



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
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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
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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
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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
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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
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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
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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			
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Age at first infusion of alglucosidase alfa. 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: years			
arithmetic mean	45.3	46.8	
standard deviation	± 12.37	± 8.62	-

Gender categorical Units: Subjects			
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Female	26	15	41
Male	34	11	45
Data not available	0	4	4

Race/Ethnicity			
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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]}
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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
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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]}
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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
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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]}
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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
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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]}
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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
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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]
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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 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
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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
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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 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
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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]
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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 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
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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]
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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 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
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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
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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/Alglucosidase Alfa
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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
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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 occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Skin Papilloma subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 26 (0.00%) 0	
Vascular disorders Aneurysm subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 2	0 / 26 (0.00%) 0	
Cardiovascular Insufficiency subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Diastolic Hypotension subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Flushing subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 5	1 / 26 (3.85%) 1	
Haematoma subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 26 (0.00%) 0	
Hot Flush subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 5	0 / 26 (0.00%) 0	
Hypertension subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 5	0 / 26 (0.00%) 0	
Hypotension subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	1 / 26 (3.85%) 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 occurrences (all)	1 / 60 (1.67%) 2	0 / 26 (0.00%) 0	
Oxygen Saturation Decreased subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Protein Urine Present subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	0 / 26 (0.00%) 0	
Specific Gravity Urine Increased subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Tandem Gait Test Abnormal subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Urine Analysis Abnormal subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 26 (3.85%) 1	
Urine Ketone Body Present subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Weight Decreased subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	1 / 26 (3.85%) 1	
White Blood Cell Count Increased subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 2	0 / 26 (0.00%) 0	
White Blood Cells Urine Positive subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Injury, poisoning and procedural complications			
Animal Bite subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 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 occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Wound subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	0 / 26 (0.00%) 0	
Cardiac disorders			
Angina Pectoris subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Atrial Hypertrophy subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Bundle Branch Block Left subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Bundle Branch Block Right subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Coronary Artery Disease subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 3	0 / 26 (0.00%) 0	
Palpitations subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 9	0 / 26 (0.00%) 0	
Tachycardia subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 26 (0.00%) 0	
Sinus Tachycardia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Tricuspid Valve Incompetence subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Ventricular Dysfunction subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 26 (3.85%) 1	

Ventricular Hypertrophy subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 26 (3.85%) 1	
Nervous system disorders			
Areflexia subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 8	2 / 26 (7.69%) 2	
Balance Disorder subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	0 / 26 (0.00%) 0	
Burning Sensation subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	0 / 26 (0.00%) 0	
Carpal Tunnel Syndrome subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	16 / 60 (26.67%) 38	3 / 26 (11.54%) 4	
Dizziness Postural subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 26 (0.00%) 0	
Facial Palsy subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 2	0 / 26 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	31 / 60 (51.67%) 113	6 / 26 (23.08%) 21	
Hyperreflexia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Hypoaesthesia subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	0 / 26 (0.00%) 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 occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Tremor subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	1 / 26 (3.85%) 2	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	0 / 26 (0.00%) 0	
Lymphadenopathy subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 6	0 / 26 (0.00%) 0	
Macrocytosis subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 26 (3.85%) 1	
Normochromic Normocytic Anaemia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 2	0 / 26 (0.00%) 0	
Spontaneous Haematoma subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 26 (3.85%) 1	
Ear and labyrinth disorders			
Cerumen Impaction subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 26 (3.85%) 1	
Auricular Swelling subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Ear Congestion subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Ear Discomfort subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 33	0 / 26 (0.00%) 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	
Presbycusis			
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 occurrences (all)	2 / 60 (3.33%) 2	0 / 26 (0.00%) 0	
Toothache subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	14 / 60 (23.33%) 17	2 / 26 (7.69%) 2	
Skin and subcutaneous tissue disorders			
Cold Sweat subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 4	0 / 26 (0.00%) 0	
Actinic Keratosis subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Decubitus Ulcer subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 2	0 / 26 (0.00%) 0	
Dermatitis Contact subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Dry Skin subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 26 (3.85%) 1	
Ecchymosis subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Erythema subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 5	0 / 26 (0.00%) 0	
Heat Rash subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Hyperhidrosis subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 14	1 / 26 (3.85%) 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 occurrences (all)	5 / 60 (8.33%) 7	2 / 26 (7.69%) 3	
Vaginal Infection subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 5	1 / 26 (3.85%) 1	
Viral Infection subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	0 / 26 (0.00%) 0	
Wound Infection subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Metabolism and nutrition disorders			
Anorexia subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 26 (3.85%) 1	
Decreased Appetite subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	0 / 26 (0.00%) 0	
Gout subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Hypernatraemia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 26 (0.00%) 0	
Hypokalaemia subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 5	0 / 26 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2006	<p>It included following statements:</p> <ol style="list-style-type: none">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