Clinical trial results:
MEA115666: A multi-centre, open-label, long term safety study of mepolizumab in asthmatic subjects who participated in the MEA112997 trial.

Summary

EudraCT number	2012-001643-51
Trial protocol	GB DE
Global end of trial date	31 May 2017

Results information

Result version number	v1 (current)
This version publication date	05 May 2018
First version publication date	05 May 2018

Trial information

Trial identification

Sponsor protocol code	115666

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	25 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 May 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to describe the long-term safety profile of mepolizumab.

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	28 September 2012
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?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 30
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Germany: 56
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Romania: 28
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	Russian Federation: 47
Country: Number of subjects enrolled	Ukraine: 45
Country: Number of subjects enrolled	Argentina: 9
Country: Number of subjects enrolled	Chile: 27
Country: Number of subjects enrolled	Australia: 25
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Korea, Republic of: 14
Worldwide total number of subjects	347
EEA total number of subjects	138

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)	301
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multi-center, open-label, long term safety study of mepolizumab in 347 asthmatic participants who participated in the MEA112997 trial and were found eligible for this study after screening and run in phase. The study was conducted at 65 centers in 13 countries from 28 Sep 2012 to 31 May 2017.

Pre-assignment

Screening details:

A total of 362 participants were screened; 4 participants were screen failures (did not meet the inclusion/exclusion criteria); 11 participants were withdrawn during the run-in period (4 did not meet the continuation criteria, 4 withdrawal by participant and 3 following physician decision).

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

Arm description:

Participants received 100 milligram (mg) of mepolizumab injected subcutaneously (SC) once every 4 weeks until participant withdrawal or mepolizumab becomes commercially available in the relevant participating country. Participants remained on standard of care asthma therapy, which was adjusted during the study, at the discretion of their 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 100 mg of mepolizumab injected SC once every 4 weeks.

Number of subjects in period 1	Mepolizumab 100 mg
Started	347
Completed	0
Not completed	347
Study closed/terminated	50
Adverse event, serious fatal	6
Physician decision	6
Consent withdrawn by subject	31
Adverse event, non-fatal	13
Product commercially available	221
Lost to follow-up	5

Lack of efficacy	11
Protocol deviation	4

Baseline characteristics

Reporting groups	
Reporting group title	Mepolizumab 100 mg
Reporting group description:	
Participants received 100 milligram (mg) of mepolizumab injected subcutaneously (SC) once every 4 weeks until participant withdrawal or mepolizumab becomes commercially available in the relevant participating country. Participants remained on standard of care asthma therapy, which was adjusted during the study, at the discretion of their physician.	

Reporting group values	Mepolizumab 100 mg	Total	
Number of subjects	347	347	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	52.2		
standard deviation	± 10.73	-	
Gender categorical Units: Subjects			
Female	224	224	
Male	123	123	
Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	8	8	
American Indian or Alaskan Native	2	2	
Asian - Central/South Asian Heritage	4	4	
Asian - East Asian Heritage	14	14	
White - Arabic/North African Heritage	7	7	
White - White/Caucasian/European Heritage	311	311	
Asian & Native Hawaiian or Other Pacific Islander	1	1	

End points

End points reporting groups

Reporting group title	Mepolizumab 100 mg

Reporting group description:

Participants received 100 milligram (mg) of mepolizumab injected subcutaneously (SC) once every 4 weeks until participant withdrawal or mepolizumab becomes commercially available in the relevant participating country. Participants remained on standard of care asthma therapy, which was adjusted during the study, at the discretion of their physician.

Primary: Number of participants who experienced on-treatment adverse events (AE) and on-treatment serious adverse events (SAE)

End point title	Number of participants who experienced on-treatment adverse events (AE) and on-treatment serious adverse events (SAE)[1]

End point description:

AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with use of a medicinal product (MP), whether or not considered related to MP. AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with use of MP. 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. As Treated (AT) Population consisted of participants who received at least one dose of open label mepolizumab. 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 of mepolizumab + 28 days.

End point type	Primary

End point timeframe:

Baseline (Week 0) to Week 240

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 is no statistical data to report.

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[2]			
Units: Participants				
AE	326			
SAE	79			

Notes:

[2] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who experienced on-treatment systemic (i.e., allergic/Immunoglobulin E [IgE]-mediated and non-allergic) and on-treatment local site reactions

End point title	Number of participants who experienced on-treatment systemic (i.e., allergic/Immunoglobulin E [IgE]-mediated and non-allergic) and on-treatment local site reactions

End point description:

Systemic and local site reactions following mepolizumab dosing as identified by the investigator and the number of participants who experienced systemic and/or local site reactions are presented. 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 of mepolizumab + 28 days.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[3]			
Units: Participants				
Systemic reactions	9			
Local site reactions	42			

Notes:

[3] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in QT interval corrected by Bazett's method (QTc[B])

End point title	Mean change from Baseline in QT interval corrected by Bazett's method (QTc[B])

End point description:

Twelve-lead ECGs were performed at Screening and every 24 weeks during the treatment period. ECG measurements were made after the participant had rested in the supine position for 5 minutes. Collection shortly after a meal or during sleep was avoided as QT prolongation can occur at these times. Baseline was the last available ECG prior to mepolizumab dosing. Change from Baseline was post-Baseline values minus Baseline values. Only those participants 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 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[4]			
Units: Milliseconds				
arithmetic mean (standard deviation)				
Week 24, n=330	4.2 (± 18.57)			
Week 48, n=319	3.2 (± 17.19)			
Week 72, n=307	-0.5 (± 16.76)			
Week 96, n=293	1.3 (± 17.92)			
Week 124, n=292	1.5 (± 19.69)			

Week 148, n=275	1.6 (± 17.84)			
Week 176, n=201	0.6 (± 18.02)			
Week 200, n=149	3.3 (± 17.02)			
Week 228, n=32	1.5 (± 20.95)			
Follow up, n=270	2.5 (± 18.71)			

Notes:

[4] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in QT interval corrected by Fridericia's method (QTc[F])

End point title	Mean change from Baseline in QT interval corrected by Fridericia's method (QTc[F])

End point description:

Twelve-lead ECGs were performed at Screening and every 24 weeks during the treatment period. ECG measurements were made after the participant had rested in the supine position for 5 minutes. Collection shortly after a meal or during sleep was avoided as QT prolongation can occur at these times. Baseline was the last available ECG prior to mepolizumab dosing. Change from Baseline was post-Baseline values minus Baseline values. Only those participants 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 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[5]			
Units: Milliseconds				
arithmetic mean (standard deviation)				
Week 24, n=330	5.1 (± 17.00)			
Week 48, n=319	4.1 (± 15.72)			
Week 72, n=307	0.2 (± 15.11)			
Week 96, n=293	2.2 (± 15.37)			
Week 124, n=292	3.2 (± 16.77)			
Week 148, n=275	2.9 (± 15.49)			
Week 176, n=201	2.0 (± 15.97)			
Week 200, n=149	4.3 (± 14.52)			
Week 228, n=32	0.4 (± 15.81)			
Follow up, n=270	3.9 (± 16.39)			

Notes:

[5] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with a maximum change from Baseline for QTc(F) and QTc(B)

End point title	Number of participants with a maximum change from Baseline for QTc(F) and QTc(B)

End point description:

Twelve-lead ECGs were performed at Screening and every 24 weeks during the treatment period. ECG measurements were made after the participant had rested in the supine position for 5 minutes. Collection shortly after a meal or during sleep was avoided as QT prolongation can occur at these times. Baseline was the last available ECG prior to mepolizumab dosing. Change from Baseline was post-Baseline values minus Baseline values. Number of participants with a maximum change from Baseline for QTc(F) and QTc(B) at any time post Baseline are presented. Only those participants who provided ECG data at baseline and post-baseline were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	342[6]			
Units: Participants				
QTc(F): < -60	0			
QTc(F): >= -60 - < -30	1			
QTc(F): >= -30 - < 0	31			
QTc(F): >= 0 - < 30	252			
QTc(F): >= 30 - < 60	55			
QTc(F): >= 60	3			
QTc(B): < -60	0			
QTc(B): >= -60 - < -30	1			
QTc(B): >= -30 - < 0	36			
QTc(B): >= 0 - < 30	228			
QTc(B): >= 30 - < 60	69			
QTc(B): >= 60	8			

Notes:

[6] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinical chemistry data of potential clinical concern

End point title	Number of participants with clinical chemistry data of potential clinical concern

End point description:

Clinical chemistry analytes with laboratory ranges defining values of potential clinical concern included sodium, potassium, calcium, phosphate, serum glucose and alanine aminotransferase. Number of participants with clinical chemistry abnormalities of potential clinical concern anytime post baseline are presented. Only those participants who provided lab data post-baseline were analyzed represented by n=X in the category titles.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[7]			
Units: Participants				
Potassium high, n=346	1			
Serum glucose high, n=346	1			
Serum glucose low, n=346	7			

Notes:

[7] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with hematology data of potential clinical concern

End point title	Number of participants with hematology data of potential clinical concern

End point description:

Hematology parameters with laboratory ranges defining values of potential clinical concern included hemoglobin, hematocrit, platelet count, white blood cell count. Number of participants with clinical hematology abnormalities of potential clinical concern anytime post baseline are presented, which only included participants with low hemoglobin values. Only those participants who provided lab data post-baseline were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	346[8]			
Units: Participants				
Participants	1			

Notes:

[8] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in vital signs-Sitting diastolic blood pressure and sitting systolic blood pressure

End point title	Mean change from Baseline in vital signs-Sitting diastolic blood pressure and sitting systolic blood pressure

End point description:

Vital signs included sitting pulse rate and sitting blood pressure (diastolic and systolic). Measurements were done pre injection with the participant sitting, having rested in this position for at least 5 minutes before each reading. Baseline was Week 0. Change from Baseline was post-Baseline values minus Baseline values. Only those participants 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 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[9]			
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
Sitting Diastolic Blood Pressure: Week 4, n=346	-1.0 (± 8.71)			
Sitting Diastolic Blood Pressure: Week 8, n=345	-1.5 (± 8.85)			
Sitting Diastolic Blood Pressure: Week 12, n=342	-0.7 (± 9.67)			
Sitting Diastolic Blood Pressure: Week 16, n=341	-1.6 (± 9.27)			
Sitting Diastolic Blood Pressure: Week 20, n=338	-1.6 (± 9.17)			
Sitting Diastolic Blood Pressure: Week 24, n=336	-0.7 (± 9.27)			
Sitting Diastolic Blood Pressure: Week 28, n=332	-1.3 (± 8.90)			
Sitting Diastolic Blood Pressure: Week 32, n=333	-1.0 (± 9.62)			
Sitting Diastolic Blood Pressure: Week 36, n=329	-1.8 (± 8.95)			
Sitting Diastolic Blood Pressure: Week 40, n=329	-1.2 (± 9.33)			
Sitting Diastolic Blood Pressure: Week 44, n=326	-1.1 (± 10.00)			
Sitting Diastolic Blood Pressure: Week 48, n=325	-0.7 (± 9.67)			
Sitting Diastolic Blood Pressure: Week 52, n=322	-1.1 (± 9.85)			
Sitting Diastolic Blood Pressure: Week 56, n=320	-1.3 (± 9.67)			
Sitting Diastolic Blood Pressure: Week 60, n=318	-0.9 (± 9.56)			
Sitting Diastolic Blood Pressure: Week 64, n=318	-1.0 (± 9.29)			
Sitting Diastolic Blood Pressure: Week 68, n=317	-1.1 (± 9.94)			
Sitting Diastolic Blood Pressure: Week 72, n=312	-1.5 (± 9.67)			
Sitting Diastolic Blood Pressure: Week 76, n=313	-1.1 (± 10.06)			

Sitting Diastolic Blood Pressure: Week 80, n=311	-1.6 (± 10.23)			
Sitting Diastolic Blood Pressure: Week 84, n=310	-1.7 (± 10.51)			
Sitting Diastolic Blood Pressure: Week 88, n=310	-1.4 (± 10.45)			
Sitting Diastolic Blood Pressure: Week 92, n=311	-1.0 (± 9.89)			
Sitting Diastolic Blood Pressure: Week 96, n=303	-1.2 (± 9.81)			
Sitting Diastolic Blood Pressure: Week 100, n=300	-0.3 (± 9.40)			
Sitting Diastolic Blood Pressure: Week 104, n=301	-1.0 (± 9.69)			
Sitting Diastolic Blood Pressure: Week 108, n=300	-0.9 (± 10.28)			
Sitting Diastolic Blood Pressure: Week 112, n=299	-0.9 (± 9.78)			
Sitting Diastolic Blood Pressure: Week 116, n=297	-0.7 (± 9.56)			
Sitting Diastolic Blood Pressure: Week 120, n=295	-0.8 (± 9.41)			
Sitting Diastolic Blood Pressure: Week 124, n=294	-1.3 (± 10.52)			
Sitting Diastolic Blood Pressure: Week 128, n=293	-1.2 (± 10.08)			
Sitting Diastolic Blood Pressure: Week 132, n=289	-1.0 (± 10.48)			
Sitting Diastolic Blood Pressure: Week 136, n=288	-0.7 (± 10.42)			
Sitting Diastolic Blood Pressure: Week 140, n=287	-0.6 (± 9.90)			
Sitting Diastolic Blood Pressure: Week 144, n=290	-0.9 (± 9.83)			
Sitting Diastolic Blood Pressure: Week 148, n=287	0.1 (± 10.22)			
Sitting Diastolic Blood Pressure: Week 152, n=284	-0.9 (± 10.17)			
Sitting Diastolic Blood Pressure: Week 156, n=275	-0.4 (± 10.44)			
Sitting Diastolic Blood Pressure: Week 160, n=265	-0.6 (± 9.93)			
Sitting Diastolic Blood Pressure: Week 164, n=242	-1.7 (± 10.83)			
Sitting Diastolic Blood Pressure: Week 168, n=232	-1.3 (± 10.46)			
Sitting Diastolic Blood Pressure: Week 172, n=226	-1.2 (± 10.18)			
Sitting Diastolic Blood Pressure: Week 176, n=212	-1.6 (± 9.84)			
Sitting Diastolic Blood Pressure: Week 180, n=200	-1.6 (± 10.42)			
Sitting Diastolic Blood Pressure: Week 184, n=184	-1.3 (± 9.94)			
Sitting Diastolic Blood Pressure: Week 188, n=180	-1.4 (± 9.81)			
Sitting Diastolic Blood Pressure: Week 192, n=176	-1.1 (± 10.25)			
Sitting Diastolic Blood Pressure: Week 196, n=175	-1.5 (± 10.18)			
Sitting Diastolic Blood Pressure: Week 200, n=172	-0.4 (± 10.07)			

Sitting Diastolic Blood Pressure: Week 204, n=169	-1.1 (± 10.25)			
Sitting Diastolic Blood Pressure: Week 208, n=157	-1.8 (± 9.48)			
Sitting Diastolic Blood Pressure: Week 212, n=146	-1.3 (± 9.53)			
Sitting Diastolic Blood Pressure: Week 216, n=130	-0.2 (± 9.55)			
Sitting Diastolic Blood Pressure: Week 220, n=67	-1.6 (± 10.85)			
Sitting Diastolic Blood Pressure: Week 224, n=54	-1.9 (± 11.97)			
Sitting Diastolic Blood Pressure: Week 228, n=37	-0.2 (± 9.60)			
Sitting Diastolic Blood Pressure: Week 232, n=5	4.6 (± 5.86)			
Sitting Diastolic Blood Pressure: Follow-up, n=306	-0.7 (± 10.03)			
Sitting Systolic Blood Pressure: Week 4, n=346	0.2 (± 10.79)			
Sitting Systolic Blood Pressure: Week 8, n=345	-0.7 (± 12.57)			
Sitting Systolic Blood Pressure: Week 12, n=342	-0.3 (± 12.59)			
Sitting Systolic Blood Pressure: Week 16, n=341	-0.5 (± 13.60)			
Sitting Systolic Blood Pressure: Week 20, n=338	-1.8 (± 13.31)			
Sitting Systolic Blood Pressure: Week 24, n=336	-0.8 (± 13.93)			
Sitting Systolic Blood Pressure: Week 28, n=332	-0.6 (± 13.61)			
Sitting Systolic Blood Pressure: Week 32, n=333	-1.0 (± 14.24)			
Sitting Systolic Blood Pressure: Week 36, n=329	-0.7 (± 14.19)			
Sitting Systolic Blood Pressure: Week 40, n=329	-0.6 (± 14.11)			
Sitting Systolic Blood Pressure: Week 44, n=326	-0.9 (± 14.87)			
Sitting Systolic Blood Pressure: Week 48, n=325	-0.1 (± 13.59)			
Sitting Systolic Blood Pressure: Week 52, n=322	-0.3 (± 13.63)			
Sitting Systolic Blood Pressure: Week 56, n=320	-0.3 (± 14.33)			
Sitting Systolic Blood Pressure: Week 60, n=318	0.0 (± 14.21)			
Sitting Systolic Blood Pressure: Week 64, n=318	-0.2 (± 13.99)			
Sitting Systolic Blood Pressure: Week 68, n=317	-1.1 (± 14.83)			
Sitting Systolic Blood Pressure: Week 72, n=312	-1.8 (± 13.16)			
Sitting Systolic Blood Pressure: Week 76, n=313	-0.8 (± 14.44)			
Sitting Systolic Blood Pressure: Week 80, n=311	-1.1 (± 14.49)			
Sitting Systolic Blood Pressure: Week 84, n=310	-1.9 (± 14.47)			
Sitting Systolic Blood Pressure: Week 88, n=310	-1.7 (± 14.94)			

Sitting Systolic Blood Pressure: Week 92, n=311	-0.3 (± 15.16)			
Sitting Systolic Blood Pressure: Week 96, n=303	0.1 (± 14.32)			
Sitting Systolic Blood Pressure: Week 100, n=300	0.7 (± 14.71)			
Sitting Systolic Blood Pressure: Week 104, n=301	0.3 (± 14.81)			
Sitting Systolic Blood Pressure: Week 108, n=300	0.5 (± 15.15)			
Sitting Systolic Blood Pressure: Week 112, n=299	-0.4 (± 14.83)			
Sitting Systolic Blood Pressure: Week 116, n=297	0.4 (± 14.31)			
Sitting Systolic Blood Pressure: Week 120, n=295	0.5 (± 14.37)			
Sitting Systolic Blood Pressure: Week 124, n=294	0.7 (± 14.80)			
Sitting Systolic Blood Pressure: Week 128, n=293	0.7 (± 14.68)			
Sitting Systolic Blood Pressure: Week 132, n=289	0.7 (± 14.51)			
Sitting Systolic Blood Pressure: Week 136, n=288	0.9 (± 16.81)			
Sitting Systolic Blood Pressure: Week 140, n=287	0.3 (± 15.48)			
Sitting Systolic Blood Pressure: Week 144, n=290	1.1 (± 15.79)			
Sitting Systolic Blood Pressure: Week 148, n=287	1.8 (± 13.59)			
Sitting Systolic Blood Pressure: Week 152, n=284	0.2 (± 15.53)			
Sitting Systolic Blood Pressure: Week 156, n=275	0.8 (± 14.56)			
Sitting Systolic Blood Pressure: Week 160, n=265	1.1 (± 15.34)			
Sitting Systolic Blood Pressure: Week 164, n=242	0.6 (± 15.51)			
Sitting Systolic Blood Pressure: Week 168, n=232	0.1 (± 14.87)			
Sitting Systolic Blood Pressure: Week 172, n=226	-0.8 (± 15.67)			
Sitting Systolic Blood Pressure: Week 176, n=212	0.4 (± 13.78)			
Sitting Systolic Blood Pressure: Week 180, n=200	0.6 (± 15.32)			
Sitting Systolic Blood Pressure: Week 184, n=184	-0.5 (± 16.36)			
Sitting Systolic Blood Pressure: Week 188, n=180	-1.0 (± 15.54)			
Sitting Systolic Blood Pressure: Week 192, n=176	-1.2 (± 16.60)			
Sitting Systolic Blood Pressure: Week 196, n=175	-0.8 (± 14.76)			
Sitting Systolic Blood Pressure: Week 200, n=172	-0.1 (± 15.28)			
Sitting Systolic Blood Pressure: Week 204, n=169	-0.4 (± 15.64)			
Sitting Systolic Blood Pressure: Week 208, n=157	-1.0 (± 16.92)			
Sitting Systolic Blood Pressure: Week 212, n=146	0.5 (± 14.98)			

Sitting Systolic Blood Pressure: Week 216, n=130	0.4 (± 15.52)			
Sitting Systolic Blood Pressure: Week 220, n=67	-4.2 (± 20.86)			
Sitting Systolic Blood Pressure: Week 224, n=54	-3.8 (± 17.87)			
Sitting Systolic Blood Pressure: Week 228, n=37	-3.6 (± 15.15)			
Sitting Systolic Blood Pressure: Week 232, n=5	-0.8 (± 6.30)			
Sitting Systolic Blood Pressure: Follow-up, n=306	0.0 (± 14.92)			

Notes:

[9] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in Vital signs-Sitting pulse rate

End point title	Mean change from Baseline in Vital signs-Sitting pulse rate

End point description:

Vital signs included sitting pulse rate and blood pressure (diastolic and systolic). Measurements were done pre injection with the participant sitting, having rested in this position for at least 5 minutes before each reading. Baseline was Week 0. Change from Baseline was post-Baseline values minus Baseline values. Only those participants 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 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[10]			
Units: Beats per minute				
arithmetic mean (standard deviation)				
Sitting Pulse Rate: Week 4, n=346	-0.3 (± 8.94)			
Sitting Pulse Rate: Week 8, n=345	1.0 (± 9.98)			
Sitting Pulse Rate: Week 12, n=342	0.0 (± 9.52)			
Sitting Pulse Rate: Week 16, n=341	-0.1 (± 10.08)			
Sitting Pulse Rate: Week 20, n=338	-0.3 (± 9.44)			
Sitting Pulse Rate: Week 24, n=337	-1.6 (± 9.83)			
Sitting Pulse Rate: Week 28, n=332	-0.2 (± 9.58)			
Sitting Pulse Rate: Week 32, n=333	-0.2 (± 9.74)			
Sitting Pulse Rate: Week 36, n=329	-0.6 (± 9.60)			
Sitting Pulse Rate: Week 40, n=329	-0.2 (± 9.56)			
Sitting Pulse Rate: Week 44, n=327	-0.4 (± 9.80)			
Sitting Pulse Rate: Week 48, n=325	-1.6 (± 9.65)			
Sitting Pulse Rate: Week 52, n=322	0.1 (± 9.56)			
Sitting Pulse Rate: Week 56, n=320	-0.3 (± 9.79)			
Sitting Pulse Rate: Week 60, n=318	-0.8 (± 9.54)			

Sitting Pulse Rate: Week 64, n=318	-0.9 (± 9.63)			
Sitting Pulse Rate: Week 68, n=317	-1.2 (± 9.51)			
Sitting Pulse Rate: Week 72, n=312	-1.8 (± 10.07)			
Sitting Pulse Rate: Week 76, n=313	-1.2 (± 9.65)			
Sitting Pulse Rate: Week 80, n=311	-0.5 (± 10.08)			
Sitting Pulse Rate: Week 84, n=310	-1.2 (± 9.80)			
Sitting Pulse Rate: Week 88, n=310	-0.6 (± 10.12)			
Sitting Pulse Rate: Week 92, n=311	-0.6 (± 9.36)			
Sitting Pulse Rate: Week 96, n=303	-1.7 (± 10.61)			
Sitting Pulse Rate: Week 100, n=300	-0.5 (± 9.81)			
Sitting Pulse Rate: Week 104, n=301	-0.9 (± 10.45)			
Sitting Pulse Rate: Week 108, n=300	-0.8 (± 10.04)			
Sitting Pulse Rate: Week 112, n=299	-0.5 (± 9.60)			
Sitting Pulse Rate: Week 116, n=297	-1.5 (± 9.33)			
Sitting Pulse Rate: Week 120, n=294	-1.2 (± 10.27)			
Sitting Pulse Rate: Week 124, n=294	-2.5 (± 10.27)			
Sitting Pulse Rate: Week 128, n=293	-1.2 (± 10.00)			
Sitting Pulse Rate: Week 132, n=289	-0.7 (± 9.20)			
Sitting Pulse Rate: Week 136, n=288	-0.6 (± 10.55)			
Sitting Pulse Rate: Week 140, n=287	-0.6 (± 9.71)			
Sitting Pulse Rate: Week 144, n=290	-0.7 (± 9.72)			
Sitting Pulse Rate: Week 148, n=287	-1.8 (± 9.82)			
Sitting Pulse Rate: Week 152, n=284	-0.9 (± 10.45)			
Sitting Pulse Rate: Week 156, n=275	-0.8 (± 9.83)			
Sitting Pulse Rate: Week 160, n=265	-0.5 (± 10.42)			
Sitting Pulse Rate: Week 164, n=242	-1.1 (± 11.07)			
Sitting Pulse Rate: Week 168, n=232	-0.5 (± 11.25)			
Sitting Pulse Rate: Week 172, n=226	-1.0 (± 9.80)			
Sitting Pulse Rate: Week 176, n=212	-2.9 (± 9.57)			
Sitting Pulse Rate: Week 180, n=200	-0.5 (± 10.01)			
Sitting Pulse Rate: Week 184, n=184	-1.3 (± 9.89)			
Sitting Pulse Rate: Week 188, n=180	-1.3 (± 10.38)			
Sitting Pulse Rate: Week 192, n=176	-1.6 (± 10.37)			
Sitting Pulse Rate: Week 196, n=175	-1.2 (± 9.79)			
Sitting Pulse Rate: Week 200, n=172	-2.3 (± 11.03)			
Sitting Pulse Rate: Week 204, n=169	-1.9 (± 10.67)			
Sitting Pulse Rate: Week 208, n=157	-0.6 (± 10.64)			
Sitting Pulse Rate: Week 212, n=146	-0.4 (± 10.09)			
Sitting Pulse Rate: Week 216, n=130	-1.4 (± 10.49)			
Sitting Pulse Rate: Week 220, n=67	0.0 (± 11.13)			
Sitting Pulse Rate: Week 224, n=54	-1.4 (± 13.19)			
Sitting Pulse Rate: Week 228, n=37	-2.4 (± 10.57)			
Sitting Pulse Rate: Week 232, n=5	-2.0 (± 16.63)			
Sitting Pulse Rate: Follow-up, n=306	-1.5 (± 10.72)			

Notes:

[10] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized rate of on-treatment exacerbations

End point title	Annualized rate of on-treatment exacerbations

End point description:

Exacerbations were defined as worsening of asthma which required use of systemic corticosteroids and/or hospitalization and/or Emergency Department visits. Data is presented as mean which is exacerbation rate/year. Exacerbation data are performed using a negative binomial model with covariates of region, annualized rate of exacerbations in the interval between MEA112997 and MEA115666 (as an ordinal variable) and baseline % predicted FEV1, and with logarithm of time on treatment as an offset variable.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[11]			
Units: Exacerbations per year				
arithmetic mean (confidence interval 95%)				
Exacerbations per year	0.68 (0.60 to 0.78)			

Notes:

[11] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in Asthma Control Questionnaire (ACQ) score

End point title	Mean change from Baseline in Asthma Control Questionnaire (ACQ) score

End point description:

The ACQ-5 is a five-item questionnaire, which was developed as a measure of participant' asthma control that was completed by the participant. The five questions enquire about the frequency and/or severity of symptoms (nocturnal awakening on waking in the morning, activity limitation, and shortness of breath, wheeze). The ACQ consists of 5 questions that are scored on a 7 point scale from 0 (totally controlled) to 6 (severely uncontrolled). The ACQ score was derived as mean of five questions: ACQ score = Question 1 (Q1)+Q2+Q3+Q4+Q5 divided by 5 where Q1, Q2,... Q5 are the scores of Q1, Q2, ..., Q5, respectively. The total score ranged from zero (no impairment/limitation) which indicated best condition to six (total impairment/ limitation) which indicated worst asthma. Baseline was Week 0. Change from Baseline was post-Baseline values minus Baseline values. Only those participants 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 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[12]			
Units: Scores on a Scale				
arithmetic mean (standard deviation)				
Week 12, n=341	-0.47 (± 0.991)			
Week 24, n=335	-0.55 (± 1.037)			
Week 36, n=327	-0.56 (± 1.088)			
Week 48, n=324	-0.55 (± 1.098)			
Week 60, n=317	-0.58 (± 1.126)			
Week 72, n=311	-0.51 (± 1.054)			
Week 84, n=308	-0.54 (± 1.090)			
Week 96, n=301	-0.44 (± 1.171)			
Week 112, n=297	-0.51 (± 1.228)			
Week 124, n=293	-0.66 (± 1.216)			
Week 136, n=287	-0.58 (± 1.215)			
Week 148, n=286	-0.54 (± 1.070)			
Week 164, n=240	-0.59 (± 1.221)			
Week 176, n=211	-0.49 (± 1.179)			
Week 188, n=178	-0.40 (± 1.310)			
Week 200, n=171	-0.45 (± 1.119)			
Week 216, n=130	-0.42 (± 1.161)			
Week 228, n=37	-0.47 (± 1.502)			
Follow-up, n=301	-0.53 (± 1.193)			

Notes:

[12] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in clinic pre-bronchodilator forced expiratory volume in 1 second (FEV1)

End point title	Mean change from Baseline in clinic pre-bronchodilator forced expiratory volume in 1 second (FEV1)

End point description:

FEV1 is forced expiratory volume in the first second. The volume of air that can be forced out in one second after taking a deep breath, an important measure of pulmonary function. Forced expiratory volume (FEV) measures how much air a person can exhale during a forced breath. FEV1 was measured

by clinic spirometry. Baseline was Week 0. Change from Baseline was post-Baseline values minus Baseline values. Only those participants 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 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[13]			
Units: Milliliters (mL)				
arithmetic mean (standard deviation)				
Week 12, n=340	124 (± 346.9)			
Week 24, n=334	144 (± 335.0)			
Week 48, n=325	98 (± 395.2)			
Week 72, n=312	91 (± 405.5)			
Week 96, n=301	51 (± 385.8)			
Week 124, n=292	85 (± 395.5)			
Week 148, n=281	17 (± 370.2)			
Week 176, n=210	45 (± 352.2)			
Week 200, n=171	8 (± 375.7)			
Week 228, n=37	-23 (± 331.9)			

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:

Immunogenicity testing included two types of assays: a binding antibody assay (anti-drug antibody; ADA) and a neutralizing antibody (NAb) assay for participants who were tested positive in the ADA assay. Blood samples were collected for the determination of anti-mepolizumab antibodies, just prior to administration of mepolizumab. Samples that test positive for anti-mepolizumab antibodies were further tested for the presence of neutralizing antibody. Number of participants with positive highest value post-Baseline have been presented. Only those participants 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 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[14]			
Units: Participants				
Positive ADA result, n=346	27			
Positive NAb result, n=27	0			

Notes:

[14] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who withdrew due to lack of efficacy

End point title	Number of participants who withdrew due to lack of efficacy

End point description:

Lack of efficacy referred to failure of expected pharmacological action of Mepolizumab. Number of participants who withdrew due to lack of efficacy are presented.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[15]			
Units: Participants				
Participants	11			

Notes:

[15] - AT Population.

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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. 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 open-label mepolizumab date and before/on last dose of mepolizumab + 28 days.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[16]			
Units: Participants				
Participants	71			

Notes:

[16] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who withdrew due to AE

End point title	Number of participants who withdrew due to AE

End point description:

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. 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. 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 who withdrew due to AE are presented.

End point type	Secondary

End point timeframe:

Baseline (Week 0) to Week 240

End point values	Mepolizumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	347[17]			
Units: Participants				
Participants	19			

Notes:

[17] - 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 open label mepolizumab date and before/on last dose of mepolizumab date + 28 days (up to 240 weeks)

Adverse event reporting additional description:

AE and SAE were collected for all participants within the As Treated Population which comprised of all participants who received at least one dose of open label mepolizumab.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Mepolizumab

Reporting group description:

Subjects will receive 100 mg of mepolizumab (in 1 ml polypropylene syringe) injected subcutaneously (SC) approximately every 4 weeks.

Serious adverse events	Mepolizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	79 / 347 (22.77%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	2 / 347 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder papilloma			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			

subjects affected / exposed	1 / 347 (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 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis superficial			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Non-cardiac chest pain			
subjects affected / exposed	1 / 347 (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 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Anaphylactic shock				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Cervical polyp				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectocele				
subjects affected / exposed	1 / 347 (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	33 / 347 (9.51%)			
occurrences causally related to treatment / all	0 / 47			
deaths causally related to treatment / all	0 / 2			
Pneumonia aspiration				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory arrest				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sleep apnoea syndrome				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Status asthmaticus				

subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic enzyme increased			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Comminuted fracture			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ligament rupture			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ligament sprain			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Subarachnoid haemorrhage				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial tachycardia				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Myocardial infarction				

subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	2 / 347 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	2 / 347 (0.58%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peroneal nerve palsy			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal claudication			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			

Lymphocytosis				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic gastritis				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Faecaloma				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric polyps				

subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Incarcerated inguinal hernia				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				
subjects affected / exposed	2 / 347 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cholestasis				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatocellular injury				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				

Renal colic				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bladder prolapse				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary incontinence				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Basedow's disease				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thyroid mass				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Bursitis				
subjects affected / exposed	2 / 347 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	2 / 347 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Lumbar spinal stenosis				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neuropathic arthropathy				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rheumatoid arthritis				
subjects affected / exposed	1 / 347 (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 / 347 (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 / 347 (1.73%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	2 / 347 (0.58%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				

subjects affected / exposed	2 / 347 (0.58%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myelitis				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	1 / 347 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				

subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Streptococcal infection			
subjects affected / exposed	1 / 347 (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 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	1 / 347 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Mepolizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	314 / 347 (90.49%)		
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	15 / 347 (4.32%)		
occurrences (all)	24		
Contusion			
subjects affected / exposed	13 / 347 (3.75%)		
occurrences (all)	15		
Ligament sprain			

subjects affected / exposed occurrences (all)	11 / 347 (3.17%) 11		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	 32 / 347 (9.22%) 43		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	 99 / 347 (28.53%) 386 16 / 347 (4.61%) 21 23 / 347 (6.63%) 31		
General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	 42 / 347 (12.10%) 129 12 / 347 (3.46%) 16		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	 13 / 347 (3.75%) 15		
Eye disorders Cataract subjects affected / exposed occurrences (all)	 14 / 347 (4.03%) 17		
Gastrointestinal disorders Toothache subjects affected / exposed occurrences (all) Diarrhoea	 22 / 347 (6.34%) 26		

subjects affected / exposed	26 / 347 (7.49%)		
occurrences (all)	38		
Abdominal pain			
subjects affected / exposed	17 / 347 (4.90%)		
occurrences (all)	18		
Abdominal pain upper			
subjects affected / exposed	15 / 347 (4.32%)		
occurrences (all)	21		
Nausea			
subjects affected / exposed	17 / 347 (4.90%)		
occurrences (all)	25		
Gastrooesophageal reflux disease			
subjects affected / exposed	14 / 347 (4.03%)		
occurrences (all)	14		
Vomiting			
subjects affected / exposed	11 / 347 (3.17%)		
occurrences (all)	13		
Dyspepsia			
subjects affected / exposed	12 / 347 (3.46%)		
occurrences (all)	15		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	69 / 347 (19.88%)		
occurrences (all)	116		
Rhinitis allergic			
subjects affected / exposed	36 / 347 (10.37%)		
occurrences (all)	55		
Oropharyngeal pain			
subjects affected / exposed	27 / 347 (7.78%)		
occurrences (all)	37		
Cough			
subjects affected / exposed	22 / 347 (6.34%)		
occurrences (all)	32		
Productive cough			

subjects affected / exposed	12 / 347 (3.46%)		
occurrences (all)	15		
Rhinorrhoea			
subjects affected / exposed	12 / 347 (3.46%)		
occurrences (all)	17		
Dysphonia			
subjects affected / exposed	11 / 347 (3.17%)		
occurrences (all)	11		
Dyspnoea			
subjects affected / exposed	11 / 347 (3.17%)		
occurrences (all)	16		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	12 / 347 (3.46%)		
occurrences (all)	16		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	63 / 347 (18.16%)		
occurrences (all)	135		
Arthralgia			
subjects affected / exposed	58 / 347 (16.71%)		
occurrences (all)	85		
Osteoarthritis			
subjects affected / exposed	20 / 347 (5.76%)		
occurrences (all)	22		
Pain in extremity			
subjects affected / exposed	40 / 347 (11.53%)		
occurrences (all)	52		
Myalgia			
subjects affected / exposed	18 / 347 (5.19%)		
occurrences (all)	28		
Musculoskeletal pain			
subjects affected / exposed	14 / 347 (4.03%)		
occurrences (all)	15		
Infections and infestations			

Viral upper respiratory tract infection				
subjects affected / exposed	169 / 347 (48.70%)			
occurrences (all)	371			
Upper respiratory tract infection				
subjects affected / exposed	81 / 347 (23.34%)			
occurrences (all)	195			
Bronchitis				
subjects affected / exposed	73 / 347 (21.04%)			
occurrences (all)	165			
Sinusitis				
subjects affected / exposed	57 / 347 (16.43%)			
occurrences (all)	111			
Influenza				
subjects affected / exposed	43 / 347 (12.39%)			
occurrences (all)	53			
Respiratory tract infection				
subjects affected / exposed	38 / 347 (10.95%)			
occurrences (all)	66			
Lower respiratory tract infection				
subjects affected / exposed	31 / 347 (8.93%)			
occurrences (all)	64			
Gastroenteritis				
subjects affected / exposed	27 / 347 (7.78%)			
occurrences (all)	32			
Pharyngitis				
subjects affected / exposed	24 / 347 (6.92%)			
occurrences (all)	32			
Urinary tract infection				
subjects affected / exposed	24 / 347 (6.92%)			
occurrences (all)	35			
Rhinitis				
subjects affected / exposed	23 / 347 (6.63%)			
occurrences (all)	29			
Respiratory tract infection viral				
subjects affected / exposed	20 / 347 (5.76%)			
occurrences (all)	27			

Viral infection subjects affected / exposed occurrences (all)	18 / 347 (5.19%) 30		
Ear infection subjects affected / exposed occurrences (all)	15 / 347 (4.32%) 21		
Acute sinusitis subjects affected / exposed occurrences (all)	14 / 347 (4.03%) 21		
Cystitis subjects affected / exposed occurrences (all)	13 / 347 (3.75%) 25		
Nasopharyngitis subjects affected / exposed occurrences (all)	13 / 347 (3.75%) 29		
Oral candidiasis subjects affected / exposed occurrences (all)	13 / 347 (3.75%) 17		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	11 / 347 (3.17%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 August 2012	Amendment 1: To clarify that the rationale and objective of the study includes long-term provision of mepolizumab therapy to participants who have severe asthma and participated in MEA112997 To clarify that only monoclonal antibodies are excluded, rather than all biologics To clarify reason for more frequent safety monitoring at the start of the study To correct Inclusion criterion 5 from Randomization Visit to Visit 2 To add exclusion criterion for significant cardiovascular disease To correct inconsistencies between protocol text and the Time and Events Table To correct bilirubin exclusion criterion at visit 2 To expand on requirements for designating a participant as lost to follow-up To add visit window for the follow-up visit To move Baseline spirometry from the screen visit to the Baseline visit To clarify that all participants will have an immunogenicity test 12 weeks after last dose To correct Section 8.3.5.2 wording "Efficacy" to "Safety" To add reference to support Appendix 6 and remove 3 references which are not cited in the protocol. To add Appendix 5 and Appendix 6 and amended Section 6.1 and Section 6.3.9. to support the determination of exclusion criteria 4.
06 March 2013	Amendment 2: To add two additional immunogenicity sample assessment time points when the 100 mg vial is introduced. To allow other syringe sizes for study drug administration To allow for study drug administration in the upper thigh or the arm To add the prohibited non-drug therapies to Section 5.7.2 To list Adverse Events and Serious Adverse Events on the same line in Table 3 To correct a formatting error for Section 4.6 To remove specific test name for confirming Hepatitis C positive sample To delete redundant text in Section 6.3.3.1 To remove from Section 6.3.7 the requirement to report outcome of pregnancy in female partners of male participants To include analyses of immunogenicity data in Section 8.3 and to clarify when interim analyses will be performed.
19 June 2015	Amendment 3: To reduce the Follow-up visit period from 12 weeks to 4 weeks post last dose of investigational product To update the time limit from reconstitution to administration of investigational product.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported