



## Clinical trial results: A Phase 4 Open Label, Prospective Study in Patients With Pompe Disease to Evaluate the Efficacy and Safety of Alglucosidase Alfa Produced at the 4000 L Scale

### Summary

EudraCT number	2015-000512-18
Trial protocol	Outside EU/EEA
Global end of trial date	29 December 2014

### Results information

Result version number	v1
This version publication date	04 July 2016
First version publication date	25 June 2015

### Trial information

#### Trial identification

Sponsor protocol code	AGLU09411/EFC12720
-----------------------	--------------------

#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01526785
WHO universal trial number (UTN)	U1111-1162-8919

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	05 March 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 December 2014
Was the trial ended prematurely?	No

Notes:

---

**General information about the trial**

---

Main objective of the trial:

The primary efficacy objective was to demonstrate comparability of treatment with alglucosidase alfa produced at the 4000L scale in subjects previously treated with 160L scale alglucosidase alfa.

---

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	09 March 2012
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 States: 113
Worldwide total number of subjects	113
EEA total number of subjects	0

Notes:

---

**Subjects enrolled per age group**

---

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	33
Children (2-11 years)	73
Adolescents (12-17 years)	6
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

---

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study was conducted in United States. A total of 113 subjects were treated between 9 March 2012 and 4 June 2014.

### Period 1

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

### Arms

<b>Arm title</b>	Alglucosidase Alfa
------------------	--------------------

Arm description:

Alglucosidase alfa produced at 4000 L scale for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase Alfa
Investigational medicinal product code	
Other name	Lumizyme®
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

4000 L alglucosidase alfa as per subject's routine practice.

<b>Number of subjects in period 1</b>	Alglucosidase Alfa
Started	113
Completed	100
Not completed	13
Consent withdrawn by subject	2
Physician decision	1
Death	2
Study Terminated by Sponsor	8

## Baseline characteristics

---

### Reporting groups

Reporting group title	Alglucosidase Alfa
-----------------------	--------------------

Reporting group description:

Alglucosidase alfa produced at 4000 L scale for 52 weeks.

---

Reporting group values	Alglucosidase Alfa	Total	
Number of subjects	113	113	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	4.8 ± 3.73	-	
Gender categorical Units: Subjects			
Female	53	53	
Male	60	60	

## End points

### End points reporting groups

Reporting group title	Alglucosidase Alfa
Reporting group description: Alglucosidase alfa produced at 4000 L scale for 52 weeks.	

### Primary: Percentage of Subjects Who were Clinically Stable or Improved at Week 52

End point title	Percentage of Subjects Who were Clinically Stable or Improved at Week 52 <sup>[1]</sup>
-----------------	---

End point description:

Clinical stability defined as absence of death due to disease progression or new dependency on invasive ventilation and; decline in cardiac status, motor function, and pulmonary function from baseline. Analysis was carried out on full analysis population defined as all subjects who receive at least 1 infusion of 4000 L alglucosidase alfa during the study.

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

End point timeframe:

Week 52

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:

Due to EudraCT format constraint, the statistical analysis could not be provided for single arm study.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	104			
Units: percentage of subjects				
number (confidence interval 95%)	83.7 (75.1 to 90.2)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Survival Rate at Week 52

End point title	Survival Rate at Week 52
-----------------	--------------------------

End point description:

Percentage of subjects who were alive at Week 52, were reported. Survival rate was calculated by Kaplan-Meier estimate. Analysis was carried out on full analysis population.

End point type	Secondary
----------------	-----------

End point timeframe:

Week 52

<b>End point values</b>	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	113			
Units: percentage of subjects				
number (confidence interval 95%)	98.1 (92.73 to 99.53)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Invasive Ventilator-Free Survival Rate at Week 52

End point title	Invasive Ventilator-Free Survival Rate at Week 52
End point description:	Percentage of subjects who were invasive ventilator-free at week 52, were reported. Invasive ventilation was defined as mechanical ventilatory support applied with the use of an endotracheal tube or tracheostomy. Invasive ventilator-free survival rate was calculated by Kaplan-Meier estimate. Analysis was carried out on full analysis population.
End point type	Secondary
End point timeframe:	Week 52

<b>End point values</b>	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: percentage of subjects				
number (confidence interval 95%)	92.4 (83.89 to 96.53)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline on Left Ventricular Mass Z-Score (LVM-Z) at Week 52

End point title	Change From Baseline on Left Ventricular Mass Z-Score (LVM-Z) at Week 52
End point description:	Z--Scores indicate the number of standard deviations (SD) from the mean in a normal distribution. A negative change from baseline indicates a decrease and positive change from baseline indicates an increase in LVM-Z score. The normal range is -2 to 2 and greater than 2 may indicate left ventricular hypertrophy. Analysis was carried out on full analysis population.
End point type	Secondary
End point timeframe:	Baseline, Week 52

<b>End point values</b>	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	67			
Units: units on a scale				
arithmetic mean (standard deviation)	-0.5 ( $\pm$ 1.71)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline on Gross Motor Function Measure-88 (GMFM-88) at Week 52

End point title	Change From Baseline on Gross Motor Function Measure-88 (GMFM-88) at Week 52
-----------------	--

End point description:

GMFM-88 (88-item measure to detect gross motor function) consists of 5 components, each measured on a 4-point Likert scale. The score for each dimension was expressed as a percentage of the maximum score for that dimension. Total score ranges from 0% to 100%, where higher scores indicate better motor functions. Analysis was carried out on full analysis population. Number of subjects analysed = subjects with baseline and Week 52 GMFM-88 data.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 52

<b>End point values</b>	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: percentage of total score				
arithmetic mean (standard deviation)	3.7 ( $\pm$ 17.46)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Forced Vital Capacity (FVC) at Week 52- At Supine Position

End point title	Change From Baseline in Forced Vital Capacity (FVC) at Week 52- At Supine Position
-----------------	--

End point description:

Analysis was carried out on full analysis population. Number of subjects analysed = subjects with baseline and Week 52 FVC data.

End point type	Secondary
End point timeframe:	
Baseline, Week 52	

<b>End point values</b>	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: percent predicted FVC				
arithmetic mean (standard deviation)	3.2 (± 11.07)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Forced Vital Capacity (FVC) at Week 52- At Sitting Position

End point title	Change From Baseline in Forced Vital Capacity (FVC) at Week 52- At Sitting Position
-----------------	---

End point description:

Analysis was carried out on full analysis population. Number of subjects analysed = subjects with baseline and Week 52 FVC data.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline, Week 52

<b>End point values</b>	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: percent predicted FVC				
arithmetic mean (standard deviation)	2.3 (± 11.8)			

### 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 52) 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' (from the first infusion of study drug up to 30 days after last infusion of study drug). Analysis was performed on safety population which included all treated subjects.

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

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	17.1
--------------------	------

### Reporting groups

Reporting group title	Alglucosidase Alfa 4000 L
-----------------------	---------------------------

Reporting group description:

Alglucosidase alfa produced at 4000 L scale for 52 weeks.

<b>Serious adverse events</b>	Alglucosidase Alfa 4000 L		
Total subjects affected by serious adverse events			
subjects affected / exposed	73 / 113 (64.60%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events			
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jugular Vein Thrombosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Central Venous Catheterisation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Therapeutic Procedure			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>General disorders and administration site conditions</b>			
<b>Chest Pain</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Chills</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Device Breakage</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Device Malfunction</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hypothermia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Oedema Peripheral</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pyrexia</b>			
subjects affected / exposed	10 / 113 (8.85%)		
occurrences causally related to treatment / all	4 / 16		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory, thoracic and mediastinal disorders</b>			

Acute Respiratory Distress Syndrome			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Acute Respiratory Failure			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Apnoea			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspiration			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atelectasis			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Bronchial Secretion Retention			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchiectasis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Chronic Respiratory Failure			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cough			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Dyspnoea</b>			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
<b>Hypoxia</b>			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Pneumonia Aspiration</b>			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Pneumothorax</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Pulmonary Granuloma</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory Disorder</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory Distress</b>			
subjects affected / exposed	16 / 113 (14.16%)		
occurrences causally related to treatment / all	0 / 23		
deaths causally related to treatment / all	0 / 2		
<b>Respiratory Failure</b>			

subjects affected / exposed	7 / 113 (6.19%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 1		
<b>Respiratory Tract Congestion</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Rhonchi</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Psychiatric disorders</b>			
<b>Mental Status Changes</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Self-Injurious Ideation</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Investigations</b>			
<b>Alanine Aminotransferase Increased</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Aspartate Aminotransferase Increased</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Blood Albumin Decreased</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gamma-Glutamyltransferase Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oxygen Saturation Decreased			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Feeding Tube Complication			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur Fracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foreign Body			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foreign Body Aspiration			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheal Obstruction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic Haemothorax			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
Bradycardia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac Arrest			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac Failure Congestive			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-Respiratory Arrest			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Cardiopulmonary Failure			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cyanosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Left Ventricular Hypertrophy			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Mitral Valve Incompetence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulseless Electrical Activity			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Sinus Tachycardia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Supraventricular Tachycardia</b>			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
<b>Tachycardia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Nervous system disorders</b>			
<b>Brain Injury</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Cerebral Ischaemia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Convulsion</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Gross Motor Delay</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Loss Of Consciousness</b>			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tremor			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Motion Sickness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eyelid Ptosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dental Caries			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Diarrhoea			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intussusception			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis Acute			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Hyperhidrosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Purpura			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary Retention			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscle Contracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular Weakness			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Adenovirus Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Bacterial Tracheitis</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Bronchiolitis</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Cellulitis</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Device Related Infection</b>			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
<b>Gastroenteritis</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Gastroenteritis Viral</b>			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Haemophilus Bacteraemia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Influenza</b>			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Klebsiella Bacteraemia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Lobar Pneumonia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Lung Infection</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Metapneumovirus Infection</b>			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Otitis Media Acute</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Parainfluenzae Virus Infection</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Periumbilical Abscess</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pneumonia</b>			

subjects affected / exposed	25 / 113 (22.12%)		
occurrences causally related to treatment / all	0 / 33		
deaths causally related to treatment / all	0 / 1		
Pneumonia Parainfluenzae Viral			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia Pseudomonal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia Respiratory Syncytial Viral			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia Viral			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory Syncytial Virus Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory Tract Infection			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Respiratory Tract Infection Viral			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Rhinovirus Infection</b>			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Sepsis</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Staphylococcal Infection</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Tracheitis</b>			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
<b>Tracheostomy Infection</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Upper Respiratory Tract Infection</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Urinary Tract Infection</b>			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Urinary Tract Infection Bacterial</b>			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection Staphylococcal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Failure To Thrive			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fluid Overload			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	Alglucosidase Alfa 4000 L		
Total subjects affected by non-serious adverse events subjects affected / exposed	113 / 113 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Cholesteatoma subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Vascular disorders Aortic Dilatation subjects affected / exposed occurrences (all)  Flushing subjects affected / exposed occurrences (all)  Haematoma subjects affected / exposed occurrences (all)  Hypertension subjects affected / exposed occurrences (all)  Hypotension subjects affected / exposed occurrences (all)  Pallor subjects affected / exposed occurrences (all)  Peripheral Coldness subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1  7 / 113 (6.19%) 13  2 / 113 (1.77%) 3  5 / 113 (4.42%) 5  2 / 113 (1.77%) 2  1 / 113 (0.88%) 1  1 / 113 (0.88%) 1		
Surgical and medical procedures Central Venous Catheterisation subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		

Ear Tube Removal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastrostomy Tube Removal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
General disorders and administration site conditions			
Abasia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Catheter Site Erythema			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Extravasation			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Catheter Site Haemorrhage			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Inflammation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Oedema			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Pain			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Catheter Site Rash			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Related Reaction			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Catheter Site Swelling			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Chest Discomfort			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Chest Pain			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	8		
Chills			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Crepitations			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Device Breakage			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Device Dislocation			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	6		
Device Issue			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Device Malfunction			
subjects affected / exposed	9 / 113 (7.96%)		
occurrences (all)	21		
Device Occlusion			
subjects affected / exposed	13 / 113 (11.50%)		
occurrences (all)	15		
Discomfort			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Disease Progression			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Energy Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Extravasation			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Feeling Hot			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gait Disturbance			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Granuloma			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	5		
Gravitational Oedema			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Influenza Like Illness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Infusion Site Extravasation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Infusion Site Swelling			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Injection Site Extravasation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Injection Site Swelling			

subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Malaise subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Oedema subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 3		
Oedema Peripheral subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Pain subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 3		
Peripheral Swelling subjects affected / exposed occurrences (all)	4 / 113 (3.54%) 5		
Pyrexia subjects affected / exposed occurrences (all)	61 / 113 (53.98%) 218		
Secretion Discharge subjects affected / exposed occurrences (all)	6 / 113 (5.31%) 9		
Thirst subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Thrombosis In Device subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Immune system disorders Drug Hypersensitivity subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Food Allergy subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		

Hypersensitivity subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 5		
Multiple Allergies subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Seasonal Allergy subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Reproductive system and breast disorders			
Genital Discomfort subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Vaginal Prolapse subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Vulvovaginal Disorder subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Vulvovaginal Erythema subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Vulvovaginal Pruritus subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Respiratory, thoracic and mediastinal disorders			
Adenoidal Hypertrophy subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Aspiration subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 3		
Atelectasis subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 6		
Bronchial Hyperreactivity			

subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Bronchial Secretion Retention			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	6		
Bronchial Wall Thickening			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Bronchomalacia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Bronchospasm			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Choking			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Cough			
subjects affected / exposed	36 / 113 (31.86%)		
occurrences (all)	105		
Dysphonia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	11		
Epistaxis			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Haemoptysis			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Hypercapnia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hypoventilation			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Hypoxia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Increased Bronchial Secretion			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Increased Upper Airway Secretion			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	11		
Increased Viscosity Of Bronchial Secretion			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Nasal Congestion			
subjects affected / exposed	16 / 113 (14.16%)		
occurrences (all)	23		
Nasal Discharge Discolouration			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nasal Dryness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Oropharyngeal Pain			
subjects affected / exposed	13 / 113 (11.50%)		
occurrences (all)	14		
Pleural Effusion			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pneumonia Aspiration			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Productive Cough			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		

Pulmonary Artery Dilatation subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Pulmonary Congestion subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Pulmonary Hypertension subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Respiratory Disorder subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Respiratory Distress subjects affected / exposed occurrences (all)	8 / 113 (7.08%) 10		
Respiratory Failure subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Respiratory Muscle Weakness subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 3		
Respiratory Tract Congestion subjects affected / exposed occurrences (all)	7 / 113 (6.19%) 8		
Respiratory Tract Haemorrhage subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 4		
Rhinitis Allergic subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Rhinorrhoea subjects affected / exposed occurrences (all)	24 / 113 (21.24%) 42		
Rhonchi subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		

Sinus Congestion			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Sleep Apnoea Syndrome			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Sneezing			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Snoring			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Sputum Discoloured			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Sputum Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Tachypnoea			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Throat Irritation			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Throat Tightness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		
Tonsillar Hypertrophy			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tracheal Ulcer			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Upper Respiratory Tract Congestion			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	14		

Upper-Airway Cough Syndrome subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		
Use Of Accessory Respiratory Muscles subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		
Wheezing subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 6		
Psychiatric disorders			
Aggression subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		
Agitation subjects affected / exposed occurrences (all)	4 / 113 (3.54%) 7		
Anxiety subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 5		
Attention Deficit/Hyperactivity Disorder subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Bruxism subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Insomnia subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 5		
Irritability subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Mental Disorder subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Mood Swings			

subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Oppositional Defiant Disorder subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Sleep Disorder subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
<b>Investigations</b>			
Alanine Aminotransferase Abnormal subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 4		
Aspartate Aminotransferase Abnormal subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all)	4 / 113 (3.54%) 5		
Atrial Pressure Increased subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Blood Alkaline Phosphatase Increased subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Blood Creatine Phosphokinase Mb Increased subjects affected / exposed occurrences (all)	7 / 113 (6.19%) 7		
Blood Creatine Phosphokinase Abnormal subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Blood Creatine Phosphokinase			

Increased			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	7		
Blood Culture Positive			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Lactate Dehydrogenase Abnormal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Blood Potassium Decreased			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Blood Pressure Decreased			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Blood Pressure Increased			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	8		
Blood Pressure Systolic Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Uric Acid Decreased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Uric Acid Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Blood Zinc Decreased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Body Temperature Increased			

subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Brain Natriuretic Peptide Increased			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Breath Sounds Abnormal			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Creatine Urine Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Creatinine Urine Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Electrocardiogram Pr Shortened			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Electrocardiogram Qt Prolonged			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Electrocardiogram St Segment Elevation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Electrocardiogram Abnormal			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Eosinophil Count Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Haematocrit Decreased			

subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Haemoglobin Decreased subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 4		
Heart Rate Increased subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 5		
Liver Function Test Abnormal subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Neutrophil Count Abnormal subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Neutrophil Count Increased subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Neutrophil Percentage Increased subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Occult Blood Positive subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Oxygen Saturation Decreased subjects affected / exposed occurrences (all)	4 / 113 (3.54%) 6		
Platelet Count Increased subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Protein Urine subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Protein Urine Present subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Pulmonary Function Test Decreased			

subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Pulse Pressure Abnormal subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Respiratory Rate Increased subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Serum Ferritin Decreased subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Specific Gravity Urine subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Sputum Culture Positive subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Staphylococcus Test Positive subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Tuberculin Test Positive subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Urine Ketone Body Present subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Urine Output Decreased subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Weight Decreased subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Weight Increased subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 3		
White Blood Cell Count Abnormal			

subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
White Blood Cell Count Increased subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Injury, poisoning and procedural complications			
Agitation Postoperative subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Animal Bite subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Animal Scratch subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Ankle Fracture subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Arthropod Bite subjects affected / exposed occurrences (all)	7 / 113 (6.19%) 8		
Arthropod Sting subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Concussion subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Contusion subjects affected / exposed occurrences (all)	6 / 113 (5.31%) 7		
Exposure To Communicable Disease subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Eye Contusion			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eye Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Face Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	11 / 113 (9.73%)		
occurrences (all)	13		
Feeding Tube Complication			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Femur Fracture			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Foreign Body			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastrointestinal Anastomotic Leak			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		
Gastrointestinal Stoma Complication			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hand Fracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Head Injury			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Humerus Fracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Joint Dislocation			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Laceration			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	6		
Laryngeal Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Ligament Sprain			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Limb Injury			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Lower Limb Fracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Overdose			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Periorbital Haemorrhage			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Post Procedural Haemorrhage			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Postoperative Fever			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Postoperative Respiratory Distress			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Procedural Nausea			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Procedural Pain			

subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	10		
Procedural Vomiting			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Scratch			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Skin Abrasion			
subjects affected / exposed	9 / 113 (7.96%)		
occurrences (all)	14		
Skin Wound			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Soft Tissue Injury			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Splinter			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Stoma Site Erythema			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Stoma Site Haemorrhage			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Stoma Site Irritation			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Stoma Site Rash			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Stoma Site Reaction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Sunburn			

subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Thermal Burn subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Tibia Fracture subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Tooth Avulsion subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Tooth Fracture subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Tooth Injury subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Tracheostomy Malfunction subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Vaccination Complication subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Wound subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Wound Dehiscence subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Congenital, familial and genetic disorders Cryptorchism subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Cardiac disorders			

Arrhythmia			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Bundle Branch Block Right			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Bradycardia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	4		
Cardiac Failure			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Cardiomyopathy			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Defect Conduction Intraventricular			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Diastolic Dysfunction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Left Ventricular Dysfunction			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Heart Valve Incompetence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pericardial Effusion			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	6		
Right Atrial Dilatation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Right Ventricular Hypertrophy			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		

Sinus Bradycardia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Sinus Tachycardia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Supraventricular Tachycardia			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	13		
Tachycardia			
subjects affected / exposed	13 / 113 (11.50%)		
occurrences (all)	21		
Wolff-Parkinson-White Syndrome			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tricuspid Valve Incompetence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Nervous system disorders</b>			
Allodynia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Areflexia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Burning Sensation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Clumsiness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Convulsion			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Dizziness			

subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
<b>Facial Paresis</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Formication</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Gross Motor Delay</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
<b>Headache</b>			
subjects affected / exposed	14 / 113 (12.39%)		
occurrences (all)	36		
<b>Hypoaesthesia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
<b>Hyporeflexia</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
<b>Hypotonia</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
<b>Lethargy</b>			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	8		
<b>Motor Developmental Delay</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Motor Dysfunction</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
<b>Muscle Contractions Involuntary</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Nystagmus</b>			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Paraesthesia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Paralysis Flaccid</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Poor Quality Sleep</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Presyncope</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Psychomotor Hyperactivity</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
<b>Somnolence</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Speech Disorder</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Tremor</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
<b>Blood and lymphatic system disorders</b>			
<b>Anaemia</b>			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	8		
<b>Eosinophilia</b>			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	7		
<b>Coagulopathy</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		

Iron Deficiency Anaemia subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Lymphadenitis subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Neutropenia subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Ear and labyrinth disorders			
Conductive Deafness subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Cerumen Impaction subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 5		
Deafness subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Deafness Neurosensory subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Deafness Unilateral subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Ear Pain subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 8		
Eustachian Tube Dysfunction subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 5		
Middle Ear Effusion			

subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 5		
Mixed Deafness subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Otorrhoea subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 3		
Tympanic Membrane Disorder subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Tympanic Membrane Perforation subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Eye disorders			
Astigmatism subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Blepharitis subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Chalazion subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Conjunctival Hyperaemia subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Dry Eye subjects affected / exposed occurrences (all)	4 / 113 (3.54%) 5		
Eye Discharge subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		
Eye Irritation subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		

Eye Pruritus			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eye Swelling			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eyelid Oedema			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eyelid Ptosis			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	6		
Hypermetropia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lid Sulcus Deepened			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Myopia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Ocular Hyperaemia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Photophobia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Strabismus			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Vision Blurred			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal Discomfort			

subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Abdominal Distension			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Abdominal Pain			
subjects affected / exposed	10 / 113 (8.85%)		
occurrences (all)	17		
Abdominal Pain Upper			
subjects affected / exposed	11 / 113 (9.73%)		
occurrences (all)	18		
Abnormal Faeces			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Anal Fissure			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Aphthous Stomatitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	20 / 113 (17.70%)		
occurrences (all)	23		
Dental Caries			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Dental Discomfort			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	55 / 113 (48.67%)		
occurrences (all)	121		
Dysphagia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Faecal Incontinence			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Faeces Discoloured			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Flatulence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Frequent Bowel Movements			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		
Gastric Ulcer			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastritis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Gastrointestinal Disorder			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	10		
Gastroesophageal Reflux Disease			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Gingival Bleeding			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Haematochezia			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Haemorrhoids			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Ileus			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Infrequent Bowel Movements			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lip Blister			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lip Ulceration			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Mouth Ulceration			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	12 / 113 (10.62%)		
occurrences (all)	20		
Oral Disorder			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Rectal Fissure			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Regurgitation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Retained Deciduous Tooth			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Retching			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Salivary Hypersecretion			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Sensitivity Of Teeth			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Teething			

subjects affected / exposed occurrences (all)	4 / 113 (3.54%) 4		
Tongue Spasm subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Tooth Deposit subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Tooth Impacted subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Toothache subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Vomiting subjects affected / exposed occurrences (all)	42 / 113 (37.17%) 112		
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		
Hepatic Fibrosis subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 3		
Alopecia subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 3		
Blister subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Cold Sweat			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Decubitus Ulcer			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Dermatitis			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Dermatitis Allergic			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Dermatitis Contact			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Dermatitis Diaper			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	6		
Dry Skin			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Ecchymosis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	9		
Excessive Granulation Tissue			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Granuloma Skin			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hyperhidrosis			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
<b>Hyperkeratosis</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
<b>Ingrowing Nail</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Ingrown Hair</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Macule</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
<b>Mechanical Urticaria</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Papule</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	3		
<b>Petechiae</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Photosensitivity Reaction</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Pruritus</b>			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	6		
<b>Pruritus Generalised</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
<b>Rash</b>			
subjects affected / exposed	31 / 113 (27.43%)		
occurrences (all)	42		
<b>Rash Erythematous</b>			

subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Rash Macular			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Rash Pruritic			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Red Man Syndrome			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Seborrhoeic Dermatitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Skin Disorder			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Skin Exfoliation			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Skin Hyperpigmentation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Skin Irritation			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Skin Lesion			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Skin Ulcer			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Swelling Face			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Urticaria			

subjects affected / exposed occurrences (all)	9 / 113 (7.96%) 28		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Haematuria			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Incontinence			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nephrolithiasis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Pollakiuria			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Proteinuria			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Urinary Hesitation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Urinary Incontinence			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Urinary Retention			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Endocrine disorders			
Precocious Puberty			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	7		
Arthropathy			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Axillary Mass			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Back Pain			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	6		
Deformity Thorax			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Foot Deformity			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Fracture Pain			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hip Deformity			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Joint Contracture			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Joint Stiffness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Joint Swelling			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Kyphosis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		

Limb Discomfort			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Muscle Contracture			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Muscle Spasms			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Muscle Tightness			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Muscular Weakness			
subjects affected / exposed	12 / 113 (10.62%)		
occurrences (all)	15		
Musculoskeletal Chest Pain			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Musculoskeletal Pain			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Musculoskeletal Stiffness			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Myopathy			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Neck Pain			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Osteopenia			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		

Pain In Extremity subjects affected / exposed occurrences (all)	16 / 113 (14.16%) 23		
Pain In Jaw subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 3		
Scoliosis subjects affected / exposed occurrences (all)	6 / 113 (5.31%) 6		
Tendinous Contracture subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Tendon Discomfort subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 3		
Tendon Disorder subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
<b>Infections and infestations</b>			
Abscess Limb subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Acarodermatitis subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Adenovirus Infection subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Atypical Pneumonia subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Bacterial Tracheitis subjects affected / exposed occurrences (all)	5 / 113 (4.42%) 7		
Beta Haemolytic Streptococcal Infection			

subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Body Tinea subjects affected / exposed occurrences (all)	3 / 113 (2.65%) 3		
Bronchiolitis subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Bronchitis subjects affected / exposed occurrences (all)	8 / 113 (7.08%) 8		
Candida Infection subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Cellulitis subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Chronic Sinusitis subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 2		
Clostridium Difficile Colitis subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 3		
Conjunctivitis subjects affected / exposed occurrences (all)	7 / 113 (6.19%) 9		
Croup Infectious subjects affected / exposed occurrences (all)	2 / 113 (1.77%) 2		
Device Related Infection subjects affected / exposed occurrences (all)	1 / 113 (0.88%) 1		
Ear Infection subjects affected / exposed occurrences (all)	12 / 113 (10.62%) 20		
Ear Lobe Infection			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Enterovirus Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Erythema Infectiosum			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Escherichia Urinary Tract Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Eye Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Folliculitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Fungal Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Fungal Skin Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Furuncle			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	11 / 113 (9.73%)		
occurrences (all)	15		
Gastroenteritis Norovirus			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gastroenteritis Viral			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Gastrointestinal Infection			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Gingival Abscess			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Gingivitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Haemophilus Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hand-Foot-And-Mouth Disease			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Herpes Zoster			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Impetigo			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	8 / 113 (7.08%)		
occurrences (all)	10		
Labyrinthitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lice Infestation			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Lip Infection			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Lobar Pneumonia			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nail Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	12 / 113 (10.62%)		
occurrences (all)	23		
Oral Candidiasis			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Oral Herpes			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Otitis Externa			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	5		
Otitis Externa Fungal			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Otitis Media			
subjects affected / exposed	23 / 113 (20.35%)		
occurrences (all)	35		
Otitis Media Acute			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	7		
Otitis Media Chronic			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	6		
Pharyngitis			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	14		
Pharyngitis Streptococcal			

subjects affected / exposed	13 / 113 (11.50%)		
occurrences (all)	24		
Pneumonia			
subjects affected / exposed	17 / 113 (15.04%)		
occurrences (all)	32		
Pneumonia Viral			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Pseudomonas Infection			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	5		
Rash Pustular			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Respiratory Syncytial Virus Infection			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
Respiratory Tract Infection			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	5		
Rhinitis			
subjects affected / exposed	6 / 113 (5.31%)		
occurrences (all)	8		
Rhinovirus Infection			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	4		
Rotavirus Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	6		
Skin Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Staphylococcal Infection			

subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	5		
Stoma Site Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Streptococcal Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Streptococcal Urinary Tract Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Subcutaneous Abscess			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Tinea Infection			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tonsillitis			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Tooth Abscess			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	3		
Tooth Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tracheitis			
subjects affected / exposed	7 / 113 (6.19%)		
occurrences (all)	12		
Tracheobronchitis			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Tracheostomy Infection			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	9		
Upper Respiratory Tract Infection			

subjects affected / exposed	49 / 113 (43.36%)		
occurrences (all)	104		
Upper Respiratory Tract Infection Bacterial			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	2		
Urinary Tract Infection			
subjects affected / exposed	19 / 113 (16.81%)		
occurrences (all)	31		
Viral Infection			
subjects affected / exposed	15 / 113 (13.27%)		
occurrences (all)	23		
Viral Rash			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	7		
Vulvovaginal Mycotic Infection			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Abnormal Weight Gain			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Decreased Appetite			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		
Dehydration			
subjects affected / exposed	5 / 113 (4.42%)		
occurrences (all)	7		
Electrolyte Imbalance			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
Failure To Thrive			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Hypoalbuminaemia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Hypochloraemia</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Hypoglycaemia</b>			
subjects affected / exposed	3 / 113 (2.65%)		
occurrences (all)	3		
<b>Hypokalaemia</b>			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences (all)	2		
<b>Iron Deficiency</b>			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences (all)	1		
<b>Vitamin D Deficiency</b>			
subjects affected / exposed	4 / 113 (3.54%)		
occurrences (all)	4		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 October 2012	6-month administrative analysis was added. -For the primary efficacy endpoint, in addition to the analysis using the full analysis set specified in the original protocol, the analysis was also to be conducted on the Per-Protocol Analysis Set. -The efficacy endpoint of left ventricular mass index Z- score (LVMI-Z) was revised to LVM-Z. -Shortening of the post-infusion observation period was changed from being allowed after a 6-month treatment period to being allowed after a 3-month treatment period. -Home infusions were changed from being allowed after 4 infusions in subjects with no history of moderate or severe infusion-associated reactions (IARs) or serious adverse events (SAEs) to being allowed after 2 infusions in subjects with no history of moderate or severe IARs or SAEs. -The Sponsor's department name, Global Patient Safety and Risk Management, was updated for a recent name change to Global Pharmacovigilance and Epidemiology. -Text was added to clarify that pulmonary function tests were not required in young subjects unable to undergo testing. -The protocol was modified to ensure that subject position during measurement of vital signs was to be recorded in the electronic case report form and that vital signs and weight were to be obtained at every study visit. -The IgG antibodies, inhibitory antibodies, and urine pregnancy testing schedules were clarified. -Text referring to subjects' previous treatment "in the commercial setting" was deleted as subjects treated with 160L scale product in other clinical trials were eligible to enroll. - Measurement of R voltage V6 and S voltage V1 were removed from the ECG. -Text was deleted to reflect that efficacy and safety results would not be summarized by baseline Pompe disease status. - The presentation of results of planned clinical laboratory assessments was clarified. -The stipulation that the Data Safety Monitoring Board (DSMB) would be comprised of 4 physicians was removed.

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported