Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Pulmaquin® in the Management of Chronic Lung Infections with Pseudomonas aeruginosa in Subjects with Non-Cystic Fibrosis Bronchiectasis, including 28 Day Open-Label Extension (ORBIT-4)

Summary

EudraCT number	2013-005366-19
Trial protocol	GB HU IT ES RO PL FR
Global end of trial date	12 October 2016

Results information

Result version number	v1 (current)
This version publication date	25 April 2018
First version publication date	25 April 2018

Trial information

Trial identification

Sponsor protocol code	ARD-3150-1202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02104245
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aradigm Corporation
Sponsor organisation address	3929 Point Eden Way, Hayward, California, United States, 94545
Public contact	Clinical Operations, Aradigm Corporation, +1 510 265 8895, JacksonA@aradigm.com
Scientific contact	Medical and Drug Development, Aradigm Corporation, +1 510 265 8838, froehlichj@aradigm.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	07 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 August 2016
Global end of trial reached?	Yes
Global end of trial date	12 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy of Linhaliq compared to placebo in the management of chronic lung infections with P. aeruginosa in subjects with non-cystic fibrosis (non-CF) bronchiectasis by evaluating the time to first pulmonary exacerbation in the Double-Blind Phase.

Protection of trial subjects:

The study was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 May 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Israel: 24
Country: Number of subjects enrolled	New Zealand: 16
Country: Number of subjects enrolled	Georgia: 28
Country: Number of subjects enrolled	Serbia: 10
Country: Number of subjects enrolled	Korea, Republic of: 14
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Romania: 17
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	United Kingdom: 43
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Australia: 26
Country: Number of subjects enrolled	Peru: 21
Country: Number of subjects enrolled	United States: 36
Country: Number of subjects enrolled	Canada: 10
Worldwide total number of subjects	304
EEA total number of subjects	119

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)	139
From 65 to 84 years	162
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

96 clinical sites screened at least one subject for the study. The sites were located in Australia, Canada, France, Georgia, Hungary, Israel, Italy, New Zealand, Peru, Poland, Romania, Serbia, South Korea, Spain, the United Kingdom, and the US. The first subject was screened on 28 May 2014, and the final subject screened on 04 August 2015.

Pre-assignment

Screening details:

533 were enrolled and screened. Subjects who met all eligibility criteria were randomized in a 2:1 ratio to receive once daily inhaled treatment with Pulmaquin or placebo.

Period 1

Period 1 title	Double-Blind Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

Liquid mixture of liposome-encapsulated and unencapsulated ciprofloxacin

Arm type	Experimental
Investigational medicinal product name	Linhaliq
Investigational medicinal product code	ARD-3150
Other name	Pulmaquin
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

The administered dose was 189 mg (6 mL) of ciprofloxacin comprised of one vial of 135 mg (3mL) liposome-encapsulated ciprofloxacin dispersion and one vial of 54 mg (3mL) free ciprofloxacin solution given once daily by oral inhalation using a nebuliser; the dosing regimen was 6 cycles of 28 days on treatment, followed by 28 days off treatment.

Arm title	Placebo

Arm description:

Liquid mixture of empty liposomes and normal saline

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

The administered dose was 6 mL placebo, comprised of one vial of 3 mL empty liposomes and one vial of 3 mL normal saline solution once daily by oral inhalation using a nebuliser; the dosing regimen was 6 cycles of 28 days on treatment, followed by 28 days off treatment.

Number of subjects in period 1	Active	Placebo
Started	206	98
Completed	178	81
Not completed	28	17
Adverse event, serious fatal	1	2
Physician decision	3	1
Consent withdrawn by subject	13	11
Adverse event, non-fatal	4	2
Other	2	-
Lost to follow-up	3	-
Lack of efficacy	1	-
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Active
Reporting group description:	
Liquid mixture of liposome-encapsulated and unencapsulated ciprofloxacin	
Reporting group title	Placebo
Reporting group description:	
Liquid mixture of empty liposomes and normal saline	

Reporting group values	Active	Placebo	Total
Number of subjects	206	98	304
Age categorical Units: Subjects			
Age continuous Units: years			
median	65.5	67.0	
full range (min-max)	18 to 90	21 to 86	-
Gender categorical Units: Subjects			
Female	134	63	197
Male	72	35	107

End points

End points reporting groups	
Reporting group title	Active
Reporting group description:	
Liquid mixture of liposome-encapsulated and unencapsulated ciprofloxacin	
Reporting group title	Placebo
Reporting group description:	
Liquid mixture of empty liposomes and normal saline	

Primary: Time to First Pulmonary Exacerbation	
End point title	Time to First Pulmonary Exacerbation
End point description:	
Median time to first pulmonary exacerbation	
End point type	Primary
End point timeframe:	
May 2014 to August 2016	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	98		
Units: Number of days				
median (confidence interval 95%)	230.0 (187.0 to 341.0)	158.0 (79.0 to 238.0)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Active v Placebo
Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0323
Method	Stratified Unweighted Log-Rank Test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.97

Secondary: Frequency of Pulmonary Exacerbations

End point title	Frequency of Pulmonary Exacerbations

End point description:

End point type	Secondary

End point timeframe:

May 2014 to August 2016

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	98		
Units: Number of Pulmonary Exacerbations				
arithmetic mean (standard error)	0.98 (± 0.09)	1.47 (± 0.11)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Active v Placebo
Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	Stratified Negative Binomial Regression
Parameter estimate	Risk ratio (RR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	0.82

Statistical analysis title	Statistical Analysis 2
Comparison groups	Active v Placebo

Number of subjects included in analysis	304
Analysis specification	Post-hoc
Analysis type	superiority
P-value	< 0.001
Method	Counting Process
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.76

Secondary: Frequency of Moderate and Severe Pulmonary Exacerbations

End point title	Frequency of Moderate and Severe Pulmonary Exacerbations
End point description:	

End point type	Secondary
End point timeframe:	
May 2014 to August 2016	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	98		
Units: Number of Pulmonary Exacerbations				
arithmetic mean (standard error)	0.78 (± 0.10)	1.27 (± 0.12)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Active v Placebo
Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Stratified Negative Binomial Regression
Parameter estimate	Risk ratio (RR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	0.77

Statistical analysis title	Statistical Analysis 2
Comparison groups	Active v Placebo
Number of subjects included in analysis	304
Analysis specification	Post-hoc
Analysis type	superiority
P-value	< 0.001
Method	Counting Process
Parameter estimate	Hazard ratio (HR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.71

Secondary: Frequency of Severe Pulmonary Exacerbations	
End point title	Frequency of Severe Pulmonary Exacerbations
End point description:	
End point type	Secondary
End point timeframe:	
May 2014 to August 2016	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	98		
Units: Number of Pulmonary Exacerbations				
arithmetic mean (standard error)	0.14 (± 0.24)	0.30 (± 0.25)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Active v Placebo

Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0031
Method	Stratified Negative Binomial Regression
Parameter estimate	Risk ratio (RR)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.74

Statistical analysis title	Statistical Analysis 2
Comparison groups	Active v Placebo
Number of subjects included in analysis	304
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.001
Method	Counting Process
Parameter estimate	Hazard ratio (HR)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.71

Adverse events

Adverse events information	
Timeframe for reporting adverse events: May 2014 to August 2016	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1
Reporting groups	
Reporting group title	Active
Reporting group description: Liquid mixture of liposome-encapsulated and unencapsulated ciprofloxacin	
Reporting group title	Placebo
Reporting group description: Liquid mixture of empty liposomes and normal saline	

Serious adverse events	Active	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 206 (16.99%)	28 / 98 (28.57%)	
number of deaths (all causes)	2	4	
number of deaths resulting from adverse events	1	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exercise tolerance decreased			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			

subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 206 (0.97%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
acute respiratory failure			
subjects affected / exposed	3 / 206 (1.46%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial secretion retention			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic respiratory failure			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cough			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	6 / 206 (2.91%)	5 / 98 (5.10%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Increased viscosity of bronchial secretion			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	3 / 206 (1.46%)	4 / 98 (4.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rhonchi			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sputum increased			
subjects affected / exposed	1 / 206 (0.49%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			

subjects affected / exposed	3 / 206 (1.46%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Breath sounds abnormal			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (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			
Avulsion fracture			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Periorbital haematoma			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
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	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoclonus			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Transient ischaemic attack			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (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 pain			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (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	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			

subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection bacterial			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	7 / 206 (3.40%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin graft infection			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sputum purulent			
subjects affected / exposed	1 / 206 (0.49%)	2 / 98 (2.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (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			
Gout			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Active	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	179 / 206 (86.89%)	95 / 98 (96.94%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Basal cell carcinoma			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	3	1	
Keratoacanthoma			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	2	
Myelofibrosis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Squamous cell carcinoma			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Cryoglobulinaemia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Hot flush			
subjects affected / exposed	3 / 206 (1.46%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Hypertension			
subjects affected / exposed	9 / 206 (4.37%)	3 / 98 (3.06%)	
occurrences (all)	14	3	
Hypotension			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Orthostatic hypotension			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Peripheral arterial occlusive disease			

subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Application site irritation			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	3 / 206 (1.46%)	1 / 98 (1.02%)	
occurrences (all)	3	1	
Chest discomfort			
subjects affected / exposed	9 / 206 (4.37%)	7 / 98 (7.14%)	
occurrences (all)	10	9	
Chest pain			
subjects affected / exposed	11 / 206 (5.34%)	4 / 98 (4.08%)	
occurrences (all)	12	4	
Chills			
subjects affected / exposed	2 / 206 (0.97%)	4 / 98 (4.08%)	
occurrences (all)	5	7	
Crepitations			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Device breakage			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Discomfort			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Exercise tolerance decreased			
subjects affected / exposed	54 / 206 (26.21%)	32 / 98 (32.65%)	
occurrences (all)	93	54	
Fatigue			

subjects affected / exposed	71 / 206 (34.47%)	49 / 98 (50.00%)		
occurrences (all)	124	99		
Hernia pain				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Influenza like illness				
subjects affected / exposed	3 / 206 (1.46%)	0 / 98 (0.00%)		
occurrences (all)	3	0		
Malaise				
subjects affected / exposed	36 / 206 (17.48%)	14 / 98 (14.29%)		
occurrences (all)	39	21		
Medical device site irritation				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Non-cardiac chest pain				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Oedema peripheral				
subjects affected / exposed	1 / 206 (0.49%)	6 / 98 (6.12%)		
occurrences (all)	1	7		
Pain				
subjects affected / exposed	4 / 206 (1.94%)	3 / 98 (3.06%)		
occurrences (all)	4	4		
Peripheral swelling				
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)		
occurrences (all)	2	1		
Product taste abnormal				
subjects affected / exposed	4 / 206 (1.94%)	0 / 98 (0.00%)		
occurrences (all)	4	0		
Pyrexia				
subjects affected / exposed	42 / 206 (20.39%)	24 / 98 (24.49%)		
occurrences (all)	62	33		
Systemic inflammatory response syndrome				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		

Vaccination site discomfort			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergy to animal			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Drug hypersensitivity			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Food allergy			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Hypersensitivity			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Seasonal allergy			
subjects affected / exposed	4 / 206 (1.94%)	0 / 98 (0.00%)	
occurrences (all)	4	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Prostatomegaly			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Asphyxia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Asthma			
subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	

Asthmatic crisis				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Bronchospasm				
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)		
occurrences (all)	1	2		
Catarrh				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Cough				
subjects affected / exposed	137 / 206 (66.50%)	71 / 98 (72.45%)		
occurrences (all)	285	192		
Diaphragmalgia				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Dry throat				
subjects affected / exposed	1 / 206 (0.49%)	3 / 98 (3.06%)		
occurrences (all)	1	3		
Dysphonia				
subjects affected / exposed	6 / 206 (2.91%)	1 / 98 (1.02%)		
occurrences (all)	6	1		
Dyspnoea				
subjects affected / exposed	106 / 206 (51.46%)	53 / 98 (54.08%)		
occurrences (all)	234	144		
Dyspnoea exertional				
subjects affected / exposed	2 / 206 (0.97%)	2 / 98 (2.04%)		
occurrences (all)	2	2		
Epistaxis				
subjects affected / exposed	5 / 206 (2.43%)	0 / 98 (0.00%)		
occurrences (all)	5	0		
Haemoptysis				

subjects affected / exposed	25 / 206 (12.14%)	18 / 98 (18.37%)	
occurrences (all)	36	30	
Hyperventilation			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Increased viscosity of bronchial secretion			
subjects affected / exposed	43 / 206 (20.87%)	24 / 98 (24.49%)	
occurrences (all)	78	41	
Nasal congestion			
subjects affected / exposed	5 / 206 (2.43%)	3 / 98 (3.06%)	
occurrences (all)	5	3	
Oropharyngeal pain			
subjects affected / exposed	10 / 206 (4.85%)	13 / 98 (13.27%)	
occurrences (all)	13	19	
Painful respiration			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Paranasal sinus discomfort			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Pharyngeal erythema			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Pleurisy			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Pleuritic pain			
subjects affected / exposed	6 / 206 (2.91%)	1 / 98 (1.02%)	
occurrences (all)	7	1	
Pneumothorax			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	9 / 206 (4.37%)	1 / 98 (1.02%)	
occurrences (all)	11	1	

Pulmonary embolism			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Pulmonary hypertension			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Pulmonary pain			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Rales			
subjects affected / exposed	13 / 206 (6.31%)	5 / 98 (5.10%)	
occurrences (all)	20	9	
Respiratory failure			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Respiratory tract congestion			
subjects affected / exposed	9 / 206 (4.37%)	8 / 98 (8.16%)	
occurrences (all)	11	8	
Rhinorrhoea			
subjects affected / exposed	11 / 206 (5.34%)	9 / 98 (9.18%)	
occurrences (all)	12	13	
Rhonchi			
subjects affected / exposed	3 / 206 (1.46%)	3 / 98 (3.06%)	
occurrences (all)	4	6	
Sinus congestion			
subjects affected / exposed	3 / 206 (1.46%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Sputum discoloured			
subjects affected / exposed	5 / 206 (2.43%)	7 / 98 (7.14%)	
occurrences (all)	7	7	
Sputum increased			
subjects affected / exposed	99 / 206 (48.06%)	62 / 98 (63.27%)	
occurrences (all)	186	155	

Sputum retention			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Tachypnoea			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Throat irritation			
subjects affected / exposed	4 / 206 (1.94%)	3 / 98 (3.06%)	
occurrences (all)	4	6	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	84 / 206 (40.78%)	48 / 98 (48.98%)	
occurrences (all)	149	114	
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 206 (0.49%)	2 / 98 (2.04%)	
occurrences (all)	1	3	
Anhedonia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	4 / 206 (1.94%)	1 / 98 (1.02%)	
occurrences (all)	4	1	
Depressed mood			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Emotional disorder			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Insomnia			

subjects affected / exposed	0 / 206 (0.00%)	3 / 98 (3.06%)	
occurrences (all)	0	3	
Irritability			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Major depression			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Middle insomnia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Mood altered			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Mood swings			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	2	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	3	
Anticonvulsant drug level increased			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Aspergillus test positive			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
blood cortisol decreased			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Blood creatine increased			

subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Blood glucose increased			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Body temperature increased			
subjects affected / exposed	3 / 206 (1.46%)	1 / 98 (1.02%)	
occurrences (all)	3	1	
Breath sounds abnormal			
subjects affected / exposed	61 / 206 (29.61%)	28 / 98 (28.57%)	
occurrences (all)	86	52	
C-reactive protein abnormal			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Chest X-ray abnormal			
subjects affected / exposed	7 / 206 (3.40%)	2 / 98 (2.04%)	
occurrences (all)	8	2	
Crystal urine present			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram change			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Forced expiratory volume decreased			
subjects affected / exposed	70 / 206 (33.98%)	33 / 98 (33.67%)	
occurrences (all)	114	55	
Forced vital capacity decreased			
subjects affected / exposed	48 / 206 (23.30%)	24 / 98 (24.49%)	
occurrences (all)	80	38	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	

Glomerular filtration rate decreased				
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)		
occurrences (all)	1	1		
Heart rate increased				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Hepatic enzyme increased				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
International normalised ratio fluctuation				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Liver function test abnormal				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Lymph node palpable				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Lymphocyte count increased				
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)		
occurrences (all)	3	0		
Medication residue present				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Neutrophil count increased				
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)		
occurrences (all)	2	1		
Platelet count increased				
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)		
occurrences (all)	2	0		
Pseudomonas test positive				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Pulmonary function test decreased				

subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Spirometry abnormal			
subjects affected / exposed	4 / 206 (1.94%)	1 / 98 (1.02%)	
occurrences (all)	5	1	
Sputum abnormal			
subjects affected / exposed	24 / 206 (11.65%)	15 / 98 (15.31%)	
occurrences (all)	38	30	
Transaminases increased			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	1 / 206 (0.49%)	3 / 98 (3.06%)	
occurrences (all)	2	3	
White blood cell count decreased			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
White blood cell count increased			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
White blood cells urine positive			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
X-ray abnormal			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Animal scratch			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Arthropod bite			

subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)		
occurrences (all)	1	1		
Arthropod sting				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Avulsion fracture				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Back injury				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Contusion				
subjects affected / exposed	5 / 206 (2.43%)	0 / 98 (0.00%)		
occurrences (all)	8	0		
Fall				
subjects affected / exposed	5 / 206 (2.43%)	0 / 98 (0.00%)		
occurrences (all)	12	0		
Foot fracture				
subjects affected / exposed	1 / 206 (0.49%)	2 / 98 (2.04%)		
occurrences (all)	1	2		
Forearm fracture				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Head injury				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Hip fracture				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Joint dislocation				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Joint injury				
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)		
occurrences (all)	2	0		
Laceration				

subjects affected / exposed	5 / 206 (2.43%)	2 / 98 (2.04%)	
occurrences (all)	5	2	
Ligament sprain			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	2	
Limb injury			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Muscle strain			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Post-traumatic neck syndrome			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Post-traumatic pain			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Procedural pain			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Rib fracture			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Skin abrasion			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Tooth fracture			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	5	0	
Wrist fracture			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	

Arrhythmia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Arrhythmia supraventricular			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Atrial fibrillation			
subjects affected / exposed	3 / 206 (1.46%)	2 / 98 (2.04%)	
occurrences (all)	3	2	
Bradycardia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Cardiac failure chronic			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Cor pulmonale chronic			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Myocardial infarction			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	5 / 206 (2.43%)	2 / 98 (2.04%)	
occurrences (all)	6	2	
Sinus tachycardia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Cluster headache			

subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Dementia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
dizziness			
subjects affected / exposed	13 / 206 (6.31%)	4 / 98 (4.08%)	
occurrences (all)	17	4	
Dizziness postural			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	13 / 206 (6.31%)	7 / 98 (7.14%)	
occurrences (all)	36	7	
Essential tremor			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	23 / 206 (11.17%)	14 / 98 (14.29%)	
occurrences (all)	33	24	
Hypogeusia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	49 / 206 (23.79%)	20 / 98 (20.41%)	
occurrences (all)	87	46	
Migraine			
subjects affected / exposed	1 / 206 (0.49%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Neuralgia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Neuropathy peripheral			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			

subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Parkinson's disease			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Resting tremor			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	2	
Sinus headache			
subjects affected / exposed	3 / 206 (1.46%)	0 / 98 (0.00%)	
occurrences (all)	4	0	
Somnolence			
subjects affected / exposed	3 / 206 (1.46%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Syncope			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Tremor			
subjects affected / exposed	2 / 206 (0.97%)	2 / 98 (2.04%)	
occurrences (all)	2	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 206 (1.94%)	0 / 98 (0.00%)	
occurrences (all)	4	0	
Eosinophilia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	0 / 206 (0.00%)	3 / 98 (3.06%)	
occurrences (all)	0	3	
White blood cell disorder			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	

Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Ear pain			
subjects affected / exposed	4 / 206 (1.94%)	5 / 98 (5.10%)	
occurrences (all)	6	5	
Excessive cerumen production			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
External ear inflammation			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Hypoacusis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Neurosensory hypoacusis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Tinnitus			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Vertigo			
subjects affected / exposed	3 / 206 (1.46%)	2 / 98 (2.04%)	
occurrences (all)	3	2	
Vertigo positional			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	2	
Diplopia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Dry eye			

subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Eye haemorrhage			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Eye pain			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Eye swelling			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Visual impairment			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Vitreous detachment			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Vitreous floaters			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	5 / 206 (2.43%)	5 / 98 (5.10%)	
occurrences (all)	7	5	
Abdominal pain upper			
subjects affected / exposed	3 / 206 (1.46%)	5 / 98 (5.10%)	
occurrences (all)	3	5	

Abdominal tenderness			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Anorectal discomfort			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Anorectal varices			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Chronic gastritis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	5 / 206 (2.43%)	2 / 98 (2.04%)	
occurrences (all)	5	2	
Dental caries			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	14 / 206 (6.80%)	10 / 98 (10.20%)	
occurrences (all)	17	11	
Dry mouth			
subjects affected / exposed	1 / 206 (0.49%)	4 / 98 (4.08%)	
occurrences (all)	1	4	
Dyspepsia			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Dysphagia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Epigastric discomfort			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Faecaloma			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	

Faeces soft			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Femoral hernia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Frequent bowel movements			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	1 / 206 (0.49%)	3 / 98 (3.06%)	
occurrences (all)	1	3	
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 206 (2.43%)	1 / 98 (1.02%)	
occurrences (all)	5	1	
Gingival pain			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids thrombosed			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Intestinal polyp			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Irritable bowel syndrome			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	

Lip pain			
subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Lip swelling			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
mouth ulceration			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	14 / 206 (6.80%)	7 / 98 (7.14%)	
occurrences (all)	19	13	
Odynophagia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Oesophagitis			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Portal hypertensive gastropathy			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Salivary gland enlargement			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Salivary hypersecretion			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Tongue ulceration			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Tooth impacted			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	

Varices oesophageal			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	6 / 206 (2.91%)	4 / 98 (4.08%)	
occurrences (all)	6	5	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	3 / 206 (1.46%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Gallbladder polyp			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Hepatic steatosis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Alopecia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Eczema			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Erythema			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			

subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Night sweats				
subjects affected / exposed	3 / 206 (1.46%)	1 / 98 (1.02%)		
occurrences (all)	3	1		
Onychomadesis				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Pain of skin				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Photosensitivity reaction				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Precancerous skin lesion				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Pruritus				
subjects affected / exposed	3 / 206 (1.46%)	4 / 98 (4.08%)		
occurrences (all)	3	4		
Purpura				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Rash				
subjects affected / exposed	7 / 206 (3.40%)	3 / 98 (3.06%)		
occurrences (all)	7	5		
Rash generalised				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Rash maculo-papular				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Rash pruritic				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Skin atrophy				

subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Skin disorder			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Skin lesion			
subjects affected / exposed	2 / 206 (0.97%)	2 / 98 (2.04%)	
occurrences (all)	2	2	
Skin reaction			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Bladder discomfort			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Micturition disorder			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Nephrolithiasis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Nocturia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 206 (6.31%)	5 / 98 (5.10%)	
occurrences (all)	14	5	
Arthritis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	8 / 206 (3.88%)	3 / 98 (3.06%)	
occurrences (all)	8	4	
Exostosis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Fibromyalgia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Joint effusion			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Joint swelling			
subjects affected / exposed	5 / 206 (2.43%)	1 / 98 (1.02%)	
occurrences (all)	5	2	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Muscle twitching			

subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	8 / 206 (3.88%)	1 / 98 (1.02%)	
occurrences (all)	8	1	
Musculoskeletal discomfort			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal pain			
subjects affected / exposed	5 / 206 (2.43%)	0 / 98 (0.00%)	
occurrences (all)	5	0	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	4 / 206 (1.94%)	7 / 98 (7.14%)	
occurrences (all)	10	8	
Neck pain			
subjects affected / exposed	1 / 206 (0.49%)	4 / 98 (4.08%)	
occurrences (all)	1	4	
Osteoarthritis			
subjects affected / exposed	3 / 206 (1.46%)	1 / 98 (1.02%)	
occurrences (all)	5	1	
Osteoporosis			
subjects affected / exposed	1 / 206 (0.49%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
pain in extremity			
subjects affected / exposed	8 / 206 (3.88%)	2 / 98 (2.04%)	
occurrences (all)	8	2	
Pain in jaw			
subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Plantar fasciitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Rheumatoid arthritis			

subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Rotator cuff syndrome			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Spinal pain			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Synovial cyst			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Tendon calcification			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Tendon disorder			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Tendonitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Tenosynovitis stenosans			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Abdominal hernia infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Abscess limb			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	4 / 206 (1.94%)	0 / 98 (0.00%)	
occurrences (all)	4	0	

Bronchitis viral			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Candida infection			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Catheter site infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Chlamydial infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Chronic sinusitis			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	3	1	
Conjunctivitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Diverticulitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	4 / 206 (1.94%)	3 / 98 (3.06%)	
occurrences (all)	5	3	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	

Fungal infection			
subjects affected / exposed	2 / 206 (0.97%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Fungal skin infection			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Gastroenteritis			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Gastroenteritis viral			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Helicobacter infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Herpes zoster			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Infectious disease carrier			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	2 / 206 (0.97%)	3 / 98 (3.06%)	
occurrences (all)	2	4	
Labyrinthitis			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	1	1	
Laryngitis			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Localised infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	

Lower respiratory tract infection bacterial				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Lyme disease				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Nasopharyngitis				
subjects affected / exposed	13 / 206 (6.31%)	6 / 98 (6.12%)		
occurrences (all)	15	7		
Nocardiosis				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Oesophageal candidiasis				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Oral candidiasis				
subjects affected / exposed	3 / 206 (1.46%)	4 / 98 (4.08%)		
occurrences (all)	3	6		
Oral herpes				
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)		
occurrences (all)	0	1		
Otitis externa				
subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)		
occurrences (all)	0	2		
Otitis media				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Otitis media acute				
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)		
occurrences (all)	1	1		
Pharyngitis				
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)		
occurrences (all)	1	0		
Pneumonia				

subjects affected / exposed	3 / 206 (1.46%)	0 / 98 (0.00%)	
occurrences (all)	3	0	
Pneumonia bacterial			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Respiratory tract infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	5 / 206 (2.43%)	4 / 98 (4.08%)	
occurrences (all)	5	7	
Sepsis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	13 / 206 (6.31%)	4 / 98 (4.08%)	
occurrences (all)	16	6	
Skin candida			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	2	0	
Sputum purulent			
subjects affected / exposed	52 / 206 (25.24%)	35 / 98 (35.71%)	
occurrences (all)	90	59	
Staphylococcal infection			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Tonsillitis			
subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Tooth abscess			
subjects affected / exposed	1 / 206 (0.49%)	2 / 98 (2.04%)	
occurrences (all)	1	2	
Tooth infection			

subjects affected / exposed	3 / 206 (1.46%)	1 / 98 (1.02%)	
occurrences (all)	4	1	
Upper respiratory tract infection			
subjects affected / exposed	8 / 206 (3.88%)	1 / 98 (1.02%)	
occurrences (all)	8	1	
Urinary tract infection			
subjects affected / exposed	10 / 206 (4.85%)	3 / 98 (3.06%)	
occurrences (all)	13	5	
Viral infection			
subjects affected / exposed	3 / 206 (1.46%)	2 / 98 (2.04%)	
occurrences (all)	3	2	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 206 (0.00%)	2 / 98 (2.04%)	
occurrences (all)	0	2	
Vulvovaginal candidiasis			
subjects affected / exposed	2 / 206 (0.97%)	4 / 98 (4.08%)	
occurrences (all)	2	5	
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 206 (0.49%)	1 / 98 (1.02%)	
occurrences (all)	2	2	
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	5 / 206 (2.43%)	0 / 98 (0.00%)	
occurrences (all)	5	0	
Dehydration			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Dyslipidaemia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Fluid retention			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	

Gout			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Hypercholesterolaemia			
subjects affected / exposed	2 / 206 (0.97%)	1 / 98 (1.02%)	
occurrences (all)	2	1	
Hyperkalaemia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Hypophagia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	
Vitamin B12 deficiency			
subjects affected / exposed	1 / 206 (0.49%)	0 / 98 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	0 / 206 (0.00%)	1 / 98 (1.02%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported