Clinical trial results:
A Phase III Double-blind, Randomized, Placebo-Controlled Study assessing the Efficacy, Safety and Tolerability of Idebenone in Patients with Duchenne Muscular Dystrophy Receiving Glucocorticoid Steroids

Summary

EudraCT number	2016-000602-10
Trial protocol	DE BE NL SE GB ES AT FR IT IE HU BG
Global end of trial date	01 December 2020

Results information

Result version number	v2 (current)
This version publication date	08 January 2023
First version publication date	26 June 2022
Version creation reason	• New data added to full data set new updated study data available
Summary attachment (see zip file)	company statement (2022-06-10_Statement_EudraCT_signed.pdf)

Trial information

Trial identification

Sponsor protocol code	SNT-III-012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02814019
WHO universal trial number (UTN)	-
Other trial identifiers	US IND: 103801

Notes:

Sponsors

Sponsor organisation name	Santhera Pharmaceuticals (Switzerland) Limited
Sponsor organisation address	Hohenrainstrasse 24, Pratteln, Switzerland, 4133
Public contact	Julien Gaudias, Santhera Pharmaceuticals (Switzerland) Limited, +41 79 811 01 98, julien.gaudias@santhera.com
Scientific contact	Julien Gaudias, Santhera Pharmaceuticals (Switzerland) Limited, +41 79 811 01 98, julien.gaudias@santhera.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	23 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 December 2020
Global end of trial reached?	Yes
Global end of trial date	01 December 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of idebenone compared to placebo, in delaying the loss of respiratory function in patients with DMD receiving glucocorticoid steroids as measured by changes in Forced Vital Capacity percent predicted (FVC %p) using clinic-based spirometry

Protection of trial subjects:

This study was conducted according to the guidelines of Good Clinical Practice (GCP), ICH E3 (CPMP/ICH/135/95), the US Code of Federal Regulations governing Protection of Human Subjects (21 CFR 50), Financial Disclosure by Clinical Investigators (21 CFR 54), Institutional Review Boards (21 CFR 56), Investigational New Drug Application (21 CFR 312), and Applications for FDA Approval to Market a New Drug (21 CFR 314), in compliance with the World Medical Assembly Declaration of Helsinki and its most recent amendments and applicable local regulatory requirements and law.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 36
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Italy: 55
Country: Number of subjects enrolled	Switzerland: 8
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	United States: 72
Worldwide total number of subjects	264
EEA total number of subjects	145

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)	28
Adolescents (12-17 years)	154
Adults (18-64 years)	82
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 395 patients were screened and 267 were enrolled in the study (132 patients each in the idebenone and placebo arms)

Period 1

Period 1 title	Baseline to Week 78 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	idebenone

Arm description:

Idebenone arm: 900 mg idebenone per day (two 150 mg tablets to be taken orally, three times a day with meals).

Arm type	Experimental
Investigational medicinal product name	idebenone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

900 mg idebenone per day (two 150 mg tablets to be taken orally, three times a day with meals).

Arm title	Placebo

Arm description:

Matching Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

two tablets to be taken orally, three times a day with meals.

Number of subjects in period 1	idebenone	Placebo
Started	132	132
Completed	99	89
Not completed	33	43
Consent withdrawn by subject	8	12
FAILURE TO MEET CONTINUATION CRITERIA	1	-
Adverse event, non-fatal	4	3
Death	3	1
xxxxxxxxxxxxxxxx	16	-
PROTOCOL-SPECIFIED WITHDRAWAL CRITERION MET	-	2
Lost to follow-up	-	3
xxxxxxx	-	21
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	idebenone
Reporting group description:	
Idebenone arm: 900 mg idebenone per day (two 150 mg tablets to be taken orally, three times a day with meals).	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo	

Reporting group values	idebenone	Placebo	Total
Number of subjects	132	132	264
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	13	15	28
Adolescents (12-17 years)	78	76	154
Adults (18-64 years)	41	41	82
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	0	0	0
Male	132	132	264

End points

End points reporting groups

Reporting group title	idebenone
Reporting group description:	
Idebenone arm: 900 mg idebenone per day (two 150 mg tablets to be taken orally, three times a day with meals).	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo	

Primary: Change From Baseline in Forced Vital Capacity Percent Predicted (FVC %p) at Week 78

End point title	Change From Baseline in Forced Vital Capacity Percent Predicted (FVC %p) at Week 78
End point description:	
Delaying the loss of respiratory function in patients with Duchenne muscular dystrophy (DMD) receiving glucocorticoid steroids as measured by changes in FVC%p (Percent Predicted Forced Vital Capacity) from Baseline to Week 78 using hospital based spirometry	
End point type	Primary
End point timeframe:	
Baseline to Week 78	

End point values	idebenone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	90		
Units: FVC %p				
least squares mean (standard deviation)				
Change From Baseline in Forced Vital Capacity Perc	-9.93 (± 7.446)	-8.39 (± 6.218)		

Statistical analyses

Statistical analysis title	Analysis of FVC%p
Statistical analysis description:	
Slope analysis assuming MNAR Estimated treatment difference of slopes (as annual rate of change in FVC%p)	
Comparison groups	idebenone v Placebo

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.9403
Method	Random Coefficient Regression Model
Parameter estimate	Median difference (net)
Point estimate	0.05
Confidence interval	
level	Other: 99.46 %
sides	2-sided
lower limit	-1.83
upper limit	1.93
Variability estimate	Standard error of the mean
Dispersion value	0.68

Notes:

[1] - Estimated treatment difference of slopes (as annual rate of change in FVC%p over 78 Weeks)

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Informed consent signature date to end of study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Reporting groups	
Reporting group title	Idebenone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Idebenone	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 132 (12.88%)	14 / 132 (10.61%)	
number of deaths (all causes)	3	1	
number of deaths resulting from adverse events	3	1	
Investigations			
Fibrin D dimer increased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count increased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin T increased			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	3 / 132 (2.27%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fat embolism			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Thoracic vertebral fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrioventricular block complete			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial fibrosis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systolic dysfunction			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Cardiogenic shock			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Surgical and medical procedures			
Orthopaedic procedure			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenotomy			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Benign intracranial hypertension			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung consolidation			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteomyelitis chronic			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Idebenone	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	121 / 132 (91.67%)	120 / 132 (90.91%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Skin papilloma			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	2	1	
Peripheral venous disease			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Hypertension			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Lymphoedema			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Ankle operation			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Mole excision			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Orthopaedic procedure			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Tenotomy			
subjects affected / exposed	1 / 132 (0.76%)	2 / 132 (1.52%)	
occurrences (all)	1	2	
Ear tube insertion			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Tooth extraction			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	11 / 132 (8.33%)	13 / 132 (9.85%)	
occurrences (all)	14	18	
Influenza like illness			
subjects affected / exposed	4 / 132 (3.03%)	3 / 132 (2.27%)	
occurrences (all)	5	3	
Fatigue			
subjects affected / exposed	3 / 132 (2.27%)	1 / 132 (0.76%)	
occurrences (all)	3	1	
Malaise			
subjects affected / exposed	3 / 132 (2.27%)	1 / 132 (0.76%)	
occurrences (all)	3	1	
Peripheral swelling			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences (all)	2	1	
Chest pain			
subjects affected / exposed	1 / 132 (0.76%)	3 / 132 (2.27%)	
occurrences (all)	1	3	
Oedema peripheral			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Vaccination site pain			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Vessel puncture site bruise			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Cyst			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Discomfort			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	3	

Hyperpyrexia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Injection site pain			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Medical device pain			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Seasonal allergy			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Social circumstances			
Walking disability			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Testicular retraction			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Genital rash			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	20 / 132 (15.15%)	16 / 132 (12.12%)	
occurrences (all)	33	20	
Oropharyngeal pain			

subjects affected / exposed	10 / 132 (7.58%)	18 / 132 (13.64%)	
occurrences (all)	13	23	
Rhinorrhoea			
subjects affected / exposed	6 / 132 (4.55%)	3 / 132 (2.27%)	
occurrences (all)	6	4	
Acute respiratory failure			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences (all)	2	1	
Nasal congestion			
subjects affected / exposed	2 / 132 (1.52%)	2 / 132 (1.52%)	
occurrences (all)	2	2	
Productive cough			
subjects affected / exposed	2 / 132 (1.52%)	2 / 132 (1.52%)	
occurrences (all)	2	2	
Sleep apnoea syndrome			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences (all)	2	1	
Asthma			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	1 / 132 (0.76%)	8 / 132 (6.06%)	
occurrences (all)	1	16	
Pulmonary congestion			
subjects affected / exposed	1 / 132 (0.76%)	2 / 132 (1.52%)	
occurrences (all)	1	2	
Respiratory distress			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Respiratory muscle weakness			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Tachypnoea			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Throat irritation			

subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Tonsillar hypertrophy			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Chronic throat clearing			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Increased upper airway secretion			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Lung consolidation			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Pulmonary embolism			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Respiratory depth decreased			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Respiratory failure			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Rhinitis allergic			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Psychiatric disorders			

Anxiety			
subjects affected / exposed	6 / 132 (4.55%)	0 / 132 (0.00%)	
occurrences (all)	7	0	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Mood altered			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Initial insomnia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Irritability			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Panic attack			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Investigations			
Bone density decreased			
subjects affected / exposed	3 / 132 (2.27%)	0 / 132 (0.00%)	
occurrences (all)	3	0	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 132 (1.52%)	3 / 132 (2.27%)	
occurrences (all)	2	3	
Blood bilirubin increased			

subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	3	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 132 (1.52%)	2 / 132 (1.52%)	
occurrences (all)	2	2	
Blood glucose increased			
subjects affected / exposed	2 / 132 (1.52%)	2 / 132 (1.52%)	
occurrences (all)	2	2	
Blood triglycerides			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences (all)	2	1	
Vitamin D decreased			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Weight increased			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences (all)	2	1	
Blood chloride decreased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Blood cholesterol increased			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Blood uric acid increased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Blood urine			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Cardiac function test abnormal			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Cardiac imaging procedure abnormal			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	

Crystal urine present			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Ejection fraction decreased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Fibrin D dimer increased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Glomerular filtration rate increased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Heart rate increased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Heart rate irregular			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Lymphocyte count decreased			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Neutrophil count increased			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Oxygen saturation decreased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Platelet count increased			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
QRS axis abnormal			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Red blood cells urine			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	

Urine analysis abnormal				
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)		
occurrences (all)	1	0		
Weight decreased				
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)		
occurrences (all)	1	1		
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)		
occurrences (all)	0	1		
Blood creatinine increased				
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)		
occurrences (all)	0	1		
Blood potassium decreased				
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)		
occurrences (all)	0	1		
Blood potassium increased				
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)		
occurrences (all)	0	1		
Blood urine present				
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)		
occurrences (all)	0	1		
Breath sounds abnormal				
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)		
occurrences (all)	0	1		
Crystal urine				
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)		
occurrences (all)	0	1		
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 132 (0.00%)	3 / 132 (2.27%)		
occurrences (all)	0	3		
Glucose urine present				
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)		
occurrences (all)	0	1		
Haemoglobin urine				

subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Haemoglobin urine present			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Hepatic enzyme increased			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Thyroid hormones increased			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Troponin T increased			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	4 / 132 (3.03%)	4 / 132 (3.03%)	
occurrences (all)	6	4	
Femur fracture			
subjects affected / exposed	4 / 132 (3.03%)	2 / 132 (1.52%)	
occurrences (all)	4	2	
Fall			
subjects affected / exposed	3 / 132 (2.27%)	4 / 132 (3.03%)	
occurrences (all)	3	4	
Injury			
subjects affected / exposed	3 / 132 (2.27%)	2 / 132 (1.52%)	
occurrences (all)	4	2	
Joint injury			
subjects affected / exposed	3 / 132 (2.27%)	2 / 132 (1.52%)	
occurrences (all)	3	2	
Muscle strain			
subjects affected / exposed	3 / 132 (2.27%)	1 / 132 (0.76%)	
occurrences (all)	3	1	
Ligament sprain			

subjects affected / exposed	2 / 132 (1.52%)	2 / 132 (1.52%)	
occurrences (all)	2	2	
Tibia fracture			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences (all)	2	1	
Arthropod bite			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Arthropod sting			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Fracture			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Skin abrasion			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Spinal fracture			
subjects affected / exposed	1 / 132 (0.76%)	2 / 132 (1.52%)	
occurrences (all)	1	2	
Wound			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Animal bite			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Epidural haemorrhage			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Face injury			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Fibula fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Foot fracture			

subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Head injury			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Humerus fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Lower limb fracture			
subjects affected / exposed	0 / 132 (0.00%)	3 / 132 (2.27%)	
occurrences (all)	0	3	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Patella fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Procedural headache			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Spinal compression fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Sunburn			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Wrist fracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			

subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Phimosis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Talipes			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Tachycardia			
subjects affected / exposed	2 / 132 (1.52%)	2 / 132 (1.52%)	
occurrences (all)	2	2	
Atrioventricular block complete			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Cardiac failure			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Cardiogenic shock			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Cardiomyopathy			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Congestive cardiomyopathy			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Left ventricular dysfunction			
subjects affected / exposed	1 / 132 (0.76%)	3 / 132 (2.27%)	
occurrences (all)	1	3	

Myocardial fibrosis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	1 / 132 (0.76%)	2 / 132 (1.52%)	
occurrences (all)	1	2	
Sinus tachycardia			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Ventricular hypokinesia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Ventricular tachycardia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Cardiac hypertrophy			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Myocardial infarction			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Pericardial effusion			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Pericarditis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Right ventricular hypertrophy			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Systolic dysfunction			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	3	
Nervous system disorders			
Headache			

subjects affected / exposed	32 / 132 (24.24%)	30 / 132 (22.73%)	
occurrences (all)	68	168	
Dizziness			
subjects affected / exposed	4 / 132 (3.03%)	3 / 132 (2.27%)	
occurrences (all)	4	3	
Migraine			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Benign intracranial hypertension			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Dystonia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Periodic limb movement disorder			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	1 / 132 (0.76%)	2 / 132 (1.52%)	
occurrences (all)	1	2	
Cluster headache			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	2	
Coma			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Encephalopathy			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Sleep disorder			

subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Leukocytosis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences (all)	2	1	
Tympanic membrane perforation			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Eustachian tube dysfunction			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Vertigo positional			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Tympanic membrane hyperaemia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Tympanic membrane scarring			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Eye disorders			

Cataract subcapsular			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Eye pruritus			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Astigmatism			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Cataract			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Dacryostenosis acquired			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	3	0	
Dry eye			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	3	0	
Eyelid oedema			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Myopia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis allergic			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Ocular hyperaemia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Vomiting			

subjects affected / exposed	18 / 132 (13.64%)	10 / 132 (7.58%)	
occurrences (all)	22	13	
Diarrhoea			
subjects affected / exposed	16 / 132 (12.12%)	22 / 132 (16.67%)	
occurrences (all)	23	31	
Constipation			
subjects affected / exposed	11 / 132 (8.33%)	8 / 132 (6.06%)	
occurrences (all)	13	6	
Nausea			
subjects affected / exposed	10 / 132 (7.58%)	8 / 132 (6.06%)	
occurrences (all)	18	10	
Abdominal pain upper			
subjects affected / exposed	9 / 132 (6.82%)	11 / 132 (8.33%)	
occurrences (all)	12	14	
Abdominal pain			
subjects affected / exposed	8 / 132 (6.06%)	7 / 132 (5.30%)	
occurrences (all)	13	10	
Dyspepsia			
subjects affected / exposed	3 / 132 (2.27%)	3 / 132 (2.27%)	
occurrences (all)	3	4	
Abdominal discomfort			
subjects affected / exposed	2 / 132 (1.52%)	3 / 132 (2.27%)	
occurrences (all)	2	3	
Flatulence			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences (all)	2	1	
Toothache			
subjects affected / exposed	2 / 132 (1.52%)	1 / 132 (0.76%)	
occurrences (all)	3	1	
Abnormal faeces			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Anal pruritus			

subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Breath odour			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Faeces soft			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal pain			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Gingival pain			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Oral disorder			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Teething			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Chronic gastritis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Dysphagia			

subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Faecaloma			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Food poisoning			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Frequent bowel movements			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Hyperchlorhydria			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Lip swelling			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Odynophagia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Catheter site pain			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Injection site reaction			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	4 / 132 (3.03%)	4 / 132 (3.03%)	
occurrences (all)	4	4	
Dry skin			
subjects affected / exposed	3 / 132 (2.27%)	0 / 132 (0.00%)	
occurrences (all)	3	0	

Eczema				
subjects affected / exposed	3 / 132 (2.27%)	5 / 132 (3.79%)		
occurrences (all)	3	4		
Dandruff				
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)		
occurrences (all)	1	0		
Dermatitis allergic				
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)		
occurrences (all)	2	0		
Dermatitis contact				
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)		
occurrences (all)	1	0		
Ecchymosis				
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)		
occurrences (all)	1	0		
Erythema				
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)		
occurrences (all)	1	1		
Mechanical urticaria				
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)		
occurrences (all)	1	0		
Pigmentation disorder				
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)		
occurrences (all)	1	0		
Pityriasis rosea				
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)		
occurrences (all)	1	0		
Psoriasis				
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)		
occurrences (all)	2	0		
Rash				
subjects affected / exposed	1 / 132 (0.76%)	4 / 132 (3.03%)		
occurrences (all)	1	4		
Rash generalised				
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)		
occurrences (all)	1	1		

Seborrhoea			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Skin ulcer			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Acne			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Dermatitis bullous			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Dyshidrotic eczema			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Ingrowing nail			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	2	
Miliaria			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Rash pruritic			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Skin discolouration			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	

Skin disorder			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	2	
Skin lesion			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Skin mass			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	11 / 132 (8.33%)	0 / 132 (0.00%)	
occurrences (all)	14	0	
Nephrolithiasis			
subjects affected / exposed	3 / 132 (2.27%)	4 / 132 (3.03%)	
occurrences (all)	4	4	
Choluria			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Glycosuria			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Haematuria			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Haemoglobinuria			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			

subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Ureterolithiasis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Ketonuria			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Proteinuria			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Urge incontinence			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Urinary hesitation			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Endocrine disorders			
Delayed puberty			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Cushingoid			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	9 / 132 (6.82%)	15 / 132 (11.36%)	
occurrences (all)	12	25	
Arthralgia			
subjects affected / exposed	7 / 132 (5.30%)	9 / 132 (6.82%)	
occurrences (all)	7	10	
Myalgia			

subjects affected / exposed	5 / 132 (3.79%)	1 / 132 (0.76%)	
occurrences (all)	6	1	
Scoliosis			
subjects affected / exposed	5 / 132 (3.79%)	1 / 132 (0.76%)	
occurrences (all)	6	1	
Pain in extremity			
subjects affected / exposed	3 / 132 (2.27%)	3 / 132 (2.27%)	
occurrences (all)	3	3	
Joint swelling			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 132 (1.52%)	2 / 132 (1.52%)	
occurrences (all)	2	2	
Osteoporosis			
subjects affected / exposed	2 / 132 (1.52%)	5 / 132 (3.79%)	
occurrences (all)	2	5	
Bone pain			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Coccydynia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Dactylitis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Flank pain			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Joint contracture			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	2	2	
Joint stiffness			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Muscle hypertrophy			

subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 132 (0.76%)	2 / 132 (1.52%)	
occurrences (all)	1	2	
Neck pain			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Tendon pain			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Chest wall mass			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Extremity contracture			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Foot deformity			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Muscle contracture			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Spinal pain			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Delirium			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	45 / 132 (34.09%)	36 / 132 (27.27%)	
occurrences (all)	68	50	
Upper respiratory tract infection			
subjects affected / exposed	18 / 132 (13.64%)	17 / 132 (12.88%)	
occurrences (all)	24	24	
Gastroenteritis			
subjects affected / exposed	11 / 132 (8.33%)	5 / 132 (3.79%)	
occurrences (all)	13	6	
Influenza			
subjects affected / exposed	11 / 132 (8.33%)	8 / 132 (6.06%)	
occurrences (all)	13	9	
Urinary tract infection			
subjects affected / exposed	6 / 132 (4.55%)	2 / 132 (1.52%)	
occurrences (all)	6	6	
Otitis media			
subjects affected / exposed	5 / 132 (3.79%)	0 / 132 (0.00%)	
occurrences (all)	5	0	
Pneumonia			
subjects affected / exposed	5 / 132 (3.79%)	0 / 132 (0.00%)	
occurrences (all)	6	0	
Rhinitis			
subjects affected / exposed	5 / 132 (3.79%)	8 / 132 (6.06%)	
occurrences (all)	6	9	
Ear infection			
subjects affected / exposed	3 / 132 (2.27%)	8 / 132 (6.06%)	
occurrences (all)	3	9	
Localised infection			
subjects affected / exposed	3 / 132 (2.27%)	2 / 132 (1.52%)	
occurrences (all)	3	2	
Lower respiratory tract infection			
subjects affected / exposed	3 / 132 (2.27%)	2 / 132 (1.52%)	
occurrences (all)	3	2	
Pharyngitis			
subjects affected / exposed	3 / 132 (2.27%)	6 / 132 (4.55%)	
occurrences (all)	3	6	

Bronchitis			
subjects affected / exposed	2 / 132 (1.52%)	3 / 132 (2.27%)	
occurrences (all)	3	5	
Dysentery			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Furuncle			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Gastroenteritis viral			
subjects affected / exposed	2 / 132 (1.52%)	3 / 132 (2.27%)	
occurrences (all)	2	3	
Respiratory tract infection			
subjects affected / exposed	2 / 132 (1.52%)	2 / 132 (1.52%)	
occurrences (all)	2	3	
Corona virus infection			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Cystitis			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Enterocolitis infectious			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Fungal skin infection			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Oral fungal infection			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	

Oral herpes			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	3	
Paronychia			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Pilonidal cyst			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Rash pustular			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Sepsis			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Skin infection			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Tinea versicolour			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	1 / 132 (0.76%)	2 / 132 (1.52%)	
occurrences (all)	1	3	
Tracheitis			
subjects affected / exposed	1 / 132 (0.76%)	2 / 132 (1.52%)	
occurrences (all)	1	3	
Viral infection			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Wound infection staphylococcal			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	

Appendicitis perforated			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Body tinea			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Eczema infected			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Gastrointestinal infection			
subjects affected / exposed	0 / 132 (0.00%)	2 / 132 (1.52%)	
occurrences (all)	0	2	
Genital infection fungal			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Groin infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Helicobacter infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Hordeolum			
subjects affected / exposed	0 / 132 (0.00%)	4 / 132 (3.03%)	
occurrences (all)	0	4	
Onychomycosis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	

Osteomyelitis chronic			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Peritonitis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Rhinovirus infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Scarlet fever			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Soft tissue infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Staphylococcal infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Tinea pedis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Wound infection			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	2	
Fat embolism			
subjects affected / exposed	1 / 132 (0.76%)	1 / 132 (0.76%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 132 (1.52%)	0 / 132 (0.00%)	
occurrences (all)	2	0	
Dehydration			

subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Folate deficiency			
subjects affected / exposed	1 / 132 (0.76%)	0 / 132 (0.00%)	
occurrences (all)	1	0	
Hyperhomocysteinaemia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Hyperuricaemia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	
Vitamin D deficiency			
subjects affected / exposed	0 / 132 (0.00%)	1 / 132 (0.76%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2016	Amendment1 1. Amendment to Inclusion criteria to introduce minimum age for study participants: 10 years old at Screening. 2. Amendment to Inclusion criteria to allow immunization with any pneumococcal polysaccharide vaccine. 3. Amendment to Section 4.4 Pregnancy to update the contraception methods for participating patients and their female partners of childbearing potential as well as the duration of required contraception after last study drug intake. 4. Amendment to Section 8.1.5 Assessment of Causality to introduce reference to the IB regarding available safety information with the study drug. 5. Introduction of Section 8.2.5 Reporting of the Suspected Unexpected Serious Adverse Reactions (SUSARs) by the Sponsor to provide definition of SUSARs and information about SUSARs reporting. 6. Minor editorial changes.
16 August 2016	Amendment 2 1. Amendment to the Synopsis and Section 2.1 Study Objectives to remove the assessment of idebenone pharmacokinetic profile in patients with DMD receiving glucocorticoid steroids 2. Amendment to the Synopsis and Section 2.2 Study Endpoints to remove the PK endpoints 3. The following Sections were amended to cross-refer to the PK substudy protocol (SIDEROS PK substudy): Synopsis Study Flow Chart 6.1 Outline of Study Procedures 6.2 Schedule of Assessments 6.3 Treatment and Storage of Biological Samples 9.3.2 Efficacy Evaluation 4. Amendment to Section 8.2.5 Reporting of the Suspected Unexpected Serious Adverse Reactions (SUSARs) by the Sponsor to also include the process for SUSAR reporting in Switzerland. 5. Amendment to Section 8.3.3 Safety Blood Sampling and Urine Analysis to clarify further testing upon an abnormal urinalysis.

08 February 2017	Amendment 3 1. Amendment to Synopsis and Section 4.1 Inclusion Criteria to specify that the 15% reproducibility of the FVC repeat refers to relative values. 2. Amendment to Synopsis and Section 4.2 Exclusion Criteria to: a. Allow the participation of patients that underwent exon-skipping or read-through gene therapy more than 6 months prior to Screening. b. Clarify the concept of symptomatic heart failure. c. Add a reference to Appendix B for the concept of hepatic impairment, which defines the Child-Pugh Score in chronic liver disease. 3. The following Sections were amended to introduce the collection of demographic data at Screening: Synopsis Study Flow Chart Section 6.1 Outline of Study Procedures Section 6.2 Schedule of Assessments Section 6.2.1 Screening Visit 4. Amendment to Section 8.1.5 Assessment of Causality to update the reference to the Investigator's Brochure regarding the list of AEs. 5. Amendment to Section 9.2.1 Intent-To-Treat Population to remove the word "violations" and replace it by "deviations". 6. Addition of Appendix B to attach the Child-Pugh score in chronic liver disease. 7. Minor editorial changes
04 September 2017	Amendment 4 v 0.9 for detailed description of the amendment see Appendix 16.1.1.1 of the CSR
20 November 2017	Amendment 5 v0.1 1. The responsible Physician of the study and the corresponding contact details have been changed. 2. Synopsis and Section 4.2 were amended: Exclusion criterion 8 has been changed to reintroduce the exclusion of patients with severe renal impairment (eGFR <30 mL/min/1.73 m2). 3. Minor clarification to Synopsis, Section 4.6 and Section 6.2.13 to specify that withdrawal criteria apply only to randomized patients. 4. The Schedule of Assessments table was corrected to remove "Randomization" mark from Visit 3/Week 13 and Visit 5/Week39. 5. Additional clarification was added to Section 8.1 for the classification of laboratory abnormalities. 6. Addition of a reference in Section 10.
20 June 2018	Amendment 6 (20 June 2018) see Appendix 16.1.1.1 of the CSR
19 May 2020	Addendum 1 (19 May 2020) – Particular measures related to COVID-19 pandemic
22 June 2020	Amendment 7 (22 June 2020) for detailed amendement description see Appendix 16.1.1.1 of CSR

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Data from an interim analysis (IA) conducted by an independent DSMB concluded that the study was unlikely to meet its PEP. Decision to terminate the study was made in October 2020 based on data from the IA. LPLV occurred on 1 Dec 2020.

Notes: