

**Clinical trial results:****An Open-label, Multicenter, Expanded Access Program For Asfotase Alfa (Human Recombinant Tissue-nonspecific Alkaline Phosphatase Fusion Protein) Treatment For Patients With Infantile - Or Juvenile-onset Hypophosphatasia (HPP)****Summary**

EudraCT number	2015-000809-39
Trial protocol	FR
Global end of trial date	08 March 2018

Results information

Result version number	v1 (current)
This version publication date	23 September 2018
First version publication date	23 September 2018

Trial information**Trial identification**

Sponsor protocol code	AA-HPP-405
-----------------------	------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02496689
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals, Inc.
Sponsor organisation address	100 College Street, New Haven, United States, 06510
Public contact	European Clinical Trial Information, Alexion Europe SAS, +33 147100606, clinicaltrials.eu@alexion.com
Scientific contact	European Clinical Trial Information, Alexion Europe SAS, +33 147100606, clinicaltrials.eu@alexion.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	08 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 March 2018
Global end of trial reached?	Yes
Global end of trial date	08 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of subcutaneous (SC) injections of asfotase alfa administered 6 times weekly (at a dose of 1 milligram/kilogram [mg/kg]) or 3 times weekly (at a dose of 2 mg/kg) at the discretion of the Investigator.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 September 2015
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	France: 12
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	23
EEA total number of subjects	12

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)	1
Children (2-11 years)	9
Adolescents (12-17 years)	1
Adults (18-64 years)	11
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 5 investigational sites: 2 sites in the United States (US) and 3 sites in France

Pre-assignment

Screening details:

The study consisted of a screening period of up to 12 weeks prior to study initiation. The duration of treatment varied by participant and ranged from 56 to 588 days. The median (mean) duration of treatment was 470.0 (357.9) days.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Perinatal/Infantile

Arm description:

Participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of 1 mg/kg 6 times per week or 2 mg/kg 3 times per week by SC injection, at the discretion of the Investigator). Participants were grouped based on age of onset of first symptoms of HPP (perinatal onset, in utero and at birth; infantile-onset, <6 months of age). Throughout the study, dose adjustments were made to account for changes in body weight.

Arm type	Experimental
Investigational medicinal product name	asfotase alfa
Investigational medicinal product code	
Other name	Strensiq®
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Asfotase alfa was administered subcutaneously.

The dose used in this study is the approved dosage (6 mg/kg/week) used in the US, European Union (EU), and other countries.

All participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of 1 mg/kg 6 times per week or 2 mg/kg 3 times per week, at the discretion of the Investigator).

Throughout the study, dose adjustments were made to account for changes in body weight.

The maximum volume of medicinal product per injection was not to exceed 1.0 milliliter (mL). If more than 1.0 mL was required, multiple injections were administered at the same time.

Throughout the study, injection sites were rotated among different body areas (the upper and lower thighs, buttocks, upper and lower abdomen, and upper arms) and were carefully monitored for sign(s) of potential reaction(s).

Arm title	Juvenile
------------------	----------

Arm description:

Participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of

1 mg/kg 6 times per week or 2 mg/kg 3 times per week by SC injection, at the discretion of the Investigator). Participants were grouped based on age of onset of first symptoms of HPP (≥ 6 months to < 18 years of age). Throughout the study, dose adjustments were made to account for changes in body weight.

Arm type	Experimental
Investigational medicinal product name	asfotase alfa
Investigational medicinal product code	
Other name	Strensiq®
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Asfotase alfa was administered subcutaneously.

The dose used in this study is the approved dosage (6 mg/kg/week) used in the US, EU, and other countries.

All participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of 1 mg/kg 6 times per week or 2 mg/kg 3 times per week, at the discretion of the Investigator).

Throughout the study, dose adjustments were made to account for changes in body weight.

The maximum volume of medicinal product per injection was not to exceed 1.0 mL. If more than 1.0 mL was required, multiple injections were administered at the same time.

Throughout the study, injection sites were rotated among different body areas (the upper and lower thighs, buttocks, upper and lower abdomen, and upper arms) and were carefully monitored for sign(s) of potential reaction(s).

Number of subjects in period 1	Perinatal/Infantile	Juvenile
Started	12	11
Received at Least 1 Dose of Study Drug	12	11
Completed	12	11

Baseline characteristics

Reporting groups

Reporting group title	Perinatal/Infantile
-----------------------	---------------------

Reporting group description:

Participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of 1 mg/kg 6 times per week or 2 mg/kg 3 times per week by SC injection, at the discretion of the Investigator). Participants were grouped based on age of onset of first symptoms of HPP (perinatal onset, in utero and at birth; infantile-onset, <6 months of age). Throughout the study, dose adjustments were made to account for changes in body weight.

Reporting group title	Juvenile
-----------------------	----------

Reporting group description:

Participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of 1 mg/kg 6 times per week or 2 mg/kg 3 times per week by SC injection, at the discretion of the Investigator). Participants were grouped based on age of onset of first symptoms of HPP (≥ 6 months to <18 years of age). Throughout the study, dose adjustments were made to account for changes in body weight.

Reporting group values	Perinatal/Infantile	Juvenile	Total
Number of subjects	12	11	23
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	1	0	1
Children (2-11 years)	5	4	9
Adolescents (12-17 years)	1	0	1
Adults (18-64 years)	5	6	11
From 65-84 years	0	1	1
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	8	7	15
Male	4	4	8
Race			
Units: Subjects			
White	4	7	11
Not Reported	8	4	12
ethnicity			
Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	7	10	17
Not Reported	4	1	5

End points

End points reporting groups

Reporting group title	Perinatal/Infantile
-----------------------	---------------------

Reporting group description:

Participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of 1 mg/kg 6 times per week or 2 mg/kg 3 times per week by SC injection, at the discretion of the Investigator). Participants were grouped based on age of onset of first symptoms of HPP (perinatal onset, in utero and at birth; infantile-onset, <6 months of age). Throughout the study, dose adjustments were made to account for changes in body weight.

Reporting group title	Juvenile
-----------------------	----------

Reporting group description:

Participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of 1 mg/kg 6 times per week or 2 mg/kg 3 times per week by SC injection, at the discretion of the Investigator). Participants were grouped based on age of onset of first symptoms of HPP (≥6 months to <18 years of age). Throughout the study, dose adjustments were made to account for changes in body weight.

Subject analysis set title	Safety Set
----------------------------	------------

Subject analysis set type	Safety analysis
---------------------------	-----------------

Subject analysis set description:

Safety Set: All participants who received ≥1 dose of study drug.

Primary: Number of Participants Experiencing Serious Adverse Events (SAEs)

End point title	Number of Participants Experiencing Serious Adverse Events (SAEs) ^[1]
-----------------	--

End point description:

The number of participants experiencing SAEs is presented for participants who received asfotase alfa in this open-label, expanded access study. The duration of treatment varied by participant, with a median duration of exposure of 502.5 days for participants in the perinatal/infantile group and 450.0 days for participants in the juvenile group. An adverse event (AE) was defined as any untoward medical occurrence in a participant administered a medicinal product that does not necessarily have a causal relationship with the treatment. AEs were classified as an SAE if the event met any one of the following criteria (at any dose): resulted in death, was life-threatening, resulted in hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was an important medical event. A summary of all SAEs and other non-serious AEs, regardless of causality, is located in the reported Adverse events module.

End point type	Primary
----------------	---------

End point timeframe:

Baseline, End of Program (EOP)

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: Justification: Quantitative statistical analysis (for example, a p-value) was not performed for this end point. Only descriptive statistics were included.

End point values	Perinatal/Infantile	Juvenile		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12 ^[2]	11 ^[3]		
Units: participants	5	0		

Notes:

[2] - Safety Set

[3] - Safety Set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from baseline through the EOP visit.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Perinatal/Infantile
-----------------------	---------------------

Reporting group description:

Participants were enrolled into this group based on age of onset of first symptoms of HPP (perinatal onset, in utero and at birth; infantile-onset, <6 months of age). Participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of 1 mg/kg 6 times per week or 2 mg/kg 3 times per week by SC injection, at the discretion of the Investigator). Throughout the study, dose adjustments were made to account for changes in body weight.

Reporting group title	Juvenile
-----------------------	----------

Reporting group description:

Participants were enrolled into this group based on age of onset of first symptoms of HPP (≥6 months to <18 years of age). Participants received a total of 6 mg/kg of asfotase alfa each week (administered at a dosage regimen of 1 mg/kg 6 times per week or 2 mg/kg 3 times per week by SC injection, at the discretion of the Investigator). Throughout the study, dose adjustments were made to account for changes in body weight.

Serious adverse events	Perinatal/Infantile	Juvenile	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)	0 / 11 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			

subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiphysiolysis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip deformity			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 2	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	Perinatal/Infantile	Juvenile	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	10 / 11 (90.91%)	
General disorders and administration site conditions			

Injection site reaction subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 15	8 / 11 (72.73%) 50	
Injection site pain subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 6	3 / 11 (27.27%) 3	
Pyrexia subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 4	0 / 11 (0.00%) 0	
Fatigue subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 11 (9.09%) 1	
Injection site bruising subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 11 (18.18%) 8	
Injection site erythema subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 11 (0.00%) 0	
Chest pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 2	
Hypothermia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	
Injection site haematoma subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	0 / 11 (0.00%) 0	
Pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Reproductive system and breast disorders			

Pelvic pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	0 / 11 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	1 / 11 (9.09%) 1	
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 11 (9.09%) 1	
Asthma subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Productive cough subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Respiratory distress subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	
Psychiatric disorders Depressed mood subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	
Investigations Crystal urine present subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 11 (18.18%) 2	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	2 / 11 (18.18%) 2	
Infusion related reaction subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 12 (8.33%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	3 / 12 (25.00%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Hypokinesia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Sensory loss			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Lymphadenopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Otorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract nuclear			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Corneal deposits			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Diplopia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Dry eye			

subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	0	
Eyelid cyst			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Photopsia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 12 (25.00%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Anal incontinence			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Defaecation urgency			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Paraesthesia oral			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Tooth loss			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	

Vomiting subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Hepatobiliary disorders Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	
Skin and subcutaneous tissue disorders Onychoclasia subjects affected / exposed occurrences (all) Acne subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Hypertrichosis subjects affected / exposed occurrences (all) Swelling face subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0	2 / 11 (18.18%) 2 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 1 / 11 (9.09%) 1	
Renal and urinary disorders Nephrolithiasis subjects affected / exposed occurrences (all) Renal mass subjects affected / exposed occurrences (all) Urinary incontinence subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	0 / 11 (0.00%) 0 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1	
Endocrine disorders Hyperparathyroidism subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	

Hyperparathyroidism secondary subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 5	2 / 11 (18.18%) 4	
Back pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	
Pain in extremity subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	1 / 11 (9.09%) 1	
Bone pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	
Epiphysiolysis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Hip deformity subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 3	0 / 11 (0.00%) 0	
Joint swelling subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	
Muscle contracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 2	
Muscle spasms subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 4	0 / 11 (0.00%) 0	
Neck pain			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 3	0 / 11 (0.00%) 0	
Wrist deformity subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3	1 / 11 (9.09%) 1	
Nasopharyngitis			
subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 8	1 / 11 (9.09%) 1	
Rhinitis			
subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 4	0 / 11 (0.00%) 0	
Gastroenteritis			
subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 11 (0.00%) 0	
Sinusitis			
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	1 / 11 (9.09%) 1	
Upper respiratory tract infection			
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 11 (9.09%) 1	
Conjunctivitis			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	
Folliculitis			
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	0 / 11 (0.00%) 0	
Influenza			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 11 (9.09%) 1	
Pharyngitis streptococcal			
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 11 (0.00%) 0	

Tracheitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	2	
Viral infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	2 / 12 (16.67%)	0 / 11 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 June 2015	The planned number of participants was changed from approximately 75 to 120 participants globally, to accurately reflect the number of participants that were planned for enrollment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The single-arm, open-label trial design, without any control group in this expanded access study, precluded any definitive conclusions about the safety or efficacy of asfotase alfa.

Notes: