00%) 2	

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