Clinical trial results:
Study MEA117106: Mepolizumab vs. Placebo as add-on treatment for frequently exacerbating COPD patients

Summary

EudraCT number	2013-004298-28
Trial protocol	SE CZ PL IT BE ES EE GR
Global end of trial date	17 January 2017

Results information

Result version number	v1
This version publication date	31 January 2018
First version publication date	31 January 2018

Trial information

Trial identification

Sponsor protocol code	117106

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	31 May 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of mepolizumab 100 mg subcutaneous (SC) given every 4 weeks compared to placebo on the frequency of moderate and severe exacerbations in chronic obstructive pulmonary disease (COPD) participants at high risk of exacerbations despite the use of optimized standard of care background therapy.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 40
Country: Number of subjects enrolled	France: 37
Country: Number of subjects enrolled	Greece: 61
Country: Number of subjects enrolled	Italy: 53
Country: Number of subjects enrolled	Norway: 12
Country: Number of subjects enrolled	Spain: 58
Country: Number of subjects enrolled	Sweden: 10
Country: Number of subjects enrolled	Czech Republic: 22
Country: Number of subjects enrolled	Estonia: 21
Country: Number of subjects enrolled	Poland: 79
Country: Number of subjects enrolled	United States: 89
Country: Number of subjects enrolled	Australia: 46
Country: Number of subjects enrolled	Canada: 106
Country: Number of subjects enrolled	Mexico: 88
Country: Number of subjects enrolled	Peru: 75
Country: Number of subjects enrolled	Russian Federation: 40
Worldwide total number of subjects	837
EEA total number of subjects	393

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)	375
From 65 to 84 years	460
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants with chronic obstructive pulmonary disease (COPD) with frequent exacerbations and on high dose inhaled corticosteroid (ICS)-based triple inhaled maintenance therapy were included in this study. Participants were randomized to receive mepolizumab 100 milligrams (mg) or placebo by subcutaneous (SC) injection every 4 weeks for 52 weeks.

Pre-assignment

Screening details:

A total of 1161 participants were enrolled of which 79 were pre-screen failures; 245 were screen failures. 836 participants were randomized and received at least one dose of study treatment and included in the modified intent to treat (mITT) population. One participant randomized to the placebo group was withdrawn without receiving study treatment.

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	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo - High stratum

Arm description:

Participants with blood eosinophil counts >=150 cells per microliter (cells/µL) at Screening or >=300 cells/µL in the 12 months prior were assigned to the high stratum group. These participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks along with their standard of care (SoC) therapy. Salbutamol metered dose inhaler (MDI) was issued for use as rescue medication throughout the study.

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:

Placebo was 0.9 percent sodium chloride solution which was administered via SC route every 4 weeks for up to 52 weeks in addition to SoC therapy.

Arm title	Mepolizumab 100 mg - High stratum

Arm description:

Participants with blood eosinophil counts >=150 cells/µL at Screening or >=300 cells/ µL in the 12 months prior were assigned to the high stratum group. These participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

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:

Mepolizumab was available as lyophilized cake which was reconstituted with Sterile water for injection prior to use. Mepolizumab 100 milligrams (mg) injection was administered via SC route every 4 weeks

up to 52 weeks in addition to SoC therapy.

Arm title	Placebo - Low stratum

Arm description:

Participants with blood eosinophil counts <150 cells/µL at Screening and no evidence of blood eosinophil counts >=300 cells/µL in the 12 months prior were assigned to the low stratum group. These participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

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:

Placebo was 0.9 percent sodium chloride solution which was administered via SC route every 4 weeks for up to 52 weeks in addition to SoC therapy.

Arm title	Mepolizumab 100 mg - Low stratum

Arm description:

Participants with blood eosinophil counts <150 cells/µL at Screening and no evidence of blood eosinophil counts >=300 cells/µL in the 12 months prior were assigned to the low stratum group. These participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

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:

Mepolizumab was available as lyophilized cake which was reconstituted with Sterile water for injection prior to use. Mepolizumab 100 milligrams (mg) injection was administered via SC route every 4 weeks up to 52 weeks in addition to SoC therapy.

Number of subjects in period 1[1]	Placebo - High stratum	Mepolizumab 100 mg - High stratum	Placebo - Low stratum
Started	229	233	190
Completed Investigational Product (IP)	185 [2]	203 [3]	148 [4]
Not completed IP	44 [5]	30 [6]	42 [7]
Withdrew IP due to: Adverse event	20 [8]	16 [9]	15 [10]
Withdrew IP Due to: Lack of efficacy	5 [11]	2 [12]	8 [13]
Withdrew IP Due to: Protocol deviation	1 [14]	3 [15]	3 [16]
Withdrew IP Due to: Lost to Follow-up	0 [17]	0 [18]	1 [19]

Withdrew IP Due to: Withdrawal by subj.	16 [20]	8 [21]	11 [22]
Withdrew IP Due to: Physician decision	2 [23]	1 [24]	4 [25]
Withdrew IP due to: Stopping criteria	0 [26]	0 [27]	0 [28]
Completed	202	213	162
Not completed	27	20	28
Adverse event, serious fatal	6	6	7
Physician decision	2	2	2
Consent withdrawn by subject	15	10	10
Adverse event, non-fatal	4	1	4
Lost to follow-up	-	-	2
Lack of efficacy	-	1	3

Number of subjects in period 1[1]	Mepolizumab 100 mg - Low stratum
Started	184
Completed Investigational Product (IP)	149 [29]
Not completed IP	35 [30]
Withdrew IP due to: Adverse event	13 [31]
Withdrew IP Due to: Lack of efficacy	2 [32]
Withdrew IP Due to: Protocol deviation	0 [33]
Withdrew IP Due to: Lost to Follow-up	2 [34]
Withdrew IP Due to: Withdrawal by subj.	15 [35]
Withdrew IP Due to: Physician decision	2 [36]
Withdrew IP due to: Stopping criteria	1 [37]
Completed	157
Not completed	27
Adverse event, serious fatal	9
Physician decision	2
Consent withdrawn by subject	11
Adverse event, non-fatal	2
Lost to follow-up	1
Lack of efficacy	2

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 other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[12] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[13] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[14] - The number of subjects at this milestone seems inconsistent with the number of subjects in the

arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[15] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[16] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[17] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[18] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[19] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[20] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[21] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[22] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[23] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[24] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[25] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that

completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[26] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[27] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[28] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[29] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[30] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[31] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[32] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[33] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[34] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[35] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

[36] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The other milestones presented represent the number of participants that completed

investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.
[37] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: The other milestones presented represent the number of participants that completed investigational product and those not completed investigational product and the reasons why participants did not complete investigational product.

Baseline characteristics

Reporting groups

Reporting group title	Placebo - High stratum

Reporting group description:

Participants with blood eosinophil counts >=150 cells per microliter (cells/µL) at Screening or >=300 cells/µL in the 12 months prior were assigned to the high stratum group. These participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks along with their standard of care (SoC) therapy. Salbutamol metered dose inhaler (MDI) was issued for use as rescue medication throughout the study.

Reporting group title	Mepolizumab 100 mg - High stratum

Reporting group description:

Participants with blood eosinophil counts >=150 cells/µL at Screening or >=300 cells/ µL in the 12 months prior were assigned to the high stratum group. These participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Reporting group title	Placebo - Low stratum

Reporting group description:

Participants with blood eosinophil counts <150 cells/µL at Screening and no evidence of blood eosinophil counts >=300 cells/µL in the 12 months prior were assigned to the low stratum group. These participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Reporting group title	Mepolizumab 100 mg - Low stratum

Reporting group description:

Participants with blood eosinophil counts <150 cells/µL at Screening and no evidence of blood eosinophil counts >=300 cells/µL in the 12 months prior were assigned to the low stratum group. These participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Reporting group values	Placebo - High stratum	Mepolizumab 100 mg - High stratum	Placebo - Low stratum
Number of subjects	229	233	190
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	65.3	65.2	65.2
standard deviation	± 8.53	± 8.36	± 8.62
Gender categorical Units: Subjects			
Female	79	84	77
Male	150	149	113
Race/Ethnicity, Customized Units: Subjects			
American Indian/ Alaska native Heritage	14	19	22
Asian- East Asian Heritage	0	2	0
Asian- Japanese Heritage	3	0	1
Black/ African American Heritage	4	2	3
White- Arabic/ North African Heritage	2	1	0

White- White/ Caucasian/ European Heritage	190	198	145
Multiple - American Indian/Alaska native and White	16	11	19

Reporting group values	Mepolizumab 100 mg - Low stratum	Total	
Number of subjects	184	836	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	66.1		
standard deviation	± 9.14	-	
Gender categorical Units: Subjects			
Female	76	316	
Male	108	520	
Race/Ethnicity, Customized Units: Subjects			
American Indian/ Alaska native Heritage	14	69	
Asian- East Asian Heritage	0	2	
Asian- Japanese Heritage	1	5	
Black/ African American Heritage	2	11	
White- Arabic/ North African Heritage	1	4	
White- White/ Caucasian/ European Heritage	143	676	
Multiple - American Indian/Alaska native and White	23	69	

Subject analysis sets

Subject analysis set title	Placebo
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks in addition to their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Subject analysis set title	Mepolizumab 100 mg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks in addition to their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Reporting group values	Placebo	Mepolizumab 100 mg	
Number of subjects	419	417	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	0	0	
standard deviation	± 0	± 0	
Gender categorical Units: Subjects			
Female	0	0	
Male	0	0	
Race/Ethnicity, Customized Units: Subjects			
American Indian/ Alaska native Heritage	0	0	
Asian- East Asian Heritage	0	0	
Asian- Japanese Heritage	0	0	
Black/ African American Heritage	0	0	
White- Arabic/ North African Heritage	0	0	
White- White/ Caucasian/ European Heritage	0	0	
Multiple - American Indian/Alaska native and White	0	0	

End points

End points reporting groups

Reporting group title	Placebo - High stratum

Reporting group description:

Participants with blood eosinophil counts >=150 cells per microliter (cells/µL) at Screening or >=300 cells/µL in the 12 months prior were assigned to the high stratum group. These participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks along with their standard of care (SoC) therapy. Salbutamol metered dose inhaler (MDI) was issued for use as rescue medication throughout the study.

Reporting group title	Mepolizumab 100 mg - High stratum

Reporting group description:

Participants with blood eosinophil counts >=150 cells/µL at Screening or >=300 cells/ µL in the 12 months prior were assigned to the high stratum group. These participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Reporting group title	Placebo - Low stratum

Reporting group description:

Participants with blood eosinophil counts <150 cells/µL at Screening and no evidence of blood eosinophil counts >=300 cells/µL in the 12 months prior were assigned to the low stratum group. These participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Reporting group title	Mepolizumab 100 mg - Low stratum

Reporting group description:

Participants with blood eosinophil counts <150 cells/µL at Screening and no evidence of blood eosinophil counts >=300 cells/µL in the 12 months prior were assigned to the low stratum group. These participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Subject analysis set title	Placebo
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks in addition to their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Subject analysis set title	Mepolizumab 100 mg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks in addition to their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Primary: Rate of moderate or severe exacerbations in participants in the high stratum

End point title	Rate of moderate or severe exacerbations in participants in the high stratum[1]

End point description:

Moderate exacerbations are defined as clinically significant exacerbations that require treatment with oral/systemic corticosteroids and/or antibiotics. Severe exacerbations are defined as clinically significant exacerbations that require in-patient hospitalization (>= 24 hours) or result in death. Moderate and severe exacerbations occurring from the start of investigational product (IP) up to the Week 52 visit, including exacerbations reported after early discontinuation from investigational product by subjects who remained in the study, were included in the analysis. The analysis was performed on the mITT high stratum (mITT-H) Population which comprised of participants in the mITT Population (all randomized participants who received at least one dose of study treatment) with blood eosinophil counts >=150 cells/µL at Screening or >=300 cells/ µL in the 12 months prior.

End point type	Primary

End point timeframe:

From randomization to Week 52

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Placebo - High stratum	Mepolizumab 100 mg - High stratum		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229[2]	233[3]		
Units: Rate per year				
number (not applicable)				
Rate per year	1.71	1.40		

Notes:

[2] - mITT-H Population

[3] - mITT-H Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis using a negative binomial model with covariates of treatment, geographic region, no.of moderate/severe exacerbations in previous year, Baseline percent predicted FEV1, smoking status and offset of log (time in on- and off-treatment period).

Comparison groups	Mepolizumab 100 mg - High stratum v Placebo - High stratum
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 [4]
Method	Negative binomial model
Parameter estimate	Rate ratio (mepolizumab/placebo)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.98

Notes:

[4] - Adjusted p-value to account for two treatment comparisons

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis using a negative binomial model with covariates of treatment, geographic region, no.of moderate/severe exacerbations in previous year, Baseline percent predicted FEV1, smoking status and offset of log (time in on- and off-treatment period).

Comparison groups	Mepolizumab 100 mg - High stratum v Placebo - High stratum

Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029 [5]
Method	Negative binomial mode
Parameter estimate	Rate ratio (mepolizumab/placebo)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.98

Notes:

[5] - Unadjusted p-value.

Primary: Rate of moderate or severe exacerbations in the mITT Population

End point title	Rate of moderate or severe exacerbations in the mITT Population

End point description:

Moderate and severe exacerbations occurring from the start of IP up to the Week 52 visit, including exacerbations reported after early discontinuation from IP by participants who remained in the study, were included in the analysis. The analysis was performed on mITT Population which comprised of all randomized participants who received at least one dose of trial medication.

End point type	Primary

End point timeframe:

From randomization to Week 52

End point values	Placebo	Mepolizumab 100 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	419[6]	417[7]		
Units: Rate per year				
number (not applicable)				
Rate per year	1.52	1.49		

Notes:

[6] - mITT Population

[7] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis using a negative binomial model with covariates of treatment, geographic region, no.of moderate/severe exacerbations in previous year, Baseline percent predicted FEV1, smoking status and offset of log (time in on- and off-treatment period).

Comparison groups	Mepolizumab 100 mg v Placebo

Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [8]
Method	Negative Binomial Model
Parameter estimate	Rate ratio (mepolizumab/placebo)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.12

Notes:

[8] - Adjusted p-value to account for two treatment comparisons

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis using a negative binomial model with covariates of treatment, geographic region, no.of moderate/severe exacerbations in previous year, Baseline percent predicted FEV1, smoking status and offset of log (time in on and off-treatment period).

Comparison groups	Mepolizumab 100 mg v Placebo
Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.731 [9]
Method	Negative binomial mode
Parameter estimate	Rate ratio (mepolizumab/placebo)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.12

Notes:

[9] - Unadjusted p-value.

Secondary: Time to first moderate/severe exacerbation in participants in the high stratum

End point title	Time to first moderate/severe exacerbation in participants in the high stratum[10]

End point description:

Kaplan Meier estimates of the probability of a moderate or severe exacerbation are expressed as the percentage of participants with an exacerbation over time (by Week 8, 16, 24, 32, 40, 48, 52). Analysis of time to first moderate/severe exacerbation was performed on the mITT-H Population and included exacerbations reported on-treatment and those reported after early discontinuation from IP by participants who remained in the study.

End point type	Secondary

End point timeframe:

From randomization to Week 52

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Placebo - High stratum	Mepolizumab 100 mg - High stratum		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229[11]	233[12]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 8	28.1 (22.7 to 34.4)	20.2 (15.6 to 26.0)		
Week 16	45.5 (39.3 to 52.3)	34.9 (29.2 to 41.5)		
Week 24	53.4 (47.0 to 60.1)	45.8 (39.6 to 52.4)		
Week 32	60.9 (54.5 to 67.4)	55.3 (49.0 to 61.8)		
Week 40	68.5 (62.2 to 74.5)	59.3 (53.0 to 65.7)		
Week 48	71.8 (65.7 to 77.6)	62.0 (55.8 to 68.3)		
Week 52	75.2 (69.3 to 80.8)	64.6 (58.3 to 70.8)		

Notes:

[11] - mITT-H Population

[12] - mITT-H Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using a Cox Proportional Hazards Model with covariates of treatment, geographic region, no. moderate/severe exacerbations in previous year, Baseline percent predicted FEV1 and smoking status

Comparison groups	Placebo - High stratum v Mepolizumab 100 mg - High stratum
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 [13]
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (Mepolizumab/placebo)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	0.94

Notes:

[13] - Adjusted p-value

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis performed using a Cox Proportional Hazards Model with covariates of treatment, geographic

region, no. moderate/severe exacerbations in previous year, Baseline percent predicted FEV1 and smoking status

Comparison groups	Placebo - High stratum v Mepolizumab 100 mg - High stratum
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 [14]
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (Mepolizumab/placebo)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	0.94

Notes:

[14] - Unadjusted p-value

Secondary: Rate of COPD exacerbations requiring an emergency department (ED) visit and/or hospitalization in participants in the high stratum

End point title	Rate of COPD exacerbations requiring an emergency department (ED) visit and/or hospitalization in participants in the high stratum[15]

End point description:

COPD exacerbations requiring an ED visit and/or hospitalization occurring from the start of IP up to the Week 52 visit, including exacerbations reported after early discontinuation from IP by participants who remained in the study, were included in the analysis. The analysis was performed on mITT-H Population.

End point type	Secondary

End point timeframe:

From randomization to Week 52

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Placebo - High stratum	Mepolizumab 100 mg - High stratum		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229[16]	233[17]		
Units: Rate per year				
number (not applicable)				
Rate per year	0.26	0.30		

Notes:

[16] - mITT-H Population

[17] - mITT-H Population

Statistical analyses

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis using a negative binomial model with covariates of treatment, geographic region, no. moderate/severe exacerbations in previous year, Baseline percent predicted FEV1, smoking status and

offset of log (time in on- and off-treatment period).

Comparison groups	Mepolizumab 100 mg - High stratum v Placebo - High stratum
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.479 [18]
Method	Negative binomial model
Parameter estimate	Rate ratio (mepolizumab/placebo)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.75

Notes:

[18] - Unadjusted p-value

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis using a negative binomial model with covariates of treatment, geographic region, no. moderate/severe exacerbations in previous year, Baseline percent predicted FEV1, smoking status and offset of log (time in on- and off-treatment period).

Comparison groups	Mepolizumab 100 mg - High stratum v Placebo - High stratum
Number of subjects included in analysis	462
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.598 [19]
Method	Negative binomial model
Parameter estimate	Rate ratio (mepolizumab/placebo)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.75

Notes:

[19] - Adjusted p-value

Secondary: Change from Baseline in mean total St. George's Respiratory Questionnaire (SGRQ) score in participants in the high stratum

End point title	Change from Baseline in mean total St. George's Respiratory Questionnaire (SGRQ) score in participants in the high stratum[20]

End point description:

The SGRQ for COPD is a 40-item questionnaire derived from the original SGRQ, designed to measure health impairment by addressing the frequency of respiratory symptoms and current state of the participant. SGRQ Total Scores ranges from 0 to 100 with higher scores indicating worse health-related quality of life and reductions indicating improvement. The Baseline value will be the last measurement collected prior to the first dose of investigational product. Change from Baseline is calculated as the post-dose visit value minus the Baseline value. Participants with a Baseline and at least one post-Baseline assessment were included in the analysis. Mean change from Baseline in SGRQ score at Week 52 has been presented.

End point type	Secondary

End point timeframe:

Baseline and Week 52

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Placebo - High stratum	Mepolizumab 100 mg - High stratum		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214[21]	226[22]		
Units: Score on SGRQ scale				
least squares mean (standard error)				
Score on SGRQ scale	-3.0 (± 1.11)	-2.8 (± 1.06)		

Notes:

[21] - mITT-H Population

[22] - mITT-H Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using mixed model repeated measures with covariates of Baseline SGRQ Total Score, geographic region, smoking status, treatment and visit, plus interaction terms for visit by Baseline and visit by treatment group.

Comparison groups	Mepolizumab 100 mg - High stratum v Placebo - High stratum
Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [23]
Method	Mixed Model Repeated Measure Analysis
Parameter estimate	Mean Difference (Mepolizumab - Placebo)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	3.2

Notes:

[23] - Adjusted p-value

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis performed using mixed model repeated measures with covariates of Baseline SGRQ Total Score, geographic region, smoking status, treatment and visit, plus interaction terms for visit by Baseline and visit by treatment group.

Comparison groups	Mepolizumab 100 mg - High stratum v Placebo - High stratum

Number of subjects included in analysis	440
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.901 [24]
Method	Mixed Model Repeated Measure Analysis
Parameter estimate	Mean Difference (Mepolizumab - Placebo)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	3.2

Notes:

[24] - Unadjusted p-value

Secondary: Change from Baseline in Mean COPD assessment test (CAT) score in participants in the high stratum

End point title	Change from Baseline in Mean COPD assessment test (CAT) score in participants in the high stratum[25]

End point description:

The CAT is an 8-item questionnaire developed for use in routine clinical practice to measure the health status of participants with COPD. Each question is assessed on a 6-point scale ranging from 0 (no impairment) to 5 (maximum impairment) with the CAT score ranging from 0-40. Higher scores indicate greater disease impact with reductions indicating improvement. The Baseline value will be the last measurement collected prior to the first dose of investigational product. Change from Baseline is calculated as the post-dose visit value minus the Baseline value. Participants with a Baseline and at least one post-Baseline assessment were included in the analysis. Mean change from Baseline in CAT score at Week 52 has been presented.

End point type	Secondary

End point timeframe:

Baseline and Week 52

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting on a subset of the arms that are contained in the baseline period.

End point values	Placebo - High stratum	Mepolizumab 100 mg - High stratum		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212[26]	224[27]		
Units: Score on CAT scale				
least squares mean (standard error)				
Score on CAT scale	0.0 (± 0.47)	-0.8 (± 0.45)		

Notes:

[26] - mITT-H Population

[27] - mITT-H Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using mixed model repeated measures with covariates of Baseline CAT score, geographic region, smoking status, treatment and visit, plus interaction terms for visit by Baseline and

visit by treatment group.

Comparison groups	Mepolizumab 100 mg - High stratum v Placebo - High stratum
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [28]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean Difference (Mepolizumab - Placebo)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.5

Notes:

[28] - Adjusted p-value

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis performed using mixed model repeated measures with covariates of Baseline CAT score, geographic region, smoking status, treatment and visit, plus interaction terms for visit by Baseline and visit by treatment group.

Comparison groups	Mepolizumab 100 mg - High stratum v Placebo - High stratum
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.244 [29]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean Difference (Mepolizumab - Placebo)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.5

Notes:

[29] - Unadjusted p-value

Secondary: Time to first moderate/severe exacerbation in the mITT Population

End point title	Time to first moderate/severe exacerbation in the mITT Population

End point description:

Kaplan Meier estimates of the probability of a moderate/severe exacerbation are expressed as the percentage of participants with an exacerbation over time (by Week 8, 16, 24, 32, 40, 48, 52). The analysis of time to first moderate/severe exacerbation was performed on the mITT population and included exacerbations reported on-treatment and those reported after early discontinuation from IP by participants who remained in the study.

End point type	Secondary

End point timeframe:

From randomization to Week 52

End point values	Placebo	Mepolizumab 100 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	419[30]	417[31]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 8	25.1 (21.3 to 29.6)	23.6 (19.8 to 28.0)		
Week 16	39.8 (35.2 to 44.6)	37.4 (32.9 to 42.3)		
Week 24	49.2 (44.5 to 54.1)	46.3 (41.6 to 51.3)		
Week 32	57.3 (52.6 to 62.2)	54.1 (49.3 to 59.0)		
Week 40	63.8 (59.1 to 68.5)	59.7 (54.9 to 64.5)		
Week 48	67.3 (62.7 to 71.9)	62.5 (57.8 to 67.2)		
Week 52	71.2 (66.6 to 75.6)	65.5 (60.7 to 70.1)		

Notes:

[30] - mITT Population

[31] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using a Cox Proportional Hazards Model with covariates of treatment, geographic region, no. moderate/severe exacerbations in previous year, Baseline percent predicted FEV1 and smoking status

Comparison groups	Mepolizumab 100 mg v Placebo
Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [32]
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (Mepolizumab/Placebo)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.05

Notes:

[32] - Adjusted p-value

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis performed using a Cox Proportional Hazards Model with covariates of treatment, geographic region, no. moderate/severe exacerbations in previous year, Baseline percent predicted FEV1 and

smoking status

Comparison groups	Mepolizumab 100 mg v Placebo
Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.16 [33]
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard ratio (Mepolizumab/Placebo)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.05

Notes:

[33] - Unadjusted p-value

Secondary: Rate of COPD exacerbations requiring ED visit and/or hospitalization in the mITT Population

End point title	Rate of COPD exacerbations requiring ED visit and/or hospitalization in the mITT Population

End point description:

COPD exacerbations requiring ED visit and/or hospitalization occurring from the start of IP up to the Week 52 visit, including exacerbations reported after early discontinuation from IP by participants who remained in the study, were included in the analysis. The analysis was performed on mITT Population.

End point type	Secondary

End point timeframe:

From randomization to Week 52

End point values	Placebo	Mepolizumab 100 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	419[34]	417[35]		
Units: Rate per year				
number (not applicable)				
Rate per year	0.26	0.29		

Notes:

[34] - mITT Population

[35] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis using a negative binomial model with covariates of treatment, geographic region, no. moderate/severe exacerbations in previous year, Baseline percent predicted FEV1, smoking status and offset of log (time in on- and off-treatment period).

Comparison groups	Placebo v Mepolizumab 100 mg

Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [36]
Method	Negative binomial model
Parameter estimate	Rate ratio (mepolizumab/placebo)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.49

Notes:

[36] - Adjusted p-value

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis using a negative binomial model with covariates of treatment, geographic region, no. moderate/severe exacerbations in previous year, Baseline percent predicted FEV1, smoking status and offset of log (time in on- and off-treatment period).

Comparison groups	Placebo v Mepolizumab 100 mg
Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.556 [37]
Method	Negative binomial model
Parameter estimate	Rate ratio (mepolizumab/placebo)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.49

Notes:

[37] - Unadjusted p-value

Secondary: Change from Baseline in mean total SGRQ score in the mITT Population

End point title	Change from Baseline in mean total SGRQ score in the mITT Population

End point description:

The SGRQ for COPD is a 40-item questionnaire derived from the original SGRQ, designed to measure health impairment by addressing the frequency of respiratory symptoms and current state of the participant. SGRQ Total Scores ranges from 0 to 100 with higher scores indicating worse health-related quality of life and reductions indicating improvement. The Baseline value will be the last measurement collected prior to the first dose of investigational product. Change from Baseline is calculated as the post-dose visit value minus the Baseline value. Mean change from Baseline in SGRQ score at Week 52 has been presented.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo	Mepolizumab 100 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	396[38]	397[39]		
Units: Score on SGRQ scale				
least squares mean (standard error)				
Score on SGRQ scale	-4.0 (± 0.81)	-3.2 (± 0.80)		

Notes:

[38] - mITT Population

[39] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using mixed model repeated measures with covariates of Baseline SGRQ Total Score, geographic region, smoking status, treatment and visit, plus interaction terms for visit by Baseline and visit by treatment group.

Comparison groups	Mepolizumab 100 mg v Placebo
Number of subjects included in analysis	793
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [40]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (Mepolizumab - Placebo)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2.9

Notes:

[40] - Adjusted p-value

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis performed using mixed model repeated measures with covariates of Baseline SGRQ Total Score, geographic region, smoking status, treatment and visit, plus interaction terms for visit by Baseline and visit by treatment group.

Comparison groups	Mepolizumab 100 mg v Placebo
Number of subjects included in analysis	793
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.532 [41]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (Mepolizumab - Placebo)
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2.9

Notes:

[41] - Unadjusted p-value

Secondary: Change from Baseline in Mean CAT score in the mITT Population

End point title	Change from Baseline in Mean CAT score in the mITT Population

End point description:

The CAT is an 8-item questionnaire developed for use in routine clinical practice to measure the health status of participants with COPD. Each question is assessed on a 6-point scale ranging from 0 (no impairment) to 5 (maximum impairment) with the CAT score ranging from 0-40. Higher scores indicate greater disease impact with reductions indicating improvement. The Baseline value will be the last measurement collected prior to the first dose of investigational product. Change from Baseline is calculated as the post-dose visit value minus the Baseline value. Participants with a Baseline and at least one post-Baseline assessment were included in the analysis. Mean change from Baseline in CAT score at Week 52 has been presented.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Placebo	Mepolizumab 100 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	392[42]	401[43]		
Units: Score on CAT scale				
least squares mean (standard error)				
Score on CAT scale	-0.4 (± 0.35)	-1.0 (± 0.34)		

Notes:

[42] - mITT Population

[43] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using mixed model repeated measures with covariates of Baseline CAT score, geographic region, smoking status, treatment and visit, plus interaction terms for visit by Baseline and visit by treatment group.

Comparison groups	Placebo v Mepolizumab 100 mg
Number of subjects included in analysis	793
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [44]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (Mepolizumab - Placebo)
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.4

Notes:

[44] - Adjusted p-value

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis performed using mixed model repeated measures with covariates of Baseline CAT score, geographic region, smoking status, treatment and visit, plus interaction terms for visit by Baseline and visit by treatment group.

Comparison groups	Placebo v Mepolizumab 100 mg
Number of subjects included in analysis	793
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.252 [45]
Method	Mixed Model Repeated Measures Analysis
Parameter estimate	Mean difference (Mepolizumab - Placebo)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.4

Notes:

[45] - Unadjusted p-value

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) collected from the start of study participation until the end of follow up (up to Week 60). On-treatment non-serious adverse events (AEs) reported from start of study treatment until 4 weeks after last dose.

Adverse event reporting additional description:

AEs and SAEs were collected in Safety Population which comprised of all randomized participants who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Placebo - High stratum

Reporting group description:

Participants with blood eosinophil counts >=150 cells/µL at Screening or >=300 cells/µL in the 12 months prior were assigned to the high stratum group. These participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Reporting group title	Placebo - Low stratum

Reporting group description:

Participants with blood eosinophil counts <150 cells/µL at Screening and no evidence of blood eosinophil counts >=300 cells/µL in the 12 months prior were assigned to the low stratum group. These participants were randomized to and received placebo by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Reporting group title	Mepolizumab 100 mg - Low stratum

Reporting group description:

Participants with blood eosinophil counts <150 cells/µL at Screening and no evidence of blood eosinophil counts >=300 cells/µL in the 12 months prior were assigned to the low stratum group. These participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Reporting group title	Mepolizumab 100 mg - High stratum

Reporting group description:

Participants with blood eosinophil counts >=150 cells/µL at Screening or >=300 cells/ µL in the 12 months prior were assigned to the high stratum group. These participants were randomized to and received mepolizumab 100 mg by SC injection every 4 weeks for up to 52 weeks along with their SoC therapy. Salbutamol MDI was issued for use as rescue medication throughout the study.

Serious adverse events	Placebo - High stratum	Placebo - Low stratum	Mepolizumab 100 mg - Low stratum
Total subjects affected by serious adverse events			
subjects affected / exposed	80 / 229 (34.93%)	51 / 190 (26.84%)	50 / 184 (27.17%)
number of deaths (all causes)	8	9	10
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			

subjects affected / exposed	2 / 229 (0.87%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal cancer recurrent			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung adenocarcinoma stage IV			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Non-small cell lung cancer			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal neoplasm			

subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal melanoma			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Small cell lung cancer			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
T-cell lymphoma			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian vein thrombosis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Non-cardiac chest pain			

subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	43 / 229 (18.78%)	31 / 190 (16.32%)	31 / 184 (16.85%)
occurrences causally related to treatment / all	0 / 61	1 / 44	0 / 42
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 3
Respiratory failure			
subjects affected / exposed	5 / 229 (2.18%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	3 / 229 (1.31%)	3 / 190 (1.58%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 229 (0.44%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alveolitis allergic			

subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumopathy			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Psychiatric disorders			
Abnormal behaviour			

subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol abuse			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Personality change due to a general medical condition			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Influenza B virus test positive			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			

subjects affected / exposed	1 / 229 (0.44%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injection related reaction			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			

subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital haematoma			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural haemorrhage			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory fume inhalation disorder			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			

subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound haemorrhage			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 229 (0.87%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	3 / 229 (1.31%)	0 / 190 (0.00%)	3 / 184 (1.63%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Acute myocardial infarction			
subjects affected / exposed	1 / 229 (0.44%)	2 / 190 (1.05%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure chronic			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block second degree			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bundle branch block left			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			

subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiopulmonary failure			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cor pulmonale			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular extrasystoles			

subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 229 (0.44%)	1 / 190 (0.53%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain injury			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sensory loss			

subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 229 (0.87%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Abdominal hernia			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			

subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal fistula			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			

subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal polyp			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute prerenal failure			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anuria			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder dilatation			

subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	1 / 229 (0.44%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			

subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	16 / 229 (6.99%)	13 / 190 (6.84%)	11 / 184 (5.98%)
occurrences causally related to treatment / all	0 / 19	0 / 15	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	2 / 229 (0.87%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bronchitis			
subjects affected / exposed	2 / 229 (0.87%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			

subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella infection			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal infection			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 229 (0.00%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonellosis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 229 (0.44%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	0 / 229 (0.00%)	2 / 190 (1.05%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	1 / 229 (0.44%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 229 (0.44%)	0 / 190 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute hepatic failure			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Mepolizumab 100 mg - High stratum		
Total subjects affected by serious adverse events			
subjects affected / exposed	65 / 233 (27.90%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colon cancer			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laryngeal cancer recurrent			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma stage IV			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-small cell lung cancer			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Renal neoplasm				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal melanoma				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small cell lung cancer				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of lung				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
T-cell lymphoma				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematoma				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subclavian vein thrombosis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Death				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised oedema				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Benign prostatic hyperplasia				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	33 / 233 (14.16%)			
occurrences causally related to treatment / all	1 / 59			
deaths causally related to treatment / all	0 / 3			
Respiratory failure				
subjects affected / exposed	5 / 233 (2.15%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			
Acute respiratory failure				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Pneumothorax				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Alveolitis allergic				

subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopneumopathy				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchospasm				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Organising pneumonia				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory arrest				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Abnormal behaviour				

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol abuse				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Personality change due to a general medical condition				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device dislocation				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Influenza B virus test positive				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femur fracture				

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fibula fracture				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injection related reaction				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaw fracture				

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laceration				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meniscus injury				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periorbital haematoma				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Procedural haemorrhage				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory fume inhalation disorder				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thermal burn				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound haemorrhage				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	4 / 233 (1.72%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				

subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute coronary syndrome				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block second degree				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bundle branch block left				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiomyopathy				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiopulmonary failure				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Congestive cardiomyopathy				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cor pulmonale				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular extrasystoles				

subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain injury			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral haematoma			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sensory loss			

subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal hernia			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulum			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhoidal haemorrhage			

subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal fistula			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal haemorrhage			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumoperitoneum			

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal polyp				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute prerenal failure				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anuria				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bladder dilatation				

subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Calculus urinary				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Bursitis				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthralgia				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar spinal stenosis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	12 / 233 (5.15%)			
occurrences causally related to treatment / all	1 / 15			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of chronic obstructive airways disease				
subjects affected / exposed	2 / 233 (0.86%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				

subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				

subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Klebsiella infection				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumococcal infection				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia klebsiella				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				

subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	1 / 233 (0.43%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rhinovirus infection				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Salmonellosis				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fluid overload				
subjects affected / exposed	0 / 233 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				

subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	1 / 233 (0.43%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute hepatic failure			
subjects affected / exposed	0 / 233 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Placebo - High stratum	Placebo - Low stratum	Mepolizumab 100 mg - Low stratum
Total subjects affected by non-serious adverse events			
subjects affected / exposed	146 / 229 (63.76%)	116 / 190 (61.05%)	108 / 184 (58.70%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 229 (1.31%)	5 / 190 (2.63%)	5 / 184 (2.72%)
occurrences (all)	6	6	5
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 229 (2.18%)	3 / 190 (1.58%)	4 / 184 (2.17%)
occurrences (all)	5	3	4
Nervous system disorders			
Headache			
subjects affected / exposed	31 / 229 (13.54%)	25 / 190 (13.16%)	18 / 184 (9.78%)
occurrences (all)	71	47	36
Dizziness			
subjects affected / exposed	6 / 229 (2.62%)	11 / 190 (5.79%)	7 / 184 (3.80%)
occurrences (all)	6	12	9
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	7 / 229 (3.06%)	5 / 190 (2.63%)	5 / 184 (2.72%)
occurrences (all)	12	6	13
Oedema peripheral			
subjects affected / exposed	5 / 229 (2.18%)	8 / 190 (4.21%)	1 / 184 (0.54%)
occurrences (all)	5	8	1
Pyrexia			
subjects affected / exposed	9 / 229 (3.93%)	4 / 190 (2.11%)	1 / 184 (0.54%)
occurrences (all)	12	6	2
Asthenia			
subjects affected / exposed	8 / 229 (3.49%)	0 / 190 (0.00%)	3 / 184 (1.63%)
occurrences (all)	8	0	3
Non-cardiac chest pain			
subjects affected / exposed	2 / 229 (0.87%)	6 / 190 (3.16%)	2 / 184 (1.09%)
occurrences (all)	2	6	2
Influenza like illness			

subjects affected / exposed	7 / 229 (3.06%)	2 / 190 (1.05%)	0 / 184 (0.00%)
occurrences (all)	8	3	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 229 (2.62%)	9 / 190 (4.74%)	8 / 184 (4.35%)
occurrences (all)	8	17	11
Nausea			
subjects affected / exposed	8 / 229 (3.49%)	4 / 190 (2.11%)	4 / 184 (2.17%)
occurrences (all)	18	6	5
Abdominal pain			
subjects affected / exposed	3 / 229 (1.31%)	9 / 190 (4.74%)	4 / 184 (2.17%)
occurrences (all)	4	9	4
Constipation			
subjects affected / exposed	5 / 229 (2.18%)	1 / 190 (0.53%)	6 / 184 (3.26%)
occurrences (all)	6	1	7
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	6 / 229 (2.62%)	12 / 190 (6.32%)	9 / 184 (4.89%)
occurrences (all)	7	13	12
Cough			
subjects affected / exposed	9 / 229 (3.93%)	6 / 190 (3.16%)	9 / 184 (4.89%)
occurrences (all)	10	7	11
Chronic obstructive pulmonary disease			
subjects affected / exposed	7 / 229 (3.06%)	8 / 190 (4.21%)	10 / 184 (5.43%)
occurrences (all)	13	13	22
Dyspnoea			
subjects affected / exposed	8 / 229 (3.49%)	4 / 190 (2.11%)	6 / 184 (3.26%)
occurrences (all)	10	4	9
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 229 (1.31%)	1 / 190 (0.53%)	2 / 184 (1.09%)
occurrences (all)	3	1	2
Pruritus			
subjects affected / exposed	1 / 229 (0.44%)	7 / 190 (3.68%)	0 / 184 (0.00%)
occurrences (all)	1	7	0
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	16 / 229 (6.99%)	15 / 190 (7.89%)	16 / 184 (8.70%)
occurrences (all)	17	17	19
Pain in extremity			
subjects affected / exposed	6 / 229 (2.62%)	10 / 190 (5.26%)	12 / 184 (6.52%)
occurrences (all)	15	12	12
Arthralgia			
subjects affected / exposed	8 / 229 (3.49%)	11 / 190 (5.79%)	4 / 184 (2.17%)
occurrences (all)	16	11	5
Myalgia			
subjects affected / exposed	4 / 229 (1.75%)	7 / 190 (3.68%)	4 / 184 (2.17%)
occurrences (all)	8	8	5
Musculoskeletal pain			
subjects affected / exposed	9 / 229 (3.93%)	3 / 190 (1.58%)	2 / 184 (1.09%)
occurrences (all)	10	4	2
Muscle spasms			
subjects affected / exposed	3 / 229 (1.31%)	7 / 190 (3.68%)	1 / 184 (0.54%)
occurrences (all)	3	7	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	32 / 229 (13.97%)	31 / 190 (16.32%)	26 / 184 (14.13%)
occurrences (all)	49	39	34
Upper respiratory tract infection			
subjects affected / exposed	10 / 229 (4.37%)	11 / 190 (5.79%)	11 / 184 (5.98%)
occurrences (all)	10	16	13
Influenza			
subjects affected / exposed	10 / 229 (4.37%)	13 / 190 (6.84%)	8 / 184 (4.35%)
occurrences (all)	13	16	12
Sinusitis			
subjects affected / exposed	7 / 229 (3.06%)	6 / 190 (3.16%)	5 / 184 (2.72%)
occurrences (all)	8	6	5
Pharyngitis			
subjects affected / exposed	12 / 229 (5.24%)	6 / 190 (3.16%)	5 / 184 (2.72%)
occurrences (all)	13	6	5
Urinary tract infection			

subjects affected / exposed	9 / 229 (3.93%)	4 / 190 (2.11%)	7 / 184 (3.80%)
occurrences (all)	12	4	8
Oral candidiasis			
subjects affected / exposed	7 / 229 (3.06%)	5 / 190 (2.63%)	6 / 184 (3.26%)
occurrences (all)	9	6	8
Pneumonia			
subjects affected / exposed	10 / 229 (4.37%)	2 / 190 (1.05%)	5 / 184 (2.72%)
occurrences (all)	11	2	5
Bronchitis			
subjects affected / exposed	7 / 229 (3.06%)	3 / 190 (1.58%)	4 / 184 (2.17%)
occurrences (all)	10	6	4
Gastroenteritis			
subjects affected / exposed	1 / 229 (0.44%)	5 / 190 (2.63%)	7 / 184 (3.80%)
occurrences (all)	1	5	7
Conjunctivitis			
subjects affected / exposed	0 / 229 (0.00%)	1 / 190 (0.53%)	6 / 184 (3.26%)
occurrences (all)	0	1	6

Non-serious adverse events	Mepolizumab 100 mg - High stratum		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	136 / 233 (58.37%)		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	7 / 233 (3.00%)		
occurrences (all)	7		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 233 (3.43%)		
occurrences (all)	8		
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 233 (10.30%)		
occurrences (all)	36		
Dizziness			
subjects affected / exposed	3 / 233 (1.29%)		
occurrences (all)	4		

General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	7 / 233 (3.00%)		
occurrences (all)	9		
Oedema peripheral			
subjects affected / exposed	8 / 233 (3.43%)		
occurrences (all)	9		
Pyrexia			
subjects affected / exposed	7 / 233 (3.00%)		
occurrences (all)	9		
Asthenia			
subjects affected / exposed	4 / 233 (1.72%)		
occurrences (all)	4		
Non-cardiac chest pain			
subjects affected / exposed	5 / 233 (2.15%)		
occurrences (all)	6		
Influenza like illness			
subjects affected / exposed	2 / 233 (0.86%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 233 (4.29%)		
occurrences (all)	11		
Nausea			
subjects affected / exposed	6 / 233 (2.58%)		
occurrences (all)	7		
Abdominal pain			
subjects affected / exposed	4 / 233 (1.72%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	5 / 233 (2.15%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	15 / 233 (6.44%)		
occurrences (all)	15		

Cough			
subjects affected / exposed	12 / 233 (5.15%)		
occurrences (all)	17		
Chronic obstructive pulmonary disease			
subjects affected / exposed	10 / 233 (4.29%)		
occurrences (all)	15		
Dyspnoea			
subjects affected / exposed	11 / 233 (4.72%)		
occurrences (all)	15		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 233 (3.00%)		
occurrences (all)	7		
Pruritus			
subjects affected / exposed	3 / 233 (1.29%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	17 / 233 (7.30%)		
occurrences (all)	20		
Pain in extremity			
subjects affected / exposed	7 / 233 (3.00%)		
occurrences (all)	7		
Arthralgia			
subjects affected / exposed	9 / 233 (3.86%)		
occurrences (all)	11		
Myalgia			
subjects affected / exposed	4 / 233 (1.72%)		
occurrences (all)	4		
Musculoskeletal pain			
subjects affected / exposed	3 / 233 (1.29%)		
occurrences (all)	5		
Muscle spasms			
subjects affected / exposed	4 / 233 (1.72%)		
occurrences (all)	4		
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	38 / 233 (16.31%)		
occurrences (all)	50		
Upper respiratory tract infection			
subjects affected / exposed	10 / 233 (4.29%)		
occurrences (all)	12		
Influenza			
subjects affected / exposed	8 / 233 (3.43%)		
occurrences (all)	9		
Sinusitis			
subjects affected / exposed	14 / 233 (6.01%)		
occurrences (all)	16		
Pharyngitis			
subjects affected / exposed	7 / 233 (3.00%)		
occurrences (all)	9		
Urinary tract infection			
subjects affected / exposed	8 / 233 (3.43%)		
occurrences (all)	9		
Oral candidiasis			
subjects affected / exposed	8 / 233 (3.43%)		
occurrences (all)	8		
Pneumonia			
subjects affected / exposed	4 / 233 (1.72%)		
occurrences (all)	4		
Bronchitis			
subjects affected / exposed	5 / 233 (2.15%)		
occurrences (all)	6		
Gastroenteritis			
subjects affected / exposed	4 / 233 (1.72%)		
occurrences (all)	4		
Conjunctivitis			
subjects affected / exposed	3 / 233 (1.29%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2013	Amendment 1: To reflect that Investigational Product will be administered by a single SC injection.
05 March 2014	Amendment 2: Removal of short form (SF)-36 health outcomes endpoint; Removal of electrocardiogram (ECG) at Visit 2; Update of ECG exclusion and discontinuation criteria; Addition of adverse event causality assessment guidance language; Update of chest x-ray randomization criterion for Germany; Wording edited for consistency and clarification of statements in multiple sections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported