



## Clinical trial results:

### A Phase 3/4 Prospective Study to Characterize the Pharmacokinetics of Alglucosidase Alfa in Patients with Pompe Disease

#### Summary

EudraCT number	2010-022231-11
Trial protocol	DE GB
Global end of trial date	20 November 2020

#### Results information

Result version number	v1 (current)
This version publication date	02 June 2021
First version publication date	02 June 2021

#### Trial information

##### Trial identification

Sponsor protocol code	AGLU07710
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01410890
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Genzyme, a Sanofi Company
Sponsor organisation address	500 Kendall Street, Cambridge, United States, 02142
Public contact	Trial Transparency Team, Genzyme, a Sanofi Company, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Genzyme, a Sanofi Company, 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	16 December 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 November 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To characterise the pharmacokinetics (PK) of alglucosidase alfa manufactured at the 4000 L scale in subjects who had a confirmed diagnosis of Pompe disease.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of paediatric and adult 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 minimised. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia might have been used to minimise distress and discomfort. Adult 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	03 November 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	India: 4
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Ukraine: 2
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	21
EEA total number of subjects	1

Notes:

<b>Subjects enrolled per age group</b>	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	2
Children (2-11 years)	7
Adolescents (12-17 years)	1
Adults (18-64 years)	11
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 12 sites in 6 countries. A total of 27 subjects were screened between 03-Nov-2014 and 23-Sep-2020, of whom 6 subjects were screen failures and 21 subjects were enrolled in the study.

### Pre-assignment

Screening details:

Out of 21 subjects, 1 subject signed the informed consent, but due to health status did not continue in the study to the treatment visit.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Alglucosidase Alfa: <18 Years

Arm description:

Subjects with less than (<) 18 years of age received intravenous (IV) infusion of Alglucosidase alfa 20 milligrams per kilogram (mg/kg) body weight on Day 1. Infusion was administered at an initial rate of approximately 1 milligrams per kilogram per hour (mg/kg/hr) with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of infusion-associated reactions (IARs), until a maximum rate of approximately 7 mg/kg/hr was reached.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase Alfa
Investigational medicinal product code	GZ419829
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV infusion of Alglucosidase alfa 20 mg/kg body weight on Day 1.

<b>Arm title</b>	Alglucosidase Alfa: >=18 Years
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Arm description:

Subjects with greater than or equal to (>=) 18 years of age received IV infusion of Alglucosidase alfa 20 mg/kg body weight on Day 1. Infusion was administered at an initial rate of approximately 1 mg/kg/hr with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of IARs, until a maximum rate of approximately 7 mg/kg/hr was reached.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase Alfa
Investigational medicinal product code	GZ419829
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV infusion of Alglucosidase alfa 20 mg/kg body weight on Day 1.

Number of subjects in period 1 <sup>[1]</sup>	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: ≥18 Years
Started	10	10
Treated	10	10
Completed	10	10

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Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 1 subject signed the informed consent, but due to health status did not continue in the study to the treatment visit.

## Baseline characteristics

### Reporting groups

Reporting group title	Alglucosidase Alfa: <18 Years
Reporting group description:	
Subjects with less than (<) 18 years of age received intravenous (IV) infusion of Alglucosidase alfa 20 milligrams per kilogram (mg/kg) body weight on Day 1. Infusion was administered at an initial rate of approximately 1 milligrams per kilogram per hour (mg/kg/hr) with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of infusion-associated reactions (IARs), until a maximum rate of approximately 7 mg/kg/hr was reached.	
Reporting group title	Alglucosidase Alfa: >=18 Years
Reporting group description:	
Subjects with greater than or equal to (>=) 18 years of age received IV infusion of Alglucosidase alfa 20 mg/kg body weight on Day 1. Infusion was administered at an initial rate of approximately 1 mg/kg/hr with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of IARs, until a maximum rate of approximately 7 mg/kg/hr was reached.	

Reporting group values	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: >=18 Years	Total
Number of subjects	10	10	20
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	5.1	41.8	
standard deviation	± 3.95	± 12.44	-
Gender categorical			
Units: Subjects			
Female	5	2	7
Male	5	8	13
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	6	8	14
Unknown or Not Reported	3	1	4
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	1	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	5	9	14
More than one race	2	0	2
Unknown or Not Reported	0	0	0
Anti-Recombinant Human Acid Alpha-Glucosidase (rhGAA) Immunoglobulin G (IgG) Antibody Status			
Positive antibody status indicated presence of anti-rhGAA IgG antibodies and negative antibody status indicated absence of anti-rhGAA IgG antibodies.			
Units: Subjects			

Positive	3	4	7
Negative	6	6	12
Missing	1	0	1

## End points

### End points reporting groups

Reporting group title	Alglucosidase Alfa: <18 Years
Reporting group description: Subjects with less than (<) 18 years of age received intravenous (IV) infusion of Alglucosidase alfa 20 milligrams per kilogram (mg/kg) body weight on Day 1. Infusion was administered at an initial rate of approximately 1 milligrams per kilogram per hour (mg/kg/hr) with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of infusion-associated reactions (IARs), until a maximum rate of approximately 7 mg/kg/hr was reached.	
Reporting group title	Alglucosidase Alfa: >=18 Years
Reporting group description: Subjects with greater than or equal to (>=) 18 years of age received IV infusion of Alglucosidase alfa 20 mg/kg body weight on Day 1. Infusion was administered at an initial rate of approximately 1 mg/kg/hr with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of IARs, until a maximum rate of approximately 7 mg/kg/hr was reached.	
Subject analysis set title	Anti-rhGAA Antibody Negative Subjects
Subject analysis set type	Full analysis
Subject analysis set description: Subjects with negative anti-rhGAA IgG antibody status at Baseline received IV infusion of Alglucosidase alfa 20 mg/kg body weight on Day 1. Infusion was administered at an initial rate of approximately 1 mg/kg/hr with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of IARs, until a maximum rate of approximately 7 mg/kg/hr was reached.	
Subject analysis set title	Anti-rhGAA Antibody Positive Subjects
Subject analysis set type	Full analysis
Subject analysis set description: Subjects with positive anti-rhGAA IgG antibody status at Baseline received IV infusion of Alglucosidase alfa 20 mg/kg body weight on Day 1. Infusion was administered at an initial rate of approximately 1 mg/kg/hr with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of IARs, until a maximum rate of approximately 7 mg/kg/hr was reached.	

### Primary: Pharmacokinetics: Maximum Observed Plasma Concentration (Cmax) of Alglucosidase Alfa

End point title	Pharmacokinetics: Maximum Observed Plasma Concentration (Cmax) of Alglucosidase Alfa <sup>[1]</sup>
End point description: Cmax was defined as maximum observed plasma concentration. Analysis was performed on all subjects who received any amount of alglucosidase alfa.	
End point type	Primary
End point timeframe: Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1	

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 endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: >=18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: nanograms per millilitre (ng/mL)				
arithmetic mean (standard deviation)	204000 (± 94600)	307000 (± 143000)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Pharmacokinetics: Time to Reach Maximum Observed Plasma Concentration (Tmax) of Alglucosidase Alfa

End point title	Pharmacokinetics: Time to Reach Maximum Observed Plasma Concentration (Tmax) of Alglucosidase Alfa <sup>[2]</sup>
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End point description:

Tmax was defined as time to reach maximum observed plasma concentration. Analysis was performed on all subjects who received any amount of alglucosidase alfa.

End point type	Primary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

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 endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: ≥18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: hours				
median (full range (min-max))	4.23 (1.92 to 6.42)	3.85 (1.42 to 5.33)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Pharmacokinetics: Area Under the Plasma Concentration-Time Curve (AUC) of Alglucosidase Alfa

End point title	Pharmacokinetics: Area Under the Plasma Concentration-Time Curve (AUC) of Alglucosidase Alfa <sup>[3]</sup>
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End point description:

AUC was defined as area under the plasma concentration-time curve from time 0 to 24 hours post-dose. Analysis was performed on all subjects who received any amount of alglucosidase alfa.

End point type	Primary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

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 endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: ≥18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: hours per nanograms per milliliter				
arithmetic mean (standard deviation)	1110000 (± 753000)	1890000 (± 969000)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Pharmacokinetics: Area Under the Concentration-time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Alglucosidase Alfa

End point title	Pharmacokinetics: Area Under the Concentration-time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUC0-last) of Alglucosidase Alfa <sup>[4]</sup>
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End point description:

AUC0-last was defined as area under the concentration-time curve from time 0 to the time of the last quantifiable concentration. Analysis was performed on all subjects who received any amount of alglucosidase alfa.

End point type	Primary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

Notes:

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

Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: ≥18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: hours per nanograms per milliliter				
arithmetic mean (standard deviation)	1040000 (± 590000)	1840000 (± 901000)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Pharmacokinetics: Terminal Elimination Half-life (T1/2) of Alglucosidase Alfa

End point title	Pharmacokinetics: Terminal Elimination Half-life (T1/2) of Alglucosidase Alfa <sup>[5]</sup>
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End point description:

T1/2 was defined as the time taken by drug to reduce to half of its initial plasma concentration. Analysis was performed on all subjects who received any amount of alglucosidase alfa.

End point type	Primary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: ≥18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: hours				
arithmetic mean (standard deviation)	5.43 (± 3.82)	3.84 (± 0.801)		

## Statistical analyses

No statistical analyses for this end point

## Primary: Pharmacokinetics: Total Systemic Clearance (CL) of Alglucosidase Alfa

End point title	Pharmacokinetics: Total Systemic Clearance (CL) of Alglucosidase Alfa <sup>[6]</sup>
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End point description:

CL of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. Analysis was performed on all subjects who received any amount of alglucosidase alfa.

End point type	Primary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

Notes:

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

Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: ≥18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Litres per hour				
arithmetic mean (standard deviation)	0.529 (± 0.613)	1.26 (± 1.24)		

## Statistical analyses

No statistical analyses for this end point

## Primary: Pharmacokinetics: Volume of Distribution at Steady State (Vss) of Alglucosidase Alfa

End point title	Pharmacokinetics: Volume of Distribution at Steady State (Vss) of Alglucosidase Alfa <sup>[7]</sup>
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End point description:

Volume of distribution (Vd) is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug. Vss is the apparent volume of distribution at steady-state. Analysis was performed on all subjects who received any amount of alglucosidase alfa.

End point type Primary

End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: ≥18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Litres				
arithmetic mean (standard deviation)	2.35 (± 2.02)	5.59 (± 3.72)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Maximum Observed Plasma Concentration of Alglucosidase Alfa in Anti-Recombinant Human Acid Alpha-Glucosidase Antibody Positive and Negative Subjects

End point title Pharmacokinetics: Maximum Observed Plasma Concentration of Alglucosidase Alfa in Anti-Recombinant Human Acid Alpha-Glucosidase Antibody Positive and Negative Subjects

End point description:

Cmax was defined as maximum observed plasma concentration. Analysis was performed on full analysis set (FAS) that included subjects who received any amount of alglucosidase alfa. Here, number of subjects analysed = subjects with available data for this endpoint.

End point type Secondary

End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

End point values	Anti-rhGAA Antibody Negative Subjects	Anti-rhGAA Antibody Positive Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: ng/mL				
arithmetic mean (standard deviation)	256000 (± 121000)	262000 (± 160000)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Time to Reach Maximum Observed Plasma Concentration in Anti-rhGAA Antibody Positive and Negative Subjects

End point title	Pharmacokinetics: Time to Reach Maximum Observed Plasma Concentration in Anti-rhGAA Antibody Positive and Negative Subjects
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End point description:

Tmax was defined as time to reach maximum observed plasma concentration. Analysis was performed on FAS that included all subjects who received any amount of alglucosidase alfa. Here, number of subjects analysed = subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

End point values	Anti-rhGAA Antibody Negative Subjects	Anti-rhGAA Antibody Positive Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: hours				
median (full range (min-max))	3.94 (1.92 to 5.27)	4.33 (1.42 to 6.42)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Terminal Elimination Half-life of Alglucosidase Alfa in Anti-rhGAA Antibody Positive and Negative Subjects

End point title	Pharmacokinetics: Terminal Elimination Half-life of Alglucosidase Alfa in Anti-rhGAA Antibody Positive and Negative Subjects
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End point description:

T1/2 was defined as the time taken by drug to reduce to half of its initial plasma concentration. Analysis was performed on FAS that included subjects who received any amount of alglucosidase alfa. Here, number of subjects analysed = subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

End point values	Anti-rhGAA Antibody Negative Subjects	Anti-rhGAA Antibody Positive Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: hours				
arithmetic mean (standard deviation)	4.68 (± 2.95)	4.79 (± 2.93)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Area Under the Concentration-time Curve From Time 0 to the Time of the Last Quantifiable Concentration of Alglucosidase Alfa in Anti-rhGAA Antibody Positive and Negative Subjects

End point title	Pharmacokinetics: Area Under the Concentration-time Curve From Time 0 to the Time of the Last Quantifiable Concentration of Alglucosidase Alfa in Anti-rhGAA Antibody Positive and Negative Subjects
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End point description:

AUC<sub>0</sub>-last was defined as area under the plasma concentration-time curve from time 0 to the time of the last quantifiable concentration. Analysis was performed on FAS that included subjects who received any amount of alglucosidase alfa. Here, number of subjects analysed = subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

End point values	Anti-rhGAA Antibody Negative Subjects	Anti-rhGAA Antibody Positive Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: hours per nanograms per milliliter				
arithmetic mean (standard deviation)	1410000 (± 865000)	1610000 (± 86800)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics: Area Under the Concentration-time Curve From Time

## 0 and Extrapolated to Infinite Time (AUC0-inf) in Anti-rhGAA Antibody Positive and Negative Subjects

End point title	Pharmacokinetics: Area Under the Concentration-time Curve From Time 0 and Extrapolated to Infinite Time (AUC0-inf) in Anti-rhGAA Antibody Positive and Negative Subjects
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End point description:

AUC0-inf was defined as area under the concentration-time curve from time 0 extrapolated to infinite time. Analysis was performed on FAS that included subjects who received any amount of alglucosidase alfa. Here, number of subjects analysed = subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

End point values	Anti-rhGAA Antibody Negative Subjects	Anti-rhGAA Antibody Positive Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: hours per nanograms per milliliter				
arithmetic mean (standard deviation)	1450000 ( $\pm$ 941000)	1700000 ( $\pm$ 985000)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Total Systemic Clearance in Anti-rhGAA Antibody Positive and Negative Subjects

End point title	Pharmacokinetics: Total Systemic Clearance in Anti-rhGAA Antibody Positive and Negative Subjects
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End point description:

CL of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. Analysis was performed on FAS that included subjects who received any amount of alglucosidase alfa. Here, number of subjects analysed = subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

End point values	Anti-rhGAA Antibody Negative Subjects	Anti-rhGAA Antibody Positive Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: Litres per hour				
arithmetic mean (standard deviation)	0.765 ( $\pm$ 0.518)	1.21 ( $\pm$ 1.60)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Volume of Distribution in Anti-rhGAA Antibody Positive and Negative Subjects

End point title	Pharmacokinetics: Volume of Distribution in Anti-rhGAA Antibody Positive and Negative Subjects
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End point description:

Vd is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug. Vss is the apparent volume of distribution at steady-state. Analysis was performed on FAS that included subjects who received any amount of alglucosidase alfa. Here, number of subjects analysed = subjects with available data for this endpoint.

End point type	Secondary
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End point timeframe:

Pre-dose and at 1, 2, 4, 8, 12, and 24 hours Post-dose on Day 1

End point values	Anti-rhGAA Antibody Negative Subjects	Anti-rhGAA Antibody Positive Subjects		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	7		
Units: Litres				
arithmetic mean (standard deviation)	5.82 (± 6.49)	7.26 (± 9.16)		

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AEs) were collected from signature of the informed consent form up to Week 4.

Adverse event reporting additional description:

Reported AEs and deaths were treatment-emergent (TEAEs) that developed/worsened in grade/became serious during 'TEAE period' (i.e., from signature of the informed consent form up to Week 4. Analysis was performed on FAS that included all subjects who received any amount of alglucosidase alfa.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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### Reporting groups

Reporting group title	Alglucosidase Alfa: <18 Years
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Reporting group description:

Subjects with <18 years of age received IV infusion of Alglucosidase alfa 20 mg/kg body weight on Day 1. Infusion was administered at an initial rate of approximately 1 mg/kg/hr with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of IARs, until a maximum rate of approximately 7 mg/kg/hr was reached.

Reporting group title	Alglucosidase Alfa: >=18 Years
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Reporting group description:

Subjects with >=18 years of age received IV infusion of Alglucosidase alfa 20 mg/kg body weight on Day 1. Infusion was administered at an initial rate of approximately 1 mg/kg/hr with allowed rate increased of 2 mg/kg/hr every 30 minutes, if there were no signs of IARs, until a maximum rate of approximately 7 mg/kg/hr was reached.

Serious adverse events	Alglucosidase Alfa: <18 Years	Alglucosidase Alfa: >=18 Years	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Respiratory Distress			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (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: 5 %

<b>Non-serious adverse events</b>	<b>Alglucosidase Alfa: &lt;18 Years</b>	<b>Alglucosidase Alfa: ≥18 Years</b>	
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 10 (40.00%)	3 / 10 (30.00%)	
Investigations			
Blood Pressure Increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Body Temperature Increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 1	
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 2	
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Pyrexia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Papule subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Urticaria subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	0 / 10 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Osteoporosis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Pain In Extremity subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Infections and infestations			

Fungal Skin Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 May 2011	Following changes were made: Updated study personnel information; clarified the timing of the 30-day follow-up visit, which was the subjects last study visit; updated language for contraception requirements and pregnancy testing for consistency within the protocol and added urine pregnancy tests and use of contraception; reevaluated sample assay requirements to minimise burden on subjects. The PK sampling timepoints were extended out to 48 hours after the end of infusion to increase assurance of characterising the half-life of the second phase of the alglucosidase alfa concentration-time curve. Adjusted PK sampling timepoints to include samples immediately before each scheduled infusion rate change to make sure the true Cmax was not missed; unified text with language of approved label, where applicable; added text that dose increase and dose reduction was not permitted unless it was due to an AE; standardised collection of complete medical history and surgical procedure information; clarified that additional testing was needed only for IARs suggestive of hypersensitivity reactions. Window for testing was expanded based on experience across the program; revised the schedule of assessments to allow sufficient time between the last study infusion and last study IgG assessment to see if there was a change in IgG titer. Required that the follow-up visit be an office visit to allow collection of an IgG sample.
17 December 2015	Following changes were made: Modified inclusion criteria to remove the upper age limit of 18 years as a means to remedy the unsatisfactory number of subjects enrolled to date. Approximately 10 subjects <18 years old and 10 subjects ≥18 years old was the target for enrollment; inclusion criteria was added and exclusion criteria was deleted to allow inclusion of subjects previously treated with alglucosidase alfa for at least 6 months; reduced number of infusions from 14 to 1, reducing study duration from approximately 30 weeks to approximately 4 to 9 weeks to enhance subjects recruitment into the study; limited collection of blood samples for PK assessment to infusion Day 1 and samples at 30, 36, 42, and 48 hours after the end of infusion were eliminated to enhance subjects recruitment into the study; eliminated determination of the exploratory biomarker urine hex4 level as a consequence of the reduced study duration; eliminated exploratory assessment of GAA activity in dried blood spot with the more focused emphasis on PK and immunology assessment.
18 July 2016	Following changes were made: modified Inclusion criteria to remove the lower age limit of 8 years of age to add the possibility to characterise PK in subjects <8 years old. Approximately 10 subjects <18 years old and 10 subjects ≥18 years old remained the target for enrollment.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported