Clinical trial results:
An Open-Label Extension Study of Patients with Late-Onset Pompe Disease Who Were Previously Enrolled in Protocol AGLU02704

Summary

EudraCT number	2006-003644-31
Trial protocol	FR NL DE
Global end of trial date	13 November 2008

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	AGLU03206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00455195
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	12 February 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 November 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this extension study is to assess the long-term safety and efficacy of Myozyme treatment in subjects with Late-Onset Pompe Disease who were previously treated under the placebo-controlled, double-blind study AGLU02704.
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); and 3) to determine the effect of Myozyme treatment on respiratory muscle weakness as measured by Forced Vital Capacity (FVC) in the upright position.

Protection of trial 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	23 March 2007
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	Netherlands: 22
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	United States: 58
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:

81 of the 90 subjects enrolled in the double-blind placebo controlled AGLU02704 (NCT00158600) study continued on to the open-label extension study AGLU03206.

Period 1

Period 1 title	Double-blind Study AGLU02704
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Alglucosidase Alfa/Alglucosidase Alfa

Arm description:

Subjects who received alglucosidase alfa during the double-blind study AGLU02704 (NCT00158600) and, if they completed the double blind study, continued alglucosidase alfa in the extension study. Both study experiences on alglucosidase alfa are represented within AGLU03206.

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:

20 mg/kg every other week (qow) until their participation in both the AGLU02704 (NCT00158600) and AGLU03206 studies combined equaled a minimum of 104 weeks.

Arm title	Placebo/Alglucosidase Alfa

Arm description:

Subjects who received placebo during the double-blind study AGLU02704 (NCT00158600), completed the double-blind study, and started alglucosidase alfa in the extension study. Only subjects' experience on alglucosidase alfa in the extension study is represented.

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:

20 mg/kg every other week (qow) for up to 52 weeks. Only the alglucosidase alfa treatment experience is included in this extension study.

Number of subjects in period 1	Alglucosidase Alfa/Alglucosidase Alfa	Placebo/Alglucosidase Alfa
Started	60	30
Completed	55	26
Not completed	5	4
Adverse Event	2	1
Death	1	-
Withdrawal by Subject	2	2
Unable to commit time to study	-	1

Period 2

Period 2 title	Extension Study AGLU03206
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Alglucosidase Alfa/Alglucosidase Alfa

Arm description:

Subjects who received alglucosidase alfa during the double-blind study AGLU02704 (NCT00158600) and, if they completed the double blind study, continued alglucosidase alfa in the extension study. Both study experiences on alglucosidase alfa are represented within AGLU03206.

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

Dosage and administration details:

20 mg/kg every other week (qow) until their participation in both the AGLU02704 (NCT00158600) and AGLU03206 studies combined equaled a minimum of 104 weeks.

Arm title	Placebo/Alglucosidase Alfa

Arm description:

Subjects who received placebo during the double-blind study AGLU02704 (NCT00158600), completed the double-blind study, and started alglucosidase alfa in the extension study. Only subjects' experience on alglucosidase alfa in the extension study is represented.

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

Dosage and administration details:

20 mg/kg every other week (qow) for up to 52 weeks. Only the alglucosidase alfa treatment experience is included in this extension study.

Number of subjects in period 2	Alglucosidase Alfa/Alglucosidase Alfa	Placebo/Alglucosidase Alfa
Started	55	26
Completed	55	26

Baseline characteristics

Reporting groups

Reporting group title	Alglucosidase Alfa/Alglucosidase Alfa

Reporting group description:

Subjects who received alglucosidase alfa during the double-blind study AGLU02704 (NCT00158600) and, if they completed the double blind study, continued alglucosidase alfa in the extension study. Both study experiences on alglucosidase alfa are represented within AGLU03206.

Reporting group title	Placebo/Alglucosidase Alfa

Reporting group description:

Subjects who received placebo during the double-blind study AGLU02704 (NCT00158600), completed the double-blind study, and started alglucosidase alfa in the extension study. Only subjects' experience on alglucosidase alfa in the extension study is represented.

Reporting group values	Alglucosidase Alfa/Alglucosidase Alfa	Placebo/Alglucosidase Alfa	Total
Number of subjects	60	30	90
Age categorical Units: Subjects			
Age continuous			
Age at first infusion of alglucosidase alfa. The Alglucosidase Alfa/Alglucosidase Alfa treatment arm includes sujects' study experience in the double-blind study (AGLU02704 (NCT00158600)) and the extension study (AGLU03206 (NCT00455195) hence 60 subjects are represented. The Placebo/Alglucosidase Alfa treatment arm includes subjects' study experience on Alglucosidase Alfa in the extension study (AGLU03206) hence 26 subjects are represented.			
Units: years			
arithmetic mean	45.3	46.8	
standard deviation	± 12.37	± 8.62	-
Gender categorical Units: Subjects			
Female	26	15	41
Male	34	11	45
Data not available	0	4	4
Race/Ethnicity			
The Alglucosidase Alfa/Alglucosidase Alfa treatment arm includes subjects' study experience in the double-blind study (AGLU02704 (NCT00158600)) and the extension study (AGLU03206 (NCT00455195) hence 60 subjects are represented. The Placebo/Alglucosidase Alfa treatment arm includes subjects' study experience on Alglucosidase Alfa in the extension study (AGLU03206) hence 26 subjects are represented.			
Units: Subjects			
Hispanic	1	1	2
Asian	1	0	1
Black or African American	0	0	0
White	57	24	81
Unknown or Not Reported	1	1	2
Data not available	0	4	4

End points

End points reporting groups

Reporting group title	Alglucosidase Alfa/Alglucosidase Alfa

Reporting group description:

Subjects who received alglucosidase alfa during the double-blind study AGLU02704 (NCT00158600) and, if they completed the double blind study, continued alglucosidase alfa in the extension study. Both study experiences on alglucosidase alfa are represented within AGLU03206.

Reporting group title	Placebo/Alglucosidase Alfa

Reporting group description:

Subjects who received placebo during the double-blind study AGLU02704 (NCT00158600), completed the double-blind study, and started alglucosidase alfa in the extension study. Only subjects' experience on alglucosidase alfa in the extension study is represented.

Reporting group title	Alglucosidase Alfa/Alglucosidase Alfa

Reporting group description:

Subjects who received alglucosidase alfa during the double-blind study AGLU02704 (NCT00158600) and, if they completed the double blind study, continued alglucosidase alfa in the extension study. Both study experiences on alglucosidase alfa are represented within AGLU03206.

Reporting group title	Placebo/Alglucosidase Alfa

Reporting group description:

Subjects who received placebo during the double-blind study AGLU02704 (NCT00158600), completed the double-blind study, and started alglucosidase alfa in the extension study. Only subjects' experience on alglucosidase alfa in the extension study is represented.

Primary: Summary of Subjects Reporting Treatment-Emergent Adverse Events For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)

End point title	Summary of Subjects Reporting Treatment-Emergent Adverse Events For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)[1][2]

End point description:

The numbers of subjects who experienced 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 with alglucosidase alfa.
Subjects with long-term exposure to alglucosidase alfa (those from the Alglucosidase Alfa/Alglucosidase Alfa treatment group) are included. Time frames are stated from the start of the double-blind study AGLU02704 (NCT00158600).
The safety population includes all subjects randomized to alglucosidase alfa treatment in AGLU02704 (NCT00158600) who received at least one infusion of alglucosidase alfa.

End point type	Primary

End point timeframe:

Week 0 to 2.5 years

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: Only descriptive data were planned to be reported for efficacy analysis.

[2] - 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: The outcome focus only those subjects who received Alglucosidase Alfa during study AGLU02704.

End point values	Alglucosidase Alfa/Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: subjects				
Subjects with any AEs	60			
Subjects with Treatment-Related AEs	37			
Subjects with Infusion-Associated Reactions	21			
Subjects with Serious AEs	15			
Subjects with Severe AEs	16			
Subjects- Discontinued Due to AEs (incl death)	3			
Subjects Who Died	1			

Statistical analyses

No statistical analyses for this end point

Primary: Baseline Values (Week 0) of Functional Endurance as Measured by Six-Minute Walk Test (6MWT) For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)

End point title	Baseline Values (Week 0) of Functional Endurance as Measured by Six-Minute Walk Test (6MWT) For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)[3][4]

End point description:

Six-Minute Walk Test (6MWT) measures the distance walked (in meters) in 6 minutes. A longer distance indicates greater endurance. Time frames are stated from the start of the double-blind study AGLU02704 (NCT00158600). Intent-to-treat population.

End point type	Primary

End point timeframe:

Week 0

Notes:

[3] - 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 were planned to be reported for efficacy analysis.

[4] - 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: The outcome focus only those subjects who received Alglucosidase Alfa during study AGLU02704.

End point values	Alglucosidase Alfa/Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: meters				
arithmetic mean (standard deviation)	332.2 (± 126.69)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline (Week 0) in the Six-Minute Walk Test (6MWT) at Week 104 For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)

End point title	Change From Baseline (Week 0) in the Six-Minute Walk Test (6MWT) at Week 104 For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)[5][6]

End point description:

Six-Minute Walk Test (6MWT) measures the distance walked (in meters) in 6 minutes. A longer distance indicates greater endurance. Time frames are stated from the start of the double-blind study AGLU02704 (NCT00158600). Change is calculated as the value minus the baseline value. Intent-to-treat population of subjects who had both baseline (Week 0) and Week 104 data.

End point type	Primary

End point timeframe:

Week 0, Week 104

Notes:

[5] - 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: Analysis was descriptive, hence no statistical analysis is reported.

[6] - 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: The outcome focus only those subjects who received Alglucosidase Alfa during study AGLU02704.

End point values	Alglucosidase Alfa/Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: meters				
arithmetic mean (standard deviation)	21.3 (± 78.02)			

Statistical analyses

No statistical analyses for this end point

Primary: Baseline Values (Week 0) for Percent Predicted Forced Vital Capacity (FVC) For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)

End point title	Baseline Values (Week 0) for Percent Predicted Forced Vital Capacity (FVC) For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)[7][8]

End point description:

Forced vital capacity (FVC) is a standard pulmonary function test used to quantify respiratory muscle weakness. 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%. Time frames are stated from the start of the double-blind study AGLU02704 (NCT00158600). Intent-to-treat population.

End point type	Primary

End point timeframe:

Week 0

Notes:

[7] - 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 were planned to be reported for efficacy analysis.

[8] - 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: The outcome focus only those subjects who received Alglucosidase Alfa during study AGLU02704.

End point values	Alglucosidase Alfa/Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: percent of predicted FVC				
arithmetic mean (standard deviation)	55.4 (± 14.44)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline (Week 0) in the Percent Predicted Forced Vital Capacity (FVC) at Week 104 For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)

End point title	Change From Baseline (Week 0) in the Percent Predicted Forced Vital Capacity (FVC) at Week 104 For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)[9][10]

End point description:

Forced vital capacity (FVC) is a standard pulmonary function test used to quantify respiratory muscle weakness. 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%. Time frames are stated from the start of the double-blind study AGLU02704 (NCT00158600). Change is calculated as the value minus the baseline value. Intent-to-treat population of subjects who had both baseline (Week 0) and Week 104 data.

End point type	Primary

End point timeframe:

Week 0, Week 104

Notes:

[9] - 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: Analysis was descriptive, hence no statistical analysis is reported.

[10] - 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: The outcome focus only those subjects who received Alglucosidase Alfa during study AGLU02704.

End point values	Alglucosidase Alfa/Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: percent of predicted FVC				
arithmetic mean (standard deviation)	0.8 (± 6.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Values (Week 0) for Percent Predicted Proximal Muscle Strength of the Lower Limbs as Measured by Quantitative Muscle Testing (QMT) For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)

End point title	Baseline Values (Week 0) for Percent Predicted Proximal Muscle Strength of the Lower Limbs as Measured by Quantitative Muscle Testing (QMT) For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)[11]

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 are 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. Intent-to-treat population.

End point type	Secondary

End point timeframe:

Week 0

Notes:

[11] - 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: The outcome focus only those subjects who received Alglucosidase Alfa during study AGLU02704.

End point values	Alglucosidase Alfa/Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: percent of predicted QMT				
arithmetic mean (standard deviation)	37.7 (± 18.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline (Week 0) for Percent Predicted Proximal Muscle Strength of the Lower Limbs as Measured by Quantitative Muscle Testing (QMT) at Week 104 For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)

End point title	Change From Baseline (Week 0) for Percent Predicted Proximal Muscle Strength of the Lower Limbs as Measured by Quantitative Muscle Testing (QMT) at Week 104 For Subjects Treated With Alglucosidase Alfa During Study AGLU02704

	(NCT00158600)[12]

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 are 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. Intent-to-treat population of subjects who had both baseline (Week 0) and Week 104 data.

End point type	Secondary

End point timeframe:

Week 0, Week 104

Notes:

[12] - 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: The outcome focus only those subjects who received Alglucosidase Alfa during study AGLU02704.

End point values	Alglucosidase Alfa/Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: percent of predicted QMT				
arithmetic mean (standard deviation)	2.1 (± 11.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Values (Week 0) for Quality of Life Related to Physical Component Score (PCS) as Measured by the Medical Outcomes Study (MOS) Short Form-36 Health Survey For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)

End point title	Baseline Values (Week 0) for Quality of Life Related to Physical Component Score (PCS) as Measured by the Medical Outcomes Study (MOS) Short Form-36 Health Survey For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)[13]

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 Score reports the four domains of physical functioning, role-physical, bodily pain, and general health and are standardized as Z-scores (scale of 0-100). Higher scores are associated with better quality of life. Time frames are stated from the start of the double-blind study AGLU02704 (NCT00158600). Intent-to-treat population of subjects with valid baseline (Week 0) PCS surveys.

End point type	Secondary

End point timeframe:

Week 0

Notes:

[13] - 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: Only descriptive data were planned to be reported for efficacy analysis.

End point values	Alglucosidase Alfa/Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: units on a scale				
arithmetic mean (standard deviation)	34.33 (± 8.934)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quality of Life Related to Physical Component Score (PCS) as Measured by the Medical Outcomes Study (MOS) Short Form-36 Health Survey For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)

End point title	Change From Baseline in Quality of Life Related to Physical Component Score (PCS) as Measured by the Medical Outcomes Study (MOS) Short Form-36 Health Survey For Subjects Treated With Alglucosidase Alfa During Study AGLU02704 (NCT00158600)[14]

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 Score reports the four domains of physical functioning, role-physical, bodily pain, and general health and is standardized as Z-scores (scale of 0-100). Higher scores are associated with better quality of life. Change is calculated as the value minus the baseline value. Time frames are stated from the start of the double-blind study AGLU02704 (NCT00158600). Intent-to-treat population of subjects who had valid baseline (Week 0) and Week 104 data.

End point type	Secondary

End point timeframe:

Week 0 , Week 104

Notes:

[14] - 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: The outcome focus only those subjects who received Alglucosidase Alfa during study AGLU02704.

End point values	Alglucosidase Alfa/Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: units on a scale				
arithmetic mean (standard deviation)	0.64 (± 7.618)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events for the Alglucosidase Alfa/Alglucosidase Alfa group cover up to 2.5 years (Week 0 to 2.5 years), and for Placebo/Alglucosidase Alfa group cover up to 1.0 year (Week 78 to 2.5 years) regardless of seriousness or relationship to study drug.

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Alglucosidase Alfa/Alglucosidase Alfa

Reporting group description:

Subjects who received alglucosidase alfa during the double-blind study AGLU02704 (NCT00158600) and, if they completed the double blind study, continued alglucosidase alfa in the extension study. Both study experiences on alglucosidase alfa are represented within AGLU03206.

Reporting group title	Placebo/Alglucosidase Alfa

Reporting group description:

Subjects who received placebo during the double-blind study AGLU02704 (NCT00158600), completed the double-blind study, and started alglucosidase alfa in the extension study. Only subjects' experience on alglucosidase alfa in the extension study is represented.

Serious adverse events	Alglucosidase Alfa/Alglucosidase Alfa	Placebo/Alglucosidase Alfa	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 60 (25.00%)	2 / 26 (7.69%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix Carcinoma Stage Ii			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aneurysm			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
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 / 26 (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 / 26 (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 / 26 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
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 / 26 (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 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal Compression Fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus Fracture			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (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 / 26 (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 / 26 (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 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 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 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			

subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Cyst			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (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			
Gastroenteritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (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 / 26 (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 / 26 (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/Alglucosidase Alfa	Placebo/Alglucosidase Alfa	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 60 (100.00%)	25 / 26 (96.15%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Skin Papilloma			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Aneurysm			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Cardiovascular Insufficiency			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Diastolic Hypotension			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Flushing			
subjects affected / exposed	3 / 60 (5.00%)	1 / 26 (3.85%)	
occurrences (all)	5	1	
Haematoma			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Hot Flush			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	5	0	
Hypertension			
subjects affected / exposed	5 / 60 (8.33%)	0 / 26 (0.00%)	
occurrences (all)	5	0	
Hypotension			
subjects affected / exposed	2 / 60 (3.33%)	1 / 26 (3.85%)	
occurrences (all)	3	1	
Raynaud's Phenomenon			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Vasoconstriction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Adverse Drug Reaction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Application Site Vesicles			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	4 / 60 (6.67%)	0 / 26 (0.00%)	
occurrences (all)	5	0	
Axillary Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Catheter Related Complication			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Catheter Site Pain			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	8	0	
Chest Discomfort			
subjects affected / exposed	7 / 60 (11.67%)	0 / 26 (0.00%)	
occurrences (all)	17	0	
Chest Pain			
subjects affected / exposed	6 / 60 (10.00%)	2 / 26 (7.69%)	
occurrences (all)	7	2	
Chills			
subjects affected / exposed	4 / 60 (6.67%)	1 / 26 (3.85%)	
occurrences (all)	5	3	
Disease Progression			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	13 / 60 (21.67%)	4 / 26 (15.38%)	
occurrences (all)	19	5	
Feeling Abnormal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Feeling Cold			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Feeling Hot			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Gait Disturbance			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Influenza Like Illness			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Infusion Site Bruising			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Infusion Site Pain			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Infusion Site Paraesthesia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Infusion Site Reaction			
subjects affected / exposed	7 / 60 (11.67%)	0 / 26 (0.00%)	
occurrences (all)	10	0	
Injection Site Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Injection Site Phlebitis			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Local Swelling			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	14	0	
Malaise			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Nodule			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Oedema Peripheral			
subjects affected / exposed	13 / 60 (21.67%)	1 / 26 (3.85%)	
occurrences (all)	19	1	
Pain			
subjects affected / exposed	6 / 60 (10.00%)	0 / 26 (0.00%)	
occurrences (all)	9	0	
Pitting Oedema			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Puncture Site Haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	12 / 60 (20.00%)	2 / 26 (7.69%)	
occurrences (all)	13	2	
Thirst			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 60 (3.33%)	1 / 26 (3.85%)	
occurrences (all)	24	2	
Seasonal Allergy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	

Reproductive system and breast disorders			
Breast Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Breast Swelling			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Breast Tenderness			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Dysmenorrhoea			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Fibrocystic Breast Disease			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Menorrhagia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Menstrual Discomfort			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Menstruation Irregular			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Pelvic Pain			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Vaginal Haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Choking			

subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	8 / 60 (13.33%)	5 / 26 (19.23%)	
occurrences (all)	9	5	
Dyspnoea			
subjects affected / exposed	9 / 60 (15.00%)	1 / 26 (3.85%)	
occurrences (all)	13	1	
Dyspnoea Exertional			
subjects affected / exposed	5 / 60 (8.33%)	0 / 26 (0.00%)	
occurrences (all)	9	0	
Epistaxis			
subjects affected / exposed	4 / 60 (6.67%)	0 / 26 (0.00%)	
occurrences (all)	9	0	
Increased Bronchial Secretion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Lung Disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Lung Infiltration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Nasal Congestion			
subjects affected / exposed	8 / 60 (13.33%)	0 / 26 (0.00%)	
occurrences (all)	9	0	
Pharyngolaryngeal Pain			
subjects affected / exposed	14 / 60 (23.33%)	3 / 26 (11.54%)	
occurrences (all)	24	3	
Postnasal Drip			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Respiratory Distress			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Respiratory Failure			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Respiratory Tract Congestion			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Rhinorrhoea			
subjects affected / exposed	3 / 60 (5.00%)	1 / 26 (3.85%)	
occurrences (all)	3	1	
Sinus Congestion			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Sleep Apnoea Syndrome			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Throat Irritation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Sneezing			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Throat Tightness			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Congestion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Wheezing			
subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Psychiatric disorders			
Anger			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Anxiety			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	5	0	

Depression			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Insomnia			
subjects affected / exposed	9 / 60 (15.00%)	0 / 26 (0.00%)	
occurrences (all)	14	0	
Post-Traumatic Stress Disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Stress			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	9	0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Blood Creatine Increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Blood Folate Decreased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Blood Glucose Increased			
subjects affected / exposed	1 / 60 (1.67%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
Blood Pressure Increased			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Blood Urine Present			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Blood Uric Acid Increased			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Body Temperature Increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Carbon Dioxide Increased			
subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Crystal Urine Present			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram Qt Corrected Interval Prolonged			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram St Segment Depression			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram T Wave Amplitude Decreased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram Abnormal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Fungus Urine Test Positive			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Glucose Urine Present			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Haematocrit Decreased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Neutrophil Count Increased			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Oxygen Saturation Decreased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Protein Urine Present			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Specific Gravity Urine Increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tandem Gait Test Abnormal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Urine Analysis Abnormal			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Urine Ketone Body Present			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Weight Decreased			
subjects affected / exposed	2 / 60 (3.33%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
White Blood Cell Count Increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
White Blood Cells Urine Positive			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Animal Bite			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Animal Scratch			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Arthropod Sting			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Arthropod Bite			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Concussion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Back Injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	9 / 60 (15.00%)	1 / 26 (3.85%)	
occurrences (all)	12	2	
Excoriation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	39 / 60 (65.00%)	13 / 26 (50.00%)	
occurrences (all)	281	52	
Femur Fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Foot Fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Humerus Fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Head Injury			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Injury Corneal			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Injury			
subjects affected / exposed	4 / 60 (6.67%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Joint Sprain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Ligament Injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Limb Crushing Injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Limb Injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Mouth Injury			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Muscle Strain			
subjects affected / exposed	6 / 60 (10.00%)	2 / 26 (7.69%)	
occurrences (all)	10	2	
Neck Injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Pelvic Fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Post-Traumatic Pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Procedural Pain			
subjects affected / exposed	9 / 60 (15.00%)	1 / 26 (3.85%)	
occurrences (all)	11	1	
Radial Nerve Injury			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Rib Fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Road Traffic Accident			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Scratch			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Skin Laceration			
subjects affected / exposed	5 / 60 (8.33%)	0 / 26 (0.00%)	
occurrences (all)	7	0	
Soft Tissue Injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tendon Injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tendon Rupture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Thermal Burn			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Tooth Fracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tooth Injury			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Traumatic Ulcer			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Vaccination Complication			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Atrial Hypertrophy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Bundle Branch Block Left			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Bundle Branch Block Right			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Coronary Artery Disease			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Palpitations			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	9	0	
Tachycardia			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Sinus Tachycardia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tricuspid Valve Incompetence			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Ventricular Dysfunction			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	

Ventricular Hypertrophy			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Nervous system disorders			
Areflexia			
subjects affected / exposed	5 / 60 (8.33%)	2 / 26 (7.69%)	
occurrences (all)	8	2	
Balance Disorder			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Burning Sensation			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Carpal Tunnel Syndrome			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	16 / 60 (26.67%)	3 / 26 (11.54%)	
occurrences (all)	38	4	
Dizziness Postural			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Facial Palsy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Headache			
subjects affected / exposed	31 / 60 (51.67%)	6 / 26 (23.08%)	
occurrences (all)	113	21	
Hyperreflexia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Hyporeflexia			

subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Intercostal Neuralgia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Lethargy			
subjects affected / exposed	2 / 60 (3.33%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Loss Of Consciousness			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Migraine			
subjects affected / exposed	4 / 60 (6.67%)	0 / 26 (0.00%)	
occurrences (all)	7	0	
Nerve Compression			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Neuralgia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	7 / 60 (11.67%)	0 / 26 (0.00%)	
occurrences (all)	17	0	
Sciatica			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Sensory Disturbance			
subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Sinus Headache			
subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Somnolence			
subjects affected / exposed	4 / 60 (6.67%)	0 / 26 (0.00%)	
occurrences (all)	6	0	
Syncope Vasovagal			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	4 / 60 (6.67%)	1 / 26 (3.85%)	
occurrences (all)	4	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 60 (6.67%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Lymphadenopathy			
subjects affected / exposed	5 / 60 (8.33%)	0 / 26 (0.00%)	
occurrences (all)	6	0	
Macrocytosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Normochromic Normocytic Anaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Spontaneous Haematoma			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Cerumen Impaction			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Auricular Swelling			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Ear Congestion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Ear Discomfort			
subjects affected / exposed	5 / 60 (8.33%)	0 / 26 (0.00%)	
occurrences (all)	33	0	
Ear Pain			

subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Hypoacusis			
subjects affected / exposed	23 / 60 (38.33%)	3 / 26 (11.54%)	
occurrences (all)	39	3	
Presbyacusis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Tinnitus			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Vertigo			
subjects affected / exposed	5 / 60 (8.33%)	0 / 26 (0.00%)	
occurrences (all)	8	0	
Vertigo Positional			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Altered Visual Depth Perception			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Asthenopia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Cataract			
subjects affected / exposed	4 / 60 (6.67%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Conjunctivitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Diplopia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Dry Eye			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	

Eye Irritation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Eye Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Eye Pruritus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Eyelid Ptosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Keratoconjunctivitis Sicca			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Photophobia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Pinguecula			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Retinal Detachment			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Vision Blurred			
subjects affected / exposed	4 / 60 (6.67%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Visual Acuity Reduced			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Visual Disturbance			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Vitreous Floaters			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	

Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Abdominal Distension			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Abdominal Mass			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Abdominal Pain			
subjects affected / exposed	5 / 60 (8.33%)	0 / 26 (0.00%)	
occurrences (all)	6	0	
Abdominal Pain Lower			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Abdominal Pain Upper			
subjects affected / exposed	6 / 60 (10.00%)	1 / 26 (3.85%)	
occurrences (all)	23	1	
Abdominal Tenderness			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Anal Fissure			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Anorectal Disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Aphthous Stomatitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Bowel Sounds Abnormal			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Chapped Lips			

subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	7 / 60 (11.67%)	0 / 26 (0.00%)	
occurrences (all)	9	0	
Crohn's Disease			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	20 / 60 (33.33%)	2 / 26 (7.69%)	
occurrences (all)	49	2	
Diverticulum Intestinal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Dry Mouth			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	7 / 60 (11.67%)	0 / 26 (0.00%)	
occurrences (all)	11	0	
Epigastric Discomfort			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Food Poisoning			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Gingivitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Haematochezia			

subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Haemorrhoids			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Inguinal Hernia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Lip Swelling			
subjects affected / exposed	2 / 60 (3.33%)	1 / 26 (3.85%)	
occurrences (all)	7	1	
Mouth Ulceration			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	15 / 60 (25.00%)	2 / 26 (7.69%)	
occurrences (all)	46	26	
Oesophageal Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Oral Pruritus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Paraesthesia Oral			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Rectal Haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Retching			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Stomach Discomfort			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Swollen Tongue			

subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Toothache			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	14 / 60 (23.33%)	2 / 26 (7.69%)	
occurrences (all)	17	2	
Skin and subcutaneous tissue disorders			
Cold Sweat			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Actinic Keratosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Decubitus Ulcer			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Dermatitis Contact			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Dry Skin			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Ecchymosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	5	0	
Heat Rash			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	6 / 60 (10.00%)	1 / 26 (3.85%)	
occurrences (all)	14	1	

Ingrowing Nail			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Photosensitivity Reaction			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Night Sweats			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	8 / 60 (13.33%)	3 / 26 (11.54%)	
occurrences (all)	23	4	
Psoriasis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	9 / 60 (15.00%)	1 / 26 (3.85%)	
occurrences (all)	18	1	
Rash Macular			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	5	0	
Rash Maculo-Papular			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Rash Pruritic			
subjects affected / exposed	4 / 60 (6.67%)	0 / 26 (0.00%)	
occurrences (all)	8	0	
Rash Papular			
subjects affected / exposed	5 / 60 (8.33%)	0 / 26 (0.00%)	
occurrences (all)	6	0	
Rosacea			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Skin Hyperpigmentation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	

Skin Inflammation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Skin Lesion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Skin Nodule			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	21	0	
Skin Odour Abnormal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Subcutaneous Nodule			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	7 / 60 (11.67%)	1 / 26 (3.85%)	
occurrences (all)	25	1	
Urticaria Contact			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Haematuria			
subjects affected / exposed	3 / 60 (5.00%)	1 / 26 (3.85%)	
occurrences (all)	6	2	
Leukocyturia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Nephrolithiasis			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Pollakiuria			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	8	0	
Pyuria			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Renal Cyst			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Urge Incontinence			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Urinary Incontinence			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Urine Flow Decreased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Urine Odour Abnormal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	25 / 60 (41.67%)	4 / 26 (15.38%)	
occurrences (all)	49	6	
Arthritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Back Pain			
subjects affected / exposed	19 / 60 (31.67%)	6 / 26 (23.08%)	
occurrences (all)	38	6	
Bone Pain			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Bursitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Buttock Pain			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Costochondritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Groin Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Flank Pain			
subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Joint Contracture			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
Joint Crepitation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Muscle Atrophy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Muscle Spasms			
subjects affected / exposed	17 / 60 (28.33%)	5 / 26 (19.23%)	
occurrences (all)	30	6	
Muscle Contracture			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Muscle Twitching			
subjects affected / exposed	6 / 60 (10.00%)	0 / 26 (0.00%)	
occurrences (all)	8	0	
Muscle Tightness			

subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	2	
Musculoskeletal Chest Pain			
subjects affected / exposed	6 / 60 (10.00%)	1 / 26 (3.85%)	
occurrences (all)	10	1	
Muscular Weakness			
subjects affected / exposed	11 / 60 (18.33%)	2 / 26 (7.69%)	
occurrences (all)	19	3	
Musculoskeletal Discomfort			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal Disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal Pain			
subjects affected / exposed	10 / 60 (16.67%)	4 / 26 (15.38%)	
occurrences (all)	21	6	
Myalgia			
subjects affected / exposed	16 / 60 (26.67%)	3 / 26 (11.54%)	
occurrences (all)	53	5	
Musculoskeletal Stiffness			
subjects affected / exposed	8 / 60 (13.33%)	0 / 26 (0.00%)	
occurrences (all)	13	0	
Nose Deformity			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Neck Pain			
subjects affected / exposed	9 / 60 (15.00%)	1 / 26 (3.85%)	
occurrences (all)	11	1	
Osteoarthritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Osteopenia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Osteoporosis			

subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Senile Ankylosing Vertebral Hyperostosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Pain In Extremity			
subjects affected / exposed	23 / 60 (38.33%)	2 / 26 (7.69%)	
occurrences (all)	44	2	
Temporomandibular Joint Syndrome			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Sensation Of Heaviness			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	6	0	
Tendonitis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Tenosynovitis Stenosans			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Acute Tonsillitis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Bronchiolitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Bronchitis			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Bronchitis Acute			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Cellulitis			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Dermatophytosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Ear Infection			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Eye Infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Folliculitis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Fungal Infection			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Fungal Skin Infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	8 / 60 (13.33%)	0 / 26 (0.00%)	
occurrences (all)	8	0	
Gastroenteritis Viral			
subjects affected / exposed	4 / 60 (6.67%)	0 / 26 (0.00%)	
occurrences (all)	7	0	
Gingival Infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Herpes Simplex			
subjects affected / exposed	4 / 60 (6.67%)	1 / 26 (3.85%)	
occurrences (all)	8	1	
Herpes Virus Infection			

subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Herpes Zoster			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	8 / 60 (13.33%)	3 / 26 (11.54%)	
occurrences (all)	13	3	
Kidney Infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Localised Infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Mucosal Infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	29 / 60 (48.33%)	8 / 26 (30.77%)	
occurrences (all)	68	10	
Otitis Media			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Pharyngitis Streptococcal			
subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Pneumonia			

subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Postoperative Wound Infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Rash Pustular			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
Respiratory Tract Infection			
subjects affected / exposed	3 / 60 (5.00%)	1 / 26 (3.85%)	
occurrences (all)	3	1	
Rhinitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	9 / 60 (15.00%)	3 / 26 (11.54%)	
occurrences (all)	17	3	
Tinea Pedis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Tonsillitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tooth Abscess			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tooth Infection			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	20 / 60 (33.33%)	6 / 26 (23.08%)	
occurrences (all)	29	6	
Urinary Tract Infection Bacterial			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
Urinary Tract Infection			

subjects affected / exposed	5 / 60 (8.33%)	2 / 26 (7.69%)	
occurrences (all)	7	3	
Vaginal Infection			
subjects affected / exposed	1 / 60 (1.67%)	1 / 26 (3.85%)	
occurrences (all)	5	1	
Viral Infection			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Wound Infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Decreased Appetite			
subjects affected / exposed	2 / 60 (3.33%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Gout			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hypernatraemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	3 / 60 (5.00%)	0 / 26 (0.00%)	
occurrences (all)	5	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2006	It included following statements: 1. Oligosaccharide testing in plasma was removed because testing in urine was deemed to be better suited for use in clinical practice as urine samples were collected non-invasively, analysis was rapid, and the concentrations were several orders of magnitude higher than in plasma. 2. Inclusion criterion was amended due to ethical concerns for requiring subjects to be treated in the placebo-controlled trial beyond the originally planned 52 weeks to be eligible to participate in the open-label trial in regions where alglucosidase alfa was not provided to subjects with late-onset Pompe disease through government reimbursement or charitable access mechanisms, as subjects in these regions may have felt that their options differ from those in regions where alglucosidase alfa was available via the mechanisms outlined. In actuality, all 81 subjects who enrolled in the Late-Onset Treatment Study (LOTS) extension completed the full 78 weeks in LOTS. 3. Guidance on the infusion rates was added to the treatments administered section, primarily that Infusion-Associated Reactions (IARs) were more likely to occur at higher infusion rates and that the infusion rate might be slowed and/or temporarily stopped in the event of an IAR. 4. Assessment of vital signs during infusion was changed to immediately prior to any infusion rate change rather than every 30 minutes and immediately prior to any infusion rate change if the time point was different. Additionally, the windows for assessment of vital signs were clarified to assure that vital signs assessments before and during infusion were to within 15 minutes before the infusion or an infusion rate change, while the window for assessment of vital signs at the completion of the post-infusion observation period remained 15 minutes before or after the set time.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported