Clinical trial results:
A Randomized, Multicenter, Multinational, Phase 3B, Open-Label, Parallel-Group Study of Fabrazyme (Agalsidase beta) in Treatment-Naive Male Pediatric Patients with Fabry Disease Without Severe Symptoms

Summary

EudraCT number	2007-005668-28
Trial protocol	GB NL PT DE CZ FR
Global end of trial date	22 June 2015

Results information

Result version number	v1 (current)
This version publication date	29 May 2016
First version publication date	29 May 2016

Trial information

Trial identification

Sponsor protocol code	AGAL06207/EFC12821

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00701415
WHO universal trial number (UTN)	-
Other trial identifiers	Study Name: FIELD (Fabrazyme:Intervening Early at Lower Dose)

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, MA, United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	19 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy (globotriaosylceramide [GL-3] clearance), Pharmacokinetics (PK), and safety parameters (including immunogenicity) for 2 alternative dose regimens of Fabrazyme (0.5 mg/kg every 2 weeks and 1.0 mg/kg every 4 weeks) in treatment-naive male pediatric subjects (≥5 years to ≤18 years of age) with Fabry disease without severe symptoms.

Protection of trial subjects:

Pediatric Subjects: The study was conducted by investigators experienced in the treatment of pediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.
Adult Subjects: Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 June 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	United States: 5
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Argentina: 6

Worldwide total number of subjects	31
EEA total number of subjects	15

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)	15
Adolescents (12-17 years)	15
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 12 sites in 9 countries. A total of 44 subjects were screened between 17 June 2008 and 12 April 2010.

Pre-assignment

Screening details:

Of 44 screened subjects, 31 subjects were randomized in 1:1 ratio to fabrazyme 0.5 mg/kg and fabrazyme 1.0 mg/kg within each age stratum (5 to ≤11 years [children] and 12 to ≤18 years [adolescents]). 13 subjects were screen failure due to failure to meet inclusion criteria or withdrawal of consent prior to all screening assessments being completed.

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	Fabrazyme 0.5 mg/kg

Arm description:

Fabrazyme 0.5 mg/kg every 2 weeks up to 260 weeks

Arm type	Experimental
Investigational medicinal product name	Fabrazyme
Investigational medicinal product code	
Other name	Agalsidase beta, Recombinant human α-galactosidase A (r-hαGAL)
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fabrazyme 0.5 mg/kg was administered every 2 weeks (up to 131 infusions), the total infusion time was not less than 45 minutes. In case of significant progression of Fabry disease, the dose was increased to 1.0 mg/kg every 2 weeks.

Arm title	Fabrazyme 1.0 mg/kg

Arm description:

Fabrazyme 1.0 mg/kg every 4 weeks up to 260 weeks

Arm type	Experimental
Investigational medicinal product name	Fabrazyme
Investigational medicinal product code	
Other name	Agalsidase beta, r-hαGAL
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fabrazyme 1.0 mg/kg was administered every 4 weeks (up to 66 infusions), the total infusion time was not less than 90 minutes. In case of significant progression of Fabry disease, the dose was increased to 1.0 mg/kg every 2 weeks.

Number of subjects in period 1	Fabrazyme 0.5 mg/kg	Fabrazyme 1.0 mg/kg
Started	16	15
Completed	15	14
Not completed	1	1
Social/family issues and needle phobia	1	-
Adverse event	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Fabrazyme 0.5 mg/kg
Reporting group description: Fabrazyme 0.5 mg/kg every 2 weeks up to 260 weeks	
Reporting group title	Fabrazyme 1.0 mg/kg
Reporting group description: Fabrazyme 1.0 mg/kg every 4 weeks up to 260 weeks	

Reporting group values	Fabrazyme 0.5 mg/kg	Fabrazyme 1.0 mg/kg	Total
Number of subjects	16	15	31
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	11.2	11.9	
standard deviation	± 4	± 4.5	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	16	15	31

End points

End points reporting groups

Reporting group title	Fabrazyme 0.5 mg/kg
Reporting group description: Fabrazyme 0.5 mg/kg every 2 weeks up to 260 weeks	
Reporting group title	Fabrazyme 1.0 mg/kg
Reporting group description: Fabrazyme 1.0 mg/kg every 4 weeks up to 260 weeks	

Primary: Skin Globotriaosylceramide (GL-3) Clearance From Superficial Skin Capillary Endothelium

End point title	Skin Globotriaosylceramide (GL-3) Clearance From Superficial Skin Capillary Endothelium[1]

End point description:

Skin biopsies were taken at Baseline, Week 52, Week 156 and Week 260 or early withdrawal and analyzed for cellular GL-3 accumulation (inclusions) by light microscopy. Each biopsy was scored for GL-3 accumulation on a severity score-scale of none, mild, moderate, severe (0-1-2-3). Scores are categorized as normal (score = 0) or abnormal (score = 1, 2 or 3). Data was summarized in terms of number of subjects with none/trace, mild, moderate and severe biopsy scores. Analysis was performed on Full analysis set (FAS) , which included all randomized subjects who received at least 1 infusion of study treatment.

End point type	Primary

End point timeframe:

Baseline, Week 52, Week 156 and Week 260

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: Since analysis is descriptive in nature, statistical data could not be provided.

End point values	Fabrazyme 0.5 mg/kg	Fabrazyme 1.0 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	15		
Units: Percentage of subjects				
number (not applicable)				
Zero (0) Skin GL-3 Score at Baseline	18.8	33.3		
Zero (0) Skin GL-3 Score at Week 52	75	80		
Zero (0) Skin GL-3 Score at Week 156	56.3	80		
Zero (0) Skin GL-3 Score at Week 260	68.8	66.7		
Mild (1) Skin GL-3 Score at Baseline	6.3	0		
Mild (1) Skin GL-3 Score at Week 52	6.3	13.3		
Mild (1) Skin GL-3 Score at Week 156	18.8	0		
Mild (1) Skin GL-3 Score at Week 260	12.5	20		
Moderate (2) Skin GL-3 Score at Baseline	75	66.7		
Moderate (2) Skin GL-3 Score at Week 52	0	0		
Moderate (2) Skin GL-3 Score at Week 156	6.3	13.3		
Moderate (2) Skin GL-3 Score at Week 260	0	6.7		

Severe (3) Skin GL-3 Score at Baseline	0	0		
Severe (3) Skin GL-3 Score at Week 52	0	0		
Severe (3) Skin GL-3 Score at Week 156	0	0		
Severe (3) Skin GL-3 Score at Week 260	0	0		
Missing Skin GL-3 Score at Baseline	0	0		
Missing Skin GL-3 Score at Week 52	18.8	6.7		
Missing Skin GL-3 Score at Week 156	18.8	6.7		
Missing Skin GL-3 Score at Week 260	18.8	6.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in GL-3 Clearance From Plasma

End point title	Percent Change from Baseline in GL-3 Clearance From Plasma

End point description:

Plasma samples were assayed for GL-3 clearance using a validated tandem mass spectrometry with an upper limit of normal plasma GL-3 level of 7.0 mg/mmol. Analysis was performed on FAS. Number of subjects analyzed=subjects with both baseline and post-baseline GL-3 plasma clearance assessment. Here 'n' signifies number of subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 12, 28, 40, 52, 80, 104, 132, 156, 184, 208, 236 and 260

End point values	Fabrazyme 0.5 mg/kg	Fabrazyme 1.0 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: percent change				
arithmetic mean (standard deviation)				
Week 12 (n=14, 11)	-52.37 (± 10.12)	-52.74 (± 6.79)		
Week 28 (n=14, 14)	-49.06 (± 15.43)	-47.55 (± 16.75)		
Week 40 (n=13, 14)	-52.01 (± 11.29)	-50.82 (± 12.87)		
Week 52 (n=14, 14)	-52.29 (± 10.48)	-45.87 (± 16.01)		
Week 80 (n=13, 14)	-52.91 (± 13.93)	-48.93 (± 14.75)		
Week 104 (n=13, 14)	-51.08 (± 20.45)	-39.92 (± 18.69)		
Week 132 (n=11, 14)	-61.39 (± 10.71)	-52.97 (± 17.1)		
Week 156 (n=11, 14)	-48.72 (± 18.48)	-44.83 (± 14.14)		

Week 184 (n=12, 14)	-53.62 (± 19.38)	-49.08 (± 17.93)		
Week 208 (n=12, 14)	-48.83 (± 16.8)	-46.09 (± 16.84)		
Week 236 (n=12, 14)	-56.44 (± 12.08)	-47.25 (± 13.04)		
Week 260 (n=11, 14)	-59.95 (± 12.39)	-46.34 (± 14.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in GL-3 Clearance From Urine

End point title	Percent Change From Baseline in GL-3 Clearance From Urine

End point description:

Plasma samples were assayed for total urine GL-3 clearance using a validated tandem mass spectrometry with an upper limit of normal of <0.030 mg/mmoL of creatinine. Analysis was performed on FAS. Number of subjects analyzed=subjects with both baseline and post-baseline GL-3 urine clearance assessment. Here 'n' signifies number of subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 12, 28, 40, 52, 80, 104, 132, 156, 184, 208, 236 and 260

End point values	Fabrazyme 0.5 mg/kg	Fabrazyme 1.0 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percent change				
arithmetic mean (standard deviation)				
Week 12 (n=15, 14)	-50.77 (± 64.59)	-63.39 (± 38.81)		
Week 28 (n=15, 15)	-50.84 (± 100.61)	-52.55 (± 58.59)		
Week 40 (n=15, 14)	-44.22 (± 105.03)	-63.87 (± 24.41)		
Week 52 (n=15, 14)	-70.1 (± 41.4)	-20.72 (± 156.1)		
Week 80 (n=14, 14)	-35.84 (± 102.31)	35.22 (± 238.61)		
Week 104 (n=14, 14)	-21.92 (± 138.78)	-56.39 (± 42.39)		
Week 132 (n=13, 14)	-48.79 (± 100.1)	-45.61 (± 48.84)		
Week 156 (n=13, 14)	-65.57 (± 52.11)	-28.92 (± 84.32)		
Week 184 (n=13, 14)	-76.54 (± 38.93)	-10.5 (± 146.86)		
Week 208 (n=13, 14)	-60.94 (± 67.99)	-50.93 (± 46.52)		
Week 236 (n=13, 14)	-69.08 (± 51.72)	-40.09 (± 77.04)		

Week 260 (n=13, 14)	-57.59 (± 93.74)	-28.27 (± 56.79)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (Week 264) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (the time from the first infusion of the study drug up to 28 days after the last infusion of study drug). Safety population included all randomized subjects who received at least one infusion of Fabrazyme.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Fabrazyme 0.5 mg/kg

Reporting group description:

Fabrazyme 0.5 mg/kg every 2 weeks up to 260 weeks

Reporting group title	Fabrazyme 1.0 mg/kg

Reporting group description:

Fabrazyme 1.0 mg/kg every 4 weeks up to 260 weeks

Serious adverse events	Fabrazyme 0.5 mg/kg	Fabrazyme 1.0 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 16 (37.50%)	5 / 15 (33.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Body Mass Index Decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Multiple Injuries			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Central Venous Catheterisation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Elective Surgery			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (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			
Paraesthesia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical Device Complication			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal Ideation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Microalbuminuria			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis Media			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinea Pedis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fabrazyme 0.5 mg/kg	Fabrazyme 1.0 mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	15 / 15 (100.00%)	
Vascular disorders			
Angiopathy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	6	0	
Hypotension			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Pallor			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	5	3	
Raynaud's Phenomenon			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Sinus Operation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 16 (18.75%)	1 / 15 (6.67%)	
occurrences (all)	10	1	
Catheter Site Pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Chest Discomfort			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Chills			
subjects affected / exposed	6 / 16 (37.50%)	2 / 15 (13.33%)	
occurrences (all)	13	2	
Face Oedema			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	5 / 16 (31.25%)	2 / 15 (13.33%)	
occurrences (all)	23	2	
Feeling Cold			
subjects affected / exposed	3 / 16 (18.75%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Feeling Hot			
subjects affected / exposed	0 / 16 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	5	
Feeling Of Body Temperature Change			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
General Physical Health Deterioration			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Influenza Like Illness			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Infusion Site Extravasation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Infusion Site Pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Injection Site Haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	7	2	
Medical Device Complication			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Oedema Peripheral			
subjects affected / exposed	3 / 16 (18.75%)	2 / 15 (13.33%)	
occurrences (all)	4	2	
Pain			
subjects affected / exposed	4 / 16 (25.00%)	3 / 15 (20.00%)	
occurrences (all)	8	6	
Pyrexia			
subjects affected / exposed	12 / 16 (75.00%)	8 / 15 (53.33%)	
occurrences (all)	36	36	
Soft Tissue Inflammation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Immune system disorders			
Allergy To Arthropod Bite			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

Reproductive system and breast disorders			
Penile Discharge			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Penile Pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Scrotal Angiokeratoma			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	2	2	
Respiratory, thoracic and mediastinal disorders			
Allergic Cough			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Allergic Respiratory Symptom			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Bronchial Obstruction			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Bronchospasm			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Catarrh			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	8 / 16 (50.00%)	5 / 15 (33.33%)	
occurrences (all)	48	13	
Dry Throat			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	3 / 16 (18.75%)	2 / 15 (13.33%)	
occurrences (all)	8	12	
Epistaxis			

subjects affected / exposed	3 / 16 (18.75%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Nasal Congestion			
subjects affected / exposed	5 / 16 (31.25%)	1 / 15 (6.67%)	
occurrences (all)	15	2	
Oropharyngeal Pain			
subjects affected / exposed	3 / 16 (18.75%)	6 / 15 (40.00%)	
occurrences (all)	7	7	
Pharyngeal Erythema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Respiratory Failure			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Respiratory Tract Congestion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Rhinitis Allergic			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Sinus Congestion			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Sneezing			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Tachypnoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Throat Irritation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Tonsillar Hypertrophy			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Congestion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Confusional State			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Depression			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Depressive Symptom			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Disorientation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dysphoria			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hallucination			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	3	0	

Listless			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Panic Attack			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Sleep Disorder			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Investigations			
Beta 2 Microglobulin Increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood Pressure Increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Body Temperature Increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Eosinophil Count Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Heart Rate Increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Neutrophil Count Increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Protein Urine Present			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Urine Albumin/Creatinine Ratio Abnormal			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vitamin B12 Decreased			

subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Vitamin D Decreased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Animal Bite			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Arthropod Bite			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Arthropod Sting			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Concussion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Ear Injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Excoriation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Frostbite			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Genital Injury			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hand Fracture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Head Injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Humerus Fracture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Joint Injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Laceration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Ligament Rupture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Ligament Sprain			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Limb Injury			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Muscle Rupture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Muscle Strain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Overdose			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Post-Traumatic Pain			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Procedural Pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Road Traffic Accident			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Skin Abrasion			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Soft Tissue Injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	4	
Tendon Rupture			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Tooth Fracture			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Wound Complication			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Wound Dehiscence			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	3	2	
Nervous system disorders			
Burning Sensation			

subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Disturbance In Attention			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	4 / 16 (25.00%)	4 / 15 (26.67%)	
occurrences (all)	8	4	
Dysgeusia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	10	0	
Headache			
subjects affected / exposed	8 / 16 (50.00%)	4 / 15 (26.67%)	
occurrences (all)	49	8	
Hypoaesthesia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Migraine			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	3	
Paraesthesia			
subjects affected / exposed	6 / 16 (37.50%)	3 / 15 (20.00%)	
occurrences (all)	59	11	
Presyncope			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Slow Response To Stimuli			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Speech Disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	4	
Eosinophilia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Leukopenia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	4	
Lymphadenopathy			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Monocytopenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Conductive Deafness			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Deafness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Deafness Bilateral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Deafness Neurosensory			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Deafness Unilateral			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Middle Ear Effusion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Otorrhoea			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Tinnitus			
subjects affected / exposed	3 / 16 (18.75%)	4 / 15 (26.67%)	
occurrences (all)	4	4	
Tympanic Membrane Hyperaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctival Hyperaemia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Corneal Deposits			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dry Eye			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Lacrimation Increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Ocular Vascular Disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Periorbital Oedema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Photophobia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vision Blurred			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Visual Acuity Reduced			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	9 / 16 (56.25%)	6 / 15 (40.00%)	
occurrences (all)	51	7	
Abdominal Pain Lower			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Abdominal Pain Upper			
subjects affected / exposed	4 / 16 (25.00%)	4 / 15 (26.67%)	
occurrences (all)	11	10	
Abdominal Tenderness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Dental Caries			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	10 / 16 (62.50%)	8 / 15 (53.33%)	
occurrences (all)	39	16	
Epigastric Discomfort			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Food Poisoning			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Frequent Bowel Movements			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal Disorder			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Irritable Bowel Syndrome			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	9 / 16 (56.25%)	7 / 15 (46.67%)	
occurrences (all)	37	14	
Oral Mucosal Erythema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Salivary Hypersecretion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	9 / 16 (56.25%)	7 / 15 (46.67%)	
occurrences (all)	43	10	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Angiokeratoma			
subjects affected / exposed	9 / 16 (56.25%)	5 / 15 (33.33%)	
occurrences (all)	33	9	
Blister			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dermatitis Contact			
subjects affected / exposed	2 / 16 (12.50%)	2 / 15 (13.33%)	
occurrences (all)	3	4	

Dry Skin			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Erythema			
subjects affected / exposed	4 / 16 (25.00%)	1 / 15 (6.67%)	
occurrences (all)	31	2	
Hyperhidrosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Miliaria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Night Sweats			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	4	
Petechiae			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Rash			
subjects affected / exposed	4 / 16 (25.00%)	1 / 15 (6.67%)	
occurrences (all)	4	1	
Rash Erythematous			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Rash Macular			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Swelling Face			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	2	1	

Telangiectasia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Umbilical Erythema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Hydronephrosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hydroureter			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Microalbuminuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Endocrine disorders			
Hyperparathyroidism Secondary			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 16 (25.00%)	1 / 15 (6.67%)	
occurrences (all)	17	1	
Back Pain			
subjects affected / exposed	2 / 16 (12.50%)	2 / 15 (13.33%)	
occurrences (all)	10	3	
Foot Deformity			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Groin Pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Haemarthrosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Joint Range Of Motion Decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Joint Swelling			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Muscle Spasms			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Muscular Weakness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Musculoskeletal Pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Neck Pain			
subjects affected / exposed	3 / 16 (18.75%)	0 / 15 (0.00%)	
occurrences (all)	4	0	
Pain In Extremity			
subjects affected / exposed	8 / 16 (50.00%)	5 / 15 (33.33%)	
occurrences (all)	40	28	
Tendonitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

Infections and infestations			
Acute Sinusitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Catheter Site Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Chlamydial Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Coxsackie Viral Infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Ear Infection			
subjects affected / exposed	5 / 16 (31.25%)	1 / 15 (6.67%)	
occurrences (all)	9	1	
Enterobiasis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Erysipelas			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	2 / 16 (12.50%)	2 / 15 (13.33%)	
occurrences (all)	7	3	
Gastroenteritis Viral			
subjects affected / exposed	3 / 16 (18.75%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Herpes Simplex			

subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Herpes Virus Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Hordeolum			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Impetigo			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Influenza			
subjects affected / exposed	3 / 16 (18.75%)	3 / 15 (20.00%)	
occurrences (all)	4	4	
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Molluscum Contagiosum			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	7 / 16 (43.75%)	5 / 15 (33.33%)	
occurrences (all)	24	20	
Oral Herpes			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	5	0	
Otitis Media Chronic			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Parasitic Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Pharyngitis Streptococcal			

subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	4	0	
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Respiratory Tract Infection			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Respiratory Tract Infection Viral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	5 / 16 (31.25%)	3 / 15 (20.00%)	
occurrences (all)	8	6	
Sinusitis			
subjects affected / exposed	3 / 16 (18.75%)	1 / 15 (6.67%)	
occurrences (all)	4	1	
Staphylococcal Infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Tinea Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Tinea Versicolour			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Tonsillitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Tooth Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Upper Respiratory Tract Infection			
subjects affected / exposed	6 / 16 (37.50%)	5 / 15 (33.33%)	
occurrences (all)	11	8	
Viral Infection			

subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	3	7	
Viral Pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Viral Rhinitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
Failure To Thrive			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Iron Deficiency			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Obesity			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Underweight			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Vitamin B12 Deficiency			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vitamin D Deficiency			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2008	It included following changes: -Total blood volume for a specific procedure or for all procedures in the protocol were removed and was detailed in the informed consent form. -Clarification and additional information given for GFRiohexol rate was added for subjects with a documented low protein intake. -The contraindications mentioned in the labeling of both Fabrazyme and Omnipaque were included in the protocol as an exclusion criteria. -The number of subjects enrolled and the number of centers were increased to increase the scientific value and robustness of the trial. Pharmacokinetic samples were not collected from all subjects. -The parameters for αGAL activity were clarified. -A window for measurement of vital signs was added.
30 April 2010	It included following changes: -The sample size of subjects was decreased (n=35) due to unforeseen difficulties including unexpectedly high screen failure rates. -Additional information/clarification was added to the protocol related to home infusions and time windows around home infusion to ensure consistency between sites in management of home infusions and the safety of subjects receiving home infusions. -Clarification related to the dose and body weight was added to allow additional flexibility due to home infusions. -Blood sampling amounts and timepoints specified to ensure enough samples were collected for PK analyses following reduction in enrollment. -Three consecutive urine samples were collected to measure kidney function. -Recording of concomitant therapies was added.
25 June 2010	It included following changes: -The infusion time window for the every 2 weeks regimen was extended from ±3 days to ±7 days to reduce the deviation rate, which was estimated to be approximately 10% and was designed to lessen the burden on subjects and was deemed acceptable from a clinical perspective provided that no 2 infusions were administered less than 7 days apart. -Infusion-associated reactions were considered related to study drug.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported