Clinical trial results:
An Open-label Ascending Dose Cohort Study to Assess the Safety, Pharmacokinetics, and Preliminary Efficacy of Avalglucosidase Alfa (NeoGAA, GZ402666) in Patients with Infantile-onset Pompe Disease Treated with Alglucosidase Alfa Who Demonstrate Clinical Decline or Sub-optimal Clinical Response

Summary

EudraCT number	2016-003475-21
Trial protocol	GB DE FR Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	08 March 2022
First version publication date	08 March 2022

Trial information

Trial identification

Sponsor protocol code	ACT14132

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03019406
WHO universal trial number (UTN)	U1111-1179-4616

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	50 Binney Street, Cambridge, Massachusetts, 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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000360-PIP20-21
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?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	22 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety profile of avalglucosidase alfa in subjects with infantile-onset Pompe disease previously treated with alglucosidase alfa.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of paediatric 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 may have been used to minimise distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 October 2017
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: 2
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	22
EEA total number of subjects	4

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)	2
Children (2-11 years)	20
Adolescents (12-17 years)	0

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 10 active centres in 5 countries. Total of 22 subjects were screened between 12 October 2017 and 03 April 2019. None of the subjects were screen failed. Subjects were assigned to treatment by using interactive response technology system.

Pre-assignment

Screening details:

Cohorts 1:avalglucosidase alfa 20 milligrams per kilogram (mg/kg) every other week (qow) & Cohort 2:avalglucosidase alfa 40 mg/kg qow. No randomisation for Cohort 1 & 2. Cohort 3(stratified by gender):avalglucosidase alfa 40 mg/kg qow(3a) or current stable alglucosidase alfa dose regimen(3b). Data reported for primary completion date (30-Sep-2019).

Period 1

Period 1 title	Primary Analysis Period (PAP):upto 25 Wk
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg

Arm description:

Avalglucosidase alfa, 20 mg/kg intravenous (IV) infusion qow for 25 weeks (Wk) in PAP.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase Alfa
Investigational medicinal product code	GZ402666
Other name	Nexviadyme and Nexviazyme
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg/kg, IV infusion qow for a total of 13 doses.

Arm title	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg

Arm description:

Avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in the PAP.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase Alfa
Investigational medicinal product code	GZ402666
Other name	Nexviadyme and Nexviazyme
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/kg, IV infusion qow for a total of 13 doses.

Arm title	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg

Arm description:

After determination of the highest tolerated avalglucosidase alfa dose in Cohort 1 and Cohort 2 (after at least 5 subjects in each Cohort 1 and Cohort 2 had received the 7th dose of avalglucosidase alfa or completed Week 13 with a minimum of 6 infusions), subjects received avalglucosidase alfa 40 mg/kg (the highest tolerated dose) IV infusion qow for 25 weeks in PAP.

Arm type	Experimental

Investigational medicinal product name	Avalglucosidase Alfa
Investigational medicinal product code	GZ402666
Other name	Nexviadyme and Nexviazyme
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/kg, IV infusion qow for a total of 13 doses.

Arm title	PAP: Cohort 3b: Alglucosidase Alfa

Arm description:

After determination of the highest tolerated avalglucosidase alfa dose in Cohort 1 and Cohort 2 (after at least 5 subjects in each Cohort 1 and Cohort 2 had received the 7th dose of avalglucosidase alfa or completed Week 13 with a minimum of 6 infusions), subjects received alglucosidase alfa at their current stable dose (defined as dose [between 20 mg/kg qow and 40 mg/kg weekly as per physician] administered regularly for a minimum of 6 months immediately prior to entry in this study) IV infusion for 25 weeks in PAP.

Arm type	Active comparator
Investigational medicinal product name	Alglucosidase alfa
Investigational medicinal product code	GZ419829
Other name	Myozyme® and Lumizyme®
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose between 20 mg/kg qow and 40 mg/kg weekly (qw) as per physician, IV infusion qow/qw for a total of 13 or 25 doses, respectively.

Number of subjects in period 1	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg
Started	6	5	5
Treated	6	5	5
Completed	6	5	5

Number of subjects in period 1	PAP: Cohort 3b: Alglucosidase Alfa
Started	6
Treated	6
Completed	6

Period 2

Period 2 title	Extension treatment period(ETP):from26Wk
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	ETP: Cohort 1: Avalglucosidase Alfa 20 mg/kg

Arm description:

Included all subjects of PAP Cohort 1 who received avalglucosidase alfa 20 mg/kg IV infusion qow for 25 weeks in PAP, followed by same treatment from Week 26 up to Week 371 in ETP.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase Alfa
Investigational medicinal product code	GZ402666
Other name	Nexviadyme and Nexviazyme
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mg/kg, IV infusion qow up to 60 infusions.

Arm title	ETP: Cohort 2: Avalglucosidase Alfa 40 mg/kg

Arm description:

Included all subjects of PAP Cohort 2 who received avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in PAP, followed by same treatment from Week 26 up to Week 371 in ETP.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase Alfa
Investigational medicinal product code	GZ402666
Other name	Nexviadyme and Nexviazyme
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/kg, IV infusion qow up to 60 infusions.

Arm title	ETP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg

Arm description:

Included all subjects of PAP Cohort 3a who received avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in PAP, followed by same treatment from Week 26 up to Week 371 in ETP.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase Alfa
Investigational medicinal product code	GZ402666
Other name	Nexviadyme and Nexviazyme
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/kg, IV infusion qow up to 60 infusions.

Arm title	ETP:Alglucosidase Alfa in PAP Then Avalglucosidase Alfa in ETP

Arm description:

Included all subjects of Cohort 3b who received alglucosidase alfa at their current stable dose (defined as dose [between 20 mg/kg qow and 40 mg/kg weekly as per physician] administered regularly for a minimum of 6 months immediately prior to entry in this study) IV infusion for 25 weeks in the PAP and after PAP, subjects were switched to receive avalglucosidase alfa 40 mg/kg IV infusion qow from Week 26 up to Week 371 in ETP.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase Alfa
Investigational medicinal product code	GZ402666
Other name	Nexviadyme and Nexviazyme
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/kg, IV infusion qow up to 60 infusions.

Number of subjects in period 2[1]	ETP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	ETP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	ETP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg
Started	6	5	5
Completed	0	0	0
Not completed	6	5	5
Ongoing	6	5	5

Number of subjects in period 2[1]	ETP:Alglucosidase Alfa in PAP Then Avalglucosidase Alfa in ETP
Started	3
Completed	0
Not completed	3
Ongoing	3

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: Subjects who completed PAP and accepted to receive avalglucosidase alfa treatment in ETP.

Baseline characteristics

Reporting groups	
Reporting group title	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg
Reporting group description: Avalglucosidase alfa, 20 mg/kg intravenous (IV) infusion qow for 25 weeks (Wk) in PAP.	
Reporting group title	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg
Reporting group description: Avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in the PAP.	
Reporting group title	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg
Reporting group description: After determination of the highest tolerated avalglucosidase alfa dose in Cohort 1 and Cohort 2 (after at least 5 subjects in each Cohort 1 and Cohort 2 had received the 7th dose of avalglucosidase alfa or completed Week 13 with a minimum of 6 infusions), subjects received avalglucosidase alfa 40 mg/kg (the highest tolerated dose) IV infusion qow for 25 weeks in PAP.	
Reporting group title	PAP: Cohort 3b: Alglucosidase Alfa
Reporting group description: After determination of the highest tolerated avalglucosidase alfa dose in Cohort 1 and Cohort 2 (after at least 5 subjects in each Cohort 1 and Cohort 2 had received the 7th dose of avalglucosidase alfa or completed Week 13 with a minimum of 6 infusions), subjects received alglucosidase alfa at their current stable dose (defined as dose [between 20 mg/kg qow and 40 mg/kg weekly as per physician] administered regularly for a minimum of 6 months immediately prior to entry in this study) IV infusion for 25 weeks in PAP.	

Reporting group values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg
Number of subjects	6	5	5
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	7.6	8.1	6.9
standard deviation	± 3.4	± 4.1	± 2.7
Gender categorical Units: Subjects			
Female	1	2	3
Male	5	3	2
Race Units: Subjects			
Asian	3	3	2
Black or African American	0	0	0
White	3	2	3

Reporting group values	PAP: Cohort 3b: Alglucosidase Alfa	Total	
Number of subjects	6	22	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	4.7		
standard deviation	± 3.2	-	
Gender categorical Units: Subjects			
Female	4	10	
Male	2	12	
Race Units: Subjects			
Asian	0	8	
Black or African American	2	2	
White	4	12	

End points

End points reporting groups

Reporting group title	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg

Reporting group description:

Avalglucosidase alfa, 20 mg/kg intravenous (IV) infusion qow for 25 weeks (Wk) in PAP.

Reporting group title	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg

Reporting group description:

Avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in the PAP.

Reporting group title	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg

Reporting group description:

After determination of the highest tolerated avalglucosidase alfa dose in Cohort 1 and Cohort 2 (after at least 5 subjects in each Cohort 1 and Cohort 2 had received the 7th dose of avalglucosidase alfa or completed Week 13 with a minimum of 6 infusions), subjects received avalglucosidase alfa 40 mg/kg (the highest tolerated dose) IV infusion qow for 25 weeks in PAP.

Reporting group title	PAP: Cohort 3b: Alglucosidase Alfa

Reporting group description:

After determination of the highest tolerated avalglucosidase alfa dose in Cohort 1 and Cohort 2 (after at least 5 subjects in each Cohort 1 and Cohort 2 had received the 7th dose of avalglucosidase alfa or completed Week 13 with a minimum of 6 infusions), subjects received alglucosidase alfa at their current stable dose (defined as dose [between 20 mg/kg qow and 40 mg/kg weekly as per physician] administered regularly for a minimum of 6 months immediately prior to entry in this study) IV infusion for 25 weeks in PAP.

Reporting group title	ETP: Cohort 1: Avalglucosidase Alfa 20 mg/kg

Reporting group description:

Included all subjects of PAP Cohort 1 who received avalglucosidase alfa 20 mg/kg IV infusion qow for 25 weeks in PAP, followed by same treatment from Week 26 up to Week 371 in ETP.

Reporting group title	ETP: Cohort 2: Avalglucosidase Alfa 40 mg/kg

Reporting group description:

Included all subjects of PAP Cohort 2 who received avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in PAP, followed by same treatment from Week 26 up to Week 371 in ETP.

Reporting group title	ETP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg

Reporting group description:

Included all subjects of PAP Cohort 3a who received avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in PAP, followed by same treatment from Week 26 up to Week 371 in ETP.

Reporting group title	ETP:Alglucosidase Alfa in PAP Then Avalglucosidase Alfa in ETP

Reporting group description:

Included all subjects of Cohort 3b who received alglucosidase alfa at their current stable dose (defined as dose [between 20 mg/kg qow and 40 mg/kg weekly as per physician] administered regularly for a minimum of 6 months immediately prior to entry in this study) IV infusion for 25 weeks in the PAP and after PAP, subjects were switched to receive avalglucosidase alfa 40 mg/kg IV infusion qow from Week 26 up to Week 371 in ETP.

Subject analysis set title	Pooled Arm ETP: Avalglucosidase Alfa 40 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Pooled arm included all subjects of Cohorts 2 and 3a who received avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in PAP, followed by same treatment from Week 26 up to Week 371 in ETP.

Primary: PAP: Number of Subjects With Treatment-emergent Adverse Events (TEAEs), Serious Treatment-emergent Adverse Events, and Adverse Event of Special Interest (AESI)

End point title	PAP: Number of Subjects With Treatment-emergent Adverse Events (TEAEs), Serious Treatment-emergent Adverse Events, and Adverse Event of Special Interest (AESI)[1]

End point description:

AE: any untoward medical occurrence in subject received study drug & did not necessarily had to have

causal relationship with treatment. TEAEs: AEs developed/worsened in grade/become serious during PAP period (from the time of 1st study drug dose up to Week 25). Serious AE(SAE): any untoward medical occurrence at any dose resulted in death, was life-threatening, required inpatient hospitalisation, prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was congenital anomaly/birth defect or was medically important event. TEAEs included SAEs & non-SAEs. AESI:AE (serious/non-serious) of scientific & medical concern specific to Sponsor's product/program, for which ongoing monitoring & immediate notification by Investigator to Sponsor required. Safety population.

End point type	Primary

End point timeframe:

From Baseline to Week 25

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 was descriptive in nature, no statistical analysis was provided.

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	5	6
Units: subjects				
Any TEAEs	5	5	5	5
Any Serious TEAEs	1	3	0	2
Any AESI	0	2	1	1

Statistical analyses

No statistical analyses for this end point

Primary: PAP: Number of Subjects With Infusion-associated Reactions (IARs)

End point title	PAP: Number of Subjects With Infusion-associated Reactions (IARs)[2]

End point description:

IARs were defined as AESIs that occurred during either the infusion or the observation period following the infusion which were deemed to be related or possibly related to the study drug. Protocol-defined IARs: An AESIs that occurred during either the infusion or the observation period following the infusion which were deemed to be related or possibly related to study drug. Algorithm-defined IARs: any TEAE meeting either 1 or 2 criteria: 1) event occurred from the start of infusion to the end of infusion plus 24 hours, and considered related to study drug, 2) If an AE time component was missing, compared AE start date with infusion start date and infusion end date. If an AE start date was between infusion start date and infusion end date plus one day, and it was related to study drug. Analysis was performed on safety population which included subjects who had received at least 1 infusion (partial or total) and were analysed according to treatment received.

End point type	Primary

End point timeframe:

From Baseline to Week 25

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 was descriptive in nature, no statistical analysis was provided.

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	5	6
Units: subjects				
Protocol-defined IARs	0	2	1	1
Algorithm-defined IARs	0	2	1	1

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Number of Subjects With Anti-drug Antibody (ADA) Response

End point title	PAP: Number of Subjects With Anti-drug Antibody (ADA) Response

End point description:

Anti-drug antibody response was categorised as: Treatment induced ADAs: ADAs developed de novo (seroconversion) following administration of study drug. Treatment boosted ADAs: pre-existing ADAs that were boosted at least two titer steps from Baseline (i.e., 4-fold increase in titers) followed by administration of study drug. Analysis was performed on the ADA evaluable population which included subjects who had received at least 1 infusion (partial or total) and had at least one ADA sample taken post-baseline after drug administration that was appropriate for ADA testing with a reportable result.

End point type	Secondary

End point timeframe:

From Baseline to Week 25

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	5	6
Units: subjects				
Treatment boosted ADA response	0	0	1	2
Treatment induced ADA response	0	1	3	1

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Pharmacokinetic (PK) Parameter: Maximum Observed Plasma Concentration (Cmax) of Avalglucosidase Alfa

End point title	PAP: Pharmacokinetic (PK) Parameter: Maximum Observed Plasma Concentration (Cmax) of Avalglucosidase Alfa[3]

End point description:

Cmax is the maximum observed plasma concentration. Analysis was performed on PK population which included PAP subjects who had received at least 1 infusion (partial or total) and had evaluable drug concentration data. Here, 'n' = number of subjects with data available for each specified category. Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point type	Secondary

End point timeframe:

Cohort 1: pre-dose; at end of infusion; and at 2, 4, 6 and 8 hours after end of infusion on Day 1 (Week 1) and Week 25 Cohort 2 and 3: pre-dose; at end of infusion; and at 2, 4, 6, 8 and 12 to 16 hours after end of infusion on Day 1 (Week 1) and Week 25

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	5	
Units: nanograms per millilitre				
arithmetic mean (standard deviation)				
Week 1 (n = 5, 4, 4)	189000 (± 56700)	403000 (± 171000)	250000 (± 45100)	
Week 25 (n = 5, 5, 5)	175000 (± 65900)	297000 (± 60100)	356000 (± 84700)	

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Pharmacokinetic Parameter: Time to Achieve Maximum Observed Plasma Concentration (Tmax) of Avalglucosidase Alfa

End point title	PAP: Pharmacokinetic Parameter: Time to Achieve Maximum Observed Plasma Concentration (Tmax) of Avalglucosidase Alfa[4]

End point description:

Tmax is the time to achieve maximum plasma concentration. Analysis was performed on PK population. Here, 'n' = number of subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point type	Secondary

End point timeframe:

Cohort 1: pre-dose; at end of infusion; and at 2, 4, 6 and 8 hours after end of infusion on Day 1 (Week 1) and Week 25 Cohort 2 and 3: pre-dose; at end of infusion; and at 2, 4, 6, 8 and 12 to 16 hours after end of infusion on Day 1 (Week 1) and Week 25

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	5	
Units: hours				
median (full range (min-max))				
Week 1 (n = 5, 4, 4)	4.43 (3.90 to 5.33)	7.00 (6.00 to 7.25)	6.83 (6.65 to 7.22)	
Week 25 (n = 5, 5, 5)	3.97 (3.77 to 4.75)	7.13 (5.67 to 7.98)	6.87 (5.03 to 7.43)	

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Pharmacokinetic Parameter: Area Under the Plasma Concentration Versus Time Curve From Time 0 to the Time of Last Quantifiable Concentration (AUC0-last) of Avalglucosidase Alfa

End point title	PAP: Pharmacokinetic Parameter: Area Under the Plasma Concentration Versus Time Curve From Time 0 to the Time of Last Quantifiable Concentration (AUC0-last) of Avalglucosidase Alfa[5]

End point description:

AUC0-last is the area under the plasma concentration versus time curve from time 0 to the time of last quantifiable concentration. Analysis was performed on PK population. Here, 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point type	Secondary

End point timeframe:

Cohort 1: pre-dose; at end of infusion; and at 2, 4, 6, and 8 hours after end of infusion on Day 1 (Week 1) and Week 25, Cohort 2 & 3: pre-dose; at end of infusion; and at 2, 4, 6, 8, and 12 to 16 hours after end of infusion on Day 1 (Week 1) and Week 25

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	5	
Units: nanograms*hours per millilitre				
arithmetic mean (standard deviation)				
Week 1 (n=5,4,4)	923000 (± 352000)	2630000 (± 972000)	1720000 (± 255000)	
Week 25 (n=5,5,5)	805000 (± 295000)	1930000 (± 348000)	2200000 (± 533000)	

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Pharmacokinetic Parameter: Terminal Half-life (t1/2) of Avalglucosidase Alfa

End point title	PAP: Pharmacokinetic Parameter: Terminal Half-life (t1/2) of Avalglucosidase Alfa[6]

End point description:

t1/2 is the time required for the plasma concentration of a drug to decrease by half of its initial concentration. Analysis was performed on PK population. Here, 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point type	Secondary

End point timeframe:

Cohort 1: pre-dose; at end of infusion; and at 2, 4, 6, and 8 hours after end of infusion on Day 1 (Week 1) and Week 25; Cohort 2 & 3: pre-dose; at end of infusion; and at 2, 4, 6, 8, and 12 to 16 hours after end of infusion on Day 1 (Week 1) and Week 25

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	5	
Units: hours				
arithmetic mean (standard deviation)				
Week 1 (n=5,4,4)	0.703 (± 0.291)	1.15 (± 0.523)	0.806 (± 0.248)	
Week 25 (n=5,5,5)	0.601 (± 0.256)	1.04 (± 0.248)	1.19 (± 0.472)	

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Pharmacokinetic Parameter: Clearance (CL) of Avalglucosidase Alfa

End point title	PAP: Pharmacokinetic Parameter: Clearance (CL) of Avalglucosidase Alfa[7]

End point description:

CL is defined as a quantitative measure of the rate at which a drug substance is removed from the body. Analysis was performed on PK population. Here, 'n' = subjects with available data for each specified

category. Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point type	Secondary

End point timeframe:

Cohort 1: pre-dose; at end of infusion; and at 2, 4, 6, and 8 hours after end of infusion on Day 1 (Week 1) and Week 25; Cohort 2 and 3: pre-dose; at end of infusion; and at 2, 4, 6, 8, and 12 to 16 hours after end of infusion on Day 1 (Week 1) and Week 2

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	5	
Units: millilitres per hours				
arithmetic mean (standard deviation)				
Week 1 (n=5,4,4)	673 (± 222)	562 (± 152)	529 (± 150)	
Week 25 (n=5,5,5)	696 (± 203)	683 (± 345)	526 (± 125)	

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Pharmacokinetic Parameter: Volume of Distribution at Steady State (Vss) of Avalglucosidase Alfa

End point title	PAP: Pharmacokinetic Parameter: Volume of Distribution at Steady State (Vss) of Avalglucosidase Alfa[8]

End point description:

Steady state volume of distribution (Vss) 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. Analysis was performed on PK population. Here, 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point type	Secondary

End point timeframe:

Cohort 1: pre-dose; at end of infusion; and at 2, 4, 6, and 8 hours after end of infusion on Day 1 (Week 1) and Week 25; Cohort 2 & 3: pre-dose; at end of infusion; and at 2, 4, 6, 8, and 12 to 16 hours after end of infusion on Day 1 (Week 1) and Week 25

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data for this endpoint was not planned to be collected and analysed for PAP: Cohort 3b: Alglucosidase Alfa arm.

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	5	
Units: millilitres				
arithmetic mean (standard deviation)				
Week 1 (n=5,4,4)	3550 (± 927)	4500 (± 882)	4300 (± 1420)	
Week 25 (n=5,5,5)	3520 (± 1180)	5350 (± 2270)	4020 (± 1390)	

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Change From Baseline in Gross Motor Function Measure-88 (GMFM-88) Test Scores at Week 25

End point title	PAP: Change From Baseline in Gross Motor Function Measure-88 (GMFM-88) Test Scores at Week 25

End point description:

GMFM-88 was developed specifically to detect quantitative changes in gross motor function. The GMFM-88 consisted of 88 items organised into 5 dimensions; lying and rolling (17 items); sitting (20 items); crawling and kneeling (14 items); standing (13 items) and walking, running and jumping (24 items). Each item was scored on a 4-point Likert scale with scores range: 0= cannot do; 1 = initiates less then [<] 10 percentage [%] of the task; 2 = partially completes [10% to <100% of the task] and 3 = task completion. The score for each dimension was expressed as a % of the maximum score for that dimension. Total percentage score was obtained by adding the percentage scores for each dimension and dividing the sum by the total number of dimensions. Total scores ranged from 0% to 100%; where higher scores indicated better motor functions. Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	4	6
Units: percentage of total score				
arithmetic mean (standard deviation)	6.50 (± 22.24)	9.80 (± 13.99)	11.00 (± 10.80)	17.00 (± 8.44)

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Number of Subjects in Gross Motor Function Classification System-Expanded and Revised (GMFCS-E and R) Scores at Baseline and Week 25

End point title	PAP: Number of Subjects in Gross Motor Function Classification System-Expanded and Revised (GMFCS-E and R) Scores at Baseline and Week 25

End point description:

GMFCS-E and R was a 5 level classification system for specific age ranges; observations were performed on 5 levels based on self-initiated movement, with emphasis on sitting, transfers, and mobility: Level I (walks without limitations), Level II (walks with limitations), Level III (walks using a hand-held mobility device), Level IV (self-mobility with limitations; may use powered mobility) and level V (transported in a manual wheel chair) (I to V). The distinctions between levels were based on functional limitations, the need for assistive mobility devices, and to a much lesser extent, quality of movement, and were designed to be meaningful in daily life. The lower level represented good motor functioning and higher level represented low motor functioning. Number of subjects in each level of classification at Baseline and Week 25 were reported. Analysis was performed on safety population.

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	5	6
Units: subjects				
Baseline: Level I	1	1	2	3
Baseline: Level II	1	2	1	0
Baseline: Level III	1	0	1	1
Baseline: Level IV	2	2	0	1
Baseline: Level V	1	0	1	1
Week 25: Level I	1	1	2	3
Week 25: Level II	1	2	1	0
Week 25: Level III	2	1	0	1
Week 25: Level IV	1	1	1	1
Week 25: Level V	1	0	1	1

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Change From Baseline in Pompe Paediatric Evaluation of Disability Inventory (Pompe-PEDI) Functional Skills Scale: Mobility Domain Test Score-Scaled Score at Week 25

End point title	PAP: Change From Baseline in Pompe Paediatric Evaluation of Disability Inventory (Pompe-PEDI) Functional Skills Scale: Mobility Domain Test Score-Scaled Score at Week 25

End point description:

Pompe-PEDI: disease specific version to assess functional capabilities and performance in children with Pompe disease from 2 months through adolescence. It comprised of Functional Skills Scale and Caregiver Assistance Scale; both scales had 3 domains: Self Care, Mobility, and Social Function. Mobility

domain was used to measure change in mobility due to changes in muscle strength; consisted of 160 mobility items for subject/legal guardian. The total number of mobility items the child was capable of, was converted to a scaled score with a range of 0 to 100, where scores near "0" indicated low capability and scores near "100" indicated high capability), where higher score was indicative of greater functional ability. Scaled scores were used to interpret individual function and progress over time. Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects with available data for this endpoint.

End point type	Secondary
End point timeframe:	
Baseline, Week 25	

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	3	6
Units: score on a scale				
arithmetic mean (standard deviation)	6.19 (± 10.55)	2.12 (± 4.04)	2.60 (± 1.72)	5.20 (± 5.95)

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Change From Baseline in Quick Motor Function Test (QMFT) Scores at Week 25

End point title	PAP: Change From Baseline in Quick Motor Function Test (QMFT) Scores at Week 25

End point description:

QMFT was observer administered test comprised of 16 items specifically difficult for subjects with Pompe disease. Each item was scored on 5-point ordinal scale ranged from 0 to 4 (higher score indicated better outcome). Total QMFT score was obtained by adding the scores of all items and ranged from 0 (unable to perform motor function tests) to 64 (normal muscle function), where higher score indicated better outcome/greater motor function. Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects with available data for this endpoint.

End point type	Secondary
End point timeframe:	
Baseline, Week 25	

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	4	6
Units: score on a scale				
arithmetic mean (standard deviation)	-0.17 (± 4.45)	3.20 (± 4.55)	4.25 (± 3.30)	5.17 (± 4.54)

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Echo-Left Ventricular Mass Z-Score (LVM Z-score) M-mode at Baseline, Week 25, and Change From Baseline at Week 25

End point title	PAP: Echo-Left Ventricular Mass Z-Score (LVM Z-score) M-mode at Baseline, Week 25, and Change From Baseline at Week 25

End point description:

Cardiac function was evaluated using LVM Z-score as assessed by echocardiogram in M-mode. Z-Scores indicated the number of standard deviations (SD) from the mean in a normal distribution. The normal range is -2 to 2 and greater than 2 may indicate left ventricular hypertrophy. A negative change from Baseline indicated a decrease and positive change from Baseline indicated an increase in LVM Z-score. In this end-point, absolute scores at Baseline and Week 25 along with change from Baseline at Week 25 in LVM Z-score were reported. Analysis was performed on safety population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	5	6
Units: Z-score				
arithmetic mean (standard deviation)				
Baseline (n=6,3,5,4)	-1.10 (± 1.07)	0.13 (± 2.39)	-0.78 (± 0.70)	-0.43 (± 0.92)
Week 25 (n=5,4,5,4)	-1.74 (± 2.01)	-1.05 (± 2.61)	-1.36 (± 0.99)	0.15 (± 1.07)
Change from Baseline at Week 25 (n=5,2,5,3)	-0.60 (± 2.16)	-0.60 (± 0.71)	-0.58 (± 0.76)	0.47 (± 1.76)

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Change From Baseline in Eyelid Position Measurements: Interpalpebral Fissure Distance (IPFD) - Left Non-Flash and Right Non-Flash at Week 25

End point title	PAP: Change From Baseline in Eyelid Position Measurements: Interpalpebral Fissure Distance (IPFD) - Left Non-Flash and Right Non-Flash at Week 25

End point description:

IPFD is the widest vertical distance (in millimetres) between the upper eyelid and the lower eyelid when the subject is looking in "primary gaze" (i.e. normal gaze when looking straight forward). Images were taken while the subject was wearing a pair of empty eyeglass frames with millimetres rulers attached as a standardised tool to measure eyelid position without camera flash. A negative change from Baseline indicated a decrease and positive change from Baseline indicated an increase in measured distance. Analysis was performed on safety population.

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	5	6
Units: millimetres				
arithmetic mean (standard deviation)				
Left non-Flash	-0.67 (± 1.54)	1.30 (± 1.48)	1.30 (± 0.76)	-0.50 (± 0.77)
Right non-Flash	-0.92 (± 1.66)	0.70 (± 1.25)	0.90 (± 1.14)	-0.25 (± 1.13)

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Change From Baseline in Eyelid Position Measurements: Left and Right Margin Reflex Distance (MRD) at Week 25

End point title	PAP: Change From Baseline in Eyelid Position Measurements: Left and Right Margin Reflex Distance (MRD) at Week 25

End point description:

The MRD is the vertical distance (in millimetres) between the light reflex and the upper eyelid when the subject was looking in "primary gaze" while fixating on a light source. Images were taken while the subjects was wearing a pair of empty eyeglass frames with millimetres rulers attached as a standardised tool to measure eyelid position. A negative change from Baseline indicated a decrease and positive change from Baseline indicated an increase in measured distance. Analysis was performed on safety population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	5	6
Units: millimetres				
arithmetic mean (standard deviation)				
Left MRD (n=6,4,4,6)	-0.08 (± 1.53)	-0.38 (± 0.85)	0.88 (± 1.11)	0.08 (± 0.74)
Right MRD (n=6,5,4,6)	-0.50 (± 1.61)	-0.50 (± 1.27)	0.63 (± 1.03)	-0.08 (± 0.74)

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Change From Baseline in Eyelid Position Measurements Assessed by Margin Pupil Distance (MPD) - Left Non- Flash and Right Non-Flash at Week 25

End point title	PAP: Change From Baseline in Eyelid Position Measurements Assessed by Margin Pupil Distance (MPD) - Left Non- Flash and Right Non-Flash at Week 25

End point description:

The MPD is the vertical distance (in millimetres) between the center of the pupil and the upper eyelid margin. Images were taken while the subject was wearing a pair of empty eyeglass frames with millimetres rulers attached as a standardised tool to measure eyelid position without camera flash. A negative change from Baseline indicated a decrease and positive change from Baseline indicated an increase in measured distance. Analysis was performed on safety population. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	5	6
Units: millimetres				
arithmetic mean (standard deviation)				
MPD Left Non-Flash (n=6,4,5,6)	-0.83 (± 1.44)	0.75 (± 1.19)	0.40 (± 0.42)	-0.50 (± 0.32)
MPD Right Non-Flash (n=6,5,5,6)	-0.25 (± 1.41)	0.50 (± 1.06)	0.30 (± 0.91)	0.00 (± 0.71)

Statistical analyses

No statistical analyses for this end point

Secondary: PAP: Change From Baseline in Creatine Kinase Value at Week 25

End point title	PAP: Change From Baseline in Creatine Kinase Value at Week 25

End point description:

Change from Baseline in Creatine kinase value (to assess muscle damage) at Week 25 were reported in this endpoint. Analysis was performed on safety population.

End point type	Secondary

End point timeframe:

Baseline, Week 25

End point values	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3b: Alglucosidase Alfa
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	5	6
Units: international units per liters				
arithmetic mean (standard deviation)	-208.67 (± 382.34)	-476.60 (± 467.20)	-421.40 (± 413.39)	-1.33 (± 51.20)

Statistical analyses

No statistical analyses for this end point

Secondary: ETP: Number of Subjects With Treatment-emergent Adverse Events, Serious Treatment-emergent Adverse Events, and Adverse Event of Special Interest

End point title	ETP: Number of Subjects With Treatment-emergent Adverse Events, Serious Treatment-emergent Adverse Events, and Adverse Event of Special Interest

End point description:

Data for this endpoint will be reported at the time of anticipated last subject last visit results posting (December 2025).

End point type	Secondary

End point timeframe:

From Week 26 to Week 371

End point values	ETP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	ETP:Alglucosidase Alfa in PAP Then Avalglucosidase Alfa in ETP	Pooled Arm ETP: Avalglucosidase Alfa 40 mg/kg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[9]	0[10]	0[11]	
Units: subjects				

Notes:

[9] - Data will be reported at time of anticipated last subject last visit results posting (Dec 2025).

[10] - Data will be reported at time of anticipated last subject last visit results posting (Dec 2025).

[11] - Data will be reported at time of anticipated last subject last visit results posting (Dec 2025).

Statistical analyses

No statistical analyses for this end point

Secondary: ETP: Number of Subjects With Infusion-associated Reactions

End point title	ETP: Number of Subjects With Infusion-associated Reactions

End point description:

Data for this endpoint will be reported at the time of anticipated last subject last visit results posting (December 2025).

End point type	Secondary

End point timeframe:

From Week 26 to Week 371

End point values	ETP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	ETP:Alglucosidase Alfa in PAP Then Avalglucosidase Alfa in ETP	Pooled Arm ETP: Avalglucosidase Alfa 40 mg/kg	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[12]	0[13]	0[14]	
Units: subjects				

Notes:

[12] - Data will be reported at time of anticipated last subject last visit results posting (Dec 2025).

[13] - Data will be reported at time of anticipated last subject last visit results posting (Dec 2025).

[14] - Data will be reported at time of anticipated last subject last visit results posting (Dec 2025).

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From Day 1 to Week 25 in PAP and from Week 26 to 102 in ETP. Safety data were planned to be collected and analysed for pooled population of subjects who received avalglucosidase alfa 40 mg/kg (Cohorts 2 and 3a of PAP) in ETP. AE collection still ongoing.

Adverse event reporting additional description:

TEAEs:AEs that developed/worsened in grade/become serious during treatment epoch(PAP:1st study drug dose in ETP/4 weeks after last infusion for those who didn't get into ETP/2 weeks after last infusion in PAP)(ETP:1st dose of study drug in ETP to last dose of study drug+4 weeks/2 weeks if subject got enrolled in another study/received ERT). Safety.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg

Reporting group description:

Avalglucosidase alfa 20 mg/kg IV infusion qow for 25 weeks in PAP.

Reporting group title	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg

Reporting group description:

Avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in PAP

Reporting group title	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg

Reporting group description:

After determination of the highest tolerated avalglucosidase alfa dose in Cohort 1 and Cohort 2 (after at least 5 subjects in each Cohort 1 and Cohort 2 had received the 7th dose of avalglucosidase alfa or completed Week 13 with a minimum of 6 infusions), subjects received avalglucosidase alfa 40 mg/kg (the highest tolerated dose) IV infusion qow for 25 weeks in PAP.

Reporting group title	PAP: Cohort 3b: Alglucosidase Alfa

Reporting group description:

After determination of the highest tolerated avalglucosidase alfa dose in Cohort 1 and Cohort 2 (after at least 5 subjects in each Cohort 1 and Cohort 2 had received the 7th dose of avalglucosidase alfa or completed Week 13 with a minimum of 6 infusions), subjects received alglucosidase alfa at their current stable dose (defined as dose [between 20 mg/kg qow and 40 mg/kg weekly as per physician] administered regularly for a minimum of 6 months immediately prior to entry in this study) IV infusion for 25 weeks in PAP. After PAP subjects received avalglucosidase alfa 40 mg/kg IV infusion qow from Week 26 up to Week371 in ETP.

Reporting group title	ETP: Avalglucosidase Alfa dose 20 mg/kg

Reporting group description:

Included all subjects of Cohort 1 who received avalglucosidase alfa 20 mg/kg IV infusion qow for 25 weeks in PAP, followed by same treatment from Week 26 up to Week 371 in ETP.

Reporting group title	Pooled Arm ETP: Avalglucosidase Alfa 40 mg/kg

Reporting group description:

Pooled arm included all subjects of Cohorts 2 and 3a who received avalglucosidase alfa 40 mg/kg IV infusion qow for 25 weeks in PAP, followed by same treatment from Week 26 up to Week 371 in ETP.

Reporting group title	ETP:Alglucosidase Alfa in PAP Then Avalglucosidase Alfa in ETP

Reporting group description:

Included all subjects of Cohort 3b who received alglucosidase alfa at their current stable dose (defined as dose [between 20 mg/kg qow and 40 mg/kg weekly as per physician] administered regularly for a minimum of 6 months immediately prior to entry in this study) IV infusion for 25 weeks in the PAP and after PAP, switched to receive avalglucosidase alfa 40 mg/kg IV infusion qow from Week 26 up to Week 371 in ETP.

Serious adverse events	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	3 / 5 (60.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Femur Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint Dislocation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post Procedural Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial Thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Tympanic Membrane Perforation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eyelid Ptosis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Strabismus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal Hypertrophy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Consolidation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Distress			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (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
Tonsillar Hypertrophy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Infection Pseudomonal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection Viral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device Malfunction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	PAP: Cohort 3b: Alglucosidase Alfa	ETP: Avalglucosidase Alfa dose 20 mg/kg	Pooled Arm ETP: Avalglucosidase Alfa 40 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	4 / 6 (66.67%)	2 / 10 (20.00%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Femur Fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint Dislocation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (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
Post Procedural Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (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
Cardiac disorders			
Atrial Thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Tympanic Membrane Perforation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (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
Eye disorders			
Eyelid Ptosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Strabismus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal Hypertrophy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (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
Lung Consolidation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (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
Respiratory Distress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar Hypertrophy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (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
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (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
Lung Infection Pseudomonal			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (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

Otitis Media			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (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	1 / 6 (16.67%)	2 / 6 (33.33%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (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
Urinary Tract Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (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
Product issues			
Device Malfunction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (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

Serious adverse events	ETP:Alglucosidase Alfa in PAP Then Avalglucosidase Alfa in ETP		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Femur Fracture			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint Dislocation			

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post Procedural Haemorrhage				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial Thrombosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pyrexia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Tympanic Membrane Perforation				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Eyelid Ptosis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Strabismus				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Adenoidal Hypertrophy				

subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung Consolidation				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Distress				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillar Hypertrophy				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Gastroenteritis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung Infection Pseudomonal				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis Media				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device Malfunction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	PAP: Cohort 1: Avalglucosidase Alfa 20 mg/kg	PAP: Cohort 2: Avalglucosidase Alfa 40 mg/kg	PAP: Cohort 3a: Avalglucosidase Alfa 40 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	5 / 5 (100.00%)	5 / 5 (100.00%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Catheter Site Oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Device Related Thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Feeling Hot			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Infusion Site Swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injection Site Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Oedema Peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)	2 / 5 (40.00%)
occurrences (all)	4	4	2
Reproductive system and breast disorders			
Genital Erosion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Bronchiectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cough			

subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	2 / 5 (40.00%)
occurrences (all)	1	1	4
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Increased Upper Airway Secretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Laryngeal Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lower Respiratory Tract Congestion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nasal Congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Oropharyngeal Pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Productive Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pulmonary Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Tonsillar Hypertrophy			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Enuresis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nightmare			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Staring			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device Occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Investigations			
Alpha-1 Acid Glycoprotein Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Faecal Calprotectin Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haemoglobin Decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Heart Rate Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Arthropod Bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Arthropod Sting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Craniocerebral Injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	2	2	0
Ligament Sprain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Muscle Strain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Procedural Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Skin Abrasion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Sunburn			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Thermal Burn			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vascular Access Complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Wound			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Pericardial Effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	2 / 5 (40.00%)
occurrences (all)	1	0	2
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymph Node Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Cerumen Impaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Deafness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Ear Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Excessive Cerumen Production			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Middle Ear Effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Otorrhoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Conjunctivochalasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye Discharge			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Eye Irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Keratopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lacrimation Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal Hernia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Aphthous Ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dental Caries			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	2 / 5 (40.00%)
occurrences (all)	0	1	2
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Faeces Soft			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Loose Tooth			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Mucous Stools			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Regurgitation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Teething			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	1	5	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	2 / 5 (40.00%)
occurrences (all)	0	3	2
Skin and subcutaneous tissue disorders			
Alopecia Areata			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Blister			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dermatitis Atopic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dermatitis Contact			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Dermatitis Diaper			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Eczema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Intertrigo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	2 / 5 (40.00%)
occurrences (all)	0	1	3
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematuria			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neurogenic Bladder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Back Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Foot Deformity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Osteopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain In Extremity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	3	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Bronchitis Viral			

subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Enterovirus Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Fungal Skin Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hand-Foot-And-Mouth Disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lung Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lung Infection Pseudomonal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nail Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Otitis Externa			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Otitis Media			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Parainfluenzae Virus Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pneumonia Pseudomonal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Stoma Site Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tinea Pedis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	2 / 5 (40.00%)
occurrences (all)	5	0	3
Urinary Tract Infection			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Urinary Tract Infection Bacterial			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Viral Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Viral Rash			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	PAP: Cohort 3b: Alglucosidase Alfa	ETP: Avalglucosidase Alfa dose 20 mg/kg	Pooled Arm ETP: Avalglucosidase Alfa 40 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	6 / 6 (100.00%)	7 / 10 (70.00%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Catheter Site Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Device Related Thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Feeling Hot			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infusion Site Swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Injection Site Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Malaise			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oedema Peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	2 / 10 (20.00%)
occurrences (all)	1	9	3
Reproductive system and breast disorders			
Genital Erosion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Bronchiectasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	13	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	2 / 10 (20.00%)
occurrences (all)	0	2	3
Increased Upper Airway Secretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Laryngeal Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lower Respiratory Tract Congestion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasal Congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Productive Cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Pulmonary Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory Tract Congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tonsillar Hypertrophy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Upper Respiratory Tract Congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Enuresis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nightmare			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Staring			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Product issues			
Device Occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alpha-1 Acid Glycoprotein Increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Faecal Calprotectin Increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Haemoglobin Decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Heart Rate Increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Arthropod Sting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Craniocerebral Injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Fall			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	2 / 10 (20.00%)
occurrences (all)	0	2	2
Ligament Sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle Strain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Procedural Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin Abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Thermal Burn			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vascular Access Complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Pericardial Effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 10 (10.00%)
occurrences (all)	0	14	1
Presyncope			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Lymph Node Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Cerumen Impaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Deafness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Excessive Cerumen Production			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
Middle Ear Effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Otorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctivochalasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye Discharge			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye Irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Keratopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lacrimation Increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Hernia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Abdominal Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Aphthous Ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dental Caries			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 10 (10.00%)
occurrences (all)	0	4	3
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Faeces Soft			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Loose Tooth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mucous Stools			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	1	6	0
Regurgitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Teething			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	3 / 6 (50.00%)	1 / 6 (16.67%)	2 / 10 (20.00%)
occurrences (all)	3	3	3
Skin and subcutaneous tissue disorders			
Alopecia Areata			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Blister			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis Atopic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis Contact			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis Diaper			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Intertrigo			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	2 / 10 (20.00%)
occurrences (all)	2	1	3
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Neurogenic Bladder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Back Pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Foot Deformity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Osteopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain In Extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Bronchitis Viral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Enterovirus Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fungal Skin Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hand-Foot-And-Mouth Disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Lung Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lung Infection Pseudomonal			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nail Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Otitis Externa			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Otitis Media			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Parainfluenzae Virus Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Pneumonia Pseudomonal			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Stoma Site Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tinea Pedis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	1 / 10 (10.00%)
occurrences (all)	1	3	1
Urinary Tract Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Urinary Tract Infection Bacterial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Viral Infection			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Viral Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	ETP:Alglucosidase Alfa in PAP Then Avalglucosidase Alfa in ETP		

Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 3 (100.00%)		
General disorders and administration site conditions			
Asthenia subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Catheter Site Oedema subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Device Related Thrombosis subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Fatigue subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Feeling Hot subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Infusion Site Swelling subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Injection Site Pain subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Malaise subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oedema Peripheral subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pyrexia subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			

Genital Erosion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Atelectasis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Bronchiectasis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Increased Upper Airway Secretion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Laryngeal Oedema			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lower Respiratory Tract Congestion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nasal Congestion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Oropharyngeal Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Productive Cough			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pulmonary Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Respiratory Tract Congestion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tonsillar Hypertrophy			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Upper Respiratory Tract Congestion			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Psychiatric disorders			
Enuresis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Nightmare			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Staring			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Product issues			
Device Occlusion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Investigations			

Alpha-1 Acid Glycoprotein Increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Faecal Calprotectin Increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Haemoglobin Decreased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Heart Rate Increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Arthropod Sting			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Craniocerebral Injury			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Ligament Sprain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Muscle Strain			

subjects affected / exposed occurrences (all) Procedural Pain subjects affected / exposed occurrences (all) Skin Abrasion subjects affected / exposed occurrences (all) Sunburn subjects affected / exposed occurrences (all) Thermal Burn subjects affected / exposed occurrences (all) Vascular Access Complication subjects affected / exposed occurrences (all) Wound subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0		
Cardiac disorders Pericardial Effusion subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all) Seizure subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0		
Blood and lymphatic system disorders			

Lymph Node Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Cerumen Impaction			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Deafness			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Ear Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Excessive Cerumen Production			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Middle Ear Effusion			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Otorrhoea			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctivochalasis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Eye Discharge			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Eye Irritation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Keratopathy			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Lacrimation Increased			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal Hernia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Abdominal Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Aphthous Ulcer			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dental Caries			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Faeces Soft			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Loose Tooth			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Mucous Stools			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Nausea				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Regurgitation				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Teething				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Toothache				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Vomiting				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Skin and subcutaneous tissue disorders				
Alopecia Areata				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Blister				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Dermatitis Atopic				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dermatitis Contact				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Dermatitis Diaper				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Eczema				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Erythema				

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Intertrigo			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Neurogenic Bladder			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Back Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Foot Deformity			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal Chest Pain			

subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Musculoskeletal Pain			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Osteopenia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Pain In Extremity			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Bronchitis Viral			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Enterovirus Infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Fungal Skin Infection			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Hand-Foot-And-Mouth Disease			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

Influenza				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Lower Respiratory Tract Infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Lung Infection				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Lung Infection Pseudomonal				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Nail Infection				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Otitis Externa				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Otitis Media				
subjects affected / exposed	1 / 3 (33.33%)			
occurrences (all)	1			
Parainfluenzae Virus Infection				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Pneumonia Pseudomonal				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			
Rhinitis				
subjects affected / exposed	0 / 3 (0.00%)			
occurrences (all)	0			

Sepsis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Stoma Site Infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tinea Pedis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Urinary Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Urinary Tract Infection Bacterial			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		
Viral Infection			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Viral Rash			
subjects affected / exposed	0 / 3 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 July 2018	Following changes were made: - Changed the sample size: Cap of 5 subjected per cohort in Stage 1, Cohort 1 and Cohort 2, was removed to alleviate constraints in conduct of the study and maximise the collection of data in pediatric subjects. At least 10 subjects will be included in Cohort 3. -Changes to endpoints: Face, Legs, Activity, Cry, and Consolability scale assessment was removed from the protocol to reduce subjects and investigational staff burden due to the limited expected value of the assessment. -Changed sampling for pharmacodynamic variables: Collection of dry blood spot had been added for determination of exploratory biomarkers in addition to samples of urine and plasma to develop alternative assays and potentially reduce blood volume needed for testing in the future. - Change to inclusion/exclusion criteria: Beta-blockers are no longer a prohibited concomitant medication as they are considered standard of care in this IOPD subject population.
24 March 2020	Following changes were made: - In order to allow study subjects to continue to receive the investigational medicinal product (IMP) after Week 145, the study had been extended to an additional period of up to 226 weeks (Week 371) or until avalglucosidase alfa was approved in the subject's country, whichever came first. - In countries where it was permitted, home infusion of avalglucosidase alfa in the extension period might be allowed. - Clarifications were given regarding the conditions for temporary IMP discontinuation with DMC consultation. - Clarifications were given regarding AESI related to LFT values that can fluctuate as part of the underlying Pompe disease. - Clarification was given in the tertiary endpoints that the Motor Skills Checklist was completed in concert with the Gross Motor Function Classification System, Expanded and Revised. - Clarification was given in the description of some tertiary endpoints. - Clarification was given regarding the possibility of additional interim analysis for regulatory purpose during the extension period. - Clarification was given regarding the order of motor assessments. - As subjects were no longer treated with alglucosidase alfa after Week 25 when entering the extension period, the collection of samples for analysis of anti-alglucosidase alfa antibodies was removed from the follow-up after PAP. - Relevant sections were updated to reflect practices as outlined in the current protocol template.
05 January 2021	Following changes were made: - Included the recommendations that were developed for the Covid-19 pandemic period and shared with the sites/Investigators. These recommendations remained applicable after the end of the pandemic, especially regarding the post-infusion surveillance period. - Relevant sections wordings were updated that were compliant with general guidance, including monitoring techniques. - Updated home infusion to harmonize across the different studies included in the avalglucosidase alfa development program.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported