Clinical trial results:
Effects of oral Levosimendan (ODM-109) on respiratory function in patients with ALS

Summary

EudraCT number	2017-002754-36
Trial protocol	IE GB BE FI AT ES NL FR IT
Global end of trial date	26 June 2020

Results information

Result version number	v1 (current)
This version publication date	27 May 2021
First version publication date	27 May 2021

Trial information

Trial identification

Sponsor protocol code	3119002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03505021
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Orion Corporation
Sponsor organisation address	Orionintie 1, Espoo, Finland, 02200
Public contact	Clinical Trials Information, Orion Corporation, +358 0104261, clinicaltrials@orionpharma.com
Scientific contact	Clinical Trials Information, Orion Corporation, +358 0104261, clinicaltrials@orionpharma.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 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2020
Global end of trial reached?	Yes
Global end of trial date	26 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to confirm that levosimendan can significantly improve respiratory function measured by supine slow vital capacity (SVC) in amyotrophic lateral sclerosis (ALS) patients.

Protection of trial subjects:

Adverse events were followed by sponsor and the independent data and safety monitoring board (DSMB).
Futility analyses were conducted by DSMB when approximately 50% and when all the subjects had been treated for 12 weeks.
The study included frequent assessment of safety measurements typical of clinical trials, including blood pressure, heart rate 12-lead ECG, safety laboratory tests and adverse events. These were performed before, during and after study drug treatment. Specific criteria were in place for the withdrawal of patients from study treatment, including increased heart rate, pregnancy and need for invasive ventilator support. The investigator could also withdraw the treatment if considered to be in the best interests of the subject. Patients were free to leave the study at any time but were also withdrawn in the event of a safety finding of clinical concern.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 June 2018
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	Canada: 47
Country: Number of subjects enrolled	Italy: 34
Country: Number of subjects enrolled	United States: 150
Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	Spain: 59
Country: Number of subjects enrolled	Sweden: 26
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Austria: 7
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Finland: 13
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	Germany: 80
Country: Number of subjects enrolled	Ireland: 5
Country: Number of subjects enrolled	Australia: 20

Worldwide total number of subjects	496
EEA total number of subjects	270

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)	328
From 65 to 84 years	166
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Patients with amyotrophic lateral sclerosis (ALS) were recruited.

Pre-assignment

Screening details:

Male or female subjects with a diagnosis of probable or definite ALS according to El Escorial revised criteria, disease duration from symptom onset of 12-48 months, written or verbal IC obtained. Able to swallow study treatment capsules. Sitting SVC between 60-90% of the predicted value at screening visit. Stable riluzole and/or edaravone allowed.

Period 1

Period 1 title	Overall trial (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	Levosimendan

Arm description:

The daily dose of oral levosimendan was 1-2 mg.

Arm type	Experimental
Investigational medicinal product name	levosimendan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

1 mg capsule in the morning and when the dose was increased to 1 mg twice daily (after two weeks), the second dose was normally taken 12 hours later.

Arm title	Placebo

Arm description:

Oral placebo matching levosimendan capsules was given once or twice daily.

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule in the morning and when the dose was increased to one capsule twice daily (after two weeks), the second dose was
normally taken 12 hours later.

Number of subjects in period 1	Levosimendan	Placebo
Started	329	167
Completed	217	112
Not completed	112	55
Adverse event, serious fatal	9	8
Consent withdrawn by subject	6	1
Disease progression	33	17
Adverse event, non-fatal	26	9
Personal reason	21	12
Other	11	5
Lost to follow-up	5	3
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	496	496	
Age categorical Units: Subjects			
Adults (18-64 years)	328	328	
From 65-84 years	166	166	
85 years and over	2	2	
Gender categorical Units: Subjects			
Female	189	189	
Male	307	307	

End points

End points reporting groups	
Reporting group title	Levosimendan
Reporting group description:	
The daily dose of oral levosimendan was 1-2 mg.	
Reporting group title	Placebo
Reporting group description:	
Oral placebo matching levosimendan capsules was given once or twice daily.	

Primary: Change from baseline to 12 weeks in supine SVC	
End point title	Change from baseline to 12 weeks in supine SVC
End point description:	
End point type	Primary
End point timeframe:	
From baseline to 12 weeks	

End point values	Levosimendan	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	147		
Units: percent of predicted				
least squares mean (confidence interval 95%)	-6.731 (-8.290 to -5.171)	-6.988 (-9.052 to -4.925)		

Statistical analyses

Statistical analysis title	Change from baseline, SVC (supine)
Statistical analysis description:	
Least square (LS) means estimate, repeated measures ANCOVA with missing data imputation	
Comparison groups	Placebo v Levosimendan
Number of subjects included in analysis	435
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8253
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.258
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.032
upper limit	2.547

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From signing an informed consent until 25 days from stopping the treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

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

Serious adverse events	Levosimendan	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	89 / 326 (27.30%)	45 / 166 (27.11%)	
number of deaths (all causes)	27	17	
number of deaths resulting from adverse events	27	17	
Vascular disorders			
AORTIC STENOSIS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTENSIVE CRISIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC DEATH			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CATHETER SITE INFLAMMATION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			
subjects affected / exposed	4 / 326 (1.23%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	3 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEATH			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 27	0 / 17	
EUTHANASIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUDDEN DEATH			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OVARIAN CYST			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	2 / 326 (0.61%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	7 / 326 (2.15%)	3 / 166 (1.81%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMPHYSEMA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERCAPNIA			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOVENTILATION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARYNGEAL OEDEMA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NASAL CONGESTION			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA ASPIRATION			
subjects affected / exposed	8 / 326 (2.45%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 9	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	9 / 326 (2.76%)	4 / 166 (2.41%)	
occurrences causally related to treatment / all	1 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY ACIDOSIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY DEPRESSION			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY DISTRESS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			

subjects affected / exposed	13 / 326 (3.99%)	5 / 166 (3.01%)	
occurrences causally related to treatment / all	0 / 13	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY MUSCLE WEAKNESS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
WHEEZING			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
INSOMNIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESTLESSNESS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
BRAIN CONTUSION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CERVICAL VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

CLAVICLE FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONTUSION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FACIAL BONES FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FALL			
subjects affected / exposed	13 / 326 (3.99%)	6 / 166 (3.61%)	
occurrences causally related to treatment / all	0 / 13	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMUR FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAND FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEAD INJURY			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIP FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
JOINT DISLOCATION			

subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
JOINT INJURY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LIP INJURY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCEDURAL PAIN			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RADIUS FRACTURE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RIB FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKULL FRACTURED BASE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL COMPRESSION FRACTURE			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBDURAL HAEMATOMA			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ULNA FRACTURE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
HYPERTROPHIC CARDIOMYOPATHY			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

CARDIAC FAILURE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY DISEASE			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY DISSECTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIASTOLIC DYSFUNCTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUS TACHYCARDIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STRESS CARDIOMYOPATHY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			

subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TACHYCARDIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (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			
AMYOTROPHIC LATERAL SCLEROSIS			
subjects affected / exposed	4 / 326 (1.23%)	3 / 166 (1.81%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRAIN INJURY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERCAPNIC COMA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTRAVENTRICULAR HAEMORRHAGE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LACUNAR STROKE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SOMNOLENCE			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UNRESPONSIVE TO STIMULI			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
BREAST CANCER			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOPHARYNGEAL CANCER			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
METASTASES TO LIVER			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
VERTIGO POSITIONAL			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPHAGIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER HAEMORRHAGE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROOESOPHAGEAL REFLUX			

DISEASE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS PARALYTIC			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PEPTIC ULCER			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
DECUBITUS ULCER			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

HYPERHIDROSIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INGROWING NAIL			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEPHROLITHIASIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROGENIC BLADDER			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URETHRAL OBSTRUCTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY RETENTION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
APPENDICITIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CATHETER SITE CELLULITIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CATHETER SITE INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROBACTER BACTERAEMIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NASOPHARYNGITIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (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	12 / 326 (3.68%)	7 / 166 (4.22%)	
occurrences causally related to treatment / all	0 / 12	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY SEPSIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (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 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SERRATIA BACTERAEMIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUSITIS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMA SITE INFECTION			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	5 / 166 (3.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION BACTERIAL			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Levosimendan	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	312 / 326 (95.71%)	157 / 166 (94.58%)	
Vascular disorders			
ARTERIOSCLEROSIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	5 / 326 (1.53%)	3 / 166 (1.81%)	
occurrences (all)	5	3	
HAEMATOMA			

subjects affected / exposed	4 / 326 (1.23%)	4 / 166 (2.41%)	
occurrences (all)	4	4	
HOT FLUSH			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
HYPERTENSION			
subjects affected / exposed	8 / 326 (2.45%)	9 / 166 (5.42%)	
occurrences (all)	8	10	
HYPOTENSION			
subjects affected / exposed	3 / 326 (0.92%)	2 / 166 (1.20%)	
occurrences (all)	4	2	
ILIAC ARTERY STENOSIS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	2	
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	5 / 326 (1.53%)	0 / 166 (0.00%)	
occurrences (all)	5	0	
PERIPHERAL COLDNESS			
subjects affected / exposed	0 / 326 (0.00%)	3 / 166 (1.81%)	
occurrences (all)	0	3	
RAYNAUD'S PHENOMENON			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
THROMBOSIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
VENOUS THROMBOSIS LIMB			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
Surgical and medical procedures			
CENTRAL VENOUS CATHETERISATION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
DENTAL IMPLANTATION			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
GASTROSTOMY			
subjects affected / exposed	4 / 326 (1.23%)	1 / 166 (0.60%)	
occurrences (all)	5	1	
MECHANICAL VENTILATION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Pregnancy, puerperium and perinatal conditions			
CEPHALHAEMATOMA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	16 / 326 (4.91%)	1 / 166 (0.60%)	
occurrences (all)	19	1	
CATHETER SITE BRUISE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
CATHETER SITE HAEMORRHAGE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
CATHETER SITE PAIN			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
CHEST DISCOMFORT			
subjects affected / exposed	4 / 326 (1.23%)	4 / 166 (2.41%)	
occurrences (all)	6	4	
CHEST PAIN			
subjects affected / exposed	9 / 326 (2.76%)	4 / 166 (2.41%)	
occurrences (all)	12	6	
CHILLS			
subjects affected / exposed	2 / 326 (0.61%)	2 / 166 (1.20%)	
occurrences (all)	2	2	
CYST			

subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
DISCOMFORT				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
DISEASE PROGRESSION				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
FATIGUE				
subjects affected / exposed	30 / 326 (9.20%)	10 / 166 (6.02%)		
occurrences (all)	33	11		
FEELING COLD				
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)		
occurrences (all)	1	1		
FEELING JITTERY				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	2	0		
GAIT DISTURBANCE				
subjects affected / exposed	9 / 326 (2.76%)	2 / 166 (1.20%)		
occurrences (all)	9	2		
INFLUENZA LIKE ILLNESS				
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)		
occurrences (all)	3	0		
MALAISE				
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)		
occurrences (all)	2	0		
MEDICAL DEVICE PAIN				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
MEDICAL DEVICE SITE ERYTHEMA				
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)		
occurrences (all)	1	1		
MEDICAL DEVICE SITE HAEMORRHAGE				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		

NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
OEDEMA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
OEDEMA PERIPHERAL			
subjects affected / exposed	26 / 326 (7.98%)	12 / 166 (7.23%)	
occurrences (all)	28	14	
PAIN			
subjects affected / exposed	11 / 326 (3.37%)	2 / 166 (1.20%)	
occurrences (all)	12	2	
PARADOXICAL DRUG REACTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PERIPHERAL SWELLING			
subjects affected / exposed	7 / 326 (2.15%)	3 / 166 (1.81%)	
occurrences (all)	7	4	
PYREXIA			
subjects affected / exposed	4 / 326 (1.23%)	4 / 166 (2.41%)	
occurrences (all)	5	5	
SECRETION DISCHARGE			
subjects affected / exposed	4 / 326 (1.23%)	3 / 166 (1.81%)	
occurrences (all)	4	3	
SWELLING FACE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
VESSEL PUNCTURE SITE BRUISE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
ALLERGY TO ARTHROPOD BITE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
CONTRAST MEDIA ALLERGY			

subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
SEASONAL ALLERGY			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
Social circumstances			
LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
ERECTILE DYSFUNCTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MENOPAUSAL SYMPTOMS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MENSTRUATION IRREGULAR			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
PROSTATITIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PROSTATOMEGALY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	

ATELECTASIS				
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)		
occurrences (all)	2	0		
BRONCHITIS CHRONIC				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
BRONCHOSPASM				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
CHOKING				
subjects affected / exposed	5 / 326 (1.53%)	2 / 166 (1.20%)		
occurrences (all)	5	2		
CHRONIC OBSTRUCTIVE PULMONARY DISEASE				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
COUGH				
subjects affected / exposed	16 / 326 (4.91%)	13 / 166 (7.83%)		
occurrences (all)	19	15		
COUGH DECREASED				
subjects affected / exposed	4 / 326 (1.23%)	0 / 166 (0.00%)		
occurrences (all)	4	0		
DIAPHRAGM MUSCLE WEAKNESS				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
DIAPHRAGMATIC PARALYSIS				
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)		
occurrences (all)	1	1		
DIAPHRAGMATIC SPASM				
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)		
occurrences (all)	3	0		
DYSPHONIA				
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)		
occurrences (all)	3	0		
DYSPNOEA				

subjects affected / exposed	54 / 326 (16.56%)	30 / 166 (18.07%)	
occurrences (all)	61	35	
DYSPNOEA AT REST			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
DYSPNOEA EXERTIONAL			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
EMPHYSEMA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
EPISTAXIS			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	2	
HYPERACTIVE PHARYNGEAL REFLEX			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HYPERVENTILATION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
HYPOVENTILATION			
subjects affected / exposed	3 / 326 (0.92%)	1 / 166 (0.60%)	
occurrences (all)	3	1	
HYPOXIA			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
INCREASED BRONCHIAL SECRETION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	3	0	
INCREASED UPPER AIRWAY SECRETION			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
INCREASED VISCOSITY OF UPPER RESPIRATORY SECRETION			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
LARYNGOSPASM			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
NASAL CONGESTION			
subjects affected / exposed	5 / 326 (1.53%)	4 / 166 (2.41%)	
occurrences (all)	5	4	
NASAL DRYNESS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
NASAL POLYPS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
NASAL PRURITUS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
OROPHARYNGEAL PAIN			
subjects affected / exposed	5 / 326 (1.53%)	6 / 166 (3.61%)	
occurrences (all)	5	6	
ORTHOPNOEA			
subjects affected / exposed	6 / 326 (1.84%)	3 / 166 (1.81%)	
occurrences (all)	6	3	
PHARYNGEAL ERYTHEMA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PLEURAL EFFUSION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	2	
PRODUCTIVE COUGH			
subjects affected / exposed	4 / 326 (1.23%)	3 / 166 (1.81%)	
occurrences (all)	5	3	
PULMONARY CONGESTION			

subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
PULMONARY MASS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
RESPIRATORY FAILURE			
subjects affected / exposed	17 / 326 (5.21%)	12 / 166 (7.23%)	
occurrences (all)	17	12	
RESPIRATORY MUSCLE WEAKNESS			
subjects affected / exposed	2 / 326 (0.61%)	3 / 166 (1.81%)	
occurrences (all)	2	3	
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
RHINITIS ALLERGIC			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
RHINORRHOEA			
subjects affected / exposed	4 / 326 (1.23%)	1 / 166 (0.60%)	
occurrences (all)	4	1	
SINUS CONGESTION			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	2	
SLEEP APNOEA SYNDROME			
subjects affected / exposed	5 / 326 (1.53%)	3 / 166 (1.81%)	
occurrences (all)	6	3	
SPUTUM RETENTION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
UPPER RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	

UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
VOCAL CORD DYSFUNCTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
WHEEZING			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
ABNORMAL DREAMS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
ADJUSTMENT DISORDER WITH DEPRESSED MOOD			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
AFFECT LABILITY			
subjects affected / exposed	6 / 326 (1.84%)	4 / 166 (2.41%)	
occurrences (all)	6	4	
AFFECTIVE DISORDER			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
AGITATION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
ANXIETY			
subjects affected / exposed	18 / 326 (5.52%)	6 / 166 (3.61%)	
occurrences (all)	18	6	
CONFUSIONAL STATE			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
DEPRESSED MOOD			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
DEPRESSION			

subjects affected / exposed	13 / 326 (3.99%)	4 / 166 (2.41%)	
occurrences (all)	13	4	
FEAR			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
HALLUCINATION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
INITIAL INSOMNIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
INSOMNIA			
subjects affected / exposed	22 / 326 (6.75%)	10 / 166 (6.02%)	
occurrences (all)	22	10	
MENTAL DISORDER			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MIDDLE INSOMNIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
PANIC ATTACK			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
RESTLESSNESS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
SLEEP DISORDER			
subjects affected / exposed	2 / 326 (0.61%)	2 / 166 (1.20%)	
occurrences (all)	2	2	
STRESS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
TENSION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Product issues			

DEVICE OCCLUSION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	6 / 326 (1.84%)	3 / 166 (1.81%)	
occurrences (all)	7	3	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 326 (1.23%)	3 / 166 (1.81%)	
occurrences (all)	5	3	
BACTERIAL TEST			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BACTERIAL TEST POSITIVE			
subjects affected / exposed	3 / 326 (0.92%)	1 / 166 (0.60%)	
occurrences (all)	3	1	
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
BLOOD CALCIUM DECREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	5 / 326 (1.53%)	2 / 166 (1.20%)	
occurrences (all)	6	2	
BLOOD FOLATE DECREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	2 / 326 (0.61%)	2 / 166 (1.20%)	
occurrences (all)	2	2	

BLOOD POTASSIUM INCREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BLOOD PRESSURE INCREASED			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
BLOOD PRESSURE ORTHOSTATIC INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
BLOOD SODIUM INCREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BLOOD THYROID STIMULATING HORMONE DECREASED			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
BLOOD THYROID STIMULATING HORMONE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
BLOOD URINE PRESENT			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BODY TEMPERATURE INCREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	6 / 326 (1.84%)	3 / 166 (1.81%)	
occurrences (all)	6	3	
CARDIAC MURMUR			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	4 / 326 (1.23%)	3 / 166 (1.81%)	
occurrences (all)	4	3	
ELECTROCARDIOGRAM T WAVE AMPLITUDE DECREASED			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
EOSINOPHIL COUNT INCREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
FORCED VITAL CAPACITY DECREASED			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	7 / 326 (2.15%)	3 / 166 (1.81%)	
occurrences (all)	7	3	
GASTRIC PH DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	2	
GLUCOSE URINE PRESENT			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
HAEMOGLOBIN DECREASED			
subjects affected / exposed	4 / 326 (1.23%)	0 / 166 (0.00%)	
occurrences (all)	4	0	
HEART RATE DECREASED			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
HEART RATE INCREASED			
subjects affected / exposed	64 / 326 (19.63%)	5 / 166 (3.01%)	
occurrences (all)	68	5	
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	2	
INTRAOCULAR PRESSURE INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
LYMPHOCYTE COUNT DECREASED			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MONOCYTE COUNT INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
NEUTROPHIL COUNT INCREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
ORTHOSTATIC HEART RATE RESPONSE INCREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
OXYGEN SATURATION DECREASED			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
PLATELET COUNT INCREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PROTEIN URINE PRESENT			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PULMONARY FUNCTION TEST DECREASED			
subjects affected / exposed	7 / 326 (2.15%)	2 / 166 (1.20%)	
occurrences (all)	7	2	
RED BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
SLOW VITAL CAPACITY DECREASED			
subjects affected / exposed	2 / 326 (0.61%)	2 / 166 (1.20%)	
occurrences (all)	2	2	
TRANSAMINASES INCREASED			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
TROPONIN INCREASED			
subjects affected / exposed	8 / 326 (2.45%)	1 / 166 (0.60%)	
occurrences (all)	9	1	
TROPONIN T INCREASED			
subjects affected / exposed	10 / 326 (3.07%)	2 / 166 (1.20%)	
occurrences (all)	10	2	
URINE ANALYSIS ABNORMAL			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	2	
URINE LEUKOCYTE ESTERASE POSITIVE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
VITAL CAPACITY DECREASED			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
WEIGHT DECREASED			
subjects affected / exposed	26 / 326 (7.98%)	15 / 166 (9.04%)	
occurrences (all)	27	15	
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
WHITE BLOOD CELLS URINE POSITIVE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
ANIMAL BITE			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	2	
ANKLE FRACTURE			

subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
BACK INJURY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BONE CONTUSION			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
BONE FISSURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BURNS SECOND DEGREE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
CLAVICLE FRACTURE			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
CONCUSSION			
subjects affected / exposed	3 / 326 (0.92%)	4 / 166 (2.41%)	
occurrences (all)	4	4	
CONTUSION			
subjects affected / exposed	21 / 326 (6.44%)	8 / 166 (4.82%)	
occurrences (all)	23	9	
CRANIOCEREBRAL INJURY			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
EYE CONTUSION			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
EYE INJURY			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
FACIAL BONES FRACTURE			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
FALL			

subjects affected / exposed	86 / 326 (26.38%)	45 / 166 (27.11%)	
occurrences (all)	150	100	
FIBULA FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
FOOT FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
GASTROSTOMY TUBE SITE COMPLICATION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HAND FRACTURE			
subjects affected / exposed	4 / 326 (1.23%)	0 / 166 (0.00%)	
occurrences (all)	4	0	
HEAD INJURY			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
HUMERUS FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HYPHAEMA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
INCISION SITE HAEMATOMA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
INCISION SITE IMPAIRED HEALING			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
JOINT DISLOCATION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
JOINT INJURY			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	

LIGAMENT RUPTURE				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
LIGAMENT SPRAIN				
subjects affected / exposed	8 / 326 (2.45%)	2 / 166 (1.20%)		
occurrences (all)	9	2		
LIMB INJURY				
subjects affected / exposed	0 / 326 (0.00%)	3 / 166 (1.81%)		
occurrences (all)	0	3		
LIP INJURY				
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)		
occurrences (all)	1	1		
MUSCLE INJURY				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
MUSCLE STRAIN				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
MUSCULOSKELETAL FOREIGN BODY				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
NASAL INJURY				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
POST LUMBAR PUNCTURE SYNDROME				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
POST-TRAUMATIC PAIN				
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)		
occurrences (all)	2	2		
PROCEDURAL PAIN				
subjects affected / exposed	5 / 326 (1.53%)	0 / 166 (0.00%)		
occurrences (all)	5	0		
RADIUS FRACTURE				

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
RIB FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	3 / 326 (0.92%)	2 / 166 (1.20%)	
occurrences (all)	3	3	
SCRATCH			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
SCROTAL HAEMATOMA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
SKIN ABRASION			
subjects affected / exposed	5 / 326 (1.53%)	1 / 166 (0.60%)	
occurrences (all)	7	1	
SKIN INJURY			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
SKIN LACERATION			
subjects affected / exposed	17 / 326 (5.21%)	12 / 166 (7.23%)	
occurrences (all)	20	15	
SPINAL FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
STOMA SITE DISCOMFORT			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
STOMA SITE PAIN			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
STOMA SITE REACTION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
THERMAL BURN			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
TOOTH FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
WOUND			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
WRIST FRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
AORTIC VALVE SCLEROSIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
ATRIAL FIBRILLATION			
subjects affected / exposed	4 / 326 (1.23%)	0 / 166 (0.00%)	
occurrences (all)	4	0	
BRADYCARDIA			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
CARDIAC DISCOMFORT			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
CARDIAC FLUTTER			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
CARDIAC HYPERTROPHY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
CARDIOMYOPATHY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	

CARDIOVASCULAR DISORDER			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
CORONARY ARTERY DISEASE			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
DIASTOLIC DYSFUNCTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
LONG QT SYNDROME			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
MITRAL VALVE INCOMPETENCE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
NODAL RHYTHM			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PALPITATIONS			
subjects affected / exposed	17 / 326 (5.21%)	4 / 166 (2.41%)	
occurrences (all)	23	4	
SINUS TACHYCARDIA			
subjects affected / exposed	13 / 326 (3.99%)	0 / 166 (0.00%)	
occurrences (all)	14	0	
TACHYCARDIA			
subjects affected / exposed	32 / 326 (9.82%)	8 / 166 (4.82%)	
occurrences (all)	41	11	
TACHYCARDIA PAROXYSMAL			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	

VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
VENTRICULAR HYPERTROPHY			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
Nervous system disorders			
AGEUSIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
AMYOTROPHIC LATERAL SCLEROSIS			
subjects affected / exposed	4 / 326 (1.23%)	4 / 166 (2.41%)	
occurrences (all)	4	4	
ATAXIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BALANCE DISORDER			
subjects affected / exposed	2 / 326 (0.61%)	3 / 166 (1.81%)	
occurrences (all)	2	3	
BURNING SENSATION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
CERVICAL RADICULOPATHY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
COGNITIVE DISORDER			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
DEMENTIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
DEPRESSED LEVEL OF CONSCIOUSNESS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
DIZZINESS			

subjects affected / exposed	21 / 326 (6.44%)	13 / 166 (7.83%)	
occurrences (all)	35	14	
DROOLING			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
DYSARTHRIA			
subjects affected / exposed	6 / 326 (1.84%)	1 / 166 (0.60%)	
occurrences (all)	6	1	
DYSGEUSIA			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	3	
FINE MOTOR SKILL DYSFUNCTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HEADACHE			
subjects affected / exposed	101 / 326 (30.98%)	36 / 166 (21.69%)	
occurrences (all)	142	49	
HYPERREFLEXIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HYPOAESTHESIA			
subjects affected / exposed	4 / 326 (1.23%)	2 / 166 (1.20%)	
occurrences (all)	4	2	
INTENTION TREMOR			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
LETHARGY			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
MENTAL IMPAIRMENT			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MIGRAINE			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
MONOPARESIS			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MUSCLE CONTRACTIONS INVOLUNTARY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MUSCLE SPASTICITY			
subjects affected / exposed	7 / 326 (2.15%)	1 / 166 (0.60%)	
occurrences (all)	7	1	
NEURALGIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
NEUROLOGICAL DECOMPENSATION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PARAESTHESIA			
subjects affected / exposed	3 / 326 (0.92%)	1 / 166 (0.60%)	
occurrences (all)	3	1	
PAROSMIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PERONEAL NERVE PALSY			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
POOR QUALITY SLEEP			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
PRESYNCOPE			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
RADIAL NERVE PALSY			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	

RESTLESS LEGS SYNDROME			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
SCIATICA			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
SOMNOLENCE			
subjects affected / exposed	6 / 326 (1.84%)	3 / 166 (1.81%)	
occurrences (all)	6	3	
SPEECH DISORDER			
subjects affected / exposed	4 / 326 (1.23%)	1 / 166 (0.60%)	
occurrences (all)	5	1	
SYNCOPE			
subjects affected / exposed	8 / 326 (2.45%)	2 / 166 (1.20%)	
occurrences (all)	8	3	
TASTE DISORDER			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
TENSION HEADACHE			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences (all)	4	0	
TREMOR			
subjects affected / exposed	4 / 326 (1.23%)	2 / 166 (1.20%)	
occurrences (all)	4	2	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	3 / 326 (0.92%)	1 / 166 (0.60%)	
occurrences (all)	3	1	
ANAEMIA MACROCYTIC			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
BASAL CELL CARCINOMA			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	3	0	
BENIGN NEOPLASM OF THYROID GLAND			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
BOWEN'S DISEASE				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
HYPOPHARYNGEAL CANCER				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
INVASIVE DUCTAL BREAST CARCINOMA				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
LEUKOCYTOSIS				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
LEUKOPENIA				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
LYMPHADENITIS				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
LYMPHOPENIA				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
MYELOPROLIFERATIVE NEOPLASM				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
NORMOCYTIC ANAEMIA				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
SCHWANNOMA				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
SQUAMOUS CELL CARCINOMA OF SKIN				

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
TINNITUS			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences (all)	5	0	
VERTIGO			
subjects affected / exposed	6 / 326 (1.84%)	3 / 166 (1.81%)	
occurrences (all)	6	3	
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
Eye disorders			
BORDERLINE GLAUCOMA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
CATARACT			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
DIPLOPIA			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences (all)	3	0	
DRY EYE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
ENTROPION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
EYE DISCHARGE			

subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
EYE HAEMATOMA				
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)		
occurrences (all)	2	0		
EYE INFLAMMATION				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
EYE IRRITATION				
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)		
occurrences (all)	3	0		
EYE PAIN				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
EYE SWELLING				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
EYELID CYST				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	2	0		
GLAUCOMA				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
IRITIS				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
LACRIMATION INCREASED				
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)		
occurrences (all)	2	0		
MACULAR DEGENERATION				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
NEOVASCULAR AGE-RELATED MACULAR DEGENERATION				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		

VISION BLURRED			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	3 / 326 (0.92%)	4 / 166 (2.41%)	
occurrences (all)	3	4	
ABDOMINAL DISTENSION			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences (all)	4	0	
ABDOMINAL PAIN			
subjects affected / exposed	12 / 326 (3.68%)	2 / 166 (1.20%)	
occurrences (all)	13	2	
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	2	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	7 / 326 (2.15%)	2 / 166 (1.20%)	
occurrences (all)	7	2	
APHTHOUS ULCER			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
CONSTIPATION			
subjects affected / exposed	38 / 326 (11.66%)	21 / 166 (12.65%)	
occurrences (all)	41	22	
DENTAL CARIES			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
DENTAL DISCOMFORT			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
DIARRHOEA			
subjects affected / exposed	26 / 326 (7.98%)	14 / 166 (8.43%)	
occurrences (all)	31	18	
DRY MOUTH			

subjects affected / exposed	3 / 326 (0.92%)	1 / 166 (0.60%)		
occurrences (all)	3	1		
DYSPEPSIA				
subjects affected / exposed	3 / 326 (0.92%)	6 / 166 (3.61%)		
occurrences (all)	4	7		
DYSPHAGIA				
subjects affected / exposed	47 / 326 (14.42%)	27 / 166 (16.27%)		
occurrences (all)	55	31		
ENTERITIS				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
ERUCTATION				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
FLATULENCE				
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)		
occurrences (all)	2	1		
FOOD POISONING				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
GASTRIC HYPERMOTILITY				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
GASTRIC ULCER				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
GASTRITIS				
subjects affected / exposed	3 / 326 (0.92%)	2 / 166 (1.20%)		
occurrences (all)	3	2		
GASTROINTESTINAL PAIN				
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)		
occurrences (all)	1	2		
GASTROOESOPHAGEAL REFLUX DISEASE				
subjects affected / exposed	7 / 326 (2.15%)	3 / 166 (1.81%)		
occurrences (all)	7	3		

HIATUS HERNIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HYPOAESTHESIA ORAL			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
IRRITABLE BOWEL SYNDROME			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
LIP SWELLING			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
MOUTH ULCERATION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
NAUSEA			
subjects affected / exposed	29 / 326 (8.90%)	15 / 166 (9.04%)	
occurrences (all)	35	17	
ODYNOPHAGIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
ORAL MUCOSAL BLISTERING			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
RETCHING			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
SALIVARY GLAND ENLARGEMENT			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
SALIVARY HYPERSECRETION			
subjects affected / exposed	22 / 326 (6.75%)	9 / 166 (5.42%)	
occurrences (all)	23	10	

TONGUE ULCERATION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
TOOTHACHE			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	2	
VOMITING			
subjects affected / exposed	2 / 326 (0.61%)	5 / 166 (3.01%)	
occurrences (all)	2	6	
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
ALOPECIA			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
BLISTER			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
DECUBITUS ULCER			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences (all)	4	0	
DERMATITIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
DERMATITIS CONTACT			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
DRY SKIN			
subjects affected / exposed	5 / 326 (1.53%)	2 / 166 (1.20%)	
occurrences (all)	5	2	
DYSHIDROTIC ECZEMA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
ECZEMA			

subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
ERYTHEMA			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
HYPERHIDROSIS			
subjects affected / exposed	2 / 326 (0.61%)	2 / 166 (1.20%)	
occurrences (all)	2	2	
INGROWING NAIL			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MILIARIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
NIGHT SWEATS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PIGMENTATION DISORDER			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
PRURITUS			
subjects affected / exposed	10 / 326 (3.07%)	4 / 166 (2.41%)	
occurrences (all)	10	4	
RASH			
subjects affected / exposed	11 / 326 (3.37%)	6 / 166 (3.61%)	
occurrences (all)	11	8	
RASH MACULAR			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
RASH PAPULAR			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
SEBORRHOEA			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
SEBORRHOEIC DERMATITIS			
subjects affected / exposed	3 / 326 (0.92%)	0 / 166 (0.00%)	
occurrences (all)	3	0	
SKIN EXFOLIATION			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	2	
SKIN IRRITATION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	3	1	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BLADDER DYSFUNCTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BLADDER PAIN			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
BLADDER SPASM			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
CHROMATURIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HAEMATURIA			
subjects affected / exposed	0 / 326 (0.00%)	3 / 166 (1.81%)	
occurrences (all)	0	4	
HYPERTONIC BLADDER			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
INCONTINENCE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	

LEUKOCYTURIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
MICTURITION URGENCY			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
NEPHROLITHIASIS			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
NOCTURIA			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
POLLAKIURIA			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
POLYURIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
PROTEINURIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
RENAL COLIC			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
RENAL FAILURE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
RENAL PAIN			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
URGE INCONTINENCE			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
URINARY INCONTINENCE			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	

URINARY RETENTION			
subjects affected / exposed	3 / 326 (0.92%)	3 / 166 (1.81%)	
occurrences (all)	3	3	
URINE ABNORMALITY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
DIABETES INSIPIDUS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	13 / 326 (3.99%)	9 / 166 (5.42%)	
occurrences (all)	15	9	
ARTHRITIS			
subjects affected / exposed	3 / 326 (0.92%)	1 / 166 (0.60%)	
occurrences (all)	3	1	
BACK PAIN			
subjects affected / exposed	14 / 326 (4.29%)	7 / 166 (4.22%)	
occurrences (all)	16	11	
BONE PAIN			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
BURSITIS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
COCCYDYNIA			
subjects affected / exposed	3 / 326 (0.92%)	1 / 166 (0.60%)	
occurrences (all)	3	1	
EXOSTOSIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
FRACTURE PAIN			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
GROIN PAIN			

subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
JOINT HYPEREXTENSION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
JOINT NOISE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
JOINT SWELLING			
subjects affected / exposed	7 / 326 (2.15%)	0 / 166 (0.00%)	
occurrences (all)	7	0	
LIMB MASS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MOBILITY DECREASED			
subjects affected / exposed	4 / 326 (1.23%)	1 / 166 (0.60%)	
occurrences (all)	5	1	
MUSCLE CONTRACTURE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MUSCLE FATIGUE			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MUSCLE SPASMS			
subjects affected / exposed	17 / 326 (5.21%)	7 / 166 (4.22%)	
occurrences (all)	21	8	
MUSCLE TIGHTNESS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
MUSCLE TWITCHING			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
MUSCULAR WEAKNESS			
subjects affected / exposed	31 / 326 (9.51%)	18 / 166 (10.84%)	
occurrences (all)	39	18	
MUSCULOSKELETAL CHEST PAIN			

subjects affected / exposed	6 / 326 (1.84%)	1 / 166 (0.60%)	
occurrences (all)	6	1	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	14 / 326 (4.29%)	8 / 166 (4.82%)	
occurrences (all)	17	8	
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	4 / 326 (1.23%)	1 / 166 (0.60%)	
occurrences (all)	4	1	
MYALGIA			
subjects affected / exposed	4 / 326 (1.23%)	3 / 166 (1.81%)	
occurrences (all)	4	3	
NECK PAIN			
subjects affected / exposed	10 / 326 (3.07%)	6 / 166 (3.61%)	
occurrences (all)	11	6	
PAIN IN EXTREMITY			
subjects affected / exposed	24 / 326 (7.36%)	6 / 166 (3.61%)	
occurrences (all)	28	6	
PAIN IN JAW			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
PERIARTHRITIS			
subjects affected / exposed	3 / 326 (0.92%)	1 / 166 (0.60%)	
occurrences (all)	4	1	
POSTURE ABNORMAL			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
SPINAL PAIN			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
TENDONITIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
TENOSYNOVITIS STENOSANS			

subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
Infections and infestations			
ALVEOLAR OSTEITIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BACTERIAL INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
BACTERIURIA			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
BLASTOMYCOSIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
BRONCHITIS			
subjects affected / exposed	7 / 326 (2.15%)	4 / 166 (2.41%)	
occurrences (all)	8	4	
CANDIDA INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
CATHETER SITE INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
CELLULITIS			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	2	
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
CONJUNCTIVITIS			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
COVID-19			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	

CYSTITIS			
subjects affected / exposed	4 / 326 (1.23%)	4 / 166 (2.41%)	
occurrences (all)	6	4	
EAR INFECTION			
subjects affected / exposed	3 / 326 (0.92%)	3 / 166 (1.81%)	
occurrences (all)	3	3	
ERYSIPELAS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
EYE INFECTION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
FUNGAL INFECTION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
FUNGAL SKIN INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
FURUNCLE			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
GASTROENTERITIS			
subjects affected / exposed	2 / 326 (0.61%)	2 / 166 (1.20%)	
occurrences (all)	2	2	
GASTROENTERITIS VIRAL			
subjects affected / exposed	6 / 326 (1.84%)	2 / 166 (1.20%)	
occurrences (all)	7	2	
GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
GENITOURINARY TRACT INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HELMINTHIC INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	

HERPES ZOSTER				
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)		
occurrences (all)	2	0		
HORDEOLUM				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
IMPETIGO				
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)		
occurrences (all)	2	0		
INFECTED BITE				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
INFECTION				
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)		
occurrences (all)	1	1		
INFLUENZA				
subjects affected / exposed	4 / 326 (1.23%)	0 / 166 (0.00%)		
occurrences (all)	4	0		
LARYNGITIS				
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)		
occurrences (all)	0	2		
LOCALISED INFECTION				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
LOWER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	4 / 326 (1.23%)	0 / 166 (0.00%)		
occurrences (all)	5	0		
MALASSEZIA INFECTION				
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)		
occurrences (all)	0	1		
MEDICAL DEVICE SITE INFECTION				
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)		
occurrences (all)	1	0		
NAIL INFECTION				

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
NASOPHARYNGITIS			
subjects affected / exposed	52 / 326 (15.95%)	26 / 166 (15.66%)	
occurrences (all)	62	31	
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
ORAL FUNGAL INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
ORAL HERPES			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
OROPHARYNGEAL CANDIDIASIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
OTITIS MEDIA CHRONIC			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
PERIODONTITIS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
PHARYNGITIS			
subjects affected / exposed	2 / 326 (0.61%)	2 / 166 (1.20%)	
occurrences (all)	2	2	
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
PNEUMONIA			
subjects affected / exposed	2 / 326 (0.61%)	5 / 166 (3.01%)	
occurrences (all)	2	5	
POST PROCEDURAL INFECTION			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
POSTOPERATIVE WOUND INFECTION			

subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
PULPITIS DENTAL			
subjects affected / exposed	2 / 326 (0.61%)	2 / 166 (1.20%)	
occurrences (all)	2	3	
PYELITIS			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	7 / 326 (2.15%)	2 / 166 (1.20%)	
occurrences (all)	7	2	
RHINITIS			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	3	
ROOT CANAL INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
SIALOADENITIS			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
SINUSITIS			
subjects affected / exposed	8 / 326 (2.45%)	3 / 166 (1.81%)	
occurrences (all)	8	3	
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
STOMA SITE INFECTION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
TONGUE FUNGAL INFECTION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
TONSILLITIS			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
TOOTH ABSCESS			

subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
TOOTH INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	13 / 326 (3.99%)	5 / 166 (3.01%)	
occurrences (all)	16	5	
URINARY TRACT INFECTION			
subjects affected / exposed	25 / 326 (7.67%)	17 / 166 (10.24%)	
occurrences (all)	31	22	
URINARY TRACT INFECTION BACTERIAL			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
VIRAL INFECTION			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 326 (0.61%)	1 / 166 (0.60%)	
occurrences (all)	2	1	
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
CACHEXIA			
subjects affected / exposed	1 / 326 (0.31%)	1 / 166 (0.60%)	
occurrences (all)	1	1	
DECREASED APPETITE			
subjects affected / exposed	10 / 326 (3.07%)	5 / 166 (3.01%)	
occurrences (all)	10	5	
DEHYDRATION			
subjects affected / exposed	1 / 326 (0.31%)	2 / 166 (1.20%)	
occurrences (all)	1	2	
DIABETES MELLITUS			

subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
GOUT			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
HYPERKALAEMIA			
subjects affected / exposed	0 / 326 (0.00%)	2 / 166 (1.20%)	
occurrences (all)	0	3	
HYPERLIPIDAEMIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HYPOKALAEMIA			
subjects affected / exposed	3 / 326 (0.92%)	2 / 166 (1.20%)	
occurrences (all)	3	2	
HYPONATRAEMIA			
subjects affected / exposed	2 / 326 (0.61%)	0 / 166 (0.00%)	
occurrences (all)	2	0	
HYPOPHAGIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
HYPOVOLAEMIA			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
IRON DEFICIENCY			
subjects affected / exposed	1 / 326 (0.31%)	0 / 166 (0.00%)	
occurrences (all)	1	0	
MALNUTRITION			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
POLYDIPSIA			
subjects affected / exposed	0 / 326 (0.00%)	1 / 166 (0.60%)	
occurrences (all)	0	1	
VITAMIN B12 DEFICIENCY			

subjects affected / exposed occurrences (all)	1 / 326 (0.31%) 1	0 / 166 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 January 2018	-Orthostatic test was added as requested by the FDA. -Instruction not to report day-to-day fluctuation in ALS signs/symptoms (e.g. dysphagia,muscular weakness) not indicating clinically significant progression of the disease as an AE was added. -Background was updated regarding new information on tirasemtiv and CK-2127101. -Number of centres was updated from 70-80 to approximately 100. -Primary and secondary efficacy evaluations were clarified to include all SVC measurements prior to 12 weeks in the statistical model. -Timing of vital sign assessments during baseline and treatment period was clarified. -Flexibility was added to timing of the second daily dose to best meet clinical needs of the subjects. -Objectives related to health care resource use were updated to be in line with home diary questions. -Data to be collected on subjects who have discontinued the study treatment were clarified, as well as the end-of-study visit assessments for these subjects
17 April 2018	-Borg scale was added to obtain subjects' perception of the intensity of dyspnoea. -Use of edaravone was allowed as it was becoming standard of care in the USA. - CK-2127107 was replaced by the generic name reldesemtiv. -Discussion of cardiac safety and possible risks were added as requested by the Medical Products Agency (MPA) Sweden. -Exclusion of patients with severe renal impairment was added as requested by the MPA Sweden. -Lactating women were excluded as requested by the Medicines and Healthcare Products Regulatory Agency (MHRA) UK. -Use of highly effective contraceptive measures was added as requested by the Federal Agency for Medicines and Health Products (FAMPH) Belgium, Italian Medicines Agency (AIFA) Italy, Health Products Regulatory Authority (HPRA) Ireland and MPA Sweden. -ECG recording procedure was clarified and in order to verify that the measured HR represents genuine resting value, repeated 12-lead ECG recordings were added in connection with criteria on dose decrease. -Unblinding procedure was changed as requested by the MHRA UK. -Back-up system of the IWRS was added as requested by the MPA Sweden. -Pregnancy test was added to all physical visits except at week 2 as requested by the FAMPH Belgium and MHRA UK. -Re-screening procedure was clarified. -A mistake regarding PK sampling was corrected: at visits 4, 5, 6, and 7 only one blood sample was collected for levosimendan, OR-1855 and OR-1896 PK

26 March 2020	This amendment was written to describe how to perform visits 7 (week 36), 8 (week 48) and/or end-of-study visit (14-25 days after visit 8) remotely in case visit to the study centre was not possible due to restriction related to COVID-19 pandemic. The telephone visit was to include all protocol assessments that could be performed remotely and was to take place within the original visit window. In addition to the telephone visit, the investigator was to make reasonable efforts to obtain 12-lead ECG, laboratory safety assessments and vital signs for each visit. These measurements could include local practitioners and resources. In case these assessments, at least vital signs, could not be obtained within a reasonable time after the visit 7 telephone contact, the benefit-risk ratio for the subject to continue in the study was to be reassessed. The following assessments were not performed at telephone visits: SVC supine, weight, sitting or orthostatic changes in vital signs, blood sampling for levosimendan, OR-1855 and OR-1896 PK, for riluzole concentration and for exploratory biomarkers, and physical examination. Table 4. Study Procedures at remote visits was created.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported