Clinical trial results:
An open-label, multicenter, multinational extension study of the long-term safety and pharmacokinetics of repeated biweekly infusions of avalglucosidase alfa (neoGAA, GZ402666) in patients with Pompe disease

Summary

EudraCT number	2013-003321-28
Trial protocol	BE NL DK DE FR
Global end of trial date	12 December 2022

Results information

Result version number	v1
This version publication date	24 December 2023
First version publication date	24 December 2023

Trial information

Trial identification

Sponsor protocol code	LTS13769

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02032524
WHO universal trial number (UTN)	U1111-1147-3439

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	450 Water Street, Cambridge, Massachusetts, United States, 02141
Public contact	Trial Transparency Team, Sanofi-Aventis Recherche & Developpement, contact-us@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi-Aventis Recherche & Developpement, contact-us@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety and pharmacokinetics (PK) of avalglucosidase alfa in participants with Pompe disease who have previously completed an avalglucosidase alfa study.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 February 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	24
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	20
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 17 centers in 7 countries. A total of 21 participants completed the open-label study TDR12857 (NCT01898364). Of which, 19 participants were enrolled in this study. There was no screening period in this study.

Pre-assignment

Screening details:

Participants who completed the open-label TDR12857 study were part of this study. This was an open-label study. As prespecified, data were analyzed and presented combinedly for studies TDR12857 and LTS13769.

Period 1

Period 1 title	TDR12857 Study
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Avalglucosidase alfa 5 mg/kg

Arm description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 5 milligram per kilogram (mg/kg) intravenous (IV) infusion every other week (qow) for up to 454 weeks.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 5 mg/kg was administered through IV infusion qow for up to 454 weeks.

Arm title	Group 1: Avalglucosidase alfa 10 mg/kg

Arm description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 432 weeks.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 10 mg/kg was administered through IV infusion qow for up to 432 weeks.

Arm title	Group 1: Avalglucosidase alfa 20 mg/kg

Arm description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 421 weeks.

Arm type	Experimental

Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 20 mg/kg was administered through IV infusion qow for up to 421 weeks.

Arm title	Group 2: Avalglucosidase alfa 5 mg/kg

Arm description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 5 mg/kg IV infusion qow for up to 424 weeks.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 5 mg/kg was administered through IV infusion qow for up to 424 weeks.

Arm title	Group 2: Avalglucosidase alfa 10 mg/kg

Arm description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 450 weeks.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 10 mg/kg was administered through IV infusion qow for up to 450 weeks.

Arm title	Group 2: Avalglucosidase alfa 20 mg/kg

Arm description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 445 weeks.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 20 mg/kg was administered through IV infusion qow for up to 445 weeks.

Number of subjects in period 1	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg
Started	4	3	3
Completed	3	3	3
Not completed	1	0	0
Wishes To Withdraw	-	-	-
Adverse Event	1	-	-

Number of subjects in period 1	Group 2: Avalglucosidase alfa 5 mg/kg	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg
Started	4	4	6
Completed	3	4	5
Not completed	1	0	1
Wishes To Withdraw	1	-	1
Adverse Event	-	-	-

Period 2

Period 2 title	LTS13769 Study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Avalglucosidase alfa 5 mg/kg

Arm description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 5 mg/kg IV infusion qow for up to 454 weeks.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 5 mg/kg was administered through IV infusion qow for up to 454 weeks.

Arm title	Group 1: Avalglucosidase alfa 10 mg/kg

Arm description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 432 weeks.

Arm type	Experimental

Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 10 mg/kg was administered through IV infusion qow for up to 432 weeks.

Arm title	Group 1: Avalglucosidase alfa 20 mg/kg

Arm description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 421 weeks.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 20 mg/kg was administered through IV infusion qow for up to 421 weeks.

Arm title	Group 2: Avalglucosidase alfa 5 mg/kg

Arm description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 5 mg/kg IV infusion qow for up to 424 weeks.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 5 mg/kg was administered through IV infusion qow for up to 424 weeks.

Arm title	Group 2: Avalglucosidase alfa 10 mg/kg

Arm description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 450 weeks.

Arm type	Experimental
Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 10 mg/kg was administered through IV infusion qow for up to 450 weeks.

Arm title	Group 2: Avalglucosidase alfa 20 mg/kg

Arm description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 445 weeks.

Arm type	Experimental

Investigational medicinal product name	Avalglucosidase alfa
Investigational medicinal product code	neoGAA, GZ402666
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Avalglucosidase alfa 20 mg/kg was administered through IV infusion qow for up to 445 weeks.

Number of subjects in period 2[1]	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg
Started	3	2	3
Completed	3	1	2
Not completed	0	1	1
Wishes To Withdraw	-	1	-
Adverse Event	-	-	1
Unspecified	-	-	-

Number of subjects in period 2[1]	Group 2: Avalglucosidase alfa 5 mg/kg	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg
Started	3	3	5
Completed	3	2	4
Not completed	0	1	1
Wishes To Withdraw	-	1	-
Adverse Event	-	-	-
Unspecified	-	-	1

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: Only eligible participants enrolled in LTS13769 study.

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Avalglucosidase alfa 5 mg/kg
Reporting group description:	
Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 5 milligram per kilogram (mg/kg) intravenous (IV) infusion every other week (qow) for up to 454 weeks.	
Reporting group title	Group 1: Avalglucosidase alfa 10 mg/kg
Reporting group description:	
Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 432 weeks.	
Reporting group title	Group 1: Avalglucosidase alfa 20 mg/kg
Reporting group description:	
Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 421 weeks.	
Reporting group title	Group 2: Avalglucosidase alfa 5 mg/kg
Reporting group description:	
Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 5 mg/kg IV infusion qow for up to 424 weeks.	
Reporting group title	Group 2: Avalglucosidase alfa 10 mg/kg
Reporting group description:	
Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 450 weeks.	
Reporting group title	Group 2: Avalglucosidase alfa 20 mg/kg
Reporting group description:	
Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 445 weeks.	

Reporting group values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg
Number of subjects	4	3	3
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	3	2
From 65-84 years	1	0	1
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	3	3	1
Male	1	0	2
Race Units: Subjects			
White	4	1	3

Black or African American	0	0	0
Not Reported	0	1	0
Multiple	0	1	0

Reporting group values	Group 2: Avalglucosidase alfa 5 mg/kg	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg
Number of subjects	4	4	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	4	5
From 65-84 years	1	0	1
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	2	1	2
Male	2	3	4
Race Units: Subjects			
White	4	3	6
Black or African American	0	1	0
Not Reported	0	0	0
Multiple	0	0	0

Reporting group values	Total		
Number of subjects	24		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	20		
From 65-84 years	4		
85 years and over	0		
Gender categorical Units: Subjects			
Female	12		
Male	12		

Race Units: Subjects			
White	21		
Black or African American	1		
Not Reported	1		
Multiple	1		

End points

End points reporting groups

Reporting group title	Group 1: Avalglucosidase alfa 5 mg/kg
Reporting group description:	
Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 5 milligram per kilogram (mg/kg) intravenous (IV) infusion every other week (qow) for up to 454 weeks.	
Reporting group title	Group 1: Avalglucosidase alfa 10 mg/kg
Reporting group description:	
Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 432 weeks.	
Reporting group title	Group 1: Avalglucosidase alfa 20 mg/kg
Reporting group description:	
Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 421 weeks.	
Reporting group title	Group 2: Avalglucosidase alfa 5 mg/kg
Reporting group description:	
Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 5 mg/kg IV infusion qow for up to 424 weeks.	
Reporting group title	Group 2: Avalglucosidase alfa 10 mg/kg
Reporting group description:	
Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 450 weeks.	
Reporting group title	Group 2: Avalglucosidase alfa 20 mg/kg
Reporting group description:	
Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 445 weeks.	
Reporting group title	Group 1: Avalglucosidase alfa 5 mg/kg
Reporting group description:	
Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 5 mg/kg IV infusion qow for up to 454 weeks.	
Reporting group title	Group 1: Avalglucosidase alfa 10 mg/kg
Reporting group description:	
Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 432 weeks.	
Reporting group title	Group 1: Avalglucosidase alfa 20 mg/kg
Reporting group description:	
Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 421 weeks.	
Reporting group title	Group 2: Avalglucosidase alfa 5 mg/kg
Reporting group description:	
Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 5 mg/kg IV infusion qow for up to 424 weeks.	
Reporting group title	Group 2: Avalglucosidase alfa 10 mg/kg
Reporting group description:	
Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 450 weeks.	
Reporting group title	Group 2: Avalglucosidase alfa 20 mg/kg
Reporting group description:	
Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 445 weeks.	
Subject analysis set title	Group 1: Avalglucosidase Alfa
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 5 or 10 or 20 mg/kg IV infusion qow for up to 454 weeks.

Subject analysis set title	Group 2: Avalglucosidase Alfa
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 5 or 10 or 20 mg/kg IV infusion qow for up to 450 weeks.

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (TESAEs), Infusion Associated Reactions (IARs) and Deaths

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (TESAEs), Infusion Associated Reactions (IARs) and Deaths[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An serious AE (SAE) is any untoward medical occurrence that results: death or life-threatening or inpatient hospitalization or prolongation of existing hospitalization or persistent or significant disability or congenital anomaly or medically important event. TEAEs are defined as AEs that develop or worsen during the on-treatment period [that is, from the time of first dose of IMP up to 4 weeks after the last administration of the IMP]. Protocol-defined IARs were defined as AEs that occur during either the infusion or post-infusion observation period (that is, up to 2 hours or longer following the infusion as per the Investigator's discretion) which were deemed to be related or possibly related to the IMP. Results are based on the safety analysis set.

End point type	Primary

End point timeframe:

From first dose of investigational medicinal product (IMP) up to 4 weeks after the last treatment administration of the IMP, a maximum up to 458 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: participants				
Any TEAEs	4	3	3	4
TESAEs	3	1	1	1
Protocol-defined IARs	2	0	2	2
Any TEAE leading to death	0	0	0	0

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: participants				
Any TEAEs	4	6		

TESAEs	1	2		
Protocol-defined IARs	0	1		
Any TEAE leading to death	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Physical Examination Abnormalities

End point title	Number of Participants With Clinically Significant Physical Examination Abnormalities[2]

End point description:

Physical examination included, at a minimum, an assessment of the participant's general appearance; skin; head, eyes, ears, nose, and throat; examinations of lymph nodes, abdomen, extremities/joints, neurological and mental status; heart and respiratory auscultation; peripheral arterial pulse; and pupil, knee, achilles, and plantar reflexes. Results are based on the safety analysis set which included all participants who received at least 1 complete infusion of IMP.

End point type	Primary

End point timeframe:

From first dose of IMP up to 4 weeks after the last treatment administration of the IMP, a maximum up to 458 weeks

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: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: participants				
Achilles Reflexes	0	0	0	0
General Appearance	0	0	0	0
Knee Reflexes	0	0	0	0
Lymph Nodes	0	0	0	0
Neurological Status	0	0	0	0

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: participants				
Achilles Reflexes	0	1		
General Appearance	0	1		
Knee Reflexes	0	1		
Lymph Nodes	0	1		

Neurological Status	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Potentially Clinically Significant Abnormalities in Biochemistry

End point title	Number of Participants With Potentially Clinically Significant Abnormalities in Biochemistry[3]

End point description:

Blood samples were collected to determine the clinical chemistry laboratory abnormalities. Results are based on the safety analysis set which included all participants who received at least 1 complete infusion of IMP. Here, mmol/L= millimoles per liter, LLN= lower limit of normal, and ULN= upper limit of normal.

End point type	Primary

End point timeframe:

From first dose of IMP up to 4 weeks after the last treatment administration of the IMP, a maximum up to 458 weeks

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: participants				
Glucose: <=3.9 mmol/L and < LLN	2	2	2	1
Glucose:>=11.1 mmol/L(unfasted);>=7 mmol/L(fasted)	2	0	1	1
Sodium: <=129 mmol/L	0	0	0	1
Sodium: >=160 mmol/L	0	0	0	0
Potassium: <3 mmol/L	0	0	0	1
Potassium: >=5.5 mmol/L	0	0	0	0
Chloride: <80 mmol/L	0	0	0	0
Chloride: >115 mmol/L	0	0	0	0
Albumin: <=25 gram per liter (g/L)	0	0	0	0
Creatinine: >=150 micromoles/L (Adults)	0	0	0	0
Creatinine: >=100% change from baseline	0	0	0	0
Creatinine: >=30% change from baseline	0	0	0	1
Urea Nitrogen: >=17 mmol/L	0	0	1	0
Aspartate Aminotransferase: >3 ULN	0	2	0	1
Aspartate Aminotransferase: >5 ULN	0	1	0	0
Aspartate Aminotransferase: >10 ULN	0	0	0	0
Alanine Aminotransferase: >3 ULN	0	2	0	1

Alanine Aminotransferase: >5 ULN	0	1	0	0
Alanine Aminotransferase: >10 ULN	0	0	0	0
Alanine Aminotransferase >3ULN and Bilirubin >2ULN	0	0	0	0
Alkaline Phosphatase: >1.5 ULN	0	0	0	0
Total Bilirubin: >1.5 ULN	1	0	1	0
Total Bilirubin: >2 ULN	0	0	0	0
Direct Bilirubin >35% Bilirubin; Bilirubin >1.5ULN	0	0	0	0

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: participants				
Glucose: <=3.9 mmol/L and < LLN	2	1		
Glucose:>=11.1 mmol/L(unfasted);>=7 mmol/L(fasted)	1	3		
Sodium: <=129 mmol/L	0	1		
Sodium: >=160 mmol/L	0	0		
Potassium: <3 mmol/L	1	0		
Potassium: >=5.5 mmol/L	0	1		
Chloride: <80 mmol/L	0	0		
Chloride: >115 mmol/L	0	0		
Albumin: <=25 gram per liter (g/L)	0	0		
Creatinine: >=150 micromoles/L (Adults)	0	1		
Creatinine: >=100% change from baseline	0	2		
Creatinine: >=30% change from baseline	0	2		
Urea Nitrogen: >=17 mmol/L	0	0		
Aspartate Aminotransferase: >3 ULN	0	0		
Aspartate Aminotransferase: >5 ULN	0	0		
Aspartate Aminotransferase: >10 ULN	0	0		
Alanine Aminotransferase: >3 ULN	0	0		
Alanine Aminotransferase: >5 ULN	0	0		
Alanine Aminotransferase: >10 ULN	0	0		
Alanine Aminotransferase >3ULN and Bilirubin >2ULN	0	0		
Alkaline Phosphatase: >1.5 ULN	0	0		
Total Bilirubin: >1.5 ULN	0	2		
Total Bilirubin: >2 ULN	0	0		
Direct Bilirubin >35% Bilirubin; Bilirubin >1.5ULN	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Potentially Clinically Significant Abnormalities in Hematology

End point title	Number of Participants With Potentially Clinically Significant Abnormalities in Hematology[4]

End point description:

Blood samples were collected to determine the hematology laboratory significant abnormalities. Results are based on the safety analysis set which included all participants who received at least 1 complete infusion of IMP. Here, v/v= volume per volume and Bk= black.

End point type	Primary

End point timeframe:

From first dose of IMP up to 4 weeks after the last treatment administration of the IMP, a maximum up to 458 weeks

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: participants				
Hemoglobin: <=115 g/L (Male); <=95 g/L (Female)	1	0	1	0
Hemoglobin: >=185 g/L (Male); >=165 g/L (Female)	0	0	0	0
Hemoglobin: Decrease from baseline >=20 g/L	1	1	1	2
Hematocrit: <=0.37 v/v (Male); <=0.32 v/v (Female)	1	0	1	1
Hematocrit: >=0.55 v/v (Male); >=0.5 v/v (Female)	0	0	0	0
Platelet Count: <100x10^9/L	0	0	0	0
Platelet Count: >=700x10^9/L	0	0	0	0
Erythrocyte Count: >=6x10^12/L	0	0	0	0
Monocytes: >0.7x10^9/L	1	0	1	1
Basophils: >0.1x10^9/L	1	0	2	1
Leukocyte Count: <3x10^9/L (Non-Bk); <2x10^9/L(Bk)	0	0	0	0
Leukocyte Count: >=16x10^9/L	0	0	0	0
Neutrophils: <1.5x10^9/L (Non-Bk); <1x10^9/L (Bk)	0	0	0	0
Lymphocytes: >4x10^9/L	0	1	0	0
Eosinophils:>0.5x10^9/L or >ULN (ULN>=0.5x10^9/L)	0	0	0	0

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: participants				
Hemoglobin: <=115 g/L (Male); <=95 g/L (Female)	0	1		
Hemoglobin: >=185 g/L (Male); >=165 g/L (Female)	1	0		
Hemoglobin: Decrease from baseline >=20 g/L	0	1		
Hematocrit: <=0.37 v/v (Male); <=0.32 v/v (Female)	1	1		
Hematocrit: >=0.55 v/v (Male); >=0.5 v/v (Female)	1	0		
Platelet Count: <100x10^9/L	0	0		
Platelet Count: >=700x10^9/L	0	0		
Erythrocyte Count: >=6x10^12/L	1	0		
Monocytes: >0.7x10^9/L	0	0		
Basophils: >0.1x10^9/L	0	0		
Leukocyte Count: <3x10^9/L (Non-Bk); <2x10^9/L(Bk)	0	0		
Leukocyte Count: >=16x10^9/L	0	0		
Neutrophils: <1.5x10^9/L (Non-Bk); <1x10^9/L (Bk)	0	0		
Lymphocytes: >4x10^9/L	0	0		
Eosinophils:>0.5x10^9/L or >ULN (ULN>=0.5x10^9/L)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Urinalysis Parameters

End point title	Change From Baseline in Urinalysis Parameters[5]

End point description:

Last on-treatment (LOT) values were collected at or just prior to the last IMP administration. Results are based on the safety analysis set which included all participants who received at least 1 complete infusion of IMP. Here, n= number of participants analyzed at specific time points, 9999= no participants were analyzed, 99999= standard deviation could not be determined when only 1 participant was analyzed, and BUN= blood urea nitrogen.

End point type	Primary

End point timeframe:

Baseline (Day 1) and last on-treatment values.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: change from baseline				

arithmetic mean (standard deviation)				
Urine BUN: LOT value (n=4,3,3,4,4,6)	60.8 (± 121.0)	-17.6 (± 268.8)	179.5 (± 157.7)	72.9 (± 25.8)
Urine hyaline casts: LOT value (n=0,1,0,0,0,0)	9999 (± 9999)	2.0 (± 99999)	9999 (± 9999)	9999 (± 9999)
Urine leukocytes: LOT value (n=0,1,0,0,0,0)	9999 (± 9999)	-1.0 (± 99999)	9999 (± 9999)	9999 (± 9999)
Urine specific gravity: LOT value (n=3,3,3,2,3,3)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.1)
Urine pH: LOT value (n=3,3,3,2,3,3)	-0.4 (± 1.3)	0.2 (± 1.0)	-0.3 (± 1.1)	0.1 (± 0.5)

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: change from baseline				
arithmetic mean (standard deviation)				
Urine BUN: LOT value (n=4,3,3,4,4,6)	37.1 (± 186.5)	118.8 (± 134.8)		
Urine hyaline casts: LOT value (n=0,1,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		
Urine leukocytes: LOT value (n=0,1,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		
Urine specific gravity: LOT value (n=3,3,3,2,3,3)	0.0 (± 0.0)	-0.0 (± 0.0)		
Urine pH: LOT value (n=3,3,3,2,3,3)	-0.8 (± 0.4)	-0.3 (± 0.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Potentially Clinically Significant Vital Signs Abnormalities

End point title	Number of Participants With Potentially Clinically Significant Vital Signs Abnormalities[6]

End point description:

Participants vital signs were examined to determine the abnormalities. Vital signs included heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP). Results are based on the safety analysis set which included all participants who received at least 1 complete infusion of IMP. Here, mmHg= millimeter of mercury and bpm= beats/minute.

End point type	Primary

End point timeframe:

From first dose of IMP up to 4 weeks after the last treatment administration of the IMP, a maximum up to 458 weeks

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: participants				
SBP:<=95 mmHg and decrease from baseline >=20 mmHg	2	2	2	2
SBP:>=160 mmHg and increase from baseline >=20mmHg	2	0	1	2
DBP:<=45 mmHg and decrease from baseline >=10 mmHg	2	0	0	2
DBP:>=110 mmHg and increase from baseline >=10mmHg	2	0	0	0
HR:<=50 bpm and decrease from baseline >=20 bpm	1	0	1	0
HR:>=120 bpm and increase from baseline >=20 bpm	2	1	2	2

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: participants				
SBP:<=95 mmHg and decrease from baseline >=20 mmHg	3	2		
SBP:>=160 mmHg and increase from baseline >=20mmHg	0	3		
DBP:<=45 mmHg and decrease from baseline >=10 mmHg	0	2		
DBP:>=110 mmHg and increase from baseline >=10mmHg	0	2		
HR:<=50 bpm and decrease from baseline >=20 bpm	1	0		
HR:>=120 bpm and increase from baseline >=20 bpm	2	4		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Body Weight Increased/Decreased

End point title	Number of Participants With Body Weight

End point description:

Body weight was measured in kilograms and collected in the electronic case report forms every 3 months throughout the duration of the study, as well as at the end of study visit. Results are based on the safety analysis set which included all participants who received at least 1 complete infusion of IMP.

End point type	Primary

End point timeframe:

From first dose of IMP up to 4 weeks after the last treatment administration of the IMP, a maximum up to 458 weeks

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: participants	1	0	0	1

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: participants	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Potentially Clinically Significant 12-Lead Electrocardiogram (ECG) Abnormalities

End point title	Number of Participants With Potentially Clinically Significant 12-Lead Electrocardiogram (ECG) Abnormalities[8]

End point description:

Standard 12-lead ECGs were recorded after at least 15 minutes in the supine position using an electrocardiographic device. The following were assessed: heart rate, rhythm, interval between the peaks of successive QRS complexes (RR), interval from the beginning of the P wave until the beginning of the QRS complex (PR), interval from start of the Q wave to the end of the S wave (QRS), interval between the start of the Q wave and the end of the T wave (QT), QT interval corrected for heart rate (QTc) automatic correction evaluation (by the ECG device), QRS axis, R voltage V6, voltage V1, left ventricular hypertrophy criteria, right ventricular hypertrophy criteria, repolarization charges, and overall cardiac impression for each participant. Results are based on the safety analysis set which included all participants who received at least 1 complete infusion of IMP. Here, BCF= Bazett's Correction Formula and FCF= Fridericia's Correction Formula.

End point type	Primary

End point timeframe:

From first dose of IMP up to 4 weeks after the last treatment administration of the IMP, a maximum up to 458 weeks

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: participants				
HR: <50 bpm	1	0	0	0
HR: <50 bpm and decrease from baseline >=20 bpm	0	0	0	0
HR: <40 bpm	0	0	0	0
HR: <40 bpm and decrease from baseline >=20 bpm	0	0	0	0
HR: <30 bpm	0	0	0	0
HR: <30 bpm and decrease from baseline >=20 bpm	0	0	0	0
HR: >90 bpm	0	2	0	0
HR: >90 bpm and increase from baseline >=20 bpm	0	2	0	0
HR: >100 bpm	0	0	1	0
HR: >100 bpm and increase from baseline >=20 bpm	0	0	0	0
HR: >120 bpm	0	0	0	0
HR: >120 bpm and increase from baseline >=20 bpm	0	0	0	0
PR Duration: > 200 millisecond (msec)	0	1	1	0
PR Duration: >200 msec and baseline increase >=25%	0	1	0	0
PR Duration: >220 msec	0	0	0	1
PR Duration: >220 msec and baseline increase >=25%	0	0	0	1
PR Duration: >240 msec	0	0	0	0
PR Duration: >240 msec and baseline increase >=25%	0	0	0	0
QRS Duration: >110 msec	0	0	1	0
QRS Duration:>110 msec and baseline increase >=25%	0	0	0	0
QRS Duration: >120 msec	0	1	1	1
QRS Duration:>120 msec and baseline increase >=25%	0	0	1	0
QTcB - BCF: >450 msec	1	1	1	2
QTcB - BCF: >480 msec	0	0	0	0
QTcB - BCF: >500 msec	0	0	0	0
QTcB - BCF: Baseline increase (30-60) msec	0	2	1	1
QTcB - BCF: Baseline increase >60 msec	0	0	0	0
QTcF - FCF: >450 msec	0	1	0	1
QTcF - FCF: >480 msec	0	0	0	0
QTcF - FCF: >500 msec	0	0	0	0
QTcF - FCF: Baseline increase (30-60) msec	0	1	0	0
QTcF - FCF: Baseline increase >60 msec	0	0	0	0

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: participants				
HR: <50 bpm	1	0		
HR: <50 bpm and decrease from baseline >=20 bpm	0	0		
HR: <40 bpm	0	0		
HR: <40 bpm and decrease from baseline >=20 bpm	0	0		
HR: <30 bpm	0	0		
HR: <30 bpm and decrease from baseline >=20 bpm	0	0		
HR: >90 bpm	0	2		
HR: >90 bpm and increase from baseline >=20 bpm	0	0		
HR: >100 bpm	0	0		
HR: >100 bpm and increase from baseline >=20 bpm	0	0		
HR: >120 bpm	0	0		
HR: >120 bpm and increase from baseline >=20 bpm	0	0		
PR Duration: > 200 millisecond (msec)	0	1		
PR Duration: >200 msec and baseline increase >=25%	0	0		
PR Duration: >220 msec	0	0		
PR Duration: >220 msec and baseline increase >=25%	0	0		
PR Duration: >240 msec	0	0		
PR Duration: >240 msec and baseline increase >=25%	0	0		
QRS Duration: >110 msec	3	4		
QRS Duration:>110 msec and baseline increase >=25%	0	0		
QRS Duration: >120 msec	0	0		
QRS Duration:>120 msec and baseline increase >=25%	0	0		
QTcB - BCF: >450 msec	1	3		
QTcB - BCF: >480 msec	0	0		
QTcB - BCF: >500 msec	0	0		
QTcB - BCF: Baseline increase (30-60) msec	1	4		
QTcB - BCF: Baseline increase >60 msec	1	0		
QTcF - FCF: >450 msec	1	0		
QTcF - FCF: >480 msec	0	0		
QTcF - FCF: >500 msec	0	0		
QTcF - FCF: Baseline increase (30-60) msec	0	1		
QTcF - FCF: Baseline increase >60 msec	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Antidrug Antibodies (ADA) Status, Positive or Negative

End point title	Number of Participants With Antidrug Antibodies (ADA) Status, Positive or Negative[9]

End point description:

ADA negative was defined as ADAs are not detected (that is, negative in screening assay or reactive in screening but negative in confirmatory assay). ADA positive was defined as ADA was detected (that is, an assay signal equal to or greater than the cut-point in the screening assay and was tested positive in the confirmatory assay). Results are based on the Pharmacodynamic (PD) analysis set which included enrolled participants without any critical deviations related to IMP administration, and for whom any PD data were available.

End point type	Primary

End point timeframe:

From first dose of IMP up to 4 weeks after the last treatment administration of the IMP, a maximum up to 458 weeks

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: participants				
ADA negative	0	1	0	1
ADA positive at baseline	0	0	0	1
ADA positive post-baseline	4	2	3	2

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: participants				
ADA negative	1	3		
ADA positive at baseline	3	1		
ADA positive post-baseline	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) of Avalglucosidase Alfa

End point title	Maximum Observed Plasma Concentration (Cmax) of Avalglucosidase Alfa[10]

End point description:

Cmax was defined as maximum plasma concentration observed. The non-compartmental pharmacokinetic (PK) analysis was performed. Results are based on the PK analysis set which included enrolled participants without any critical deviations related to IMP administration, and for whom any PK data were available.

End point type	Primary

End point timeframe:

Predose (prior to infusion), end of the infusion and at 1, 4, 8, 12, and 24 hours post-dose on Week 312

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase Alfa	Group 2: Avalglucosidase Alfa		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	5		
Units: microgram per milliliter (mcg/mL)				
geometric mean (geometric coefficient of variation)	269 (± 16)	234 (± 24)		

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Real Time (AUClast) of Avalglucosidase Alfa

End point title	Area Under the Plasma Concentration Versus Time Curve From Time Zero to the Real Time (AUClast) of Avalglucosidase Alfa[11]

End point description:

AUClast was calculated using the trapezoidal method from time zero to the real time. The non-compartmental PK analysis was performed. Results are based on the PK analysis set which included enrolled participants without any critical deviations related to IMP administration, and for whom any PK data were available.

End point type	Primary

End point timeframe:

Predose (prior to infusion), end of the infusion and at 1, 4, 8, 12, and 24 hours post-dose on Week 312

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase Alfa	Group 2: Avalglucosidase Alfa		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	4		
Units: hour*mcg/mL				
geometric mean (geometric coefficient of variation)	1350 (± 24)	1290 (± 21)		

Statistical analyses

No statistical analyses for this end point

Primary: Time Corresponding to the Last Concentration (Tlast) of Avalglucosidase Alfa

End point title	Time Corresponding to the Last Concentration (Tlast) of Avalglucosidase Alfa[12]

End point description:

Tlast was defined as time corresponding to the last concentration above the limit of quantification, Clast. The noncompartmental PK analysis was performed. Results are based on the PK analysis set which included enrolled participants without any critical deviations related to IMP administration, and for whom any PK data were available.

End point type	Primary

End point timeframe:

Predose (prior to infusion), end of the infusion and at 1, 4, 8, 12, and 24 hours post-dose on Week 312

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase Alfa	Group 2: Avalglucosidase Alfa		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	4		
Units: hour				
median (full range (min-max))	25.84 (25.65 to 27.73)	27.6 (7.5 to 29.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Terminal Half-Life (t1/2z) of Avalglucosidase Alfa

End point title	Terminal Half-Life (t1/2z) of Avalglucosidase Alfa[13]

End point description:

t1/2z was calculated according to the following equation: t1/2z = 0.693/λz. Where, λz is the slope of the regression line of the terminal phase of the plasma concentration versus time curve. Half-life was calculated by taking the regression of at least 3 points. The non-compartmental PK analysis was performed. Results are based on the PK analysis set which included enrolled participants without any critical deviations related to IMP administration, and for whom any PK data were available.

End point type	Primary

End point timeframe:

Predose (prior to infusion), end of the infusion and at 1, 4, 8, 12, and 24 hours post-dose on Week 312

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase Alfa	Group 2: Avalglucosidase Alfa		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	4		
Units: hour				
geometric mean (geometric coefficient of variation)	1.62 (± 9)	1.79 (± 8)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Total Body Clearance Steady-State (CLss) of Avalglucosidase Alfa

End point title	Apparent Total Body Clearance Steady-State (CLss) of Avalglucosidase Alfa[14]

End point description:

CLss was calculated using the following equation: CLss= dose/AUC. The non-compartmental PK analysis was performed. Results are based on the PK analysis set which included enrolled participants without any critical deviations related to IMP administration, and for whom any PK data were available.

End point type	Primary

End point timeframe:

Predose (prior to infusion), end of the infusion and at 1, 4, 8, 12, and 24 hours post-dose on Week 312

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase Alfa	Group 2: Avalglucosidase Alfa		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	3		
Units: liter/hour				
geometric mean (geometric coefficient of variation)	0.90 (± 24)	1.06 (± 12)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution Steady-State (Vss) of Avalglucosidase Alfa

End point title	Apparent Volume of Distribution Steady-State (Vss) of Avalglucosidase Alfa[15]

End point description:

Vss was calculated using the following equation: Vz= CLss/λz. The non-compartmental PK analysis was performed. Results are based on the PK analysis set which included enrolled participants without any critical deviations related to IMP administration, and for whom any PK data were available.

End point type	Primary

End point timeframe:

Predose (prior to infusion), end of the infusion and at 1, 4, 8, 12, and 24 hours post-dose on Week 312

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was performed for the primary endpoint.

End point values	Group 1: Avalglucosidase Alfa	Group 2: Avalglucosidase Alfa		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	3		
Units: liter				
geometric mean (geometric coefficient of variation)	3.04 (± 13)	3.8 (± 24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skeletal Muscle Magnetic Resonance Imaging (MRI) Up to Week 442

End point title	Change From Baseline in Skeletal Muscle Magnetic Resonance Imaging (MRI) Up to Week 442

End point description:

Skeletal muscle MRI performed prior to muscle needle or open biopsy procedure using both qualitative (T1) and quantitative (T2, dixon) modalities to assess disease severity and detect treatment effects. Trophicity changes was evaluated for 5 muscle groups, including upper leg muscles [quadriceps (Q), hamstring (H)] and lower leg muscles [triceps (TS), extensors (LE), fibularis (F)]. Measured area of each muscle group, cross-sectional area (CSA) was provided. T2 multi-slice multi-spin echo and B1 mapping was provide a quantitative measure of disease activity within muscles. Three-point dixon imaging was provided quantification of fat content in muscles [dixon fat fraction (DFF)]. The DFF was combined with CSA measurements to provide muscle mass index (MMI). Results are based on the PD analysis set.
Here, n= number of participants analyzed at specific time points, 9999= no participants were analyzed, 99999= standard deviation could not be determined when only 1 participant was analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 104 and 442

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: millimeter square				
arithmetic mean (standard deviation)				

Week 104: CSA - F muscle (n=0,0,2,3,2,3)	9999 (± 9999)	9999 (± 9999)	57.4 (± 3.9)	-0.9 (± 46.9)
Week 104: CSA - H muscle (n=0,0,2,3,2,3)	9999 (± 9999)	9999 (± 9999)	123.0 (± 254.7)	-135.7 (± 138.7)
Week 104: CSA - LE muscle (n=0,0,2,3,2,3)	9999 (± 9999)	9999 (± 9999)	23.2 (± 60.2)	23.1 (± 19.1)
Week 104: CSA - Q muscle (n=0,0,2,3,2,3)	9999 (± 9999)	9999 (± 9999)	303.3 (± 49.5)	-27.6 (± 45.8)
Week 104: CSA - TS muscle (n=0,0,2,3,2,3)	9999 (± 9999)	9999 (± 9999)	283.6 (± 123.7)	-310.0 (± 383.2)
Week 104: DFF - F muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	0.9 (± 0.1)	1.4 (± 2.2)
Week 104: DFF - H muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	5.7 (± 3.3)	-0.2 (± 2.6)
Week 104: DFF - LE muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	0.9 (± 0.1)	0.8 (± 2.2)
Week 104: DFF - Q muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	2.3 (± 1.4)	-0.5 (± 2.3)
Week 104: DFF - TS muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	0.4 (± 0.3)	1.4 (± 1.7)
Week 104: MMI - F muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	44.8 (± 8.3)	-13.8 (± 40.4)
Week 104: MMI - H muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	-131.6 (± 77.0)	-100.9 (± 150.3)
Week 104: MMI - LE muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	12.4 (± 59.9)	9.8 (± 34.2)
Week 104: MMI - Q muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	149.2 (± 135.2)	-9.4 (± 65.9)
Week 104: MMI - TS muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	236.8 (± 122.2)	-299.6 (± 402.6)
Week 104: T2 - F muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	-0.6 (± 0.6)	0.5 (± 2.4)
Week 104: T2 - H muscle (n=0,0,1,3,1,3)	9999 (± 9999)	9999 (± 9999)	0.7 (± 99999)	1.6 (± 3.2)
Week 104: T2 - LE muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	-0.8 (± 1.6)	2.0 (± 2.2)
Week 104: T2 - Q muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	0.8 (± 1.0)	0.5 (± 2.7)
Week 104: T2 - TS muscle (n=0,0,2,3,1,3)	9999 (± 9999)	9999 (± 9999)	-0.3 (± 0.3)	0.5 (± 1.7)
Week 104: T2 with B1 - F muscle (n=0,0,2,3,1,1)	9999 (± 9999)	9999 (± 9999)	-0.5 (± 0.7)	0.5 (± 2.2)
Week 104: T2 with B1 - H muscle (n=0,0,1,3,1,2)	9999 (± 9999)	9999 (± 9999)	-0.4 (± 99999)	2.3 (± 4.6)
Week 104: T2 with B1 - LE muscle (n=0,0,2,3,1,1)	9999 (± 9999)	9999 (± 9999)	-0.6 (± 1.9)	2.0 (± 2.2)
Week 104: T2 with B1 - Q muscle (n=0,0,2,3,1,2)	9999 (± 9999)	9999 (± 9999)	0.9 (± 0.7)	0.7 (± 2.8)
Week 104: T2 with B1 - TS muscle (n=0,0,2,3,1,1)	9999 (± 9999)	9999 (± 9999)	-0.3 (± 0.4)	0.1 (± 1.2)
Week 442: CSA - F muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: CSA - H muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: CSA - LE muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: CSA - Q muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: CSA - TS muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: DFF - F muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

Week 442: DFF - H muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: DFF - LE muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: DFF - Q muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: DFF - TS muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: MMI - F muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: MMI - H muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: MMI - LE muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: MMI - Q muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: MMI - TS muscle (n=0,0,0,0,1,1)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 - F muscle (n=1,0,0,0,1,1)	-4.1 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 - H muscle (n=1,0,0,0,1,1)	-6.0 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 - LE muscle (n=1,0,0,0,1,1)	-2.5 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 - Q muscle (n=1,0,0,0,1,1)	-0.5 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 - TS muscle (n=1,0,0,0,1,1)	-3.5 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 with B1 - F muscle (n=1,0,0,0,0,0)	-4.1 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 with B1 - H muscle (n=0,0,0,0,0,0)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 with B1 - LE muscle (n=1,0,0,0,0,0)	-3.6 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 with B1 - Q muscle (n=1,0,0,0,0,0)	-0.3 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 442: T2 with B1 - TS muscle (n=1,0,0,0,0,0)	-3.2 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: millimeter square				
arithmetic mean (standard deviation)				
Week 104: CSA - F muscle (n=0,0,2,3,2,3)	46.1 (± 81.2)	26.7 (± 40.0)		
Week 104: CSA - H muscle (n=0,0,2,3,2,3)	70.6 (± 368.1)	215.2 (± 126.1)		
Week 104: CSA - LE muscle (n=0,0,2,3,2,3)	107.9 (± 145.0)	39.1 (± 26.6)		
Week 104: CSA - Q muscle (n=0,0,2,3,2,3)	134.0 (± 569.4)	193.3 (± 103.3)		
Week 104: CSA - TS muscle (n=0,0,2,3,2,3)	-3.5 (± 334.6)	226.0 (± 172.3)		

Week 104: DFF - F muscle (n=0,0,2,3,1,3)	-0.7 (± 99999)	0.3 (± 1.1)		
Week 104: DFF - H muscle (n=0,0,2,3,1,3)	-0.3 (± 99999)	3.4 (± 3.9)		
Week 104: DFF - LE muscle (n=0,0,2,3,1,3)	-0.3 (± 99999)	-0.2 (± 1.3)		
Week 104: DFF - Q muscle (n=0,0,2,3,1,3)	0.2 (± 99999)	2.4 (± 3.6)		
Week 104: DFF - TS muscle (n=0,0,2,3,1,3)	-0.3 (± 99999)	0.9 (± 0.5)		
Week 104: MMI - F muscle (n=0,0,2,3,1,3)	-5.8 (± 99999)	21.8 (± 41.6)		
Week 104: MMI - H muscle (n=0,0,2,3,1,3)	-149.7 (± 99999)	49.2 (± 139.0)		
Week 104: MMI - LE muscle (n=0,0,2,3,1,3)	7.5 (± 99999)	34.9 (± 33.2)		
Week 104: MMI - Q muscle (n=0,0,2,3,1,3)	-256.0 (± 99999)	120.7 (± 166.3)		
Week 104: MMI - TS muscle (n=0,0,2,3,1,3)	-210.5 (± 99999)	181.4 (± 143.7)		
Week 104: T2 - F muscle (n=0,0,2,3,1,3)	0.8 (± 99999)	0.0 (± 0.6)		
Week 104: T2 - H muscle (n=0,0,1,3,1,3)	-1.4 (± 99999)	0.2 (± 0.7)		
Week 104: T2 - LE muscle (n=0,0,2,3,1,3)	1.7 (± 99999)	-0.3 (± 0.7)		
Week 104: T2 - Q muscle (n=0,0,2,3,1,3)	-1.3 (± 99999)	1.0 (± 0.6)		
Week 104: T2 - TS muscle (n=0,0,2,3,1,3)	-0.9 (± 99999)	0.4 (± 0.6)		
Week 104: T2 with B1 - F muscle (n=0,0,2,3,1,1)	1.4 (± 99999)	0.3 (± 99999)		
Week 104: T2 with B1 - H muscle (n=0,0,1,3,1,2)	-2.3 (± 99999)	-0.4 (± 1.6)		
Week 104: T2 with B1 - LE muscle (n=0,0,2,3,1,1)	0.7 (± 99999)	-2.1 (± 99999)		
Week 104: T2 with B1 - Q muscle (n=0,0,2,3,1,2)	-1.4 (± 99999)	1.6 (± 0.6)		
Week 104: T2 with B1 - TS muscle (n=0,0,2,3,1,1)	-1.3 (± 99999)	0.5 (± 99999)		
Week 442: CSA - F muscle (n=0,0,0,0,1,1)	-41.8 (± 99999)	-55.6 (± 99999)		
Week 442: CSA - H muscle (n=0,0,0,0,1,1)	-461.1 (± 99999)	-30.2 (± 99999)		
Week 442: CSA - LE muscle (n=0,0,0,0,1,1)	-102.7 (± 99999)	-68.9 (± 99999)		
Week 442: CSA - Q muscle (n=0,0,0,0,1,1)	-644.7 (± 99999)	19.8 (± 99999)		
Week 442: CSA - TS muscle (n=0,0,0,0,1,1)	-220.9 (± 99999)	-82.3 (± 99999)		
Week 442: DFF - F muscle (n=0,0,0,0,1,1)	2.1 (± 99999)	0.8 (± 99999)		
Week 442: DFF - H muscle (n=0,0,0,0,1,1)	10.1 (± 99999)	0.6 (± 99999)		
Week 442: DFF - LE muscle (n=0,0,0,0,1,1)	1.6 (± 99999)	-0.0 (± 99999)		
Week 442: DFF - Q muscle (n=0,0,0,0,1,1)	9.7 (± 99999)	0.8 (± 99999)		
Week 442: DFF - TS muscle (n=0,0,0,0,1,1)	1.8 (± 99999)	0.5 (± 99999)		
Week 442: MMI - F muscle (n=0,0,0,0,1,1)	-53.4 (± 99999)	-54.9 (± 99999)		

Week 442: MMI - H muscle (n=0,0,0,0,1,1)	-412.7 (± 99999)	-44.0 (± 99999)		
Week 442: MMI - LE muscle (n=0,0,0,0,1,1)	-109.6 (± 99999)	-64.9 (± 99999)		
Week 442: MMI - Q muscle (n=0,0,0,0,1,1)	-1085.4 (± 99999)	-21.5 (± 99999)		
Week 442: MMI - TS muscle (n=0,0,0,0,1,1)	-288.6 (± 99999)	-85.1 (± 99999)		
Week 442: T2 - F muscle (n=1,0,0,0,1,1)	0.7 (± 99999)	0.1 (± 99999)		
Week 442: T2 - H muscle (n=1,0,0,0,1,1)	-9.1 (± 99999)	2.2 (± 99999)		
Week 442: T2 - LE muscle (n=1,0,0,0,1,1)	1.4 (± 99999)	0.6 (± 99999)		
Week 442: T2 - Q muscle (n=1,0,0,0,1,1)	1.0 (± 99999)	3.4 (± 99999)		
Week 442: T2 - TS muscle (n=1,0,0,0,1,1)	1.8 (± 99999)	-0.0 (± 99999)		
Week 442: T2 with B1 - F muscle (n=1,0,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		
Week 442: T2 with B1 - H muscle (n=0,0,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		
Week 442: T2 with B1 - LE muscle (n=1,0,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		
Week 442: T2 with B1 - Q muscle (n=1,0,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		
Week 442: T2 with B1 - TS muscle (n=1,0,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skeletal Muscle Biopsy Up to Week 312

End point title	Change From Baseline in Skeletal Muscle Biopsy Up to Week 312

End point description:

Skeletal muscle needle or open biopsy was performed on the lower extremity (quadriceps) muscle to assess glycogen content. The MRI appearance of the muscle was used to determine the level (axial slice position) that the biopsy procedure should target (avoiding fatty replaced tissue). Glycogen content was measured by histomorphometric analysis or severity grading to determine how effectively avalglucosidase alfa was able to remove glycogen from muscle. Results are based on the PD analysis set which included enrolled participants without any critical deviations related to IMP administration, and for whom any PD data were available. Here, n= number of participants analyzed at specific time points, 9999= no participants were analyzed and 99999= standard deviation could not be determined when only 1 participant was analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 27, 104, 208, 260 and 312

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: percentage of glycogen				
arithmetic mean (standard deviation)				
Left quadriceps muscle: Week 27 (n=1,0,2,3,1,3)	0.8 (± 99999)	9999 (± 9999)	0.9 (± 0.1)	-3.6 (± 6.4)
Left quadriceps muscle: Week 104 (n=0,0,0,2,0,0)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	-4.8 (± 9.9)
Left quadriceps muscle: Week 260 (n=0,0,0,1,0,0)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	-4.3 (± 99999)
Right quadriceps muscle: Week 27 (n=3,2,1,0,2,0)	-1.7 (± 3.3)	0.5 (± 1.5)	-1.1 (± 99999)	9999 (± 9999)
Right quadriceps muscle: Week 104 (n=0,0,0,0,1,0)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Right quadriceps muscle: Week 208 (n=0,0,0,0,1,0)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Right quadriceps muscle: Week 312 (n=0,0,0,0,1,0)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: percentage of glycogen				
arithmetic mean (standard deviation)				
Left quadriceps muscle: Week 27 (n=1,0,2,3,1,3)	0.5 (± 99999)	-0.4 (± 0.4)		
Left quadriceps muscle: Week 104 (n=0,0,0,2,0,0)	9999 (± 9999)	9999 (± 9999)		
Left quadriceps muscle: Week 260 (n=0,0,0,1,0,0)	9999 (± 9999)	9999 (± 9999)		
Right quadriceps muscle: Week 27 (n=3,2,1,0,2,0)	2.0 (± 1.0)	9999 (± 9999)		
Right quadriceps muscle: Week 104 (n=0,0,0,0,1,0)	-2.8 (± 99999)	9999 (± 9999)		
Right quadriceps muscle: Week 208 (n=0,0,0,0,1,0)	-3.8 (± 99999)	9999 (± 9999)		
Right quadriceps muscle: Week 312 (n=0,0,0,0,1,0)	-5.4 (± 99999)	9999 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Urinary Glucose Tetrasaccharide (Hex4) Level Up to Week 442

End point title	Change From Baseline in Urinary Glucose Tetrasaccharide

	(Hex4) Level Up to Week 442

End point description:

The Hex4, a tetraglucose oligomer, has been shown to be elevated in the urine of participants with Pompe disease. Hence, determination of Hex4 levels may be a means by which the efficacy of treatments were monitored. Urine samples were collected prior to IMP infusion for the assessment of urinary Hex4 concentrations. Results are based on the PD analysis set which included enrolled participants without any critical deviations related to IMP administration, and for whom any PD data were available. Here, n= number of participants analyzed at specific time points, 9999= no participants were analyzed and 99999= standard deviation could not be determined when only 1 participant was analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 52, 78, 104, 130, 156, 182, 208, 234, 260, 286, 312, 338, 364, 390, 416 and 442

End point values	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg	Group 2: Avalglucosidase alfa 5 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: mmol per mole				
arithmetic mean (standard deviation)				
Week 1 (n=1,0,0,0,0,0)	0.5 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 3 (n=3,3,3,4,4,6)	-0.6 (± 0.2)	-1.9 (± 1.6)	-0.9 (± 0.5)	-0.9 (± 1.0)
Week 5 (n=4,3,3,4,4,5)	-1.0 (± 0.5)	-0.2 (± 0.4)	-1.0 (± 1.1)	0.2 (± 0.7)
Week 7 (n=4,3,3,4,4,6)	-1.2 (± 1.1)	-2.2 (± 1.7)	-0.6 (± 1.3)	-0.7 (± 0.8)
Week 9 (n=4,3,3,4,4,6)	-0.6 (± 1.7)	-2.4 (± 3.2)	0.5 (± 0.7)	0.0 (± 1.3)
Week 11 (n=4,3,3,4,4,6)	-0.1 (± 1.9)	-2.7 (± 2.6)	0.4 (± 1.0)	0.1 (± 0.8)
Week 13 (n=4,3,3,4,4,6)	-1.3 (± 1.3)	-5.0 (± 3.4)	-1.6 (± 1.5)	0.5 (± 0.7)
Week 15 (n=4,3,3,4,4,6)	-1.4 (± 0.5)	-6.2 (± 3.3)	-1.4 (± 0.5)	0.6 (± 1.5)
Week 17 (n=4,3,3,3,4,5)	-1.0 (± 0.3)	-6.7 (± 2.1)	-1.5 (± 1.2)	-0.0 (± 1.4)
Week 19 (n=3,3,3,4,4,5)	-2.3 (± 2.4)	-6.5 (± 2.5)	-1.6 (± 1.0)	0.3 (± 3.1)
Week 21 (n=3,3,3,4,4,5)	-2.3 (± 2.1)	-6.5 (± 2.2)	-1.8 (± 1.3)	0.1 (± 2.2)
Week 23 (n=3,3,3,4,4,5)	-1.7 (± 1.7)	-5.3 (± 1.3)	-0.7 (± 1.4)	0.7 (± 3.1)
Week 25 (n=3,3,3,4,4,5)	-2.5 (± 3.0)	-4.5 (± 1.0)	-1.3 (± 2.3)	0.3 (± 3.7)
Week 27 (n=1,0,0,0,0,0)	-2.6 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Week 52 (n=3,2,3,3,3,5)	-1.8 (± 1.6)	-4.1 (± 5.2)	-2.0 (± 2.0)	0.2 (± 2.7)
Week 78 (n=3,2,3,3,3,5)	-1.9 (± 1.3)	-3.5 (± 5.0)	-2.9 (± 3.2)	-0.9 (± 2.4)
Week 104 (n=3,1,3,3,3,5)	-3.0 (± 2.9)	-6.4 (± 99999)	-2.8 (± 3.4)	0.8 (± 3.8)
Week 130 (n=3,1,3,2,3,5)	-4.0 (± 3.9)	-9.8 (± 99999)	-2.4 (± 3.3)	-1.4 (± 3.9)
Week 156 (n=3,1,3,3,3,4)	-3.6 (± 3.1)	-10.4 (± 99999)	-1.9 (± 3.2)	-1.4 (± 3.2)
Week 182 (n=3,1,3,3,2,5)	-3.5 (± 2.6)	-11.6 (± 99999)	-2.2 (± 2.7)	-3.1 (± 3.2)
Week 208 (n=3,1,3,3,3,4)	-3.2 (± 3.2)	-6.5 (± 99999)	-2.6 (± 3.9)	-3.9 (± 3.5)
Week 234 (n=3,1,1,3,3,4)	-3.4 (± 3.2)	-3.8 (± 99999)	-4.4 (± 99999)	-4.1 (± 2.5)
Week 260 (n=2,1,3,2,3,4)	-1.9 (± 0.4)	-10.1 (± 99999)	-1.7 (± 4.0)	-5.9 (± 0.1)
Week 286 (n=1,0,0,2,2,1)	-7.9 (± 99999)	9999 (± 9999)	9999 (± 9999)	-3.6 (± 2.2)
Week 312 (n=3,0,2,2,2,2)	-3.6 (± 3.0)	9999 (± 9999)	-4.3 (± 3.9)	-4.6 (± 1.9)
Week 338 (n=0,1,2,1,2,4)	9999 (± 9999)	-0.4 (± 99999)	-4.2 (± 5.5)	-4.9 (± 99999)
Week 364 (n=1,0,0,0,0,0)	-2.9 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

Week 390 (n=1,0,0,1,0,2)	-2.6 (± 99999)	9999 (± 9999)	9999 (± 9999)	-1.3 (± 99999)
Week 416 (n=0,1,2,2,1,1)	9999 (± 9999)	-12.5 (± 99999)	-1.9 (± 3.2)	-4.7 (± 2.5)
Week 442 (n=1,0,0,0,1,1)	-8.5 (± 99999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)

End point values	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: mmol per mole				
arithmetic mean (standard deviation)				
Week 1 (n=1,0,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		
Week 3 (n=3,3,3,4,4,6)	-0.5 (± 1.1)	-0.2 (± 1.5)		
Week 5 (n=4,3,3,4,4,5)	-0.5 (± 1.1)	-1.5 (± 2.0)		
Week 7 (n=4,3,3,4,4,6)	-0.3 (± 1.1)	-1.2 (± 2.3)		
Week 9 (n=4,3,3,4,4,6)	-0.7 (± 1.3)	-2.2 (± 2.7)		
Week 11 (n=4,3,3,4,4,6)	-0.5 (± 1.7)	-2.5 (± 3.3)		
Week 13 (n=4,3,3,4,4,6)	-0.7 (± 1.3)	-2.7 (± 3.6)		
Week 15 (n=4,3,3,4,4,6)	-1.0 (± 1.3)	-3.4 (± 4.8)		
Week 17 (n=4,3,3,3,4,5)	-0.9 (± 1.3)	-3.4 (± 4.5)		
Week 19 (n=3,3,3,4,4,5)	-0.8 (± 1.8)	-4.0 (± 5.9)		
Week 21 (n=3,3,3,4,4,5)	-0.8 (± 1.7)	-4.4 (± 5.6)		
Week 23 (n=3,3,3,4,4,5)	-0.9 (± 1.9)	-2.9 (± 5.5)		
Week 25 (n=3,3,3,4,4,5)	-0.8 (± 1.9)	-3.1 (± 5.0)		
Week 27 (n=1,0,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		
Week 52 (n=3,2,3,3,3,5)	-1.2 (± 2.0)	-3.4 (± 5.4)		
Week 78 (n=3,2,3,3,3,5)	-1.5 (± 1.8)	-3.5 (± 5.5)		
Week 104 (n=3,1,3,3,3,5)	-1.9 (± 1.5)	-3.6 (± 4.1)		
Week 130 (n=3,1,3,2,3,5)	-1.9 (± 1.6)	-3.1 (± 3.9)		
Week 156 (n=3,1,3,3,3,4)	-2.6 (± 1.8)	-4.8 (± 7.9)		
Week 182 (n=3,1,3,3,2,5)	-1.8 (± 0.4)	-3.9 (± 6.5)		
Week 208 (n=3,1,3,3,3,4)	-1.7 (± 0.6)	-5.9 (± 9.5)		
Week 234 (n=3,1,1,3,3,4)	-2.9 (± 1.2)	-4.9 (± 7.1)		
Week 260 (n=2,1,3,2,3,4)	-2.9 (± 1.7)	-5.6 (± 8.8)		
Week 286 (n=1,0,0,2,2,1)	-2.0 (± 0.6)	-0.5 (± 99999)		
Week 312 (n=3,0,2,2,2,2)	-1.9 (± 0.7)	-2.0 (± 0.2)		
Week 338 (n=0,1,2,1,2,4)	-1.8 (± 0.4)	-5.7 (± 8.2)		
Week 364 (n=1,0,0,0,0,0)	9999 (± 9999)	9999 (± 9999)		
Week 390 (n=1,0,0,1,0,2)	9999 (± 9999)	-10.5 (± 11.7)		
Week 416 (n=0,1,2,2,1,1)	-2.9 (± 99999)	-0.7 (± 99999)		
Week 442 (n=1,0,0,0,1,1)	-1.9 (± 99999)	-0.7 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs data was collected from first dose of IMP up to 4 weeks after the last dose of IMP administration (maximum exposure duration: up to 454 weeks).
Death data were collected from first dose of IMP up to the end of the study.

Adverse event reporting additional description:

Analysis was performed on the safety analysis set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Group 1: Avalglucosidase alfa 5 mg/kg

Reporting group description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 5 mg/kg IV infusion qow for up to 454 weeks.

Reporting group title	Group 1: Avalglucosidase alfa 10 mg/kg

Reporting group description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 432 weeks.

Reporting group title	Group 1: Avalglucosidase alfa 20 mg/kg

Reporting group description:

Participants who were treatment-naïve to alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 421 weeks.

Reporting group title	Group 2: Avalglucosidase alfa 5 mg/kg

Reporting group description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 5 mg/kg IV infusion qow for up to 424 weeks.

Reporting group title	Group 2: Avalglucosidase alfa 10 mg/kg

Reporting group description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 10 mg/kg IV infusion qow for up to 450 weeks.

Reporting group title	Group 2: Avalglucosidase alfa 20 mg/kg

Reporting group description:

Participants who were previously treated with alglucosidase alfa received avalglucosidase alfa 20 mg/kg IV infusion qow for up to 445 weeks.

Serious adverse events	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Carcinoma Cell Type Unspecified Stage Iv			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Renal Cell Carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic Dilatation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (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
Deep Vein Thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Extravasation Blood			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hypotension			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Artery Stenosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (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
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Labour Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (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			
Chest Discomfort			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
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			
Acute Respiratory Failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Electrocardiogram Q Wave Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Injury, poisoning and procedural complications			
Clavicle Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Fractured Sacrum			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Postimplantation Syndrome			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Myocardial Infarction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Myocardial Ischaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (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
Nervous system disorders			
Chronic Inflammatory Demyelinating Polyradiculoneuropathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic Stroke			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (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
Gastrointestinal disorders			
Gastric Ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Rectal Haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (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
Volvulus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Renal and urinary disorders			
Renal Failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (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
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	Group 2: Avalglucosidase alfa 5 mg/kg	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	2 / 6 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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 Carcinoma Cell Type Unspecified Stage Iv			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Cell Carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic Aneurysm			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Aortic Dilatation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Arteritis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Deep Vein Thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extravasation Blood			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Peripheral Artery Stenosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Labour Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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			
Chest Discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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

Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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			
Acute Respiratory Failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Distress			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Investigations			
Electrocardiogram Q Wave Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Clavicle Fracture			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured Sacrum			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postimplantation Syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Subcutaneous Haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial Ischaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Nervous system disorders			
Chronic Inflammatory Demyelinating Polyradiculoneuropathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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

Ischaemic Stroke			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Gastrointestinal disorders			
Gastric Ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Volvulus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal Failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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			
Cystitis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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
Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (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 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Group 1: Avalglucosidase alfa 5 mg/kg	Group 1: Avalglucosidase alfa 10 mg/kg	Group 1: Avalglucosidase alfa 20 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Melanocytic Naevus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin Cancer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Squamous Cell Carcinoma			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Hot Flush			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Pallor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pregnancy, puerperium and perinatal conditions			
Afterbirth Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pregnancy			
subjects affected / exposed	0 / 4 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
General disorders and administration site conditions			
Application Site Reaction			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Chest Pain			

subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Catheter Site Erythema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chest Discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Facial Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gait Disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Feeling Hot			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	5	4	0
Infusion Site Extravasation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infusion Site Oedema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Influenza Like Illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Impaired Healing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Illness			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infusion Site Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infusion Site Rash			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Infusion Site Reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion Site Swelling			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Injection Site Bruising			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection Site Swelling			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Injection Site Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Vaccination Site Reaction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	9	1	1
Peripheral Swelling			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Oedema Peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Immune system disorders			
Allergy To Arthropod Bite			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Drug Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Seasonal Allergy			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Pregnancy Of Partner			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pelvic Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ovarian Cyst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Heavy Menstrual Bleeding			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endometrial Thickening			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	0	4	2
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Allergic Respiratory Symptom			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Choking			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chronic Respiratory Failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
Dyspnoea			
subjects affected / exposed	3 / 4 (75.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Epistaxis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hyperventilation			

subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoventilation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Increased Upper Airway Secretion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal Congestion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Painful Respiration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Paranasal Sinus Discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary Mass			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary Congestion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pleural Effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory Failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Restrictive Pulmonary Disease			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Sinus Congestion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sinus Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Tracheal Polyp			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Panic Attack			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	7	0	0
Depression			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Delusional Disorder, Persecutory Type			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Anxiety			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Product issues			
Device Occlusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Antimitochondrial Antibody Positive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Antinuclear Antibody Positive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Chloride Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Calcium Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Creatinine Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Potassium Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Lactic Acid Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Potassium Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Sodium Decreased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Pressure Decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood Urea Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Body Temperature Increased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Breath Sounds Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoglobin Decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hepatic Enzyme Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intraocular Pressure Increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lipoprotein (A) Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Oxygen Saturation Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary Function Test Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Streptococcus Test Positive			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Troponin T Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Troponin Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine Analysis Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight Decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Weight Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Adverse Event Following Immunisation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthropod Bite			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Avulsion Fracture			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Bone Contusion			

subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Chest Injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Electric Shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epicondylitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	3 / 4 (75.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	8	0	1
Foot Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Head Injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion Related Reaction			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Iliotibial Band Syndrome			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Ligament Sprain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb Injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle Strain			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Patella Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post-Traumatic Pain			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Procedural Pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Pulmonary Contusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Road Traffic Accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin Laceration			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin Abrasion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thermal Burn			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Subdural Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Traumatic Haematoma			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conduction Disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mitral Valve Incompetence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mitral Valve Prolapse			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Myocardial Ischaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Tachycardia Paroxysmal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Ventricular Extrasystoles			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ventricular Arrhythmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Cervical Radiculopathy			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Cognitive Disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	12	1	0
Headache			
subjects affected / exposed	3 / 4 (75.00%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	15	12	8
Dysaesthesia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dizziness Postural			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Lethargy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Migraine With Aura			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Paraesthesia			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Sensory Loss			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sedation Complication			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Sinus Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tension Headache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Speech Disorder			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Iron Deficiency Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Leukocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Splenomegaly			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness Unilateral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear Pain			
subjects affected / exposed	3 / 4 (75.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Ear Discomfort			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eye disorders			
Cataract			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	2
Conjunctival Haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry Eye			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eye Irritation			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye Pruritus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eyelid Ptosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling Of Eyelid			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vision Blurred			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Abdominal Distension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Abdominal Mass			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Abdominal Pain Upper			
subjects affected / exposed	0 / 4 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2

Diarrhoea			
subjects affected / exposed	4 / 4 (100.00%)	1 / 3 (33.33%)	3 / 3 (100.00%)
occurrences (all)	10	3	3
Dyspepsia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Diverticulum Intestinal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Gastritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Haematochezia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Glossodynia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hiatus Hernia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Irritable Bowel Syndrome			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lip Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Lip Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malpositioned Teeth			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Melaena			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peptic Ulcer			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Oral Mucosal Blistering			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	13	1	1
Toothache			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Swollen Tongue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Salivary Hypersecretion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	5	1	0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic Steatosis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic Fibrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Actinic Keratosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ecchymosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis Allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hand Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Myxoid Cyst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Palmar Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Precancerous Skin Lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	9	1	0
Rosacea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin Lesion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Skin Striae			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Renal Colic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine Flow Decreased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal Cyst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	8	1	2
Back Pain			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	2	2	2
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Coccydynia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diffuse Idiopathic Skeletal Hyperostosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Greater Trochanteric Pain Syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Groin Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Jaw Clicking			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Intervertebral Disc Degeneration			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint Instability			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle Rigidity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Joint Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle Spasms			
subjects affected / exposed	4 / 4 (100.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	8	2	1
Muscular Weakness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Muscle Tightness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Myopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	11	15	3
Neck Pain			

subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Osteoarthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteochondrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteoporosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain In Extremity			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	5	1	1
Pain In Jaw			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tendon Disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Spinal Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Tendonitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Torticollis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Acute Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Covid-19			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear Infection			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Eye Infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fungal Skin Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Gastrointestinal Viral Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Herpes Zoster			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Gastrointestinal Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastroenteritis Viral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oral Herpes			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	14	3	0
Influenza			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Nasopharyngitis			
subjects affected / exposed	2 / 4 (50.00%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	6	6	8
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Otitis Media			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post Procedural Infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rectal Abscess			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	0	1	2
Tooth Abscess			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tooth Infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Viral Tonsillitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary Tract Infection			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Upper Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			

subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrolyte Imbalance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Iron Deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypovolaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 2: Avalglucosidase alfa 5 mg/kg	Group 2: Avalglucosidase alfa 10 mg/kg	Group 2: Avalglucosidase alfa 20 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Melanocytic Naevus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin Cancer			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Squamous Cell Carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	7
Hot Flush			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Flushing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	9	0	1
Pallor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pregnancy, puerperium and perinatal conditions			
Afterbirth Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pregnancy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Application Site Reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Asthenia			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	8
Chest Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Catheter Site Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest Discomfort			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Facial Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Gait Disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Feeling Hot			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	3	0	6
Infusion Site Extravasation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion Site Oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza Like Illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	4
Impaired Healing			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion Site Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Infusion Site Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion Site Reaction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infusion Site Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection Site Bruising			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Injection Site Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection Site Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Vaccination Site Reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	4
Peripheral Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	2
Oedema Peripheral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Immune system disorders			
Allergy To Arthropod Bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Drug Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Seasonal Allergy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Social circumstances			
Pregnancy Of Partner			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pelvic Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ovarian Cyst			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Heavy Menstrual Bleeding			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Endometrial Thickening			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Asthma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Allergic Respiratory Symptom			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Choking			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Chronic Respiratory Failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	4
Epistaxis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Hyperventilation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoventilation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Increased Upper Airway Secretion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nasal Congestion			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Painful Respiration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oropharyngeal Pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	1	2	3
Paranasal Sinus Discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pulmonary Mass			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pulmonary Congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pleural Effusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Respiratory Failure			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Restrictive Pulmonary Disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus Congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sleep Apnoea Syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tracheal Polyp			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Upper Respiratory Tract Congestion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Psychiatric disorders			
Panic Attack			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Depression			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Delusional Disorder, Persecutory Type			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Product issues			
Device Occlusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Investigations			
Antimitochondrial Antibody Positive			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Antinuclear Antibody Positive			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood Chloride Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood Calcium Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood Creatinine Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Blood Potassium Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood Lactic Acid Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood Potassium Increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood Sodium Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood Pressure Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood Urea Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Body Temperature Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breath Sounds Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Electrocardiogram Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haemoglobin Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Intraocular Pressure Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lipoprotein (A) Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oxygen Saturation Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Pulmonary Function Test Decreased			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Streptococcus Test Positive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Troponin T Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Troponin Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urine Analysis Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Weight Decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Weight Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Adverse Event Following Immunisation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Arthropod Bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Avulsion Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bite			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bone Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest Injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Electric Shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Epicondylitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Fall			
subjects affected / exposed	4 / 4 (100.00%)	1 / 4 (25.00%)	4 / 6 (66.67%)
occurrences (all)	11	1	19
Foot Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Head Injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Infusion Related Reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Iliotibial Band Syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament Sprain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Limb Injury			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle Strain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Patella Fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Post-Traumatic Pain			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	4	0	2
Procedural Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Road Traffic Accident			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Skin Laceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin Abrasion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Thermal Burn			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Subdural Haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tooth Fracture			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Traumatic Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	4
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Conduction Disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Mitral Valve Incompetence			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Mitral Valve Prolapse			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Myocardial Ischaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tachycardia Paroxysmal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ventricular Extrasystoles			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ventricular Arrhythmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Nervous system disorders			
Cervical Radiculopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cognitive Disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	6	0	4
Headache			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	16	0	22
Dysaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness Postural			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Migraine With Aura			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Neuralgia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Sensory Loss			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Sedation Complication			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tension Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Speech Disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	2

Iron Deficiency Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lymphadenopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Deafness Unilateral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ear Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ear Discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Conjunctival Haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dry Eye			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye Irritation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eye Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Eyelid Ptosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Lacrimation Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Swelling Of Eyelid			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vision Blurred			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Abdominal Distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal Mass			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Abdominal Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
Abdominal Pain Upper			
subjects affected / exposed	3 / 4 (75.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1

Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	2 / 6 (33.33%)
occurrences (all)	4	3	2
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Diverticulum Intestinal			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Glossodynia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hiatus Hernia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Irritable Bowel Syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Lip Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lip Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Malpositioned Teeth			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Peptic Ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral Mucosal Blistering			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	4	2	2
Toothache			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Swollen Tongue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Salivary Hypersecretion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hepatitis			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatic Steatosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatic Fibrosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Actinic Keratosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dermatitis Allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Hand Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Myxoid Cyst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Palmar Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Precancerous Skin Lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	3
Rash			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Rosacea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin Lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin Striae			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal Colic			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urine Flow Decreased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Renal Cyst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 4 (25.00%)	4 / 6 (66.67%)
occurrences (all)	5	1	21
Back Pain			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	2	0	10
Arthritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Coccydynia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Diffuse Idiopathic Skeletal Hyperostosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Flank Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Greater Trochanteric Pain Syndrome			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Groin Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Jaw Clicking			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Intervertebral Disc Degeneration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Joint Instability			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle Rigidity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint Swelling			
subjects affected / exposed	3 / 4 (75.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Muscle Spasms			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	2 / 6 (33.33%)
occurrences (all)	1	1	2
Muscular Weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle Tightness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal Chest Pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	4
Myopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Myalgia			

subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	9	0	6
Neck Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	9
Osteoarthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Osteopenia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Osteochondrosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Osteoporosis			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pain In Extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	5
Pain In Jaw			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rotator Cuff Syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tendon Disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Spinal Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Torticollis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Infections and infestations			
Acute Sinusitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Covid-19			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	3	3
Ear Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	3
Eye Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fungal Skin Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Furuncle			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal Viral Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Herpes Zoster			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis Viral			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Oral Herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Nasopharyngitis			
subjects affected / exposed	4 / 4 (100.00%)	3 / 4 (75.00%)	2 / 6 (33.33%)
occurrences (all)	8	5	10
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Otitis Media			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2

Post Procedural Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	4
Rectal Abscess			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	2 / 4 (50.00%)	2 / 4 (50.00%)	2 / 6 (33.33%)
occurrences (all)	3	3	3
Tonsillitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Tooth Abscess			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tooth Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral Tonsillitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Upper Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Viral Upper Respiratory Tract Infection			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	3 / 6 (50.00%)
occurrences (all)	4	1	8
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	4
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Electrolyte Imbalance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Iron Deficiency			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypovolaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2013	• Change to the inclusion criteria. • Change to the study duration. • Change to the interim analysis.
25 July 2014	• Change to the frequency of antibody testing. • Clarification of collection of baseline demographic characteristics. • Addition of time window for study assessments and IMP administration. • Change to the frequency of assessment of body weight. • Clarification of safety assessments. • Clarification of frequency of periodic safety reviews. • Clarification to the handling of IMP. • Clarification of requirement for assessment of vital signs at the end of the post-infusion observation period. • Clarification of immunogenicity assessments. • Clarification of future use of samples. • Clarification of required frequency of pregnancy tests. • Clarification of adverse event of special interest of pregnancy. • Clarification of collection of participant race or ethnicity. • Clarification of follow-up period. • Clarification of obligations of the Sponsor. • Clarification of coordinating Investigator.
29 January 2016	• 20 mg/kg body weight qow was selected as the final avalglucosidase alfa dose for the extension study. • Change to the visit schedule for participants switching from 5 mg/kg qow or 10 mg/kg qow to 20 mg/kg qow.
27 November 2017	• Added option of home infusion of IMP for participants meeting all eligibility requirements in regions where home infusion is deemed appropriate.
06 September 2019	• To comply with the Data Monitoring Committee recommendation with regards to home infusions. • To reference the Investigator's Brochure in the protocol. • To extend the additional follow-up period until avalglucosidase alfa was approved in the participant's country. • To comply with the United Kingdom position regarding the protocol language with regards to the study follow-up period duration.
21 December 2020	• To include the recommendations that were developed for the Coronavirus Disease 2019 pandemic period and were shared with the sites/Investigators. These recommendations were remained applicable after the end of the pandemic, especially the information regarding the post-infusion surveillance period. • To revise the text in Sections 12 (regulatory, ethical, and study oversight considerations), 13 (study monitoring), and 14 (additional requirements) as per the current Sanofi protocol template to use the updated wordings that are compliant with general guidance, including monitoring techniques. • To update Section 8.1 (investigational medicinal products) for details regarding home infusions to harmonize this text 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