Clinical trial results:
The efficacy and safety of erdosteine in the long-term therapy of chronic obstructive pulmonary disease (COPD). A 12-month, randomised, double-blind, placebo-controlled, parallel group, multicenter study.

Summary

EudraCT number	2008-008192-34
Trial protocol	IT GB CZ FR DK SK BE BG
Global end of trial date	03 February 2014

Results information

Result version number	v2
This version publication date	03 December 2016
First version publication date	13 November 2016
Version creation reason	• Correction of full data set we have to update non releated AE due to imput error.
Summary attachment (see zip file)	Study Synopsis (RESTORE SYNOPSIS.pdf)

Trial information

Trial identification

Sponsor protocol code	ERD-01-08/EP

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01032304
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Edmond Pharma Srl
Sponsor organisation address	S.S. dei Giovi 131, Paderno Dugnano (Mi), Italy, 20037
Public contact	Pozzi Edoardo, Edmond Pharma, +39 029500461, edoardo.pozzi@recipharm.com
Scientific contact	Pozzi Edoardo , Edmond Pharma, +39 029500461, edoardo.pozzi@recipharm.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	27 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal objective of the study is to evaluate if erdosteine is effective in reducing the risk of acute exacerbations in patients affected by moderate-to-severe COPD during a 12-month treatment period.

Protection of trial subjects:

The efficacy of erdosteine has been evaluated using the experimental drug as add-on to a regular maintenance therapy of COPD. Patients continued their standard treatment for COPD, established by the physician according to the best clinical practice and guidelines. Since patients, in any case, receive the appropriate COPD standard treatment, the administration of placebo to half of them do not posed particular ethical concerns, while being at the same time scientifically sounded in order to establish the additional benefits of adding erdosteine to regular maintenance COPD treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2009
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	United Kingdom: 22
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Bulgaria: 14
Country: Number of subjects enrolled	Czech Republic: 100
Country: Number of subjects enrolled	Denmark: 16
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Italy: 109
Country: Number of subjects enrolled	Romania: 126
Country: Number of subjects enrolled	Poland: 114
Country: Number of subjects enrolled	Slovakia: 11
Worldwide total number of subjects	528
EEA total number of subjects	528

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)	254
From 65 to 84 years	274
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient in 02-11-2009; last patient in 15/02/2013 . Countries involved: Italy, United Kingdom, Denmark, Czech Republic, France, Poland, Romania, Bulgaria, Slovakia and Belgium.

Pre-assignment

Screening details:

Outpatients of both sexes, aged between 40 and 80 years with diagnosis of COPD (Stage II and III according to GOLD 2007); with a stable therapeutic regimen for COPD for at least 8 weeks prior to inclusion, 61 screening failure were registered due to consent withdrown or lost to visit 1

Pre-assignment period milestones

Number of subjects started	528
Number of subjects completed	467

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 61

Period 1

Period 1 title	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:

blinded capsules erdosteine 300 mg

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

Dosage and administration details:

300 mg BID

Arm title	Placebo

Arm description:

Placebo

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

Dosage and administration details:

300 mg BID

Number of subjects in period 1[1]	Active	Placebo
Started	228	239
Completed	203	213
Not completed	25	26
Adverse event, serious fatal	1	2
Consent withdrawn by subject	14	20
Adverse event, non-fatal	10	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: the worldwide number enrolled corresponds to the enrolled patients (528 pts). During 2 weeks run-in period before randomization 61 pts. have been excluded for physicians decision. 467 pts have been randomized.

Baseline characteristics

Reporting groups	
Reporting group title	overall period

Reporting group description: -

Reporting group values	overall period	Total	
Number of subjects	467	467	
Age categorical			
patient aged between 40 and 80 years			
Units: Subjects			
40-80 yrs	467	467	
Age continuous			
Units: years			
median	64.8		
standard deviation	± 8.34	-	
Gender categorical			
Units: Subjects			
Female	122	122	
Male	345	345	
Population characteristic			
Units: Subjects			
COPD	467	467	

End points

End points reporting groups

Reporting group title	Active
Reporting group description: blinded capsules erdosteine 300 mg	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: overall number of exacerbations

End point title	overall number of exacerbations
End point description:	
End point type	Primary
End point timeframe: treatment period	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	239		
Units: exact number				
exacerbations	196	261		

Statistical analyses

Statistical analysis title	overall exacerbations rate

Statistical analysis description:

A predefined analysis of exacerbation frequency was performed using a Poisson regression model, with the covariates of treatment, age, sex, Body Mass Index, and FEV1 at the baseline to estimate the rate ratio. The natural logarithm of the duration, expressed as months in the study, was used as an offset variable to correct for differences in the time individuals spent under observation.

Comparison groups	Active v Placebo
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Poisson regression estimate

Confidence interval	
level	95 %
sides	2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: treatment duration 12 mounths	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	erdosteine
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Serious adverse events	erdosteine	placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 228 (17.98%)	33 / 239 (13.81%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events			
Investigations			
laringoscopy			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (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			
carbonon monoxide poisoning			
alternative dictionary used: MedDRA 17.1			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
transient cerebrovascular insufficency			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (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 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aneurysm			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Stroke in evolution			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
atrial fibrillation			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
heart failure			
subjects affected / exposed	2 / 228 (0.88%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			

Aortic bypass			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
chest/epigastric pain			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystectomy			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder empyema			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
COPD exacerbation			
subjects affected / exposed	16 / 228 (7.02%)	16 / 239 (6.69%)	
occurrences causally related to treatment / all	0 / 22	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 228 (1.75%)	5 / 239 (2.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			

subjects affected / exposed	1 / 228 (0.44%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia aspiration			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
cancer			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
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			
vertebral pain			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	erdosteine	placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	228 / 228 (100.00%)	206 / 239 (86.19%)	
Surgical and medical procedures			

Infiltration anaesthesia			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Liver function test abnormal			
subjects affected / exposed	1 / 228 (0.44%)	2 / 239 (0.84%)	
occurrences (all)	1	2	
Chills			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	2 / 228 (0.88%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Asthenia			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Haemoptysis			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	0 / 228 (0.00%)	4 / 239 (1.67%)	
occurrences (all)	0	5	
Insomnia			
subjects affected / exposed	0 / 228 (0.00%)	2 / 239 (0.84%)	
occurrences (all)	0	2	
Tooth abscess			
subjects affected / exposed	1 / 228 (0.44%)	1 / 239 (0.42%)	
occurrences (all)	2	1	
Toothache			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	2	
Weight decreased			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Viral infection			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Bronchopneumopathy			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	5 / 228 (2.19%)	4 / 239 (1.67%)	
occurrences (all)	5	6	
Chest pain			
subjects affected / exposed	2 / 228 (0.88%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	2 / 228 (0.88%)	3 / 239 (1.26%)	
occurrences (all)	2	3	
Throat irritation			
subjects affected / exposed	1 / 228 (0.44%)	4 / 239 (1.67%)	
occurrences (all)	1	4	
Dyspnoea			
subjects affected / exposed	3 / 228 (1.32%)	8 / 239 (3.35%)	
occurrences (all)	3	9	
Sputum discoloured			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Painful respiration			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 228 (0.44%)	1 / 239 (0.42%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	

COPD exacerbations			
subjects affected / exposed	99 / 228 (43.42%)	136 / 239 (56.90%)	
occurrences (all)	185	258	
Investigations			
Mitral valve replacement			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Chest injury			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 228 (0.44%)	1 / 239 (0.42%)	
occurrences (all)	1	1	
Cardiac disorder			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	1 / 228 (0.44%)	2 / 239 (0.84%)	
occurrences (all)	1	2	
Arrhythmia			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Coronary artery disease			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	8 / 228 (3.51%)	1 / 239 (0.42%)	
occurrences (all)	9	1	
Hypocalcaemia			
subjects affected / exposed	1 / 228 (0.44%)	1 / 239 (0.42%)	
occurrences (all)	1	1	
Tachycardia paroxysmal			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	

Nervous system disorders			
Anxiety			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	2 / 228 (0.88%)	0 / 239 (0.00%)	
occurrences (all)	3	0	
Dizziness			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Anaemia folate deficiency			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Hypoxia			
subjects affected / exposed	1 / 228 (0.44%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Arterial disorder			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Corneal abrasion			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Pain			

subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 228 (0.88%)	3 / 239 (1.26%)	
occurrences (all)	4	3	
Reflux gastritis			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	2 / 228 (0.88%)	1 / 239 (0.42%)	
occurrences (all)	3	1	
Dyspepsia			
subjects affected / exposed	1 / 228 (0.44%)	6 / 239 (2.51%)	
occurrences (all)	1	6	
Gastric ulcer			
subjects affected / exposed	2 / 228 (0.88%)	0 / 239 (0.00%)	
occurrences (all)	2	0	
Acidosis			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Bladder spasm			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Cholecystitis			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Salivary hypersecretion			

subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 228 (0.44%)	1 / 239 (0.42%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Infection			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 228 (0.44%)	1 / 239 (0.42%)	
occurrences (all)	1	1	
Urinary tract inflammation			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Proteinuria			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	4 / 228 (1.75%)	1 / 239 (0.42%)	
occurrences (all)	4	0	
Incontinence			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Diabetes mellitus			
subjects affected / exposed	2 / 228 (0.88%)	1 / 239 (0.42%)	
occurrences (all)	2	1	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	3 / 228 (1.32%)	3 / 239 (1.26%)	
occurrences (all)	3	3	
Contusion			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Bite			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Fibromyalgia			
subjects affected / exposed	1 / 228 (0.44%)	2 / 239 (0.84%)	
occurrences (all)	1	2	
Joint abscess			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
occurrences (all)	0	1	
Bone pain			
subjects affected / exposed	2 / 228 (0.88%)	1 / 239 (0.42%)	
occurrences (all)	2	1	
Oedema			
subjects affected / exposed	2 / 228 (0.88%)	1 / 239 (0.42%)	
occurrences (all)	0	0	
Infections and infestations			
Influenza			
subjects affected / exposed	3 / 228 (1.32%)	3 / 239 (1.26%)	
occurrences (all)	3	3	
Pyrexia			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Mycobacterial infection			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	0 / 228 (0.00%)	2 / 239 (0.84%)	
occurrences (all)	0	2	
Pneumonia			

subjects affected / exposed	1 / 228 (0.44%)	1 / 239 (0.42%)	
occurrences (all)	2	1	
Viraemia			
subjects affected / exposed	1 / 228 (0.44%)	2 / 239 (0.84%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Hyper HDL cholesterolaemia			
subjects affected / exposed	1 / 228 (0.44%)	0 / 239 (0.00%)	
occurrences (all)	1	0	
Cachexia			
subjects affected / exposed	0 / 228 (0.00%)	1 / 239 (0.42%)	
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