Clinical trial results:
The objective of the study was to evaluate the efficacy of mepolizumab 100 mg subcutaneous (SC) compared to placebo, given every 4 weeks in liquid formulation by safety syringe (SS) to Chronic Obstructive Pulmonary Disorder (COPD) participants at high risk of exacerbations despite the use of optimized COPD maintenance therapy.

Summary

EudraCT number	2018-001540-56
Trial protocol	PL HU ES NL DK BE DE SE IE IT GR AT
Global end of trial date	08 August 2024

Results information

Result version number	v1 (current)
This version publication date	20 August 2025
First version publication date	20 August 2025

Trial information

Trial identification

Sponsor protocol code	208657

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04133909
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	79 New Oxford Street, London, United Kingdom, WC1A 1DG
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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	08 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 August 2024
Global end of trial reached?	Yes
Global end of trial date	08 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the study was to evaluate the efficacy of mepolizumab 100 mg subcutaneous (SC) compared to placebo, given every 4 weeks in liquid formulation by safety syringe (SS) to COPD participants at high risk of exacerbations despite the use of optimized Chronic Obstructive Pulmonary Disorder (COPD) maintenance therapy.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 October 2019
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	Australia: 15
Country: Number of subjects enrolled	India: 79
Country: Number of subjects enrolled	Israel: 119
Country: Number of subjects enrolled	New Zealand: 29
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Denmark: 68
Country: Number of subjects enrolled	France: 52
Country: Number of subjects enrolled	Germany: 377
Country: Number of subjects enrolled	Greece: 21
Country: Number of subjects enrolled	Ireland: 6
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Netherlands: 41
Country: Number of subjects enrolled	Spain: 108
Country: Number of subjects enrolled	Sweden: 41
Country: Number of subjects enrolled	United Kingdom: 549
Country: Number of subjects enrolled	Hungary: 74
Country: Number of subjects enrolled	Poland: 270
Country: Number of subjects enrolled	China: 179
Country: Number of subjects enrolled	Korea, Republic of: 37
Country: Number of subjects enrolled	Taiwan: 2

Country: Number of subjects enrolled	Argentina: 371
Country: Number of subjects enrolled	Brazil: 28
Country: Number of subjects enrolled	Mexico: 18
Country: Number of subjects enrolled	Canada: 46
Country: Number of subjects enrolled	United States: 746
Worldwide total number of subjects	3306
EEA total number of subjects	1088

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)	1357
From 65 to 84 years	1926
85 years and over	23

Subject disposition

Recruitment

Recruitment details:

The study enrolled 806 participants from multiple locations and regions worldwide.

Pre-assignment

Screening details:

Among 806 participants, 2 were randomized in error and subsequently withdrawn from study (1 from the Mepolizumab 100 mg group and 1 from the Placebo group) without receiving any study intervention. The modified intention-to- treat (mITT) population consisted of 804 participants who were randomized and received at least 1 dose of trial medication.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Mepolizumab 100 mg

Arm description:

Participants with Chronic Obstructive Pulmonary Disease (COPD) received a 100 milligrams (mg) dose of mepolizumab as a subcutaneous injection every 4 weeks. Participants remained in the study for an assessment period of minimum of 52 weeks and a maximum of 104 weeks.

Arm type	Experimental
Investigational medicinal product name	Mepolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Eligible participants received Mepolizumab 100 mg SC injection every 4 weeks.

Arm title	Placebo

Arm description:

Participants with COPD received a matching placebo as a subcutaneous injection every 4 weeks. Participants remained in the study for an assessment period of minimum of 52 weeks and a maximum of 104 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received matching placebo every 4 weeks.

Number of subjects in period 1[1]	Mepolizumab 100 mg	Placebo
Started	403	401
Completed	339	331
Not completed	64	70
Adverse event, serious fatal	11	11
Physician decision	4	7
Consent withdrawn by subject	40	35
Adverse event, non-fatal	4	5
Lost to follow-up	3	5
Lack of efficacy	2	7

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: Total 3306 participants enrolled, 806 participants were randomized. Among 806 participants 2 participants were randomized in error and subsequently withdrawn from the study (one from the Mepolizumab 100 mg group and one from the Placebo group) without receiving any study intervention.

Baseline characteristics

Reporting groups	
Reporting group title	Mepolizumab 100 mg
Reporting group description:	
Participants with Chronic Obstructive Pulmonary Disease (COPD) received a 100 milligrams (mg) dose of mepolizumab as a subcutaneous injection every 4 weeks. Participants remained in the study for an assessment period of minimum of 52 weeks and a maximum of 104 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants with COPD received a matching placebo as a subcutaneous injection every 4 weeks. Participants remained in the study for an assessment period of minimum of 52 weeks and a maximum of 104 weeks.	

Reporting group values	Mepolizumab 100 mg	Placebo	Total
Number of subjects	403	401	804
Age categorical Units: Subjects			
19-64 years	143	173	316
>=65 years	260	228	488
Age continuous			
The Modified Intent-to-treat (mITT) population consisted of 804 participants who were randomized and received at least one dose of the trial medication.			
Units: years			
arithmetic mean	66.4	66	
standard deviation	± 8.10	± 7.91	-
Sex: Female, Male			
The mITT population consisted of 804 participants who were randomized and received at least one dose of the trial medication.			
Units: Participants			
Female	127	126	253
Male	276	275	551
Race/Ethnicity, Customized			
The 'All Other Races' category (Asian, American Indian or Alaska Native, Black or African American, and Mixed Race where 0<n<11) are combined into one category to maintain participant confidentiality and privacy. The mITT population consisted of 804 participants who were randomized and received at least one dose of the trial medication.			
Units: Subjects			
White	338	335	673
All Other Races	65	66	131

End points

End points reporting groups

Reporting group title	Mepolizumab 100 mg

Reporting group description:

Participants with Chronic Obstructive Pulmonary Disease (COPD) received a 100 milligrams (mg) dose of mepolizumab as a subcutaneous injection every 4 weeks. Participants remained in the study for an assessment period of minimum of 52 weeks and a maximum of 104 weeks.

Reporting group title	Placebo

Reporting group description:

Participants with COPD received a matching placebo as a subcutaneous injection every 4 weeks. Participants remained in the study for an assessment period of minimum of 52 weeks and a maximum of 104 weeks.

Primary: Annualized rate of moderate or severe exacerbations

End point title	Annualized rate of moderate or severe exacerbations

End point description:

Annualized rate of moderate or severe exacerbations were assessed. Moderate exacerbations are defined as clinically significant exacerbations that require treatment with oral or systemic corticosteroids and/or antibiotics. Severe exacerbations are defined per protocol as clinically significant exacerbations that require in-patient hospitalization (i.e., greater than or equal to [>=] 24 hours) or result in death. The analysis was performed on Modified Intent-to-Treat (mITT) population which included all randomized participants who received at least one dose of trial medication. Participants were analyzed by randomized treatment.

End point type	Primary

End point timeframe:

Up to Week 104

End point values	Mepolizumab 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	401		
Units: Exacerbations per year				
least squares mean (confidence interval 95%)	0.80 (0.70 to 0.91)	1.01 (0.89 to 1.15)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis performed using a negative binomial model with covariates of treatment group, geographic region, number of moderate or severe exacerbations in previous year (less than or equal to [<=]2, 3, >=4 as ordinal), baseline percent (%) predicted Forced expiratory volume in one second (FEV1) and smoking status (current vs. former smoker), and with logarithm (time on- and off-treatment) as an offset variable.

Comparison groups	Placebo v Mepolizumab 100 mg

Number of subjects included in analysis	804
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Negative binomial model
Parameter estimate	Rate ratio (Mepolizumab 100 mg/Placebo)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.94

Secondary: Time to first moderate or severe exacerbation

End point title	Time to first moderate or severe exacerbation

End point description:

The time to first moderate or severe exacerbation was determined as the number of days from the date of first dose to the date of the first moderate or severe exacerbation. Kaplan-Meier estimate of the cumulative percentage of participants with a moderate or severe exacerbation within each treatment arm over time were produced. The analysis was performed on mITT population which included all randomized participants who received at least one dose of trial medication. Participants were analyzed by randomized treatment.

End point type	Secondary

End point timeframe:

At week 8,16, 24, 32, 40, 48, 52, 56, 64, 72, 80, 88, 96, 104

End point values	Mepolizumab 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	401		
Units: Percentage of Participants				
number (confidence interval 95%)				
At week 8	11.3 (8.5 to 14.8)	15.1 (11.9 to 19.0)		
At week 16	21.6 (17.9 to 26.0)	25.6 (21.6 to 30.2)		
At week 24	28.3 (24.2 to 33.1)	35.4 (30.9 to 40.3)		
At week 32	33.6 (29.1 to 38.5)	41.6 (36.9 to 46.7)		
At week 40	39.8 (35.1 to 44.8)	47.1 (42.3 to 52.2)		
At week 48	44.9 (40.1 to 50.1)	51.4 (46.6 to 56.5)		
At week 52	46.1 (41.2 to 51.2)	53.4 (48.5 to 58.5)		
At week 56	46.7 (41.7 to 51.9)	54.0 (49.0 to 59.2)		
At week 64	51.4 (45.8 to 57.2)	58.9 (53.3 to 64.6)		

At week 72	55.9 (49.8 to 62.2)	60.5 (54.7 to 66.4)		
At week 80	59.0 (52.6 to 65.5)	62.3 (56.2 to 68.4)		
At week 88	60.6 (54.1 to 67.2)	64.2 (57.9 to 70.5)		
At week 96	62.3 (55.6 to 69.0)	67.2 (60.5 to 73.8)		
At week 104	64.5 (57.5 to 71.4)	68.3 (61.4 to 74.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Estimated from a Cox Proportional Hazards Model with covariates of treatment group, geographic region, number of moderate or severe exacerbations in previous year (<=2, 3, >=4 as ordinal), baseline % predicted FEV1 and smoking status (current vs former).

Comparison groups	Mepolizumab 100 mg v Placebo
Number of subjects included in analysis	804
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.93

Secondary: Percentage of COPD Assessment test (CAT) Responders with >=2 point Reduction from Baseline at Week 52

End point title	Percentage of COPD Assessment test (CAT) Responders with >=2 point Reduction from Baseline at Week 52

End point description:

The CAT is an 8-item questionnaire used to measure the health status of participants with COPD. Participants rated their experience on a 6-point scale, ranging from 0 (no impairment) to 5 (maximum impairment), with a scoring range of 0-40. Higher scores indicate greater disease impact, and lower score indicates lesser disease impact. Participants were considered responders if they had a 2-point or more improvement (reduction) in CAT Score from baseline. Participants who withdrew from the study prior to Week 52 were included in the analysis as non-responders. The baseline value was the last measurement collected prior to the first dose of investigational product. The analysis was performed on mITT population which included all randomized participants who received at least one dose of trial medication. Participants were analyzed by randomized treatment. Only those participants with data available at the baseline were analyzed. Percentages were rounded-off to the nearest whole number.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Mepolizumab 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	391	394		
Units: Percentage of participants				
number (not applicable)	41	46		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

A logistic regression model was used to compare the proportion of responders between the mepolizumab and placebo arms in the mITT and mITT2 populations. The model includes fixed categorical covariates (treatment group, smoking status, geographic region) and a fixed continuous covariate (baseline score).

Comparison groups	Placebo v Mepolizumab 100 mg
Number of subjects included in analysis	785
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.161
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.09

Secondary: Percentage of St. George's Respiratory Questionnaire for COPD (SGRQ) Total Score Responders with >=4-point Reduction from Baseline at Week 52

End point title	Percentage of St. George's Respiratory Questionnaire for COPD (SGRQ) Total Score Responders with >=4-point Reduction from Baseline at Week 52

End point description:

The St George’s Respiratory Questionnaire for COPD (SGRQ-C) is a 40-item questionnaire. The total SGRQ score is calculated by summing up the weights of all positively answered items across the entire questionnaire, dividing by the total possible weight for all questionnaire items. The total score was expressed as a percentage of overall impairment, with 0 (best possible health status) and 100 (the worst possible health status). Higher scores indicated greater impairment of health, and lower scores indicate a lesser impairment on health. A participant was considered a responder if they had a 4-point or more improvement (reduction) in the SGRQ-C total score from baseline. Participants who withdrew from the study prior to Week 52 were included in the analysis as non- responders. mITT population involved. Participants were analyzed by randomized treatment. Only those participants with data available at the baseline were analyzed. Percentages were rounded off to the nearest whole number.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Mepolizumab 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	390	393		
Units: Percentage of participants				
number (not applicable)	50	46		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

A logistic regression model was used to compare the proportion of responders between the mepolizumab and placebo arms in the mITT and mITT2 populations. The model includes fixed categorical covariates (treatment group, smoking status, geographic region) and a fixed continuous covariate (baseline score).

Comparison groups	Placebo v Mepolizumab 100 mg
Number of subjects included in analysis	783
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.291
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.57

Secondary: Annualized rate of Exacerbations Requiring Emergency Department (ED) visit and/or Hospitalization

End point title	Annualized rate of Exacerbations Requiring Emergency Department (ED) visit and/or Hospitalization

End point description:

Annualized rate of exacerbations requiring ED visit or hospitalization were evaluated. This included moderate exacerbations which led to a visit to the Emergency Department (ED) and severe exacerbations, were defined as clinically significant exacerbations that require in-patient hospitalization (>= 24 hours) or result in death. The analysis was performed on mITT population which included all randomized participants who received at least one dose of trial medication. Participants were analyzed by randomized treatment.

End point type	Secondary

End point timeframe:

Up to Week 104

End point values	Mepolizumab 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	401		
Units: Exacerbations per year				
least squares mean (confidence interval 95%)	0.13 (0.10 to 0.18)	0.20 (0.15 to 0.27)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis performed using a negative binomial model with covariates of treatment group, geographic region, number of moderate/severe exacerbations in previous year (<=2, 3, >=4 as ordinal), baseline % predicted FEV1 and smoking status (current vs. former smoker), and with logarithm (time on- and off-treatment) as an offset variable. Estimates based on weighting applied to each level of class variable determined from observed proportions.

Comparison groups	Mepolizumab 100 mg v Placebo
Number of subjects included in analysis	804
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032
Method	Negative binomial model
Parameter estimate	Rate ratio (Mepolizumab 100/Placebo)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.96

Secondary: Percentage of Evaluating Respiratory Symptoms in COPD (E-RS: COPD) responders with >=2 point reduction from Baseline

End point title	Percentage of Evaluating Respiratory Symptoms in COPD (E-RS: COPD) responders with >=2 point reduction from Baseline

End point description:

E-RS: COPD consists of 11 items from 14 item Exacerbations of Chronic Pulmonary Disease Tool (EXACT) instrument (completed each evening using an eDiary). E-RS: COPD is intended to capture information related to respiratory symptoms of COPD: breathlessness, cough, sputum production, chest congestion, and chest tightness. The E-RS: COPD has a scoring range of 0 (no symptoms)-40 (most severe symptoms), higher scores indicate more severe symptoms. A participant is considered a responder if they have a 2-unit or more improvement (reduction) in their average E-RS: COPD total score during a 4-week period prior to Week 52 (Weeks 49-52) compared to baseline. Average of daily scores in 4-weekly intervals were calculated; data is presented for Weeks 49-52. Participants who withdrew from study prior to start of Weeks 49-52 time-period were included in analysis as a non-responder. mITT population involved, including only those with baseline data. Percentages were rounded to nearest whole number.

End point type	Secondary

End point timeframe:

Baseline and 4-weeks prior to Week 52

End point values	Mepolizumab 100 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	403	399		
Units: Percentage of participants				
number (not applicable)	31	34		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

A logistic regression model was used to compare the proportion of responders between the mepolizumab and placebo arms in the mITT and mITT2 populations. The model includes fixed categorical covariates (treatment group, smoking status, geographic region) and a fixed continuous covariate (baseline score).

Comparison groups	Placebo v Mepolizumab 100 mg
Number of subjects included in analysis	802
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.209
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.12

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 104

Adverse event reporting additional description:

Data for All-Cause Mortality, Serious and Other (Non-Serious) Adverse Events were collected for the mITT population (all randomized participants, excluding those who were randomized in error). Safety population included all randomized participants who received at least one dose of trial medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants with COPD received a matching placebo as a subcutaneous injection every 4 weeks. Participants remained in the study for an assessment period of minimum of 52 weeks and a maximum of 104 weeks.

Reporting group title	Mepolizumab 100 mg

Reporting group description:

Participants with Chronic Obstructive Pulmonary Disease (COPD) received a 100 milligrams (mg) dose of mepolizumab as a subcutaneous injection every 4 weeks. Participants remained in the study for an assessment period of minimum of 52 weeks and a maximum of 104 weeks.

Serious adverse events	Placebo	Mepolizumab 100 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	115 / 401 (28.68%)	101 / 403 (25.06%)	
number of deaths (all causes)	11	11	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			

subjects affected / exposed	1 / 401 (0.25%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma stage I			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	2 / 401 (0.50%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			

subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	2 / 401 (0.50%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell carcinoma			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer metastatic			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tracheal cancer			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 401 (0.25%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 401 (0.25%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Embolism arterial			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypotension			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			

subjects affected / exposed	0 / 401 (0.00%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Chest discomfort			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
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			
Acute respiratory failure			
subjects affected / exposed	1 / 401 (0.25%)	3 / 403 (0.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	56 / 401 (13.97%)	48 / 403 (11.91%)	
occurrences causally related to treatment / all	0 / 78	0 / 74	
deaths causally related to treatment / all	0 / 3	0 / 2	
Chronic respiratory disease			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	0 / 401 (0.00%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung opacity			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal polyps			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	2 / 401 (0.50%)	4 / 403 (0.99%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	3 / 401 (0.75%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	3 / 401 (0.75%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device loosening			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Brain scan abnormal			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycobacterium tuberculosis complex test negative			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			

subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 401 (0.25%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoconiosis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural intestinal perforation			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pneumothorax			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			

subjects affected / exposed	2 / 401 (0.50%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	3 / 401 (0.75%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Angina unstable			
subjects affected / exposed	2 / 401 (0.50%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (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	1 / 401 (0.25%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 401 (0.25%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Left ventricular dysfunction			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 401 (0.25%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			

subjects affected / exposed	2 / 401 (0.50%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 401 (0.00%)	3 / 403 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 401 (0.25%)	4 / 403 (0.99%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Ventricular tachycardia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
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 occlusion			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (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 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinsonism			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	3 / 401 (0.75%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	3 / 401 (0.75%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polyp			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastric ulcer			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 401 (0.00%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin plaque			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Angiokeratoma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous emphysema			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (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			
subjects affected / exposed	2 / 401 (0.50%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 401 (0.50%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
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			
Arthritis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 401 (0.25%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	2 / 401 (0.50%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			

subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 401 (0.25%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	6 / 401 (1.50%)	4 / 403 (0.99%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 3	
Bronchitis			

subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 401 (0.25%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 401 (0.50%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	5 / 401 (1.25%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia pseudomonal			

subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	17 / 401 (4.24%)	14 / 403 (3.47%)	
occurrences causally related to treatment / all	0 / 22	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 401 (0.25%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 401 (0.00%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal abscess			

subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site abscess			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypervolaemia			

subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 401 (0.00%)	1 / 403 (0.25%)	
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: 3 %

Non-serious adverse events	Placebo	Mepolizumab 100 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	182 / 401 (45.39%)	195 / 403 (48.39%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	26 / 401 (6.48%)	16 / 403 (3.97%)	
occurrences (all)	29	16	
Nervous system disorders			
Headache			
subjects affected / exposed	28 / 401 (6.98%)	32 / 403 (7.94%)	
occurrences (all)	41	62	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 401 (2.99%)	22 / 403 (5.46%)	
occurrences (all)	19	23	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	15 / 401 (3.74%)	13 / 403 (3.23%)	
occurrences (all)	17	15	
Dyspnoea			
subjects affected / exposed	21 / 401 (5.24%)	19 / 403 (4.71%)	
occurrences (all)	38	30	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 401 (4.24%)	23 / 403 (5.71%)	
occurrences (all)	20	29	
Back pain			
subjects affected / exposed	23 / 401 (5.74%)	26 / 403 (6.45%)	
occurrences (all)	38	46	
Infections and infestations			
COVID-19			
subjects affected / exposed	47 / 401 (11.72%)	48 / 403 (11.91%)	
occurrences (all)	48	52	
Influenza			
subjects affected / exposed	18 / 401 (4.49%)	19 / 403 (4.71%)	
occurrences (all)	20	24	
Nasopharyngitis			
subjects affected / exposed	35 / 401 (8.73%)	41 / 403 (10.17%)	
occurrences (all)	46	57	
Upper respiratory tract infection			
subjects affected / exposed	20 / 401 (4.99%)	24 / 403 (5.96%)	
occurrences (all)	30	40	
Pneumonia			
subjects affected / exposed	17 / 401 (4.24%)	18 / 403 (4.47%)	
occurrences (all)	20	24	
Urinary tract infection			
subjects affected / exposed	7 / 401 (1.75%)	18 / 403 (4.47%)	
occurrences (all)	7	20	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2019	Amendment 1
18 July 2019	Amendment 3
13 September 2019	Amendment 4
16 October 2020	Amendment 5
06 December 2021	Amendment 6

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported