Clinical trial results:
AN OPEN-LABEL, FIXED-SEQUENCE, ASCENDING-DOSE, FIRST-IN-HUMAN STUDY TO ASSESS THE SAFETY, TOLERABILITY, PHARMACOKINETICS, PHARMACODYNAMICS, AND EFFICACY OF INTRAVENOUS INFUSIONS OF ATB200 CO-ADMINISTERED WITH ORAL AT2221 IN ADULT SUBJECTS WITH POMPE DISEASE

Summary

EudraCT number	2015-004798-34
Trial protocol	GB DE NL
Global end of trial date	22 August 2024

Results information

Result version number	v1 (current)
This version publication date	31 August 2025
First version publication date	31 August 2025

Trial information

Trial identification

Sponsor protocol code	ATB200-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02675465
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amicus Therapeutics
Sponsor organisation address	47 Hulfish Street, Princeton, United States, 08542
Public contact	MedInfo@amicusrx.com, Amicus Therapeutics, 001 609662-2000, MedInfo@amicusrx.com
Scientific contact	MedInfo@amicusrx.com, Amicus Therapeutics, 001 609662-2000, MedInfo@amicusrx.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	26 February 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 July 2024
Global end of trial reached?	Yes
Global end of trial date	22 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of single ascending doses of intravenously (IV) infused ATB200.

To evaluate the safety and tolerability of single ascending doses of IV infused ATB200 as a fixed dose, co-administered with ascending oral doses of AT2221.

To characterize the pharmacokinetics (PK) of single ascending doses of IV infused ATB200.

To characterize the single- and multiple-dose PK of IV infused 20 mg/kg ATB200 when co-administered with oral 130 mg or 260 mg AT2221.

To characterize the PK of single- and multiple-oral doses of 130 mg or 260 mg AT2221 when co-administered with IV infused ATB200.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the countries in which the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	29
EEA total number of subjects	4

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	26
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	29
Number of subjects completed	29

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

ERT-experienced ambulatory subjects with Pompe disease who had been on ERT for 2 to 6 years prior to enrollment and were able to walk at least 200 meters in the 6-minute walk test (6MWT)

Arm type	Experimental
Investigational medicinal product name	cipaglucosidase alfa
Investigational medicinal product code	
Other name	ATB200
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Up to 20 milligram (mg)/kilogram (kg) intravenous (IV) infusion over a 4-hour duration every 2 weeks.

Investigational medicinal product name	AT2221
Investigational medicinal product code	
Other name	miglustat
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Up to 260 mg 1 hour prior to cipaglucosidase alfa infusion every 2 weeks. Subjects fasted for at least 2 hours before and 2 hours after administration of miglustat.

Arm title	Cohort 2

Arm description:

ERT-experienced non-ambulatory subjects with Pompe disease who had been on ERT for at least 2 years prior to enrollment

Arm type	Experimental
Investigational medicinal product name	cipaglucosidase alfa
Investigational medicinal product code	
Other name	ATB200
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 milligram (mg)/kilogram (kg) intravenous (IV) infusion over a 4-hour duration every 2 weeks.

Investigational medicinal product name	AT2221
Investigational medicinal product code	
Other name	miglustat
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

miglustat 260 mg 1 hour prior to cipaglucosidase alfa infusion every 2 weeks. Subjects fasted for at least 2 hours before and 2 hours after administration of miglustat.

Arm title	Cohort 3

Arm description:

ERT-naive ambulatory subjects with Pompe disease who were able to walk at least 200 meters in the 6MWT

Arm type	Experimental
Investigational medicinal product name	cipaglucosidase alfa
Investigational medicinal product code	
Other name	ATB200
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 milligram (mg)/kilogram (kg) intravenous (IV) infusion over a 4-hour duration every 2 weeks.

Investigational medicinal product name	AT2221
Investigational medicinal product code	
Other name	miglustat
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

miglustat 260 mg 1 hour prior to cipaglucosidase alfa infusion every 2 weeks. Subjects fasted for at least 2 hours before and 2 hours after administration of miglustat.

Arm title	Cohort 4

Arm description:

ERT-experienced ambulatory subjects with Pompe disease who had been on ERT for at least 7 years prior to enrollment and were able to walk at least 75 meters in the 6MWT

Arm type	Experimental
Investigational medicinal product name	cipaglucosidase alfa
Investigational medicinal product code	
Other name	ATB200
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 milligram (mg)/kilogram (kg) intravenous (IV) infusion over a 4-hour duration every 2 weeks.

Investigational medicinal product name	AT2221
Investigational medicinal product code	
Other name	miglustat
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

miglustat 260 mg 1 hour prior to cipaglucosidase alfa infusion every 2 weeks. Subjects fasted for at least 2 hours before and 2 hours after administration of miglustat.

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	11	6	6
Completed	8	4	6
Not completed	3	2	0
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	1	-	-
Physician decision	1	-	-
Adverse event, non-fatal	1	1	-

Number of subjects in period 1	Cohort 4
Started	6
Completed	6
Not completed	0
Adverse event, serious fatal	-
Consent withdrawn by subject	-
Physician decision	-
Adverse event, non-fatal	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
ERT-experienced ambulatory subjects with Pompe disease who had been on ERT for 2 to 6 years prior to enrollment and were able to walk at least 200 meters in the 6-minute walk test (6MWT)	
Reporting group title	Cohort 2
Reporting group description:	
ERT-experienced non-ambulatory subjects with Pompe disease who had been on ERT for at least 2 years prior to enrollment	
Reporting group title	Cohort 3
Reporting group description:	
ERT-naive ambulatory subjects with Pompe disease who were able to walk at least 200 meters in the 6MWT	
Reporting group title	Cohort 4
Reporting group description:	
ERT-experienced ambulatory subjects with Pompe disease who had been on ERT for at least 7 years prior to enrollment and were able to walk at least 75 meters in the 6MWT	

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	11	6	6
Age categorical Units: Subjects			
18 to 64 years	10	6	5
65 years and older	1	0	1
Age continuous Units: years			
arithmetic mean	49.4	41.5	49.3
standard deviation	± 9.53	± 18.12	± 15.11
Gender categorical Units: Subjects			
Female	2	2	5
Male	9	4	1

Reporting group values	Cohort 4	Total	
Number of subjects	6	29	
Age categorical Units: Subjects			
18 to 64 years	5	26	
65 years and older	1	3	
Age continuous Units: years			
arithmetic mean	40.8		
standard deviation	± 17.03	-	
Gender categorical Units: Subjects			
Female	4	13	
Male	2	16	

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description:	
ERT-experienced ambulatory subjects with Pompe disease who had been on ERT for 2 to 6 years prior to enrollment and were able to walk at least 200 meters in the 6-minute walk test (6MWT)	
Reporting group title	Cohort 2
Reporting group description:	
ERT-experienced non-ambulatory subjects with Pompe disease who had been on ERT for at least 2 years prior to enrollment	
Reporting group title	Cohort 3
Reporting group description:	
ERT-naive ambulatory subjects with Pompe disease who were able to walk at least 200 meters in the 6MWT	
Reporting group title	Cohort 4
Reporting group description:	
ERT-experienced ambulatory subjects with Pompe disease who had been on ERT for at least 7 years prior to enrollment and were able to walk at least 75 meters in the 6MWT	

Primary: Incidence of Treatment-emergent Adverse Events (TEAEs), Treatment-emergent Serious Adverse Events (TESAEs), and Adverse Events (AEs) Leading to Discontinuation of Study Drug

End point title	Incidence of Treatment-emergent Adverse Events (TEAEs), Treatment-emergent Serious Adverse Events (TESAEs), and Adverse Events (AEs) Leading to Discontinuation of Study Drug[1]
End point description:	
Safety was evaluated by number of subjects with TEAE, TESAE, and AE leading to discontinuation during the study period	
End point type	Primary
End point timeframe:	
Entire study	

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: No statistical analyses performed on safety data in this open-label study.

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	6	6	6
Units: Number of subjects				
Subjects with TEAEs	11	6	6	6
Subjects with SAEs	7	4	4	6
Subjects with AE leading to discontinuation	1	2	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Plasma GAA Activity Levels as Measured by Maximum Observed Plasma Concentration (Cmax).

End point title	Plasma GAA Activity Levels as Measured by Maximum Observed Plasma Concentration (Cmax).[2][3]

End point description:

Plasma GAA levels (Cmax) measured in Cohorts 1 and 3 following 1st and 3rd doses of cipaglucosidase alfa + miglustat

End point type	Primary

End point timeframe:

18 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: PK analysis only performed in Cohorts 1 and 3.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analysis only performed in Cohorts 1 and 3.

End point values	Cohort 1	Cohort 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[4]	5[5]		
Units: nmol/ml/hr				
geometric mean (geometric coefficient of variation)				
ATB200 20 mg/kg + AT2221 260 mg (dose 1)	108836 (± 20.5)	132400 (± 14.3)		
ATB200 20 mg/kg + AT2221 260 mg (dose 3)	119624 (± 25.7)	105842 (± 15.4)		

Notes:

[4] - 10 subjects had PK sample available after dose 1; 11 subjects had PK sample available after dose 2

[5] - 5 subjects had PK sample available after dose 1; 6 subjects had PK sample available after dose 2

Statistical analyses

No statistical analyses for this end point

Primary: Plasma GAA Activity Levels as Measured by Time to Reach the Maximum Observed Plasma Concentration (Tmax)

End point title	Plasma GAA Activity Levels as Measured by Time to Reach the Maximum Observed Plasma Concentration (Tmax)[6][7]

End point description:

Plasma GAA levels (Tmax) measured in Cohorts 1 and 3 following 1st and 3rd doses of cipaglucosidase alfa + miglustat.

End point type	Primary

End point timeframe:

18 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: PK analysis only performed in Cohorts 1 and 3.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analysis only performed in Cohorts 1 and 3.

End point values	Cohort 1	Cohort 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[8]	5[9]		
Units: h				
median (full range (min-max))				
ATB200 20 mg/kg + AT2221 260 mg (dose 1)	3.49 (3.47 to 4.00)	3.97 (3.47 to 4.00)		
ATB200 20 mg/kg + AT2221 260 mg (dose 3)	3.57 (3.35 to 4.00)	3.66 (3.50 to 3.98)		

Notes:

[8] - 10 subjects had PK sample available after dose 1; 11 subjects had PK sample available after dose 2

[9] - 5 subjects had PK sample available after dose 1; 6 subjects had PK sample available after dose 2

Statistical analyses

No statistical analyses for this end point

Primary: Plasma GAA Activity Levels as Measured by Area Under the Plasma Drug Concentration-time Curve (AUC)

End point title	Plasma GAA Activity Levels as Measured by Area Under the Plasma Drug Concentration-time Curve (AUC)[10][11]

End point description:

Plasma GAA levels (AUC) measured in Cohorts 1 and 3 following 1st and 3rd doses of cipaglucosidase alfa + miglustat. End point not assessed in Cohorts 2 and 4.

End point type	Primary

End point timeframe:

18 weeks

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: PK analysis only performed in Cohorts 1 and 3.

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analysis only performed in Cohorts 1 and 3.

End point values	Cohort 1	Cohort 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[12]	5[13]		
Units: h nmol/mL/h				
geometric mean (geometric coefficient of variation)				
ATB200 20 mg/kg + AT2221 260 mg (dose 1)	608180 (± 23.7)	762484 (± 22.0)		
ATB200 20 mg/kg + AT2221 260 mg (dose 3)	670754 (± 29.4)	638984 (± 18.1)		

Notes:

[12] - 10 subjects had PK sample available after dose 1; 11 subjects had PK sample available after dose 2

[13] - 5 subjects had PK sample available after dose 1; 6 subjects had PK sample available after dose 2

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 6-minute Walk Distance (6MWD)

End point title	Change From Baseline in 6-minute Walk Distance (6MWD)[14]

End point description:

Motor function was measured in ambulatory subjects (Cohorts 1, 3, and 4) using 6MWD (meters). Motor function was evaluated using the Efficacy Population consisting of all enrolled subjects who took at least 1 dose of study drug (20 mg/kg cipaglucosidase alfa + 260 mg miglustat co-administration) and had both a baseline and at least 1 post-baseline assessment for any efficacy endpoint. Month 60 assessment available for 9 subjects in Cohort 1, 6 subjects in Cohort 3, and 4 subjects in Cohort 4.

End point type	Secondary

End point timeframe:

Baseline, Month 60

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 6-minute walk distance (6MWD) only performed in ambulatory subjects (Cohorts 1, 3, and 4)

End point values	Cohort 1	Cohort 3	Cohort 4	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	4	
Units: meters				
arithmetic mean (standard deviation)				
Change from baseline to Month 60 in 6MWD	9.2 (± 49.89)	-34.9 (± 118.80)	27.7 (± 74.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pulmonary Function Tests

End point title	Change From Baseline in Pulmonary Function Tests

End point description:

Pulmonary function was measured by sitting and supine % predicted forced vital capacity (ppFVC) in Cohorts 1, 2, 3, and 4. Pulmonary function was evaluated using the Efficacy Population consisting of all enrolled subjects who took at least 1 dose of study drug (20 mg/kg cipaglucosidase alfa + 260 mg miglustat co-administration) and had both a baseline and at least 1 post-baseline assessment for any efficacy endpoint. Ten subjects in Cohort 1 had a post-baseline assessment.

End point type	Secondary

End point timeframe:

Baseline, Month 60

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	1	6[15]	5[16]
Units: percent				
arithmetic mean (standard deviation)				
Sitting ppFVC: Change from baseline to Month 60	-2.8 (± 10.93)	-8.0 (± 0)	5.0 (± 8.07)	3.8 (± 3.27)

Supine ppFVC: Change from baseline to Month 60	0.8 (± 7.59)	-1.0 (± 0)	1.2 (± 9.34)	5.5 (± 5.80)

Notes:

[15] - At Month 60, 6 subjects had sitting FVC value; 5 subjects had supine FVC value.

[16] - At Month 60, 5 subjects had sitting FVC value; 4 subjects had supine FVC value.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Muscle Strength Tests

End point title	Change From Baseline in Muscle Strength Tests

End point description:

Muscle strength was measured by total manual muscle test (MMT) score. Total MMT score ranges from 0 to 80 based on all 16 muscle groups, which are right/left shoulder abduction, right/left shoulder adduction, right/left elbow flexion, right/left elbow extension, right/left hip flexion, right/left hip abduction, right/left knee flexion, and right/left knee extension. Higher scores indicate less disease impact on muscle functions. Total MMT score was evaluated using the Efficacy Population consisting of all enrolled subjects who took at least 1 dose of study drug (20 mg/kg cipaglucosidase alfa + 260 mg miglustat co-administration) in Stage 3 and had both a baseline and at least 1 post-baseline assessment for any efficacy endpoint. Number of participants analyzed per cohort represents the number of subjects assessed at the specific visit for the parameter.

End point type	Secondary

End point timeframe:

Baseline, Month 60

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	3	5	5
Units: score on scale				
arithmetic mean (standard deviation)				
Total MMT score: Change from baseline to Month 60	2.0 (± 5.20)	0.0 (± 4.36)	1.0 (± 3.54)	3.4 (± 4.83)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fatigue Severity Score (FSS)

End point title	Change From Baseline in Fatigue Severity Score (FSS)

End point description:

The FSS consists of 9 questions, each scored on a scale from 1 (“completely disagree”) to 7 (“completely agree”). The total score ranges from 9 to 63, with higher values representing higher level of fatigue due to the disease condition. The Efficacy Population consists of all enrolled subjects who took at least 1 dose of study drug (20 mg/kg cipaglucosidase alfa + 260 mg miglustat co-administration) in Stage 3 and had both a baseline and at least 1 post-baseline assessment for any efficacy endpoint. Number of participants analyzed for FSS are those in each cohort who completed the assessment at baseline and Month 60.

End point type	Secondary

End point timeframe:

Baseline, Month 60

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	4
Units: score on scale				
arithmetic mean (standard deviation)				
FSS score: Change from baseline to Month 60	0.9 (± 11.48)	-4.3 (± 7.23)	-0.5 (± 8.67)	-14.0 (± 15.25)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Overall Physical Wellbeing (Subject's Global Impression of Change [SGIC], Question 1)

End point title	Change From Baseline in Overall Physical Wellbeing (Subject's Global Impression of Change [SGIC], Question 1)

End point description:

The Subject's Global Impression of Change overall physical wellbeing (question 1) is scored on a 7-point rating scale. Improved = response of 5 or higher, No change = response of 4, and Declined = response of 3 or lower. The Efficacy Population consists of all enrolled subjects who took at least 1 dose of study drug (20 mg/kg cipaglucosidase alfa + 260 mg miglustat co-administration) in Stage 3 and had both a baseline and at least 1 post-baseline assessment for any efficacy endpoint. Number of participants analyzed for SGIC question 1 are those in each cohort who completed the assessment at baseline and Month 60.

End point type	Secondary

End point timeframe:

Baseline, Month 60

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	2	6	5
Units: participants				
Improved	3	0	3	4
No change	2	2	1	0
Declined	3	0	2	1

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Overall Physical Wellbeing (Physician's Global Impression of Change [PGIC])

End point title	Change From Baseline in Overall Physical Wellbeing (Physician's Global Impression of Change [PGIC])

End point description:

The Physician's Global Impression of Change overall physical wellbeing is scored on a 7-point rating scale. Improved = response of 5 or higher, No change = response of 4, and Declined = response of 3 or lower. The Efficacy Population consists of all enrolled subjects who took at least 1 dose of study drug (20 mg/kg cipaglucosidase alfa + 260 mg miglustat co-administration) in Stage 3 and had both a baseline and at least 1 post-baseline assessment for any efficacy endpoint. Number of participants analyzed for PGIC are those in each cohort who completed the assessment at baseline and Month 60.

End point type	Secondary

End point timeframe:

Baseline, Month 60

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	5
Units: participants				
Improved	2	1	2	2
No change	3	2	4	3
Declined	3	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Stage 2 Period 5 + Stage 3 + Stage 4 (cipaglucosidase alfa 20 mg/kg + miglustat 260 mg)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
ERT-experienced ambulatory subjects with Pompe disease who had been on ERT for 2 to 6 years prior to enrollment and were able to walk at least 200 meters in the 6-minute walk test (6MWT)	
Reporting group title	Cohort 2
Reporting group description:	
ERT-experienced non-ambulatory subjects with Pompe disease who had been on ERT for at least 2 years prior to enrollment	
Reporting group title	Cohort 3
Reporting group description:	
ERT-naive ambulatory subjects with Pompe disease who were able to walk at least 200 meters in the 6MWT	
Reporting group title	Cohort 4
Reporting group description:	
ERT-experienced ambulatory subjects with Pompe disease who had been on ERT for at least 7 years prior to enrollment and were able to walk at least 75 meters in the 6MWT	

Serious adverse events	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)	4 / 6 (66.67%)	4 / 6 (66.67%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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

Haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Hypotension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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 swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Pharyngeal oedema			

subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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
Wheezing			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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
Limb injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Traumatic haematoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Arrhythmia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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

Cardiac arrest			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	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
Supraventricular tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Femoral hernia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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
Nephrolithiasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	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
Dupuytren's contracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (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
Diverticulitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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

Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	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
Postoperative wound infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (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
Septic shock			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	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 / 1	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			

subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chills				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral swelling				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Cough				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Pharyngeal oedema				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wheezing			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Limb injury			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic haematoma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Supraventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral hernia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dupuytren's contracture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Postoperative wound infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	6 / 6 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Benign neoplasm of thyroid gland			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Papilloma			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin papilloma			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Deep vein thrombosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Hot flush			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	4
Hypertension			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	2	0	3
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Orthostatic hypotension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pallor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral venous disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Infusion site swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Asthenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Catheter site bruise			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Catheter site pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			

subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	5
Chest pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Chills			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	3
Complication associated with device			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Fatigue			
subjects affected / exposed	3 / 11 (27.27%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	5	1	5
Feeling abnormal			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Feeling jittery			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
General physical health deterioration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Infusion site pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Nodule			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	4
Peripheral swelling			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pyrexia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	7
Swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vaccination site pain			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Seasonal allergy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			

Amenorrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Atrophic vulvovaginitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Erectile dysfunction			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Metrorrhagia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vaginal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	4	1	8
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	1	1	2
Dyspnoea exertional			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Epistaxis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Increased upper airway secretion			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			

subjects affected / exposed	2 / 11 (18.18%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Oropharyngeal pain			
subjects affected / exposed	4 / 11 (36.36%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	6	3	4
Productive cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rales			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory acidosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory tract congestion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Upper respiratory tract congestion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Initial insomnia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			
Blood glucose decreased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Blood pressure increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Blood testosterone decreased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood urine present			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
C-reactive protein increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Culture wound positive			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eosinophil count increased			

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Forced expiratory volume decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Forced vital capacity decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Lipoprotein (a) increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mycobacterium test positive			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Prostatic specific antigen increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Protein urine			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Transaminases increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitamin D decreased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ankle fracture			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Arthropod sting			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Bone contusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	4 / 6 (66.67%)
occurrences (all)	2	1	23
Fall			
subjects affected / exposed	6 / 11 (54.55%)	2 / 6 (33.33%)	6 / 6 (100.00%)
occurrences (all)	36	4	43
Fibula fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Joint injury			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Ligament sprain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Limb injury			

subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lumbar vertebral fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	4 / 6 (66.67%)
occurrences (all)	2	1	11
Post procedural complication			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rib fracture			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Road traffic accident			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	4
Skin laceration			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Snake bite			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Spinal compression fracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tendon rupture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Tissue injury			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tooth fracture			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Vaccination complication			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	2
Wound			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Atrial fibrillation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Bundle branch block right			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Cardiac flutter			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cyanosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Left atrial enlargement			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3

Sinus tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Supraventricular tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	9
Ventricular hypertrophy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Burning sensation			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	2
Carpal tunnel syndrome			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cognitive disorder			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	3 / 11 (27.27%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	5	0	4
Dizziness postural			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Dysarthria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Dysstasia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Facial paresis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	4 / 11 (36.36%)	1 / 6 (16.67%)	4 / 6 (66.67%)
occurrences (all)	11	1	8
Hemiplegic migraine			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Lacunar infarction			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Migraine			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	4 / 6 (66.67%)
occurrences (all)	0	0	13
Migraine with aura			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	4
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Post herpetic neuralgia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Radial nerve palsy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sciatica			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lymphadenopathy mediastinal			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Thrombocytosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Deafness unilateral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ear discomfort			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Ear pain			

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tinnitus			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Vertigo			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	1	1	2
Vertigo positional			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	3
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cataract			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Chalazion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Diplopia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Glaucoma			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ocular discomfort			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	4
Abdominal pain			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	2	1	2
Abdominal pain lower			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	3 / 11 (27.27%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	4	0	2
Anal fissure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Haemorrhoids			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Inguinal hernia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Large intestine polyp			
subjects affected / exposed	3 / 11 (27.27%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Lip swelling			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 11 (27.27%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	5	1	16
Rectal haemorrhage			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Regurgitation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Swollen tongue			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	8
Diarrhoea			
subjects affected / exposed	4 / 11 (36.36%)	3 / 6 (50.00%)	4 / 6 (66.67%)
occurrences (all)	12	3	13
Dry mouth			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dysphagia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Enteritis			

subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	8	1	0
Food poisoning			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Gastritis erosive			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatic cyst			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Blister			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Dry skin			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Ecchymosis			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Ingrowing nail			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	9
Rash			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	4 / 6 (66.67%)
occurrences (all)	0	1	11
Rash erythematous			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Skin discolouration			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Skin oedema			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	4
Skin mass			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Bilirubinuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Calculus bladder			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hyperthyroidism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypothyroidism			

subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Thyroid mass			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 11 (54.55%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	11	1	10
Back pain			
subjects affected / exposed	6 / 11 (54.55%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	8	1	6
Bursitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Clubbing			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dupuytren's contracture			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Groin pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Joint hyperextension			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint noise			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Joint swelling			

subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Medial tibial stress syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Muscle fatigue			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	5 / 11 (45.45%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	11	0	6
Muscle tightness			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	7	1	0
Muscle twitching			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	3 / 11 (27.27%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	3	2	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Musculoskeletal pain			
subjects affected / exposed	3 / 11 (27.27%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	4	0	3
Myalgia			
subjects affected / exposed	4 / 11 (36.36%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	15	0	5
Neck mass			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Osteoarthritis			

subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Osteopenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Osteoporosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	3 / 11 (27.27%)	2 / 6 (33.33%)	3 / 6 (50.00%)
occurrences (all)	13	4	8
Pain in jaw			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rotator cuff syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Soft tissue swelling			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Synovial cyst			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	2	3	2

COVID-19			
subjects affected / exposed	5 / 11 (45.45%)	0 / 6 (0.00%)	4 / 6 (66.67%)
occurrences (all)	6	0	8
Conjunctivitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	3
Cystitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eye infection bacterial			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Fungal skin infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Graft infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Hordeolum			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Influenza			
subjects affected / exposed	4 / 11 (36.36%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	10	1	1
Labyrinthitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	5
Nasopharyngitis			
subjects affected / exposed	9 / 11 (81.82%)	3 / 6 (50.00%)	4 / 6 (66.67%)
occurrences (all)	19	4	5
Oral herpes			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Oral viral infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Sepsis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	3 / 11 (27.27%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	7	1	3

Tooth abscess			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	4 / 11 (36.36%)	0 / 6 (0.00%)	4 / 6 (66.67%)
occurrences (all)	5	0	17
Urinary tract infection			
subjects affected / exposed	2 / 11 (18.18%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	7	1	13
Viral infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Viral pharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	6
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	0	1	5
Alkalosis hypochloraemic			
subjects affected / exposed	2 / 11 (18.18%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Decreased appetite			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fluid overload			

subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	0 / 11 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	4
Hypokalaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Hypomagnesaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Metabolic alkalosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Vitamin D deficiency			
subjects affected / exposed	1 / 11 (9.09%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	1	1

Non-serious adverse events	Cohort 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Papilloma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin papilloma			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Orthostatic hypotension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pallor			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Peripheral venous disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Infusion site swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Catheter site bruise			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Catheter site pain				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	3			
Chest discomfort				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Chest pain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Chills				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	5			
Complication associated with device				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Oedema peripheral				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Fatigue				
subjects affected / exposed	5 / 6 (83.33%)			
occurrences (all)	13			
Feeling abnormal				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Feeling hot				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Feeling jittery				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Gait disturbance				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
General physical health deterioration				

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infusion site extravasation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infusion site pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nodule			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	3		
Vaccination site pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Seasonal allergy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Atrophic vulvovaginitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Erectile dysfunction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metrorrhagia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Increased upper airway secretion			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rales			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory acidosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Respiratory tract congestion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Rhinitis allergic			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper respiratory tract congestion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Anxiety				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Depression				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Initial insomnia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Insomnia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Investigations				
Blood glucose decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Blood pressure increased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Blood testosterone decreased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Blood uric acid increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Blood urine present				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Body temperature increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
C-reactive protein increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Culture wound positive				

subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Eosinophil count increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Forced expiratory volume decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Forced vital capacity decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lipoprotein (a) increased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Mycobacterium test positive				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Prostatic specific antigen increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Protein urine				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
SARS-CoV-2 test positive				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Transaminases increased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Vitamin D decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			

White blood cells urine positive			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ankle fracture			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Arthropod sting			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bone contusion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Fall			
subjects affected / exposed	4 / 6 (66.67%)		
occurrences (all)	27		
Fibula fracture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Joint injury			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Ligament sprain			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Limb injury				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Lumbar vertebral fracture				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Muscle strain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Post procedural complication				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Rib fracture				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Road traffic accident				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Skin abrasion				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	4			
Skin laceration				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Snake bite				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Spinal compression fracture				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Tendon rupture				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Thermal burn				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tissue injury			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tooth fracture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vaccination complication			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Wound			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Atrial fibrillation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Atrioventricular block first degree			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bundle branch block right			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cardiac flutter			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cyanosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Left atrial enlargement			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Palpitations			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Supraventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ventricular hypertrophy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Burning sensation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Carpal tunnel syndrome			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cognitive disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dizziness postural			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysarthria			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dysstasia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Facial paresis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Headache				
subjects affected / exposed	6 / 6 (100.00%)			
occurrences (all)	15			
Hemiplegic migraine				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Hypoaesthesia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lacunar infarction				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Migraine				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	5			
Migraine with aura				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Paraesthesia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Post herpetic neuralgia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Presyncope				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Radial nerve palsy				

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Tremor			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Iron deficiency anaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lymphadenopathy mediastinal			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Thrombocytosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Deafness unilateral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ear discomfort			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vertigo positional			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cataract			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chalazion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Diplopia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Glaucoma			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ocular discomfort			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

Vision blurred subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Abdominal distension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Abdominal pain subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2			
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2			
Anal fissure subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Constipation subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1			
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1			
Haemorrhoids subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Inguinal hernia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Large intestine polyp				

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lip swelling				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Mouth ulceration				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	5 / 6 (83.33%)			
occurrences (all)	13			
Rectal haemorrhage				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Regurgitation				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Swollen tongue				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Toothache				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Vomiting				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	4			
Diarrhoea				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	3			
Dry mouth				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Dysphagia				

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Enteritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Food poisoning			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastritis erosive			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hepatic cyst			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blister			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dermatitis contact			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dry skin			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Ecchymosis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Eczema				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Erythema				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Hyperhidrosis				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Ingrowing nail				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Night sweats				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Rash				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Rash erythematous				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Rash maculo-papular				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Rash pruritic				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Skin discolouration				

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Skin oedema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Skin lesion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Skin mass subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Renal and urinary disorders			
Bilirubinuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Calculus bladder subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Dysuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Haematuria subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Proteinuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Endocrine disorders			
Autoimmune thyroiditis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Hyperthyroidism			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Thyroid mass			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 6 (83.33%)		
occurrences (all)	8		
Back pain			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	3		
Bursitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Clubbing			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dupuytren's contracture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Joint hyperextension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Joint noise			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Joint swelling				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Medial tibial stress syndrome				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Muscle fatigue				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Muscle spasms				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Muscle tightness				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Muscle twitching				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Muscular weakness				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Musculoskeletal chest pain				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Musculoskeletal pain				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Myalgia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Neck mass				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Neck pain				

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Osteoarthritis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Osteopenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Osteoporosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pain in jaw			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Plantar fasciitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Rotator cuff syndrome			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Soft tissue swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Spinal pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Synovial cyst			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Tendonitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Bronchitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
COVID-19				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	4			
Conjunctivitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Cystitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Ear infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Eye infection bacterial				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Folliculitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Fungal skin infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastroenteritis viral				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Graft infection				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Herpes zoster				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			

Hordeolum				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Labyrinthitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	3			
Oral herpes				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Oral viral infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Paronychia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pharyngitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Sepsis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			

Sinusitis			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Tooth abscess			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	8		
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Viral pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Alkalosis hypochloraemic			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dehydration			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Fluid overload			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolic alkalosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2015	The protocol was amended to include details pertaining to subject monitoring for 48 hours at the start of infusion in Stage 1 and conduct of subject monitoring in Stage 2.
11 February 2016	Addition of a 24-month, open-label extension phase and roll-over enrollment for subjects who complete Stages 1 and 2 (Cohort 1) to the extension stage (Stage 3). Introduction of new cohorts into the study (Cohorts 2 and 3; original group of subjects in Amendment 1 was renamed Cohort 1), with separate enrollment criteria, sentinel dosing, and planned analyses specified for Cohorts 2 and 3. Addition of objectives and study assessments for long-term efficacy and safety.
19 July 2016	Clarifications to study inclusion/exclusion criteria, prohibited medications and acceptable contraception methods, and interim analysis. Updates to Schedule of Assessments, including modifications to the schedule of vital sign assessments. Addition of text pertaining to immunological testing of up to 6 months for subjects confirmed positive for anti-rhGAA antibodies upon study completion or subject discontinuation. Clarification of the extent of follow-up for subjects with adverse events. Adjustments to PK blood sampling in Schedule of Assessments for Stages 3 and 4.
16 December 2016	Collection of available historical antibody information. Patient-reported outcomes and functional assessments for Months 15 and 21 of Stage 3 and at the End of PK visit for Cohort 1 subjects, as well as for Months 3, 9, 15, and 21 for Cohorts 2 and 3. Revision of Global Impression of Change form and timing of assessments (Months 6, 12, 15, 18, and 24 of Stage 3 for Cohort 1 and Months 3, 9, 15, 18, and 21 for Cohorts 2 and 3). Changes in pre-laboratory testing requirements and acceptable forms of contraception. Correction of statistical comparisons for PK data.
16 February 2018	Implementation of home ERT infusion, as allowed by the principal investigator, regulatory authorities, and/or local ethics committees. Introduction of a new cohort (Cohort 4) into the study and a new study stage (Stage 4 [open-label extension]). Clarifications regarding Stage 3 study design, post-infusion monitoring, under-dosing reporting, PK sample collection and analysis for Cohorts 1 and 3, pulmonary function assessments, interim analyses, and application of statistical methods for non-PK parameters. Addition of sparse blood sampling for plasma total GAA protein concentrations from Cohorts 1 and 3. Addition of follow-up safety visit assessment and retrospective data collection. Change in number of subjects planned for enrollment (approximately 21 to 32).
30 April 2018	Clarification of description, reporting, and management of IARs. Updates to list of acceptable methods of contraception. Modification of laboratory testing procedures for Stage 3 (Cohort 4) and Stage 4 (all cohorts).
03 October 2018	Addition of ~10 subjects for enrollment in Cohort 4, increasing the study sample size from approximately 18 to 24 subjects to approximately 18 to 34 subjects. Modifications to inclusion criteria 29, 32, and 33, specifically for Cohort 4 subjects. Addition of a UK-specific section for acceptable methods of contraception. Addition of PROMIS® instruments to the patient-reported outcomes and activity monitoring to the exploratory assessments for Cohort 4 in Stage 3. Creation of a separate Schedule of Assessments for Cohort 4 and an update to study conduct considerations.

10 January 2019	Decrease in the number of subjects for Cohort 4 from ~10 subjects to 6 to 8 subjects. Update regarding home infusion eligibility. Modification of follow-up immunological testing duration for subjects who are confirmed to have a positive result for anti-rhGAA antibodies upon study completion or discontinuation. Modification of Cohort 4 assessments. Addition of Section 8.8: Criteria for Termination of the Study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported