Clinical trial results:
Study 201312: A Multi-Centre, Open-Label, Study of Mepolizumab in a Subset of Subjects with a History of Life Threatening/Seriously Debilitating Asthma Who Participated in the MEA115661 Trial

Summary

EudraCT number	2014-000314-54
Trial protocol	IT DE NL ES GB BE CZ Outside EU/EEA
Global end of trial date	05 October 2017

Results information

Result version number	v1
This version publication date	14 April 2018
First version publication date	14 April 2018

Trial information

Trial identification

Sponsor protocol code	201312

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 February 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To provide extended treatment with mepolizumab to subjects with a history of life threatening or seriously debilitating asthma and a history of improved disease control while receiving mepolizumab as defined by this protocol

Protection of trial subjects:

Numbing cream or spray was permitted at the site of injection and rescue medications (salbutamol/albuterol) are available to the participant throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 May 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Ethical reason
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	France: 42
Country: Number of subjects enrolled	Germany: 36
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Netherlands: 19
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Ukraine: 11
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Argentina: 11
Country: Number of subjects enrolled	Australia: 12
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	Chile: 10
Country: Number of subjects enrolled	Japan: 25
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	United States: 33
Country: Number of subjects enrolled	Korea, Republic of: 19

Worldwide total number of subjects	339
EEA total number of subjects	183

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)	6
Adults (18-64 years)	277
From 65 to 84 years	56
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was an open-label, long-term study of mepolizumab 100 milligram (mg) administered subcutaneously (SC), in addition to standard of care (SOC), in eligible participants with severe eosinophilic asthma, who completed the MEA115661 Exit Visit (Visit 14). The study enrolled participants across 18 countries.

Pre-assignment

Screening details:

A total of 340 participants were screened for the study, of which one participant was screening failure, and 339 participants received the study treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Mepolizumab 100 mg SC

Arm description:

Participants received mepolizumab 100 mg administered via SC injection into the upper arm or thigh approximately every 4 weeks for 172 weeks. Participants remained on standard of care asthma therapy which could be adjusted during the study at the discretion of the physician.

Arm type	Experimental
Investigational medicinal product name	Mepolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received mepolizumab 100 mg administered via SC injection into the upper arm or thigh approximately every 4 weeks for 172 weeks.

Number of subjects in period 1	Mepolizumab 100 mg SC
Started	339
Completed	0
Not completed	339
Study closed/terminated	153
Adverse event, serious fatal	1
Consent withdrawn by subject	15
Adverse event, non-fatal	2
Product commercially available	159
Lost to follow-up	4
Subject met Liver Stopping Criteria	1

Lack of efficacy	2
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	Mepolizumab 100 mg SC

Reporting group description:

Participants received mepolizumab 100 mg administered via SC injection into the upper arm or thigh approximately every 4 weeks for 172 weeks. Participants remained on standard of care asthma therapy which could be adjusted during the study at the discretion of the physician.

Reporting group values	Mepolizumab 100 mg SC	Total	
Number of subjects	339	339	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 52.9 ± 13.08	 -	
Gender categorical Units: Subjects			
Female	178	178	
Male	161	161	
Race/Ethnicity, Customized Units: Subjects			
Asian-Central/South Asian Heritage	2	2	
Asian-East Asian Heritage	19	19	
Asian-Japanese Heritage	26	26	
Asian-South East Asian Heritage	4	4	
Black or African American	4	4	
White-Arabic/North African Heritage	7	7	
White-White/Caucasian/European Heritage	277	277	

End points

End points reporting groups

Reporting group title	Mepolizumab 100 mg SC

Reporting group description:

Participants received mepolizumab 100 mg administered via SC injection into the upper arm or thigh approximately every 4 weeks for 172 weeks. Participants remained on standard of care asthma therapy which could be adjusted during the study at the discretion of the physician.

Primary: Annualized rate of on-treatment exacerbations per year

End point title	Annualized rate of on-treatment exacerbations per year[1]

End point description:

Exacerbations are defined as the worsening of asthma which requires use of systemic corticosteroids intravenous (IV) or oral steroid like prednisone, for at least 3 days or a single intramuscular (IM) corticosteroid (CS) dose is required. For maintenance systemic corticosteroids, at least double the existing maintenance dose for at least 3 days was required) and/or hospitalization and/or emergency department (ED) visit. On-Treatment data between first dose date and earliest of Withdrawal date/last dose + 28 days was considered for analysis. Analysis of the number of exacerbations was performed using a negative binomial generalized linear model. As Treated (AT) Population included all participants who received at least one dose of mepolizumab within study 201312.

End point type	Primary

End point timeframe:

Baseline (Week 0) to Week 172

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[2]			
Units: Exacerbations per year				
arithmetic mean (confidence interval 95%)				
Exacerbations per year	0.93 (0.81 to 1.06)			

Notes:

[2] - AT Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any on-treatment adverse event (AE) or on-treatment serious AE (SAE)

End point title	Number of participants with any on-treatment adverse event (AE) or on-treatment serious AE (SAE)[3]

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect,

any other situation according to medical or scientific judgment that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention or event associated with liver injury and impaired liver function were categorized as SAE. On-treatment AEs and on-treatment SAEs are the events occurring on/after the first dose of open-label mepolizumab date and before/on last dose+28 days.

End point type	Primary

End point timeframe:

Baseline (Week 0) to Week 172

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[4]			
Units: Participants				
Any AE	315			
Any SAE	84			

Notes:

[4] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in asthma control questionnaire (ACQ)-5 on-treatment score

End point title	Mean change from Baseline in asthma control questionnaire (ACQ)-5 on-treatment score

End point description:

The ACQ-5 is a five-item questionnaire developed as a measure of participants asthma control. The five questions enquire about the frequency and/or severity of symptoms (nocturnal awakening on waking in the morning, activity limitation, shortness of breath, wheeze). The response options for all these questions consist of a 0 (no impairment/limitation) to 6 (total impairment/ limitation) scale. The overall ACQ score is calculated as the mean of the 5 questions and therefore ranges between 0 (totally controlled) and 6 (severely uncontrolled). Baseline was considered as the latest assessment prior to first dose of mepolizumab in this study. The change from Baseline is defined as the difference between the value of the endpoint at the time point of interest and Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[5]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Week 12, n=333	-0.16 (± 1.096)			

Week 24, n=333	-0.15 (± 1.131)			
Week 36, n=326	-0.21 (± 1.089)			
Week 48, n=328	-0.17 (± 0.965)			
Week 60, n=307	-0.18 (± 1.066)			
Week 72, n=282	-0.08 (± 1.145)			
Week 84, n=254	-0.03 (± 1.151)			
Week 96, n=212	-0.12 (± 0.976)			
Week 108, n=190	-0.06 (± 1.057)			
Week 120, n=164	-0.01 (± 1.244)			
Week 132, n=135	-0.09 (± 1.089)			
Week 144, n=73	0.34 (± 1.220)			
Week 156, n=23	0.07 (± 0.962)			
Week 168, n=6	-0.33 (± 0.935)			

Notes:

[5] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in on-treatment clinic pre-bronchodilator FEV1

End point title	Mean change from Baseline in on-treatment clinic pre-bronchodilator FEV1

End point description:

FEV1 is defined as the volume of air forcefully expelled from the lungs in 1 second. Pre-bronchodilator FEV1 measurements were taken by spirometry at Baseline and Weeks 24, 48, 72, 96, 120, 144 and 168. Spirometry was performed within 1 hour of the Baseline assessment. Baseline was considered as the latest assessment prior to first dose of mepolizumab in this study. The change from Baseline is defined as the difference between the value of the endpoint at the time point of interest and Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles). Data between first dose date and earliest of Withdrawal date/last dose + 28 days considered on-treatment.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[6]			
Units: Milliliter				
arithmetic mean (standard deviation)				
Week 24, n=332	67 (± 382.9)			

Week 48, n=325	27 (± 404.6)			
Week 72, n=289	30 (± 406.0)			
Week 96, n=223	47 (± 433.7)			
Week 120, n=169	34 (± 369.9)			
Week 144, n=88	14 (± 374.9)			
Week 168, n=15	78 (± 302.9)			

Notes:

[6] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants withdrawn from the study due to lack of efficacy and adverse events

End point title	Number of participants withdrawn from the study due to lack of efficacy and adverse events

End point description:

AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. Number of participants withdrawn due to lack of efficacy and adverse events from the study have been presented.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[7]			
Units: Participants				
Withdrawals due to lack of efficacy	2			
Withdrawals due to adverse events	3			

Notes:

[7] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants hospitalized due to adverse events including asthma exacerbations

End point title	Number of participants hospitalized due to adverse events including asthma exacerbations

End point description:

AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or is a congenital anomaly/birth defect or is medically significant or all events of

possible drug induced liver injury with hyperbilirubinemia. Number of participants requiring hospitalization due to an on-treatment serious adverse event including asthma exacerbations are presented. On-treatment SAEs are the events occurring on/after the first dose of mepolizumab date and before/on last dose of mepolizumab + 28 days.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[8]			
Units: Participants				
Participants	78			

Notes:

[8] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with AEs including both systemic (allergic and non-allergic) and local site reactions

End point title	Number of participants with AEs including both systemic (allergic and non-allergic) and local site reactions

End point description:

AEs were collected from the Baseline visit until the follow-up visit (Week 172). Participants were monitored to evaluate the AEs of systemic and local site reaction. AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. On treatment AEs were defined as events occurring from the first dose until 28 days after the last dose of mepolizumab. Number of participants with AEs including both systemic (i.e. allergic/immunoglobulin (Ig)E-mediated and non-allergic) and local site reactions have been presented.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[9]			
Units: Participants				
Any systemic events	2			
Any local site reactions	14			

Notes:

[9] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in QT interval corrected by Bazett's method (QTcB) and QT interval corrected by Fridericia's method (QTcF) values for 12-lead electrocardiogram (ECG)

End point title	Mean change from Baseline in QT interval corrected by Bazett's method (QTcB) and QT interval corrected by Fridericia's method (QTcF) values for 12-lead electrocardiogram (ECG)

End point description:

Twelve-lead ECG measurements were recorded after the participant has rested in the supine position for 5 minutes. The ECG was obtained before lung function testing followed by other study procedures. Baseline was considered as the latest assessment prior to first dose of mepolizumab in this study. The change from Baseline is defined as the difference between the value of the endpoint at the time point of interest and Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles)..

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[10]			
Units: Milliseconds				
arithmetic mean (standard deviation)				
QTcB, Week 24, n=301	0.1 (± 16.90)			
QTcB, Week 48, n=294	-0.9 (± 17.27)			
QTcB, Week 72, n=269	-2.9 (± 18.13)			
QTcB, Week 96, n=221	-0.6 (± 17.96)			
QTcB, Week 144, n=131	0.5 (± 21.07)			
QTcB, Week 172, n=16	1.8 (± 22.08)			
QTcF, Week 24, n=301	-1.1 (± 14.61)			
QTcF, Week 48, n=294	-1.3 (± 14.08)			
QTcF, Week 72, n=269	-3.7 (± 15.68)			
QTcF, Week 96, n=221	-0.8 (± 16.18)			
QTcF, Week 144, n=131	0.0 (± 17.88)			
QTcF, Week 172, n=16	1.7 (± 17.06)			

Notes:

[10] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with maximum change from Baseline in QTcB and QTcF interval for ECG assessed at any time post Baseline

End point title	Number of participants with maximum change from Baseline in QTcB and QTcF interval for ECG assessed at any time post Baseline

End point description:

Twelve-lead ECG measurements were recorded after the participant has rested in the supine position for 5 minutes. The ECG was obtained before lung function testing followed by other study procedures.

Baseline was considered as the latest assessment prior to first dose of mepolizumab in this study. The change from Baseline is defined as the difference between the value of the endpoint at the time point of interest and Baseline value. Participants with maximum change from Baseline were summarised at any time post Baseline for the following categories <-60, >=-60 to <-30, >=-30 to <0, >=0 to <30, >=30 to <60 and >=60. QTc intervals shown at any time post Baseline are the maximum seen in each participant over the course of the trial.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	305[11]			
Units: Participants				
QTcB, <-60	0			
QTcB, >=-60 to <-30	1			
QTcB, >=-30 to < 0	70			
QTcB, >= 0 to < 30	196			
QTcB, >= 30 to < 60	35			
QTcB, >=60	3			
QTcF, <-60	0			
QTcF, >=-60 to <-30	1			
QTcF, >=-30 to < 0	77			
QTcF, >= 0 to < 30	199			
QTcF, >= 30 to < 60	28			
QTcF, >=60	0			

Notes:

[11] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systolic blood pressure and diastolic blood pressure

End point title	Change from Baseline in systolic blood pressure and diastolic blood pressure

End point description:

Vital sign measurements including systolic blood pressure (SBP) and diastolic blood pressure (DBP) were done pre-injection with the participants sitting, having rested in this position for at least 5 minutes before each reading. They were taken before measurement of any clinic lung function tests or ECGs at the specified time point. Baseline was considered as the latest assessment prior to first dose of mepolizumab in this study. The change from Baseline is defined as the difference between the value of the endpoint at the time point of interest and Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles). 99999 indicates data is not available.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[12]			
Units: Millimeter of mercury				
arithmetic mean (standard deviation)				
SBP, Week 4, n=333	1.8 (± 11.26)			
SBP, Week 8, n=334	0.6 (± 11.75)			
SBP, Week 12, n=337	1.5 (± 12.48)			
SBP, Week 16, n=334	2.0 (± 12.35)			
SBP, Week 20, n=327	1.2 (± 13.69)			
SBP, Week 24, n=333	1.8 (± 13.35)			
SBP, Week 28, n=330	1.4 (± 13.56)			
SBP, Week 32, n=324	1.0 (± 13.43)			
SBP, Week 36, n=330	0.8 (± 13.00)			
SBP, Week 40, n=327	1.6 (± 13.44)			
SBP, Week 44, n=327	1.2 (± 12.75)			
SBP, Week 48, n=329	1.8 (± 13.22)			
SBP, Week 52, n=325	1.5 (± 13.31)			
SBP, Week 56, n=324	2.0 (± 13.52)			
SBP, Week 60, n=315	2.0 (± 13.17)			
SBP, Week 64, n=307	2.5 (± 13.37)			
SBP, Week 68, n=286	2.5 (± 13.46)			
SBP, Week 72, n=281	2.3 (± 13.35)			
SBP, Week 76, n=274	2.3 (± 12.31)			
SBP, Week 80, n=265	3.5 (± 13.58)			
SBP, Week 84, n=255	2.7 (± 14.01)			
SBP, Week 88, n=245	1.5 (± 13.70)			
SBP, Week 92, n=218	0.7 (± 13.24)			
SBP, Week 96, n=208	1.2 (± 13.39)			
SBP, Week 100, n=199	1.0 (± 12.43)			
SBP, Week 104, n=197	2.4 (± 13.38)			
SBP, Week 108, n=192	1.7 (± 12.76)			
SBP, Week 112, n=182	1.8 (± 14.12)			
SBP, Week 116, n=177	1.9 (± 14.66)			
SBP, Week 120, n=167	1.9 (± 13.63)			
SBP, Week 124, n=152	2.5 (± 14.88)			
SBP, Week 128, n=151	2.6 (± 14.15)			
SBP, Week 132, n=139	1.0 (± 14.37)			
SBP, Week 136, n=112	2.3 (± 14.94)			
SBP, Week 140, n=91	-0.9 (± 16.53)			
SBP, Week 144, n=77	2.3 (± 14.13)			
SBP, Week 148, n=62	0.6 (± 13.02)			
SBP, Week 152, n=35	0.6 (± 11.33)			
SBP, Week 156, n=32	1.5 (± 15.73)			
SBP, Week 160, n=14	4.4 (± 9.48)			
SBP, Week 164, n=8	7.0 (± 15.07)			
SBP, Week 168, n=1	-4.0 (± 99999)			

DBP, Week 4, n=333	0.1 (± 8.41)			
DBP, Week 8, n=334	-0.8 (± 8.81)			
DBP, Week 12, n=337	0.2 (± 9.25)			
DBP, Week 16, n=334	0.5 (± 9.30)			
DBP, Week 20, n=327	-0.7 (± 10.35)			
DBP, Week 24, n=333	-0.2 (± 9.40)			
DBP, Week 28, n=330	0.1 (± 8.88)			
DBP, Week 32, n=324	-0.1 (± 10.44)			
DBP, Week 36, n=330	-0.4 (± 10.12)			
DBP, Week 40, n=327	-0.6 (± 9.24)			
DBP, Week 44, n=327	0.1 (± 9.39)			
DBP, Week 48, n=329	0.2 (± 9.71)			
DBP, Week 52, n=325	-0.1 (± 9.83)			
DBP, Week 56, n=324	0.7 (± 9.77)			
DBP, Week 60, n=315	-0.5 (± 10.40)			
DBP, Week 64, n=307	-0.4 (± 9.92)			
DBP, Week 68, n=286	-0.1 (± 10.04)			
DBP, Week 72, n=281	-0.3 (± 10.13)			
DBP, Week 76, n=274	-0.2 (± 9.92)			
DBP, Week 80, n=265	0.7 (± 9.83)			
DBP, Week 84, n=255	-0.6 (± 10.05)			
DBP, Week 88, n=245	-0.3 (± 9.22)			
DBP, Week 92, n=218	-0.9 (± 9.10)			
DBP, Week 96, n=208	-0.2 (± 9.17)			
DBP, Week 100, n=199	-0.7 (± 10.04)			
DBP, Week 104, n=197	0.1 (± 10.21)			
DBP, Week 108, n=192	0.1 (± 9.89)			
DBP, Week 112, n=182	0.0 (± 10.17)			
DBP, Week 116, n=177	-0.1 (± 10.31)			
DBP, Week 120, n=167	0.4 (± 9.74)			
DBP, Week 124, n=152	-0.3 (± 11.11)			
DBP, Week 128, n=151	0.6 (± 9.58)			
DBP, Week 132, n=139	-0.5 (± 10.10)			
DBP, Week 136, n=112	0.1 (± 9.89)			
DBP, Week 140, n=91	-1.8 (± 9.68)			
DBP, Week 144, n=77	-0.6 (± 10.92)			
DBP, Week 148, n=62	-0.7 (± 11.03)			
DBP, Week 152, n=35	-1.0 (± 8.97)			
DBP, Week 156, n=32	-2.0 (± 10.42)			
DBP, Week 160, n=14	2.9 (± 7.92)			
DBP, Week 164, n=8	1.9 (± 8.06)			
DBP, Week 168, n=1	5.0 (± 99999)			

Notes:

[12] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in pulse rate

End point title	Change from Baseline in pulse rate

End point description:

Vital sign measurements including pulse rate was done pre-injection with the participants sitting, having rested in this position for at least 5 minutes before each reading. They were taken before measurement of any clinic lung function tests or ECGs at the specified time point. Baseline was considered as the latest assessment prior to first dose of mepolizumab in this study. The change from Baseline is defined as the difference between the value of the endpoint at the time point of interest and Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles). 99999 indicates data is not available.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[13]			
Units: Beats per minute				
arithmetic mean (standard deviation)				
Pulse rate, Week 4, n=334	2.1 (± 9.98)			
Pulse rate, Week 8, n=333	2.3 (± 10.65)			
Pulse rate, Week 12, n=337	2.6 (± 11.05)			
Pulse rate, Week 16, n=334	2.1 (± 11.03)			
Pulse rate, Week 20, n=327	2.7 (± 11.10)			
Pulse rate, Week 24, n=333	1.2 (± 11.22)			
Pulse rate, Week 28, n=330	2.8 (± 10.43)			
Pulse rate, Week 32, n=324	2.7 (± 11.44)			
Pulse rate, Week 36, n=330	2.6 (± 11.02)			
Pulse rate, Week 40, n=327	2.7 (± 11.09)			
Pulse rate, Week 44, n=327	2.7 (± 12.05)			
Pulse rate, Week 48, n=329	0.4 (± 10.63)			
Pulse rate, Week 52, n=325	1.7 (± 10.48)			
Pulse rate, Week 56, n=324	2.1 (± 11.36)			
Pulse rate, Week 60, n=315	2.1 (± 10.97)			
Pulse rate, Week 64, n=307	2.7 (± 10.96)			
Pulse rate, Week 68, n=286	2.9 (± 11.32)			
Pulse rate, Week 72, n=281	2.0 (± 11.15)			
Pulse rate, Week 76, n=274	2.8 (± 11.15)			
Pulse rate, Week 80, n=265	3.3 (± 11.45)			
Pulse rate, Week 84, n=255	3.2 (± 12.21)			
Pulse rate, Week 88, n=245	2.4 (± 11.98)			
Pulse rate, Week 92, n=218	2.4 (± 12.42)			
Pulse rate, Week 96, n=208	0.0 (± 11.16)			
Pulse rate, Week 100, n=199	1.8 (± 12.30)			
Pulse rate, Week 104, n=197	2.3 (± 12.29)			
Pulse rate, Week 108, n=192	2.2 (± 11.34)			
Pulse rate, Week 112, n=182	2.3 (± 12.35)			
Pulse rate, Week 116, n=177	2.0 (± 12.06)			
Pulse rate, Week 120, n=167	1.2 (± 12.19)			
Pulse rate, Week 124, n=152	2.3 (± 12.56)			
Pulse rate, Week 128, n=151	1.5 (± 11.69)			
Pulse rate, Week 132, n=139	2.2 (± 12.46)			

Pulse rate, Week 136, n=112	2.0 (± 11.68)			
Pulse rate, Week 140, n=92	0.7 (± 11.45)			
Pulse rate, Week 144, n=77	-1.5 (± 11.92)			
Pulse rate, Week 148, n=62	-0.5 (± 11.68)			
Pulse rate, Week 152, n=35	-0.6 (± 13.80)			
Pulse rate, Week 156, n=32	-0.4 (± 12.94)			
Pulse rate, Week 160, n=14	1.5 (± 13.24)			
Pulse rate, Week 164, n=8	1.4 (± 21.23)			
Pulse rate, Week 168, n=1	36.0 (± 99999)			

Notes:

[13] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with positive anti-mepolizumab binding antibodies (ADA) and neutralizing antibodies (NAb)

End point title	Number of participants with positive anti-mepolizumab binding antibodies (ADA) and neutralizing antibodies (NAb)

End point description:

Blood samples were collected for the determination of ADA just prior to administration of mepolizumab. Samples that tested positive for anti-mepolizumab antibodies were further tested for the presence of NAb. The highest value post-Baseline visit are based on each participant's highest post-Baseline titer. NAb assay result was only presented for participants with positive ADA assay. Highest value post-Baseline would be positive for a participant who had both negative and positive post-Baseline results. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[14]			
Units: Participants				
Highest value post-Baseline, ADA, positive, n=335	6			
Highest value post-Baseline, ADA, Negative, n=335	329			
Highest value post-Baseline, NAb, positive, n=6	0			
Highest value post-Baseline, NAb, Negative, n=6	6			

Notes:

[14] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Potential Clinical Importance values for change from Baseline relative to the reference range for clinical chemistry parameters at any time post-Baseline

End point title	Number of participants with Potential Clinical Importance values for change from Baseline relative to the reference range for clinical chemistry parameters at any time post-Baseline

End point description:

Blood samples were collected to assess clinical chemistry laboratory parameters. Number of participants with Potential Clinical Importance values for change from Baseline relative to the reference range at any time post-Baseline are presented. Any time post Baseline = all visits (including scheduled and unscheduled) post-Baseline. Participants are counted in the category that their value changes to (low, normal or high), unless there was no change in their category. If lab value category was unchanged, participants were recorded in the "To Normal or No Change" category. Alanine Aminotransferase=ALT. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	339[15]			
Units: Participants				
Glucose, To low, n=336	1			
Glucose, To Normal or No Change, n=336	334			
Glucose, To high, n=336	1			
ALT, To low, n=337	0			
ALT, To Normal or No Change, n=337	337			
ALT, To high, n=337	0			
Calcium, To low, n=336	0			
Calcium, To Normal or No Change, n=336	336			
Calcium, To high, n=336	0			
Phosphate, To low, n=336	0			
Phosphate, To Normal or No Change, n=336	336			
Phosphate, To high, n=336	0			
Potassium, To low, n=336	0			
Potassium, To Normal or No Change, n=336	336			
Potassium, To high, n=336	0			
Sodium, To low, n=336	1			
Sodium, To Normal or No Change, n=336	335			
Sodium, To high, n=336	0			

Notes:

[15] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Potential Clinical Importance values for change from Baseline relative to the reference range for hematology parameters at any time post-Baseline

End point title	Number of participants with Potential Clinical Importance values for change from Baseline relative to the reference range for hematology parameters at any time post-Baseline

End point description:

Blood samples were collected to assess hematology laboratory parameters. Number of participants with Potential Clinical Importance values for change from Baseline relative to the reference range at any time post-Baseline are presented. Any time post Baseline = all visits (including scheduled and unscheduled) post-Baseline. Participants are counted in the category that their value changes to (low, normal or high), unless there was no change in their category. If lab value category was unchanged, participants were recorded in the "To Normal or No Change" category.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 172

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	336[16]			
Units: Participants				
Hematocrit, To low	1			
Hematocrit, To Normal or No Change	335			
Hematocrit, To high	0			
Hemoglobin, To low	1			
Hemoglobin, To Normal or No Change	335			
Hemoglobin, To high	0			
Leukocytes, To low	1			
Leukocytes, To Normal or No Change	335			
Leukocytes, To high	0			
Platelets, To low	1			
Platelets, To Normal or No Change	335			
Platelets, To high	0			

Notes:

[16] - AT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The on-treatment AEs and on-treatment SAEs are the events which happened on/after the first dose of mepolizumab date and before/on last dose of mepolizumab date + 28 days (up to 172 weeks)

Adverse event reporting additional description:

AEs and SAEs were collected for all participants within the As Treated Population which comprised of all participants who received at least one dose of mepolizumab.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Mepolizumab 100 mg SC

Reporting group description:

Participants received mepolizumab 100 mg administered via SC injection into the upper arm or thigh approximately every 4 weeks for 172 weeks. Participants remained on standard of care asthma therapy which could be adjusted during the study at the discretion of the physician.

Serious adverse events	Mepolizumab 100 mg SC		
Total subjects affected by serious adverse events			
subjects affected / exposed	84 / 339 (24.78%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colon neoplasm			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			

subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Cyst			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anaphylactic shock			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Food allergy			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Endometrial hyperplasia			

subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	34 / 339 (10.03%)		
occurrences causally related to treatment / all	0 / 51		
deaths causally related to treatment / all	0 / 1		
Nasal polyps			
subjects affected / exposed	4 / 339 (1.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Status asthmaticus			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			

Anxiety disorder				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Foot fracture				
subjects affected / exposed	3 / 339 (0.88%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Fracture				
subjects affected / exposed	2 / 339 (0.59%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Joint injury				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ligament rupture				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Rib fracture				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tendon injury				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Congenital anomaly				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aortic valve stenosis				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Arrhythmia			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hemiparesis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
IIIrd nerve paralysis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Glaucoma			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal adhesions			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dental cyst			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Neurodermatitis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary incontinence			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteonecrosis			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pain in extremity				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Polyarthritis				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	6 / 339 (1.77%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	3 / 339 (0.88%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	3 / 339 (0.88%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	2 / 339 (0.59%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	2 / 339 (0.59%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchitis				

subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis infectious				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia haemophilus				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia staphylococcal				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				

subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Mepolizumab 100 mg SC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	288 / 339 (84.96%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 339 (4.13%)		
occurrences (all)	15		
Nervous system disorders			
Headache			
subjects affected / exposed	57 / 339 (16.81%)		
occurrences (all)	160		
Dizziness			
subjects affected / exposed	15 / 339 (4.42%)		
occurrences (all)	19		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 339 (4.72%)		
occurrences (all)	23		
Influenza like illness			
subjects affected / exposed	15 / 339 (4.42%)		
occurrences (all)	17		
Injection site reaction			
subjects affected / exposed	15 / 339 (4.42%)		
occurrences (all)	48		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	16 / 339 (4.72%)		
occurrences (all)	17		
Nausea			
subjects affected / exposed	15 / 339 (4.42%)		
occurrences (all)	16		
Vomiting			
subjects affected / exposed	14 / 339 (4.13%)		
occurrences (all)	32		
Gastrooesophageal reflux disease			

subjects affected / exposed	11 / 339 (3.24%)		
occurrences (all)	13		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	52 / 339 (15.34%)		
occurrences (all)	78		
Oropharyngeal pain			
subjects affected / exposed	25 / 339 (7.37%)		
occurrences (all)	31		
Cough			
subjects affected / exposed	22 / 339 (6.49%)		
occurrences (all)	27		
Dyspnoea			
subjects affected / exposed	13 / 339 (3.83%)		
occurrences (all)	14		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	14 / 339 (4.13%)		
occurrences (all)	17		
Rash			
subjects affected / exposed	14 / 339 (4.13%)		
occurrences (all)	18		
Pruritus			
subjects affected / exposed	13 / 339 (3.83%)		
occurrences (all)	17		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	17 / 339 (5.01%)		
occurrences (all)	18		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	41 / 339 (12.09%)		
occurrences (all)	51		
Arthralgia			
subjects affected / exposed	32 / 339 (9.44%)		
occurrences (all)	48		

Pain in extremity			
subjects affected / exposed	15 / 339 (4.42%)		
occurrences (all)	16		
Musculoskeletal pain			
subjects affected / exposed	14 / 339 (4.13%)		
occurrences (all)	16		
Myalgia			
subjects affected / exposed	11 / 339 (3.24%)		
occurrences (all)	11		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	143 / 339 (42.18%)		
occurrences (all)	270		
Bronchitis			
subjects affected / exposed	64 / 339 (18.88%)		
occurrences (all)	106		
Upper respiratory tract infection			
subjects affected / exposed	64 / 339 (18.88%)		
occurrences (all)	110		
Sinusitis			
subjects affected / exposed	62 / 339 (18.29%)		
occurrences (all)	115		
Influenza			
subjects affected / exposed	42 / 339 (12.39%)		
occurrences (all)	52		
Respiratory tract infection			
subjects affected / exposed	20 / 339 (5.90%)		
occurrences (all)	23		
Gastroenteritis			
subjects affected / exposed	19 / 339 (5.60%)		
occurrences (all)	20		
Lower respiratory tract infection			
subjects affected / exposed	18 / 339 (5.31%)		
occurrences (all)	28		
Rhinitis			

subjects affected / exposed	18 / 339 (5.31%)		
occurrences (all)	31		
Urinary tract infection			
subjects affected / exposed	17 / 339 (5.01%)		
occurrences (all)	19		
Pharyngitis			
subjects affected / exposed	15 / 339 (4.42%)		
occurrences (all)	22		
Ear infection			
subjects affected / exposed	12 / 339 (3.54%)		
occurrences (all)	15		
Viral upper respiratory tract infection			
subjects affected / exposed	12 / 339 (3.54%)		
occurrences (all)	14		
Pneumonia			
subjects affected / exposed	11 / 339 (3.24%)		
occurrences (all)	11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2014	Amendment 1: The primary purpose of Amendment 01 was to change three entry criteria to ensure those participants with a history of seriously debilitating asthma and a history of improved disease control continue to receive mepolizumab in 201312. The amendment also included a number of additional corrections and edits.
14 November 2014	Amendment 2: The primary reason for Amendment 2 was to insert entry criterion number 8. There are also minor changes to clarify the participant scenarios added during Amendment 1 and an administrative change to update the Medical Monitors.
19 June 2015	Amendment 3: The primary reason for Amendment 3 was to increase the treatment duration and to remove the Follow-up visit. There was also a change to the investigational product (IP) administration process and clarification to the IP post dose monitoring process. The amendment also included a standardization of the collection of concomitant medications.
06 July 2015	Amendment 4: To correct some errors in Appendix 9 to reflect the amendments made within the main protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported