



Clinical trial results:

An Exploratory, Open-Label Study of the Safety and Efficacy of High Dose or High Dosing Frequency Alglucosidase Alfa Treatment in Patients With Pompe Disease Who Do Not Have an Optimal Response to the Standard Dose Regimen

Summary

EudraCT number	2015-000582-31
Trial protocol	Outside EU/EEA
Global end of trial date	21 July 2010

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	28 June 2015

Trial information

Trial identification

Sponsor protocol code	AGLU03306
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00483379
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, 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	22 October 2010
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 July 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this exploratory study is to evaluate the safety and efficacy of alternative dosing regimens of alglucosidase alfa in subjects with Pompe disease who have not demonstrated an optimal response to the standard dosing regimen of 20 mg/kg every other week after a minimum of 6 months treatment immediately prior to study entry.

Protection of trial subjects:

Paediatric subjects: The study was conducted by investigators experienced in the treatment of pediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Adult Subjects: Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 May 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	Canada: 1
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	13
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	1
Children (2-11 years)	5
Adolescents (12-17 years)	3
Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Fourteen subjects were screened and enrolled; however, one withdrew before receiving any study infusions due to the burden of weekly trips to the medical centre.

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Alglucosidase Alfa 20 mg/kg Every Week

Arm description:

Subjects were treated with alglucosidase alfa every week for 52 weeks. This was the 'frequent dose' arm.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase alfa
Investigational medicinal product code	
Other name	Recombinant human acid glucosidase, Myozyme®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg/kg/week

Arm title	Alglucosidase Alfa 40 mg/kg Every Other Week
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Arm description:

Subjects were treated with alglucosidase alfa every other week for 52 weeks. This was the 'high dose' arm.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase alfa
Investigational medicinal product code	
Other name	Recombinant human acid glucosidase, Myozyme®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/kg

Number of subjects in period 1	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week
Started	6	7
Completed	4	7
Not completed	2	0
'Adverse Event '	1	-

Withdrawal by Subject	1	-
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Period 2

Period 2 title	Extension Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Alglucosidase Alfa 20 mg/kg Every Week

Arm description:

Alglucosidase Alfa every Week until commercial supply became available.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase alfa
Investigational medicinal product code	
Other name	Recombinant human acid glucosidase, Myozyme
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg/kg

Arm title	Alglucosidase Alfa 40 mg/kg Every Other Week
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Arm description:

Alglucosidase Alfa every week until commercial supply became available.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase alfa
Investigational medicinal product code	
Other name	Recombinant human acid glucosidase, Myozyme®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/kg

Number of subjects in period 2^[1]	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week
Started	1	2
Completed	1	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Three subjects participated into the extension period.

Baseline characteristics

Reporting groups

Reporting group title	Alglucosidase Alfa 20 mg/kg Every Week
Reporting group description: Subjects were treated with alglucosidase alfa every week for 52 weeks. This was the 'frequent dose' arm.	
Reporting group title	Alglucosidase Alfa 40 mg/kg Every Other Week
Reporting group description: Subjects were treated with alglucosidase alfa every other week for 52 weeks. This was the 'high dose' arm.	

Reporting group values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week	Total
Number of subjects	6	7	13
Age categorical Units: Subjects			
<18 years	4	5	9
>= 18 and <=65 years	2	2	4
>65 years	0	0	0
Age continuous Units: years arithmetic mean standard deviation	23.3 ± 27.75	16.8 ± 15.56	-
Gender categorical Units: Subjects			
Female	2	3	5
Male	4	4	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	6	6	12
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Life-stage of Disease Onset Units: Subjects			
Infantile-onset Pompe Disease	4	5	9
Late-onset Pompe Disease	2	2	4
Parameter in Clinical Decline			
Subject counts of the parameter in clinical decline (cardiac, respiratory or motor skills as compared to their condition prior to the beginning alglucosidase alfa treatment) for which subjects were included in the study.			
Units: Subjects			
Cardiac	0	0	0
Respiratory	1	1	2
Motor Skills	5	6	11

Cross-Reactive Immunologic Material (CRIM) Assay Result Units: Subjects			
Positive	0	3	3
Negative	1	0	1
Unknown	5	4	9

End points

End points reporting groups

Reporting group title	Alglucosidase Alfa 20 mg/kg Every Week
Reporting group description: Subjects were treated with alglucosidase alfa every week for 52 weeks. This was the 'frequent dose' arm.	
Reporting group title	Alglucosidase Alfa 40 mg/kg Every Other Week
Reporting group description: Subjects were treated with alglucosidase alfa every other week for 52 weeks. This was the 'high dose' arm.	
Reporting group title	Alglucosidase Alfa 20 mg/kg Every Week
Reporting group description: Alglucosidase Alfa every Week until commercial supply became available.	
Reporting group title	Alglucosidase Alfa 40 mg/kg Every Other Week
Reporting group description: Alglucosidase Alfa every week until commercial supply became available.	

Primary: Subjects' Efficacy Response During the Treatment Period as Compared to Baseline for Subjects With Respiratory Decline on Standard Treatment

End point title	Subjects' Efficacy Response During the Treatment Period as Compared to Baseline for Subjects With Respiratory Decline on Standard Treatment ^[1]
End point description: Subjects were enrolled based on clinical decline or sub-optimal clinical response in cardiac, respiratory and/or motor function parameters pre-study while on standard treatment. Each subject was evaluated at Week 52 for change from baseline in the criteria that declined; respiratory decline as measured by change in ventilator use is summarized in this outcome. Ventilator use might have improved (less use of ventilator support), had no change, or worsened (more use of ventilator support). Each subject served as his or her own control. All subjects who enrolled due to decline in respiratory function while on standard treatment.	
End point type	Primary
End point timeframe: Baseline, Week 52	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: As the analysis was descriptive, no statistical analysis is provided.

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: Subjects				
Improved	0	0		
No change (on invasive ventilator for 24 hrs)	0	1		
Worsened	0	0		
Not evaluated	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Subjects' Efficacy Response During the Treatment Period as Compared to Baseline for Subjects With Motor Function Decline on Standard Treatment

End point title	Subjects' Efficacy Response During the Treatment Period as Compared to Baseline for Subjects With Motor Function Decline on Standard Treatment ^[2]
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End point description:

Subjects were enrolled based on clinical decline or sub-optimal clinical response in cardiac, respiratory and/or motor function parameters pre-study while on standard treatment. Each subject was evaluated at Week 52 for change from baseline in the criteria that declined; motor function decline primarily based on Gross Motor Function Measure 66 and Pompe Pediatric Evaluation of Disability Inventory results is summarized. Subjects could gain motor function (improve), had no change (declined stopped), or continued loss (worsened). Each subject served as his or her own control. All subjects who enrolled due to decline in motor function while on standard treatment.

End point type	Primary
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End point timeframe:

Baseline, Week 52

Notes:

[2] - 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: As the analysis was descriptive, no statistical analysis is provided.

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: subjects				
Gained gross or fine motor skills	2	4		
No change	1	2		
Continued motor loss	1	0		
Not evaluated	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Subjects Reporting Treatment-Emergent Adverse Events During the Treatment Period

End point title	Summary of Subjects Reporting Treatment-Emergent Adverse Events During the Treatment Period ^[3]
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End point description:

Overall safety summary of subjects experiencing Adverse Events (AEs), Serious Adverse Events (SAEs),

treatment-related AEs, and Infusion Associated Reactions (IARs). Summary is based on Treatment-emergent AEs (TEAEs), defined as AEs that occurred following the initiation of study treatment. Safety population comprised of all subjects who received intervention.

End point type	Primary
End point timeframe:	
Day 1 up to Week 52	

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: As the analysis was descriptive, no statistical analysis is provided.

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: subjects				
Subjects with AEs	6	7		
Related AEs	0	2		
Not related AEs	6	7		
Mild AEs	6	6		
Moderate AEs	3	2		
Severe AEs	2	0		
AEs leading to discontinuation from study	1	0		
Deaths	1	0		
Infusion Associated Reactions	0	2		
Serious AEs	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Values for Left Ventricular Mass (LVM) Z-Scores

End point title	Baseline Values for Left Ventricular Mass (LVM) Z-Scores
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End point description:

Z-Scores indicate the number of standard deviations (SD) from the mean in a normal distribution. Negative values indicate a smaller than mean LVM and values higher than 0 indicate a larger LVM than the mean. The normal range is -2 to 2 and greater than 2 may indicate left ventricular hypertrophy. The Z-scores for all parameters are calculated with reference to the normative data from the Children's Hospital, Boston, MA (Colan, 1992, J Am Coll Cardiol) based on the reference population with matched body surface area (BSA). Z-scores for LVM were provided by the central cardiologist. Full analysis population of subjects with LVM data.

End point type	Secondary
End point timeframe:	
Day 0	

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Z-score				
median (full range (min-max))	0.3 (-1.2 to 6.3)	-0.3 (-1.2 to 2.2)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in Left Ventricular Mass (LVM) Z-Score at Week 52
End point description:	
Z-Scores indicate the number of standard deviations (SD) from the mean in a normal distribution. A negative change from baseline indicates a decrease and positive change from baseline an increase in LVM Z-score. The normal range is -2 to 2 and greater than 2 may indicate left ventricular hypertrophy. The Z-scores for all parameters are calculated with reference to the normative data from the Children's Hospital, Boston, MA (Colan, 1992, J Am Coll Cardiol) based on the reference population with matched body surface area (BSA). Z-scores for LVM were provided by the central cardiologist. Full analysis population of subjects with LVM data at both timepoints.	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Z-score				
median (full range (min-max))	0.3 (-0.8 to 1.2)	0.4 (-0.1 to 0.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Values for Left Ventricular Mass Index (LVMI)

End point title	Baseline Values for Left Ventricular Mass Index (LVMI)
End point description:	
Cardiac pathophysiology was assessed by a central cardiologist using left ventricular mass index (LVMI) measured by echocardiogram at Baseline. Left Ventricular Mass is adjusted to the subject's body surface	

area in the calculation of LVMI. Full analysis population of subjects with LVMI data.

End point type	Secondary
End point timeframe:	
Day 0	

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: g/m ²				
median (full range (min-max))	62.1 (49 to 187.3)	56.5 (45.4 to 73.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Left Ventricular Mass Index (LVMI) at Week 52

End point title	Change From Baseline in Left Ventricular Mass Index (LVMI) at Week 52
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End point description:

Cardiac pathophysiology was assessed by a central cardiologist using left ventricular mass index (LVMI) measured by echocardiogram at Baseline and after 12 months of treatment (Week 52). Left Ventricular Mass is adjusted to the subject's body surface area in the calculation of LVMI. Full analysis population of subjects with LVMI data at both timepoints.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: g/m ²				
median (full range (min-max))	12.5 (-10.9 to 15.5)	4 (-5.3 to 5.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Ventilator Use at Last Assessment (Approximately Week 52)

End point title	Change From Baseline in Ventilator Use at Last Assessment (Approximately Week 52)
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End point description:

The change from baseline in ventilator use at the last assessment is summarized as improved (less use of ventilator support), no change, worsened (increased use of ventilator support), and did not use ventilator support. Full analysis population. The subject in the worsened category died after week 52.

End point type	Secondary
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End point timeframe:

Baseline, approximately Week 52

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: subjects				
Improved	0	0		
No change	2	3		
Worsened	1	0		
Did not use ventilator	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Strength Measured by the Manual Muscle Testing (MMT) Total Score at Week 52

End point title	Change From Baseline in Body Strength Measured by the Manual Muscle Testing (MMT) Total Score at Week 52
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End point description:

Body strength is measured by the MMT score on a scale of 0-10 with higher scores representing greater body strength. Full analysis population of subjects ≥ 8 years old. Due to the age restriction and small study population, the number of subjects analyzed is too small for results to be meaningful.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: subjects				

Notes:

[4] - Reason is provided in outcome description.

[5] - Reason is provided in outcome description.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Values of Raw Scores for Gross Motor Function Measure 66 (GMFM-66) Results

End point title	Baseline Values of Raw Scores for Gross Motor Function Measure 66 (GMFM-66) Results
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End point description:

The Gross Motor Function Measure 66 contains sixty-six questions with a total raw score range of 0 - 198. Raw scores are derived from the following dimensions: Lying and rolling = 12; Sitting = 45; Crawling and kneeling = 30; Standing = 39; Walking, running and jumping = 72. Higher scores indicate better gross motor functions. Full analysis population.

End point type	Secondary
End point timeframe:	
Day 0	

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: units on a scale				
arithmetic mean (standard deviation)	65 (± 60.52)	82.8 (± 84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Raw Scores for Gross Motor Function Measure 66 (GMFM-66) Results at Week 52

End point title	Change From Baseline in Raw Scores for Gross Motor Function Measure 66 (GMFM-66) Results at Week 52
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End point description:

The Gross Motor Function Measure 66 contains sixty-six questions with a total raw score range of 0 - 198. Raw scores are derived from the following dimensions: Lying and rolling = 12; Sitting = 45; Crawling and kneeling = 30; Standing = 39; Walking, running and jumping = 72. Higher scores indicate better gross motor functions. Full analysis population.

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

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: units on a scale				
arithmetic mean (standard deviation)	6 (± 8.49)	6.7 (± 6.12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Values in Mobility as Measured by the Pompe Pediatric Evaluation of Disability Inventory (Pompe PEDI)

End point title	Baseline Values in Mobility as Measured by the Pompe Pediatric Evaluation of Disability Inventory (Pompe PEDI)
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End point description:

The Pompe PEDI is a disease specific version of the PEDI that was developed to assess functional capabilities and performance in children with Pompe disease from 2 months through adolescence. Baseline results for the mobility domain are reported. Scaled scores are used as an evaluative measure of change in performance over time with acquisition of new skills or new levels of independence. The range of scores is from 0-100 with scores near "0" reflecting low capability and scores near "100" reflecting high capability. Full analysis population.

End point type	Secondary
End point timeframe:	
Day 0	

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: units on a scale				
arithmetic mean (standard deviation)	38.3 (± 20.94)	46.8 (± 21.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mobility as Measured by the Pompe Pediatric Evaluation of Disability Inventory (Pompe PEDI) at Week 52

End point title	Change From Baseline in Mobility as Measured by the Pompe Pediatric Evaluation of Disability Inventory (Pompe PEDI) at Week 52
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End point description:

The Pompe PEDI is a disease specific version of the PEDI that was developed to assess functional capabilities and performance in children with Pompe disease from 2 months through adolescence. Change from baseline results for the mobility domain are reported. Scaled scores are used as an evaluative measure of change in performance over time with acquisition of new skills or new levels of independence. The range of scores is from 0-100 with scores near "0" reflecting low capability and scores near "100" reflecting high capability. Full analysis population.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	7		
Units: units on a scale				
arithmetic mean (standard deviation)	0.6 (± 4.28)	3.5 (± 3.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Values for Normative Physical Component Summary of Medical Outcomes Study Short Form Health Survey (SF-36)

End point title	Baseline Values for Normative Physical Component Summary of Medical Outcomes Study Short Form Health Survey (SF-36)
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End point description:

Health related quality of life is measured using the Physical Component Summary (PCS) score of the Medical Outcomes Study (MOS) Short Form Health Survey (SF-36) for subjects ≥14 years of age. SF-36 normative-based scoring has a mean of 50 and a standard deviation of 10. Higher scores represent better quality of life. Full analysis population of subjects ≥ 14 years old.

End point type	Secondary
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End point timeframe:

Day 0

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: units on a scale				
arithmetic mean (standard deviation)	31.3 (± 2.84)	36 (± 9.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Normative Physical Component Summary of Medical Outcomes Study Short Form Health Survey (SF-36) at Week 52

End point title	Change From Baseline in Normative Physical Component Summary of Medical Outcomes Study Short Form Health Survey (SF-36) at Week 52
End point description: Health related quality of life is measured using the Physical Component Summary (PCS) score of the Medical Outcomes Study (MOS) Short Form Health Survey (SF-36) for subjects ≥14 years of age. SF-36 normative-based scoring has a mean of 50 and a standard deviation of 10. Higher scores represent better quality of life. Full analysis population of subjects >= 14 years old.	
End point type	Secondary
End point timeframe: Baseline, Week 52	

End point values	Alglucosidase Alfa 20 mg/kg Every Week	Alglucosidase Alfa 40 mg/kg Every Other Week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	3		
Units: units on a scale				
arithmetic mean (standard deviation)	2.5 (± 0)	4.4 (± 11.24)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment period AEs were collected up to week 52. Extension period AEs were collected following completion of the treatment period until the product was commercially available (up to week 118).

Adverse event reporting additional description:

In the event a single participant has experienced both a serious and a non-serious form of the same adverse event term, the subjects has been included in the numerator ("number of affected participants") of both adverse event tables. Events are listed independent of relationship to treatment reported.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.0
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Reporting groups

Reporting group title	Extension: Alglucosidase Alfa 20 mg/kg Every Week
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Reporting group description:

Alglucosidase Alfa every Week until commercial supply became available.

Reporting group title	Treatment: Alglucosidase Alfa 40 mg/kg Every Other Week
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Reporting group description:

Subjects were treated with alglucosidase alfa every other week for 52 weeks. This was the 'high dose' arm.

Reporting group title	Treatment: Alglucosidase Alfa 20 mg/kg Every Week
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Reporting group description:

Subjects were treated with alglucosidase alfa every week for 52 weeks. This was the 'frequent dose' arm.

Reporting group title	Extension: Alglucosidase Alfa 40 mg/kg Every Other Week
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Reporting group description:

Alglucosidase Alfa every week until commercial supply became available.

Serious adverse events	Extension: Alglucosidase Alfa 20 mg/kg Every Week	Treatment: Alglucosidase Alfa 40 mg/kg Every Other Week	Treatment: Alglucosidase Alfa 20 mg/kg Every Week
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	1 / 7 (14.29%)	2 / 6 (33.33%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Investigations			
Weight Decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fibula Fracture			

subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular Tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory Failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infections and infestations			
Device Related Infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serious adverse events			
	Extension: Alglucosidase Alfa 40 mg/kg Every Other Week		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Investigations Weight Decreased subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 2 (0.00%) 0 / 0 0 / 0		
Injury, poisoning and procedural complications Fibula Fracture subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 2 (0.00%) 0 / 0 0 / 0		
Cardiac disorders Supraventricular Tachycardia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 2 (0.00%) 0 / 0 0 / 0		
Gastrointestinal disorders Dysphagia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 2 (0.00%) 0 / 0 0 / 0		
Respiratory, thoracic and mediastinal disorders Respiratory Failure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 2 (0.00%) 0 / 0 0 / 0		
Infections and infestations Device Related Infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 2 (0.00%) 0 / 0 0 / 0 0 / 2 (0.00%) 0 / 0 0 / 0		

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

Non-serious adverse events	Extension: Alglucosidase Alfa 20 mg/kg Every Week	Treatment: Alglucosidase Alfa 40 mg/kg Every Other Week	Treatment: Alglucosidase Alfa 20 mg/kg Every Week
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	7 / 7 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Blood Pressure Fluctuation			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Adverse Drug Reaction			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Generalised Oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Atelectasis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	0	3	1
Increased Bronchial Secretion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oropharyngeal Pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vasomotor Rhinitis			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Investigations			
Aspiration Tracheal Abnormal			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood Calcium Increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Breath Sounds Abnormal			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Heart Rate Irregular			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Prostatic Specific Antigen Increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
White Blood Cells Urine Positive			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Protein Urine Present subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Injury, poisoning and procedural complications			
Arthropod Bite subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Contusion subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0
Epicondylitis subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Excoriation subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1	1 / 7 (14.29%) 2	1 / 6 (16.67%) 2
Muscle Strain subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Vaccination Complication subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Cardiac disorders			
Right Ventricular Hypertrophy subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Tachycardia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	1 / 6 (16.67%) 1
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1	0 / 7 (0.00%) 0	0 / 6 (0.00%) 0

Hypotonia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 3	0 / 6 (0.00%) 0
Presyncope subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Restless Legs Syndrome subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Somnolence subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Blood and lymphatic system disorders Lymphadenitis subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0
Eye disorders Dry Eye subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Eyelid Ptosis subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Gastrointestinal disorders			

Abdominal Discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Amalgam Tattoo			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal Pain Upper			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Anal Fissure			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Aphthous Stomatitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
Haematochezia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Dermatitis Diaper			
subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	1 / 6 (16.67%)
occurrences (all)	0	2	2
Eczema			

subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash Erythematous			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Rash Macular			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Muscle Spasms			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Back Pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	0	1	2
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Pain In Extremity			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Abscess Limb			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Acute Sinusitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Candidiasis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Ear Infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Device Related Infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fungal Skin Infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastroenteritis Viral			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Gastrointestinal Viral Infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2

Otitis Media Acute			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Otitis Media			
subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Pneumococcal Infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	4
Sinusitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash Pustular			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Tooth Abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Subcutaneous Abscess			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 1 (0.00%)	3 / 7 (42.86%)	2 / 6 (33.33%)
occurrences (all)	0	4	3

Streptococcal Infection subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0
Urinary Tract Infection subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Varicella subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	0 / 6 (0.00%) 0
Viral Infection subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	2 / 6 (33.33%) 2
Metabolism and nutrition disorders			
Dehydration subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	2 / 6 (33.33%) 2
Gout subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 6 (16.67%) 1
Non-serious adverse events	Extension: Alglucosidase Alfa 40 mg/kg Every Other Week		
Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 2 (50.00%)		

Vascular disorders Blood Pressure Fluctuation subjects affected / exposed occurrences (all) Hypotension subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
General disorders and administration site conditions Adverse Drug Reaction subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Generalised Oedema subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Atelectasis subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 1 / 2 (50.00%) 1		

Increased Bronchial Secretion subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Oropharyngeal Pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Vasomotor Rhinitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Investigations			
Aspiration Tracheal Abnormal subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Blood Calcium Increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Breath Sounds Abnormal subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Heart Rate Irregular subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Prostatic Specific Antigen Increased subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
White Blood Cells Urine Positive subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Protein Urine Present subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Injury, poisoning and procedural complications			
Arthropod Bite subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Contusion			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Epicondylitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Excoriation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Muscle Strain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Vaccination Complication			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Right Ventricular Hypertrophy			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypotonia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Presyncope			

subjects affected / exposed occurrences (all) Restless Legs Syndrome subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Blood and lymphatic system disorders Lymphadenitis subjects affected / exposed occurrences (all) Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Eye disorders Dry Eye subjects affected / exposed occurrences (all) Eyelid Ptosis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Gastrointestinal disorders Abdominal Discomfort subjects affected / exposed occurrences (all) Amalgam Tattoo subjects affected / exposed occurrences (all) Abdominal Pain Upper	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Anal Fissure			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Aphthous Stomatitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Haematochezia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis Diaper			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Rash Erythematous subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Rash Macular subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Musculoskeletal and connective tissue disorders Muscle Spasms subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Back Pain subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Myalgia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Pain In Extremity subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Infections and infestations Abscess Limb subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Acute Sinusitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Cellulitis subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		

Candidiasis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Ear Infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Device Related Infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Fungal Skin Infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastroenteritis Viral			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastrointestinal Viral Infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hordeolum			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Otitis Media Acute			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Otitis Media			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pneumococcal Infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rash Pustular			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Tooth Abscess			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Subcutaneous Abscess			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Streptococcal Infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Urinary Tract Infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Varicella			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Viral Infection subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Metabolism and nutrition disorders			
Dehydration subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Gout subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2007	Changed age stratification for randomization from 16 years to 18 years. Added assessment of the Pompe PEDI for all patients and the MOS SF-36 for subjects ≥ 14 years of age. Scope of echocardiogram (ECHO) assessments was reduced to focus on key measurements, including LVM, LVMI, left posterior wall thickness, shortening fraction, and ejection fraction.
02 October 2007	Exclude subjects negative for Cross-Reactive Immunologic Material (CRIM), to remove the analysis of results by CRIM status, and to increase the enrollment limit from 12 to 14 because 1 of the subjects enrolled prior to the amendment was found to be CRIM. Physician's global assessment of the subject's clinical status by organ system was removed. GMFM-88 was replaced by the GMFM-66. Risk section of introduction was updated. Revised text to emphasize that written informed consent must be obtained before randomization. Added screening/baseline assessment of retrospective, related AEs that occurred during previous clinical study and/or commercial Myozyme treatment.
11 October 2008	The pre-specified end date for enrollment was removed.
28 April 2009	Added an extension period to the study after the 52-week study period to allow late-onset subjects access to treatment until commercial alglucosidase alfa became available.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This small exploratory study lacked a parallel control arm at the standard dose for a longer period; decline in respiratory or motor function prior to study was not collected systematically, thus change from baseline observations are inconclusive.

Notes: