



Clinical trial results:

Randomized, Double-Blind, Placebo-Controlled Study of the Safety, Efficacy and Pharmacokinetics of Myozyme in Patients With Late-Onset Pompe Disease.

Summary

EudraCT number	2005-002759-42
Trial protocol	DE
Global end of trial date	28 September 2007

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	12 June 2015

Trial information

Trial identification

Sponsor protocol code	AGLU02704
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00158600
WHO universal trial number (UTN)	-

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	21 November 2007
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 September 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study are: 1) to evaluate the safety profile of Myozyme; 2) to determine the effect of Myozyme treatment on functional endurance as measured by the Six Minute Walk Test (6MWT) 3) to determine the effect of Myozyme treatment on respiratory muscle weakness as measured by Forced Vital Capacity (FVC) in the upright position ; and 4) to determine in a subset of subjects the PK profile of Myozyme in subjects with late-onset Pompe disease. The study will be considered to have met its primary efficacy objective if a statistically significant treatment effect of Myozyme over placebo is demonstrated in the 6 MWT distance walked.

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	06 September 2005
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	France: 10
Country: Number of subjects enrolled	United States: 58
Country: Number of subjects enrolled	Netherlands: 22
Worldwide total number of subjects	90
EEA total number of subjects	32

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)	1
Adolescents (12-17 years)	3
Adults (18-64 years)	81
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

One hundred subjects screened and 90 enrolled.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Alglucosidase Alfa
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Arm description:

Alglucosidase alfa for 78 weeks.

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

Dosage and administration details:

Alglucosidase alfa at 20 milligrams (mg)/kilogram (kg) of body weight every other week (qow).

Arm title	Placebo
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Arm description:

Placebo for 78 weeks.

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

Dosage and administration details:

Placebo matched to alglucosidase alfa every other week (qow).

Number of subjects in period 1	Alglucosidase Alfa	Placebo
Started	60	30
Completed	55	26
Not completed	5	4
unable to commit time to study	-	1
Adverse Event	2	1

Death	1	-
Withdrawal by Subject	2	2

Baseline characteristics

Reporting groups

Reporting group title	Alglucosidase Alfa
Reporting group description: Alglucosidase alfa for 78 weeks.	
Reporting group title	Placebo
Reporting group description: Placebo for 78 weeks.	

Reporting group values	Alglucosidase Alfa	Placebo	Total
Number of subjects	60	30	90
Age categorical Units: Subjects			

Age continuous			
Age at First Infusion			
Units: years			
arithmetic mean	45.3	42.6	
standard deviation	± 12.37	± 11.63	-
Gender categorical Units: Subjects			
Female	26	19	45
Male	34	11	45
Race/Ethnicity Units: Subjects			
Hispanic	1	1	2
Asian	1	1	2
Black or African American	0	0	0
White	57	27	84
Unknown or not reported	1	1	2

End points

End points reporting groups

Reporting group title	Alglucosidase Alfa
Reporting group description: Alglucosidase alfa for 78 weeks.	
Reporting group title	Placebo
Reporting group description: Placebo for 78 weeks.	

Primary: Summary of Subjects Reporting Treatment-Emergent Adverse Events

End point title	Summary of Subjects Reporting Treatment-Emergent Adverse Events ^[1]
End point description: Overall safety summary of subjects experiencing Adverse Events (AEs), Serious Adverse Events (SAEs), treatment-related AEs, and Infusion Associated Reactions (IARs). Summary is based on Treatment-emergent AEs (TEAEs), defined as AEs that occurred following the initiation of study treatment, i.e., alglucosidase alfa or placebo. All subjects who received any amount of study treatment comprise the safety population. Subjects were considered, for safety analysis, to be in the treatment group of the treatment they actually received. Missing or invalid safety or resource utilization data were not replaced.	
End point type	Primary
End point timeframe: weeks 0-78	

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	Alglucosidase Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	30		
Units: subjects				
Subjects with Any AEs	60	30		
Subjects with Treatment-Related AEs	32	17		
Subjects with Infusion-Associated Reactions	17	7		
Subjects with SAEs	13	6		
Subjects with Severe AEs	14	10		
Subjects who Discontinued Due to AEs (incl death)	3	1		
Subjects who Died	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Mean Distance Walked as Measured by Six-minute Walk Test (6MWT) at Weeks 0 and 78, and Mean Change From Baseline

End point title	Mean Distance Walked as Measured by Six-minute Walk Test (6MWT) at Weeks 0 and 78, and Mean Change From Baseline
End point description:	
Mean distance walked gives an indication of functional endurance. The greater the distance, the greater the endurance. Mean values of distance walked in a six-minute walk test are offered for baseline, week 78 (or last available observation), and the mean change from baseline (at week 78 or last available post-baseline observation). Intent-to-Treat (ITT) population. Last observation carried forward. The last available distance walked for one subject was the Baseline visit; therefore, this subject was excluded from the change from baseline calculation.	
End point type	Primary
End point timeframe:	
weeks 0, 78	

End point values	Alglucosidase Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	30		
Units: meters				
arithmetic mean (standard deviation)				
Distance Walked at Baseline	332.2 (± 126.69)	317.93 (± 132.29)		
Distance Walked at Last Available Observation	357.85 (± 141.32)	313.07 (± 144.69)		
Change at Last Available Observation from Baseline	26.08 (± 64.41)	-4.87 (± 45.24)		

Statistical analyses

Statistical analysis title	Alglucosidase Alfa vs Placebo
Statistical analysis description:	
The difference between alglucosidase alfa and placebo treatment groups in change in distance walked from baseline to last observation was estimated by ANCOVA after adjusting for baseline value and randomization strata.	
Comparison groups	Alglucosidase Alfa v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0347 ^[2]
Method	ANCOVA
Parameter estimate	Difference
Point estimate	28.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.07
upper limit	54.17

Notes:

[2] - The threshold for determining statistical significance was 0.05. A fixed testing sequence procedure was used to preserve an overall error rate of 5% for the co-primary efficacy endpoints by linking the test of FVC to the result of 6MWT.

Primary: Percent of Predicted Forced Vital Capacity (FVC)

End point title	Percent of Predicted Forced Vital Capacity (FVC)
End point description: Forced vital capacity is a standard pulmonary function test used to quantify respiratory muscle weakness. Forced vital capacity (FVC) is the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. Predicted forced vital capacity is based on a formula using sex, age and height of a person, and is an estimate of healthy lung capacity. Percent of predicted FVC = (observed value)/(predicted value) * 100%. ITT population. Last observation carried forward.	
End point type	Primary
End point timeframe: weeks 0, 78	

End point values	Alglucosidase Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	30		
Units: percent predicted FVC				
arithmetic mean (standard deviation)				
Baseline (week 0)	55.43 (± 14.44)	53 (± 15.66)		
Week 78 (or last observation)	56.71 (± 16.3)	50.7 (± 14.88)		
Change at Week 78 from Baseline	1.25 (± 5.55)	-2.3 (± 4.33)		

Statistical analyses

Statistical analysis title	Alglucosidase Alfa vs Placebo
Statistical analysis description: The difference between alglucosidase alfa and placebo treatment groups in change in % predicted FVC from baseline to last observation was estimated by ANCOVA after adjusting for baseline value and randomization strata.	
Comparison groups	Alglucosidase Alfa v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0055 [3]
Method	ANCOVA
Parameter estimate	Difference
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	5.77

Notes:

[3] - The threshold for determining statistical significance is 0.05. A fixed testing sequence procedure was used to preserve an overall error rate of 5% for the co-primary efficacy endpoints by linking the test of FVC to the result of 6MWT.

Primary: Recombinant Human Acid Alpha-Glucosidase (rhGAA) Pharmacokinetic

Parameters: Area Under the Curve (AUC)

End point title	Recombinant Human Acid Alpha-Glucosidase (rhGAA) Pharmacokinetic Parameters: Area Under the Curve (AUC) ^{[4][5]}
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End point description:

Area under the plasma concentration versus time curve from time zero (pre-dose) to 16 hours after the end of infusion. Blood sample time points were 0 (before the start of the infusion), 1 and 2 hours after the start of infusion, end of the infusion, and then 0.25, 0.5, 1, 2, 3, 4, 8, 12, and 16 hours after the end of the infusion (with a 5-minute window for time-points after the start of infusion). Pooled figures combine the values for the three timeframes. The subgroup of subjects for whom pharmacokinetic samples were obtained was based on those study sites that could accommodate pharmacokinetic sampling needs.

End point type	Primary
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End point timeframe:

weeks 0, 12 and 52

Notes:

[4] - 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: Only descriptive data are reported for pharmacokinetic analysis.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Pharmacokinetic data were measured only for alglucosidase alfa, hence data were provided for this arm only.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: ug*h/mL				
arithmetic mean (standard deviation)				
Week 0	2672.47 (± 1139.85)			
Week 12	2386.76 (± 555.09)			
Week 52	2699.28 (± 999.97)			
Pooled	2586.17 (± 933.28)			

Statistical analyses

No statistical analyses for this end point

Primary: Recombinant Human Acid Alpha-Glucosidase (rhGAA) Pharmacokinetic Parameters: Mean Maximum Plasma Concentration(Cmax)

End point title	Recombinant Human Acid Alpha-Glucosidase (rhGAA) Pharmacokinetic Parameters: Mean Maximum Plasma Concentration(Cmax) ^{[6][7]}
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End point description:

Maximum plasma concentration observed in blood samples taken at the following time points: 0 (before the start of the infusion), 1 and 2 hours after the start of infusion, end of the infusion, and then 0.25, 0.5, 1, 2, 3, 4, 8, 12, and 16 hours after the end of the infusion (with a 5-minute window for time-points after the start of infusion). Pooled figures combine the values for the three timeframes. The subgroup of subjects for whom pharmacokinetic samples were obtained was based on those study sites that could accommodate pharmacokinetic sampling needs.

End point type	Primary
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End point timeframe:

weeks 0, 12, 52

Notes:

[6] - 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: Only descriptive data are reported for pharmacokinetic analysis.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Pharmacokinetic data were measured only for alglucosidase alfa, hence data were provided for this arm only.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 0	385237 (± 105585)			
Week 12	349269 (± 78620)			
Week 52	369744 (± 88203)			
Pooled	368083 (± 91721)			

Statistical analyses

No statistical analyses for this end point

Primary: Recombinant Human Acid Alpha-Glucosidase (rhGAA) Pharmacokinetic Parameters: Mean Time to Maximum Plasma Concentration(Tmax)

End point title	Recombinant Human Acid Alpha-Glucosidase (rhGAA) Pharmacokinetic Parameters: Mean Time to Maximum Plasma Concentration(Tmax) ^{[8][9]}
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End point description:

Time to maximum plasma concentration observed in blood samples taken at the following time points: 0 (before the start of the infusion), 1 and 2 hours after the start of infusion, end of the infusion, and then 0.25, 0.5, 1, 2, 3, 4, 8, 12, and 16 hours after the end of the infusion (with a 5-minute window for time-points after the start of infusion). Pooled figures combine the values for the three timeframes. The subgroup of subjects for whom pharmacokinetic samples were obtained was based on those study sites that could accommodate pharmacokinetic sampling needs.

End point type	Primary
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End point timeframe:

weeks 0, 12, 52

Notes:

[8] - 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: Only descriptive data are reported for pharmacokinetic analysis.

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Pharmacokinetic data were measured only for alglucosidase alfa, hence data were provided for this arm only.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: hours				
arithmetic mean (standard deviation)				
Week 0	3.62 (± 0.33)			
Week 12	3.62 (± 0.28)			
Week 52	3.64 (± 0.31)			
Pooled	3.63 (± 0.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Predicted Proximal Muscle Strength of the Lower Limbs as Measured by Quantitative Muscle Testing (QMT)

End point title	Percent Predicted Proximal Muscle Strength of the Lower Limbs as Measured by Quantitative Muscle Testing (QMT)
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End point description:

Quantitative muscle testing (QMT) is a standardized system to measure muscle force production during maximal voluntary isometric contraction. QMT data were collected directly from sensors into laptop computers. Predicted normal values for QMT are based on a formula using sex, age and body mass index of a person, and is an estimate of healthy muscle force. Percent of predicted QMT = (observed value)/(predicted value) * 100%. The QMT Leg Score is the average of the bilateral means for percent predicted knee flexors and extensors. A value of 100% indicates 'normal' muscle strength. ITT population. Last observation carried forward.

End point type	Secondary
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End point timeframe:

weeks 0, 78

End point values	Alglucosidase Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	30		
Units: percent predicted QMT				
arithmetic mean (standard deviation)				
Baseline (week 0)	37.69 (± 18.88)	32.49 (± 18.24)		
Week 78 (or last available observation)	39.05 (± 21.83)	30.4 (± 20.54)		
Change at Week 78 from Baseline	1.22 (± 9.88)	-2.08 (± 5.11)		

Statistical analyses

Statistical analysis title	Alglucosidase Alfa vs Placebo
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Statistical analysis description:

The difference between alglucosidase alfa and placebo treatment groups in change in QMT from baseline to last observation was estimated by ANCOVA after adjusting for baseline value and randomization strata.

Comparison groups	Alglucosidase Alfa v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1093 ^[10]
Method	ANCOVA
Parameter estimate	Difference
Point estimate	3.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	7.08

Notes:

[10] - The threshold for determining statistical significance is 0.05. No adjustment for multiple comparison was made for secondary efficacy endpoints.

Secondary: Health-related Quality of Life Survey Values Related to Physical Components as Measured by the Medical Outcomes Study (MOS) Short Form-36 Health Survey

End point title	Health-related Quality of Life Survey Values Related to Physical Components as Measured by the Medical Outcomes Study (MOS) Short Form-36 Health Survey
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End point description:

The Medical Outcomes Study Short Form (MOS SF)-36 questionnaire consists of 36 items grouped into 8 domains designed to assess generic health-related quality of life in healthy and ill adult populations. Physical Component Scores (PCS) report the four domains of physical functioning, role-physical, bodily pain, and general health. Higher scores are associated with better quality of life. All questions are scored on a scale from 0 to 100, with 100 representing the highest level of functioning possible. The PCS scores are reported. ITT population. Last observation carried forward.

End point type	Secondary
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End point timeframe:

weeks 0, 78

End point values	Alglucosidase Alfa	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	30		
Units: Units on a scale				
arithmetic mean (standard deviation)				
PCS at Baseline (week 0)	34.33 (± 8.93)	34.91 (± 7.26)		
PCS at Week 78 (or last available observation)	35.11 (± 9.84)	36.47 (± 9.57)		

Statistical analyses

Statistical analysis title	Alglucosidase Alfa vs Placebo
Statistical analysis description:	
The difference between alglucosidase alfa and placebo treatment groups in change in PCS from baseline to last observation was estimated by ANCOVA after adjusting for baseline value and randomization strata.	
Comparison groups	Alglucosidase Alfa v Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8333 ^[11]
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.83
upper limit	3.09

Notes:

[11] - The threshold for determining statistical significance is 0.05. No adjustment for multiple comparison was made for secondary efficacy endpoints.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected following the initiation of treatment (ie alglucosidase alfa or placebo) up to the end of study (0 - 78 weeks) regardless of seriousness or relationship to investigational product

Adverse event reporting additional description:

Reported AEs and deaths are treatment-emergent that is AEs and deaths that occurred following the initiation of study treatment i.e. alglucosidase alfa or placebo.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	9.1
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Reporting groups

Reporting group title	Alglucosidase Alfa
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Reporting group description:

Alglucosidase alfa for 78 weeks.

Reporting group title	Placebo
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Reporting group description:

Placebo for 78 weeks.

Serious adverse events	Alglucosidase Alfa	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 60 (21.67%)	6 / 30 (20.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus Fracture			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aneurysm			

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary Artery Disease			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular Tachycardia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain Stem Ischaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Headache			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
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			
Chest Discomfort			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Upper			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung Disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Throat Tightness			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioneurotic Oedema			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septal Panniculitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Flank Pain			

subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Alglucosidase Alfa	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 60 (100.00%)	30 / 30 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic Naevus			

subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 30 (3.33%) 1	
Vascular disorders			
Aneurysm			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Diastolic Hypotension			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Flushing			
subjects affected / exposed	3 / 60 (5.00%)	2 / 30 (6.67%)	
occurrences (all)	5	2	
Haematoma			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Hot Flush			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Hypertension			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
Hypotension			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Phlebitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Raynaud's Phenomenon			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Vasoconstriction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Application Site Vesicles		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Asthenia		
subjects affected / exposed	3 / 60 (5.00%)	4 / 30 (13.33%)
occurrences (all)	3	8
Axillary Pain		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	2	0
Catheter Related Complication		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Catheter Site Pain		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	7	0
Catheter Site Related Reaction		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Chest Discomfort		
subjects affected / exposed	6 / 60 (10.00%)	1 / 30 (3.33%)
occurrences (all)	15	1
Chest Pain		
subjects affected / exposed	4 / 60 (6.67%)	1 / 30 (3.33%)
occurrences (all)	4	1
Chills		
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)
occurrences (all)	3	4
Fatigue		
subjects affected / exposed	7 / 60 (11.67%)	6 / 30 (20.00%)
occurrences (all)	9	14
Feeling Abnormal		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Feeling Cold		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	2	0

Feeling Hot		
subjects affected / exposed	3 / 60 (5.00%)	2 / 30 (6.67%)
occurrences (all)	4	3
Feeling Hot And Cold		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Gait Disturbance		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	2	0
Hangover		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Influenza Like Illness		
subjects affected / exposed	2 / 60 (3.33%)	4 / 30 (13.33%)
occurrences (all)	2	5
Infusion Site Bruising		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	2	0
Infusion Site Pain		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	2	0
Infusion Site Paraesthesia		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Infusion Site Reaction		
subjects affected / exposed	5 / 60 (8.33%)	0 / 30 (0.00%)
occurrences (all)	6	0
Injection Site Phlebitis		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Local Swelling		
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)
occurrences (all)	14	2
Malaise		
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)
occurrences (all)	3	0

Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Oedema Peripheral			
subjects affected / exposed	10 / 60 (16.67%)	3 / 30 (10.00%)	
occurrences (all)	12	5	
Pain			
subjects affected / exposed	5 / 60 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	8	1	
Pitting Oedema			
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
Puncture Site Haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Thirst			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	8 / 60 (13.33%)	8 / 30 (26.67%)	
occurrences (all)	8	11	
Vessel Puncture Site Haematoma			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	4	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	24	0	
Reproductive system and breast disorders			
Breast Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Breast Swelling			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Breast Tenderness			

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Dysmenorrhoea			
subjects affected / exposed	0 / 60 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
Fibrocystic Breast Disease			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Genital Pruritus Female			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Menstrual Discomfort			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Menstruation Irregular			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Scrotal Cyst			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Vaginal Haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	2	
Bronchospasm			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	6 / 60 (10.00%)	5 / 30 (16.67%)	
occurrences (all)	6	5	
Dyspnoea			

subjects affected / exposed	7 / 60 (11.67%)	4 / 30 (13.33%)
occurrences (all)	10	6
Dyspnoea Exertional		
subjects affected / exposed	4 / 60 (6.67%)	0 / 30 (0.00%)
occurrences (all)	5	0
Epistaxis		
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)
occurrences (all)	8	0
Increased Bronchial Secretion		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	5
Lung Disorder		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Lung Infiltration		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Nasal Congestion		
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)
occurrences (all)	2	3
Paranasal Sinus Hypersecretion		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Pharyngolaryngeal Pain		
subjects affected / exposed	12 / 60 (20.00%)	5 / 30 (16.67%)
occurrences (all)	19	9
Postnasal Drip		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	2	0
Rales		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Respiratory Distress		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	1
Respiratory Failure		

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Respiratory Tract Congestion			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	3	0	
Rhinorrhoea			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	2	2	
Sinus Congestion			
subjects affected / exposed	2 / 60 (3.33%)	3 / 30 (10.00%)	
occurrences (all)	2	3	
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Sneezing			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	2	
Throat Irritation			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Throat Tightness			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Wheezing			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	2 / 60 (3.33%)	3 / 30 (10.00%)	
occurrences (all)	4	3	
Depression			
subjects affected / exposed	1 / 60 (1.67%)	2 / 30 (6.67%)	
occurrences (all)	3	2	

Insomnia			
subjects affected / exposed	6 / 60 (10.00%)	2 / 30 (6.67%)	
occurrences (all)	7	2	
Panic Attack			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	2	
Stress			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	9	0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Blood Creatine Phosphokinase Mb Increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	2	
Blood Folate Decreased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Blood Glucose Increased			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Blood Parathyroid Hormone Increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Blood Pressure Increased			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	
occurrences (all)	3	2	

Blood Thyroid Stimulating Hormone Increased		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Blood Urine Present		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Blood Uric Acid Increased		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Carbon Dioxide Increased		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Electrocardiogram Qt Corrected Interval Prolonged		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	1
Eosinophil Count Increased		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Glucose Urine Present		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Forced Expiratory Volume Decreased		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Heart Rate Irregular		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
International Normalised Ratio Decreased		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Lymph Node Palpable		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Neutrophil Count Increased		

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Oxygen Saturation Decreased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Protein Total Increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	2	
Protein Urine Present			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Specific Gravity Urine Decreased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Urine Ketone Body Present			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Vitamin D Decreased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Weight Decreased			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Weight Increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
White Blood Cell Count Increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
White Blood Cells Urine Positive			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Accident			

subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Animal Bite		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Arthropod Bite		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Arthropod Sting		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	1
Back Injury		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Contusion		
subjects affected / exposed	4 / 60 (6.67%)	6 / 30 (20.00%)
occurrences (all)	6	7
Excoriation		
subjects affected / exposed	0 / 60 (0.00%)	3 / 30 (10.00%)
occurrences (all)	0	4
Fall		
subjects affected / exposed	39 / 60 (65.00%)	20 / 30 (66.67%)
occurrences (all)	154	120
Femur Fracture		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Foot Fracture		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Humerus Fracture		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	1
Injury		
subjects affected / exposed	4 / 60 (6.67%)	1 / 30 (3.33%)
occurrences (all)	4	1
Injury Corneal		

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Joint Dislocation		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Joint Sprain		
subjects affected / exposed	1 / 60 (1.67%)	2 / 30 (6.67%)
occurrences (all)	1	2
Laceration		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Ligament Injury		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Limb Crushing Injury		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Limb Injury		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Muscle Strain		
subjects affected / exposed	4 / 60 (6.67%)	4 / 30 (13.33%)
occurrences (all)	5	5
Periorbital Haematoma		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Procedural Pain		
subjects affected / exposed	9 / 60 (15.00%)	3 / 30 (10.00%)
occurrences (all)	11	6
Repetitive Strain Injury		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Rib Fracture		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	2	1
Road Traffic Accident		

subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Skeletal Injury			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Skin Laceration			
subjects affected / exposed	4 / 60 (6.67%)	1 / 30 (3.33%)	
occurrences (all)	5	1	
Tendon Injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Thermal Burn			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Tooth Fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Traumatic Ulcer			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Vaccination Complication			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Bundle Branch Block Left			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Bundle Branch Block Right			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	

Coronary Artery Disease subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 2	0 / 30 (0.00%) 0	
Palpitations subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 9	1 / 30 (3.33%) 1	
Sinus Tachycardia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 30 (0.00%) 0	
Tachycardia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 30 (0.00%) 0	
Tricuspid Valve Incompetence subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 30 (0.00%) 0	
Nervous system disorders			
Areflexia subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 4	2 / 30 (6.67%) 2	
Balance Disorder subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 30 (3.33%) 1	
Burning Sensation subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	0 / 30 (0.00%) 0	
Carpal Tunnel Syndrome subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	1 / 30 (3.33%) 1	
Disturbance In Attention subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 30 (3.33%) 1	
Dizziness subjects affected / exposed occurrences (all)	14 / 60 (23.33%) 31	6 / 30 (20.00%) 14	
Dizziness Postural			

subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	2	0
Dysgeusia		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	17
Facial Palsy		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Head Discomfort		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	4
Headache		
subjects affected / exposed	24 / 60 (40.00%)	15 / 30 (50.00%)
occurrences (all)	91	129
Hyperreflexia		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Hypoaesthesia		
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)
occurrences (all)	2	3
Hyporeflexia		
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)
occurrences (all)	2	1
Intercostal Neuralgia		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	2	0
Intracranial Hypotension		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Lethargy		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	4	0
Loss Of Consciousness		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	3	0
Migraine		

subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	
occurrences (all)	5	4	
Nerve Compression			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	6 / 60 (10.00%)	4 / 30 (13.33%)	
occurrences (all)	16	10	
Poor Quality Sleep			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Sinus Headache			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Somnolence			
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)	
occurrences (all)	5	0	
Syncope Vasovagal			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	2	
Tremor			
subjects affected / exposed	4 / 60 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	4	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Lymphadenopathy			
subjects affected / exposed	5 / 60 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	6	0	
Macrocytosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Normochromic Normocytic Anaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	

Ear and labyrinth disorders			
Auricular Swelling			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Ear Congestion			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Ear Discomfort			
subjects affected / exposed	4 / 60 (6.67%)	1 / 30 (3.33%)	
occurrences (all)	23	1	
Ear Pain			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	
occurrences (all)	3	4	
Hypoacusis			
subjects affected / exposed	20 / 60 (33.33%)	7 / 30 (23.33%)	
occurrences (all)	22	7	
Presbycusis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Tympanic Membrane Disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Tympanic Membrane Scarring			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	4 / 60 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	6	0	
Eye disorders			
Altered Visual Depth Perception			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Asthenopia			

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Cataract			
subjects affected / exposed	4 / 60 (6.67%)	2 / 30 (6.67%)	
occurrences (all)	4	2	
Conjunctivitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Diplopia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Dry Eye			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Eye Irritation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Eye Pruritus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Lacrimation Increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Photophobia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Vision Blurred			
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)	
occurrences (all)	3	0	
Visual Disturbance			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Vitreous Floaters			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Abdominal Discomfort		
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)
occurrences (all)	2	2
Abdominal Distension		
subjects affected / exposed	1 / 60 (1.67%)	2 / 30 (6.67%)
occurrences (all)	1	2
Abdominal Mass		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Abdominal Pain		
subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)
occurrences (all)	4	3
Abdominal Pain Lower		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	2	0
Abdominal Pain Upper		
subjects affected / exposed	6 / 60 (10.00%)	2 / 30 (6.67%)
occurrences (all)	23	3
Constipation		
subjects affected / exposed	6 / 60 (10.00%)	0 / 30 (0.00%)
occurrences (all)	8	0
Dental Caries		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Diarrhoea		
subjects affected / exposed	18 / 60 (30.00%)	13 / 30 (43.33%)
occurrences (all)	43	20
Diverticulum		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Dry Mouth		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Dyspepsia		
subjects affected / exposed	5 / 60 (8.33%)	0 / 30 (0.00%)
occurrences (all)	8	0

Dysphagia		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Epigastric Discomfort		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Flatulence		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	2	0
Food Poisoning		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	2	0
Gastrointestinal Disorder		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Gastrooesophageal Reflux Disease		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	4	0
Glossodynia		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Haematochezia		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Hiatus Hernia		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Inguinal Hernia		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Lip Swelling		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	3	0
Nausea		
subjects affected / exposed	11 / 60 (18.33%)	10 / 30 (33.33%)
occurrences (all)	38	49

Oesophageal Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Oral Mucosal Blistering			
subjects affected / exposed	0 / 60 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Oral Pruritus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Paraesthesia Oral			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Retching			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Stomach Discomfort			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Swollen Tongue			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Toothache			
subjects affected / exposed	1 / 60 (1.67%)	4 / 30 (13.33%)	
occurrences (all)	1	6	
Vomiting			
subjects affected / exposed	13 / 60 (21.67%)	3 / 30 (10.00%)	
occurrences (all)	16	5	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	2	
Blister			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	3	
Cold Sweat			

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	4	0
Decubitus Ulcer		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Dermatitis Contact		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Drug Eruption		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Ecchymosis		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Eczema		
subjects affected / exposed	0 / 60 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	2
Erythema		
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)
occurrences (all)	5	1
Heat Rash		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Hyperhidrosis		
subjects affected / exposed	5 / 60 (8.33%)	0 / 30 (0.00%)
occurrences (all)	10	0
Ingrowing Nail		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Photosensitivity Reaction		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	2	0
Pruritus		
subjects affected / exposed	6 / 60 (10.00%)	1 / 30 (3.33%)
occurrences (all)	15	1
Rash		

subjects affected / exposed	6 / 60 (10.00%)	3 / 30 (10.00%)
occurrences (all)	10	5
Rash Macular		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	5	0
Rash Maculo-Papular		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	4	0
Rash Papular		
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)
occurrences (all)	4	0
Rash Pruritic		
subjects affected / exposed	4 / 60 (6.67%)	1 / 30 (3.33%)
occurrences (all)	7	3
Skin Burning Sensation		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Skin Lesion		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Skin Nodule		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	21	0
Skin Odour Abnormal		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Skin Warm		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Subcutaneous Nodule		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Telangiectasia		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Urticaria		

subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 15	0 / 30 (0.00%) 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	
occurrences (all)	4	1	
Leukocyturia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Nephrolithiasis			
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)	
occurrences (all)	4	0	
Pollakiuria			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	2	2	
Pyuria			
subjects affected / exposed	1 / 60 (1.67%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Urinary Incontinence			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Urine Flow Decreased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Urine Odour Abnormal			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	18 / 60 (30.00%)	9 / 30 (30.00%)	
occurrences (all)	27	21	
Back Pain			

subjects affected / exposed	14 / 60 (23.33%)	7 / 30 (23.33%)
occurrences (all)	22	15
Bone Pain		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	1
Bursitis		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Buttock Pain		
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)
occurrences (all)	4	1
Costochondritis		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Exostosis		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Flank Pain		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	1
Foot Deformity		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Groin Pain		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Joint Range Of Motion Decreased		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Joint Swelling		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Muscle Atrophy		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Muscle Contracture		

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Muscle Spasms		
subjects affected / exposed	14 / 60 (23.33%)	6 / 30 (20.00%)
occurrences (all)	18	7
Muscle Tightness		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	2
Muscle Twitching		
subjects affected / exposed	5 / 60 (8.33%)	1 / 30 (3.33%)
occurrences (all)	7	1
Muscular Weakness		
subjects affected / exposed	6 / 60 (10.00%)	3 / 30 (10.00%)
occurrences (all)	8	4
Musculoskeletal Chest Pain		
subjects affected / exposed	5 / 60 (8.33%)	1 / 30 (3.33%)
occurrences (all)	6	1
Musculoskeletal Discomfort		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Musculoskeletal Disorder		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Musculoskeletal Pain		
subjects affected / exposed	8 / 60 (13.33%)	2 / 30 (6.67%)
occurrences (all)	14	3
Musculoskeletal Stiffness		
subjects affected / exposed	8 / 60 (13.33%)	1 / 30 (3.33%)
occurrences (all)	11	1
Myalgia		
subjects affected / exposed	12 / 60 (20.00%)	5 / 30 (16.67%)
occurrences (all)	40	14
Neck Pain		
subjects affected / exposed	7 / 60 (11.67%)	5 / 30 (16.67%)
occurrences (all)	9	11
Nose Deformity		

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Osteopenia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Osteoporosis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Pain In Extremity			
subjects affected / exposed	15 / 60 (25.00%)	7 / 30 (23.33%)	
occurrences (all)	27	25	
Plantar Fasciitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Scoliosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	2	
Sensation Of Heaviness			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	6	1	
Temporomandibular Joint Syndrome			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Tendon Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Tendonitis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	4	1	
Tenosynovitis Stenosans			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	2	1	

Cellulitis		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Bronchopneumonia		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Dermatophytosis		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Cystitis		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	2	2
Eye Infection		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Folliculitis		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Fungal Infection		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Fungal Skin Infection		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Gastroenteritis		
subjects affected / exposed	5 / 60 (8.33%)	1 / 30 (3.33%)
occurrences (all)	5	1
Gastroenteritis Viral		
subjects affected / exposed	3 / 60 (5.00%)	3 / 30 (10.00%)
occurrences (all)	5	3
Gastrointestinal Infection		
subjects affected / exposed	0 / 60 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	2
Genital Infection		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1

Gingival Infection		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Herpes Simplex		
subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)
occurrences (all)	6	4
Herpes Virus Infection		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Influenza		
subjects affected / exposed	5 / 60 (8.33%)	7 / 30 (23.33%)
occurrences (all)	8	8
Kidney Infection		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	1
Laryngitis		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Localised Infection		
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)
occurrences (all)	1	1
Mucosal Infection		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Nasopharyngitis		
subjects affected / exposed	25 / 60 (41.67%)	16 / 30 (53.33%)
occurrences (all)	45	25
Otitis Media		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Postoperative Wound Infection		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0
Rash Pustular		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1

Respiratory Tract Infection		
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)
occurrences (all)	3	0
Rhinitis		
subjects affected / exposed	0 / 60 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	2
Sinusitis		
subjects affected / exposed	4 / 60 (6.67%)	4 / 30 (13.33%)
occurrences (all)	5	5
Tinea Pedis		
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)
occurrences (all)	4	0
Tonsillitis		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Tooth Infection		
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)
occurrences (all)	2	1
Upper Respiratory Tract Infection		
subjects affected / exposed	11 / 60 (18.33%)	3 / 30 (10.00%)
occurrences (all)	16	3
Urinary Tract Infection		
subjects affected / exposed	5 / 60 (8.33%)	4 / 30 (13.33%)
occurrences (all)	6	7
Vaginal Infection		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	4	0
Viral Infection		
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)
occurrences (all)	2	2
Vulvovaginal Mycotic Infection		
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	1
Wound Infection		
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)
occurrences (all)	1	0

Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Diabetes Mellitus Non-Insulin-Dependent			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Hypernatraemia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)	
occurrences (all)	5	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 September 2005	<ul style="list-style-type: none">- Subjects who transferred to regional investigational sites after 6 months of treatment could complete the remaining infusion visits at the transfer site. The Week 38 and Week 52 or early withdrawal infusions were no longer required to be done at the primary site.- Conduct of the 6MWT at Screening/Baseline was changed from 2 tests performed on the same day to testing on 2 consecutive days.- Inclusion criterion, which required the subject to have a forced expiratory volume in the first second of the FVC maneuver (FEV1)/FVC value of 70% predicted in the upright position, was deleted. The purpose of this criterion was to identify subjects with confounding obstructive disease that was NOT related to Pompe disease. However, weakness in the supporting respiratory muscles could prevent subjects from exhaling sufficient volume in the first second of the FVC maneuver (FEV1), causing what appears to be mild obstructive involvement in addition to the restrictive involvement caused by diaphragmatic weakness.- Exclusion for major congenital anomaly was limited to those that in the judgment of the Investigator would significantly interfere with study compliance, including all prescribed evaluations and follow-up activities.
26 May 2006	<ul style="list-style-type: none">- The infusion rate schedule was adjusted to a maximum rate of approximately 7 mg/kg/hr to assist in Infusion-associated reaction (IAR) management, consistent with infantile-onset studies of Pompe disease conducted by Genzyme. In Protocol Amendment 3, this infusion rate schedule was subsequently designated as "recommended" to allow investigator discretion in setting the infusion rate.
16 August 2006	<ul style="list-style-type: none">- The infusion rate schedule as adjusted in Amendment 2 was designated as "recommended" to allow investigator discretion in setting the infusion rate.-It proposed an adaptive, information-based design.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported