



## 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
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##### **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:

<b>Subjects enrolled per age group</b>	
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
<b>Arm title</b>	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.

<b>Arm title</b>	Placebo
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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.

<b>Number of subjects in period 1</b>	Active	Placebo
Started	206	98
Completed	178	81
Not completed	28	17
Adverse event, serious fatal	1	2
Consent withdrawn by subject	13	11
Physician decision	3	1
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 full range (min-max)	65.5 18 to 90	67.0 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

<b>Statistical analysis title</b>	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

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**Secondary: Frequency of Pulmonary Exacerbations**

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End point title	Frequency of Pulmonary Exacerbations
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End point description:

End point type	Secondary
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End point timeframe:

May 2014 to August 2016

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<b>End point values</b>	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 ( $\pm$ 0.09)	1.47 ( $\pm$ 0.11)		

**Statistical analyses**

<b>Statistical analysis title</b>	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

<b>Statistical analysis title</b>	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

<b>Statistical analysis title</b>	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

<b>Statistical analysis title</b>	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	

<b>End point values</b>	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

<b>Statistical analysis title</b>	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

<b>Statistical analysis title</b>	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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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### Reporting groups

Reporting group title	Active
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Reporting group description:

Liquid mixture of liposome-encapsulated and unencapsulated ciprofloxacin

Reporting group title	Placebo
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Reporting group description:

Liquid mixture of empty liposomes and normal saline

<b>Serious adverse events</b>	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	
<b>Haemoptysis</b>			
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	
<b>Hypoxia</b>			
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	
<b>Increased viscosity of bronchial secretion</b>			
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	
<b>Pulmonary oedema</b>			
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	
<b>Respiratory failure</b>			
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	
<b>Rhonchi</b>			
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	
<b>Sputum increased</b>			
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	
<b>Wheezing</b>			

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	
<b>Investigations</b>			
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	
<b>Injury, poisoning and procedural complications</b>			
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	
<b>Gastrointestinal disorders</b>			
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	
<b>Hepatobiliary disorders</b>			
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	
<b>Skin and subcutaneous tissue disorders</b>			
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	
<b>Musculoskeletal and connective tissue disorders</b>			
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	
<b>Infections and infestations</b>			
<b>Bronchiolitis</b>			
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	
<b>Bronchitis</b>			
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	
<b>Infective exacerbation of chronic obstructive airways disease</b>			
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	
<b>Influenza</b>			
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	
<b>Lower respiratory tract infection</b>			
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	
<b>Lower respiratory tract infection bacterial</b>			
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	
<b>Lung infection</b>			
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	
<b>Pneumonia</b>			

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 %

<b>Non-serious adverse events</b>	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 occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 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 occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Immune system disorders			
Allergy to animal subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Drug hypersensitivity subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Food allergy subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Hypersensitivity subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Seasonal allergy subjects affected / exposed occurrences (all)	4 / 206 (1.94%) 4	0 / 98 (0.00%) 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	2 / 206 (0.97%) 2	0 / 98 (0.00%) 0	
Prostatomegaly subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Asphyxia subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Asthma subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	2 / 98 (2.04%) 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 occurrences (all)	1 / 206 (0.49%) 1	1 / 98 (1.02%) 1	
Spirometry abnormal subjects affected / exposed occurrences (all)	4 / 206 (1.94%) 5	1 / 98 (1.02%) 1	
Sputum abnormal subjects affected / exposed occurrences (all)	24 / 206 (11.65%) 38	15 / 98 (15.31%) 30	
Transaminases increased subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Weight decreased subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 2	3 / 98 (3.06%) 3	
White blood cell count decreased subjects affected / exposed occurrences (all)	2 / 206 (0.97%) 2	0 / 98 (0.00%) 0	
White blood cell count increased subjects affected / exposed occurrences (all)	2 / 206 (0.97%) 2	0 / 98 (0.00%) 0	
White blood cells urine positive subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
X-ray abnormal subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Injury, poisoning and procedural complications			
Animal bite subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Animal scratch subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 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 occurrences (all)	2 / 206 (0.97%) 2	0 / 98 (0.00%) 0	
Eye haemorrhage subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Eye pain subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	1 / 98 (1.02%) 1	
Eye swelling subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Lacrimation increased subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Vision blurred subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Visual impairment subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Vitreous detachment subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Vitreous floaters subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
<b>Gastrointestinal disorders</b>			
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Abdominal pain subjects affected / exposed occurrences (all)	5 / 206 (2.43%) 7	5 / 98 (5.10%) 5	
Abdominal pain upper subjects affected / exposed occurrences (all)	3 / 206 (1.46%) 3	5 / 98 (5.10%) 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
Gastroesophageal 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 occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	6 / 206 (2.91%) 6	4 / 98 (4.08%) 5	
Hepatobiliary disorders			
Cholelithiasis subjects affected / exposed occurrences (all)	3 / 206 (1.46%) 3	0 / 98 (0.00%) 0	
Gallbladder polyp subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Skin and subcutaneous tissue disorders			
Actinic keratosis subjects affected / exposed occurrences (all)	2 / 206 (0.97%) 2	0 / 98 (0.00%) 0	
Alopecia subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Dermatitis subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Dry skin subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	1 / 98 (1.02%) 1	
Eczema subjects affected / exposed occurrences (all)	2 / 206 (0.97%) 2	1 / 98 (1.02%) 1	
Erythema subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 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 occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Skin disorder subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Skin lesion subjects affected / exposed occurrences (all)	2 / 206 (0.97%) 2	2 / 98 (2.04%) 2	
Skin reaction subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Renal and urinary disorders			
Bladder discomfort subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Dysuria subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Haematuria subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	1 / 98 (1.02%) 1	
Micturition disorder subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Nephrolithiasis subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Nocturia subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Pollakiuria subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	1 / 98 (1.02%) 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 occurrences (all)	2 / 206 (0.97%) 2	1 / 98 (1.02%) 1	
Rotator cuff syndrome subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Spinal osteoarthritis subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	1 / 98 (1.02%) 1	
Spinal pain subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Synovial cyst subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Tendon calcification subjects affected / exposed occurrences (all)	0 / 206 (0.00%) 0	1 / 98 (1.02%) 1	
Tendon disorder subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Tendonitis subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Tenosynovitis stenosaurs subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
<b>Infections and infestations</b>			
Abdominal hernia infection subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Abscess limb subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	0 / 98 (0.00%) 0	
Bronchitis subjects affected / exposed occurrences (all)	4 / 206 (1.94%) 4	0 / 98 (0.00%) 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

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported