Clinical trial results:
A Phase III double-blind, randomised, placebo controlled trial of long term therapy on Exacerbation Rate in patients with stable COPD using Doxycycline

Summary

EudraCT number	2012-002199-15
Trial protocol	GB
Global end of trial date	12 July 2017

Results information

Result version number	v1 (current)
This version publication date	18 December 2019
First version publication date	18 December 2019

Trial information

Trial identification

Sponsor protocol code	12/0036

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02305940
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensingston Campus, London, United Kingdom, SW7 2AZ
Public contact	Jadwiga A Wedzicha, Imperial College London, j.wedzicha@imperial.ac.uk
Scientific contact	Jadwiga A Wedzicha, Imperial College London, j.wedzicha@imperial.ac.uk

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	02 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 July 2017
Global end of trial reached?	Yes
Global end of trial date	12 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal research question/objective is to assess whether the use of an antibiotic for 12 months by a group of patients with COPD reduces their rate of COPD exacerbations (periodic flare-ups of COPD symptoms) compared to a control group, taking a placebo.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 222
Worldwide total number of subjects	222
EEA total number of subjects	222

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)	50
From 65 to 84 years	172
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was between July 2014 and July 2017.

Pre-assignment

Screening details:

222 participants were eligible for the study

Period 1

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

Blinding implementation details:

The eligible and clinically stable participants randomisation into groups of 1:1 and patients remained blinded to treatment allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Doxycycline

Arm description:

Doxycycline: An oral dose of 100 mg once daily.

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

Dosage and administration details:

Oral dose of 100 mg once daily, for a total duration of 52 weeks.

Arm title	Placebo

Arm description:

Placebo one capsule daily

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

Dosage and administration details:

Oral dose of one capsule once daily for 52 weeks.

Number of subjects in period 1	Doxycycline	Placebo
Started	110	112
Completed	89	94
Not completed	21	18
Consent withdrawn by subject	10	7
death	4	1
Adverse event, non-fatal	-	3
Lost to follow-up	6	5
Protocol deviation	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Doxycycline
Reporting group description:	
Doxycycline: An oral dose of 100 mg once daily.	
Reporting group title	Placebo
Reporting group description:	
Placebo one capsule daily	

Reporting group values	Doxycycline	Placebo	Total
Number of subjects	110	112	222
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
geometric mean	68.8	67	
standard deviation	± 8	± 8	-
Gender categorical			
Units: Subjects			
Female	46	50	96
Male	64	62	126

End points

End points reporting groups

Reporting group title	Doxycycline

Reporting group description:

Doxycycline: An oral dose of 100 mg once daily.

Reporting group title	Placebo

Reporting group description:

Placebo one capsule daily

Primary: Rate of Exacerbations

End point title	Rate of Exacerbations[1]

End point description:

Rate of exacerbations (per person/year) recorded from date of drug issue until date of end of treatment visit.

End point type	Primary

End point timeframe:

12 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Rate of exacerbations (per person/year) recorded from date of drug issue until date of end of treatment visit.

End point values	Doxycycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: Exacerbations / year				
median (inter-quartile range (Q1-Q3))	2 (1 to 4)	3 (1 to 5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Expiratory Volume in 1 Sec (FEV1)

End point title	Forced Expiratory Volume in 1 Sec (FEV1)

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Doxycycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	94		
Units: litres				
arithmetic mean (confidence interval 95%)	-0.017 (-010 to 0.06)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Treatments
Comparison groups	Doxycycline v Placebo
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.22
Method	Mixed models analysis

Secondary: Total SGRQ score

End point title	Total SGRQ score

End point description:

The St George's Respiratory Questionnaire (SGRQ) is an instrument for the measuring of Health-Related Quality-of-Life in patients with diseases of airways obstruction.
All scales have a score range between 0 and 100 with higher scores indicating a worse quality of life.

End point type	Secondary

End point timeframe:

12 months

End point values	Doxycycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	94		
Units: score				
geometric mean (confidence interval 95%)	5.20 (1.80 to 8.70)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Treatments
Comparison groups	Doxycycline v Placebo

Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0034
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	8.7

Secondary: Adherence of the Participants

End point title	Adherence of the Participants

End point description:

Adherence as measured using pill counts, the odds of a patient being adherent (taking their pill) on a given day.

End point type	Secondary

End point timeframe:

12 months

End point values	Doxycycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: odds of taking pill				
arithmetic mean (confidence interval 95%)	0.87 (0.43 to 1.80)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Treatments
Comparison groups	Doxycycline v Placebo
Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.71
Method	Regression, Linear
Parameter estimate	Log odds ratio
Point estimate	0.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.8

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 14 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	Doxycycline
Reporting group description: Doxycycline: An oral dose of 100 mg once daily.	
Reporting group title	Placebo
Reporting group description: Placebo: Oral dose of one capsule once daily.	

Serious adverse events	Doxycycline	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 110 (30.91%)	23 / 112 (20.54%)	
number of deaths (all causes)	4	1	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Sarcoma diagnosis			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic prostate cancer			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer diagnosis			
subjects affected / exposed	0 / 110 (0.00%)	2 / 112 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Trauma to left thumb requiring surgical correction			

subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Two night hospital stay due to broken arm requiring surgery			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trauma with fracture of 6 ribs pneumothorax			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospital admission, left rib exacerbation COPD			
subjects affected / exposed	0 / 110 (0.00%)	2 / 112 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospital admission, right hip			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
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 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina secondary to iron deficiency			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death of patient, out of hospital cardiac arrest			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Fast AF complicated by pulmonary oedema			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Admission for percutaneous coronary intervention and insertion of stent into LAD			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dilated cardiomyopathy and mild pulmonary hypertension			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical chest pain with raised troponin			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death of patient, myocardial infarction			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial fibrillation with fast ventricular response, leading to left ventricular failure			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular systolic dysfunction			

subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina attack			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Elective orthopaedic surgery, correction of longstanding leg deformity			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Elective left total hip replacement			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Elective admission for laparotomy for division of adhesions + sigmoidopexy			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Admission for craniotomy			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonic clonic seizure, alcohol related?			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
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			
Unknown			

subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death of patient			
subjects affected / exposed	2 / 110 (1.82%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 2	0 / 0	
Consolidation A&E attendance			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right arm and right leg weakness, unable to smile + shaking			
subjects affected / exposed	0 / 110 (0.00%)	2 / 112 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
suspected DVT			
subjects affected / exposed	0 / 110 (0.00%)	2 / 112 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Small bowel obstruction			
subjects affected / exposed	2 / 110 (1.82%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
perforated diverticulum			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallstone cholecystitis diagnosed			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Incarcerated abdominal wall hernia			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowel blockage			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung cancer diagnosis			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spontaneous secondary pneumothorax			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Elective admission for Endobronchial valve insertion			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death of patient, diagnosed with metastatic lung cancer			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Hepatocellular carcinoma diagnosed			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Elective Trans-Urethral Resection of Prostate with 2 day admission			

subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Kidney Injury and Sepsis			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left sided hydronephrosis			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia requiring 6 day admission			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia and Multi-organ failure			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Community acquired pneumonia complicated by fast AF, initially treated as COPD exacerbation.			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospital acquired pneumonia			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suspected aspiration treated for chest infection			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Aspirate pneumonia			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Community acquired pneumonia			
subjects affected / exposed	0 / 110 (0.00%)	2 / 112 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Doxycycline	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 110 (8.18%)	23 / 112 (20.54%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Elective prostate biopsy			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Vascular disorders			
Peripheral Vascular Disease			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Elective shoulder replacement			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Cardiac disorders			
Acute Coronary Syndrome			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			

Tonic Clonic Seizure			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Nausea and skin flushing red			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Accidental unblinding of patient			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
A&E attendance, facial swelling following tooth extraction			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
SAE to exclude PE			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Atypical non-cardiac chest pain			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Admission to exclude PE			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Admission with sepsis			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Admission with atypical chest pain			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Elective admission for investigations to assess suitability for lung transplantation			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences (all)	1	0	

Right sided uncoordination			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences (all)	1	0	
Elective admission for assessment for ongoing non-invasive ventilation			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Likely oesophageal spasm			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Elective cholecystectomy			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences (all)	1	0	
Gastritis/oesophagitis			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences (all)	1	0	
Elective left inguinal hernia repair			
subjects affected / exposed	1 / 110 (0.91%)	0 / 112 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Scrotal abscess			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Infected sebaceous cyst on scrotum			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Elective urological operation			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	

Elective prostate/urethral surgery			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Endocrine disorders			
Admission with palpitations, hyperthyroidism			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 110 (0.00%)	2 / 112 (1.79%)	
occurrences (all)	0	2	
New diagnosis polymyalgia rheumatica			
subjects affected / exposed	0 / 110 (0.00%)	1 / 112 (0.89%)	
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