Clinical trial results:
MEA115661: A Multi-centre, Open-label, Long-term Safety Study of Mepolizumab in Asthmatic Subjects who participated in the MEA115588 or MEA115575 trials

Summary

EudraCT number	2012-001644-21
Trial protocol	BE GB DE IT ES NL CZ
Global end of trial date	13 March 2015

Results information

Result version number	v1 (current)
This version publication date	10 June 2016
First version publication date	10 June 2016

Trial information

Trial identification

Sponsor protocol code	MEA115661

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	17 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety profile of mepolizumab in subjects receiving long-term treatment

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 May 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	40 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 40
Country: Number of subjects enrolled	Australia: 15
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Canada: 51
Country: Number of subjects enrolled	Chile: 22
Country: Number of subjects enrolled	Czech Republic: 13
Country: Number of subjects enrolled	France: 77
Country: Number of subjects enrolled	Germany: 83
Country: Number of subjects enrolled	Italy: 51
Country: Number of subjects enrolled	Japan: 43
Country: Number of subjects enrolled	Korea, Republic of: 42
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	Netherlands: 23
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Russian Federation: 17
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Ukraine: 16
Country: Number of subjects enrolled	United Kingdom: 27
Country: Number of subjects enrolled	United States: 66

Worldwide total number of subjects	651
EEA total number of subjects	335

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)	23
Adults (18-64 years)	531
From 65 to 84 years	97
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was an extension of MEA115588 (NCT01691521) and MEA115575 (NCT01691508). Participants who completed the prior studies were offered to enroll in this study. Assessments that were captured as part of exit visit for MEA115588 and MEA115575 served as Baseline visit for this study.

Pre-assignment

Screening details:

651 participants who completed the study MEA115588 or MEA115575 were enrolled in this study. Participants meeting all the inclusion criteria and none of the exclusion criteria received their first mepolizumab dose at Visit 1 and continued to receive mepolizumab subcutaneous (SC) injections approximately every 4 weeks for 12 months.

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 milligrams (mg) administered via subcutaneous (SC) injection into the upper arm or thigh approximately every 4 weeks for 12 months. 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	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Mepolizumab 100mg was administered subcutaneously into the upper arm or thigh approximately every 4 weeks for 12 months. Prior to administration, each vial of mepolizumab was reconstituted and swirled gently to enable complete dissolution of the product.

Number of subjects in period 1	Mepolizumab 100 mg SC
Started	651
Completed	585
Not completed	66
Physician decision	9
Consent withdrawn by subject	14
Adverse event, non-fatal	11
Protocol defined stopping criteria	2
Lost to follow-up	3

Lack of efficacy	19
Protocol deviation	8

Baseline characteristics

Reporting groups	
Reporting group title	Mepolizumab 100 mg SC
Reporting group description:	
Participants received mepolizumab 100 milligrams (mg) administered via subcutaneous (SC) injection into the upper arm or thigh approximately every 4 weeks for 12 months. 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	651	651	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51.1		
standard deviation	± 13.87	-	
Gender categorical Units: Subjects			
Female	360	360	
Male	291	291	
Customized, Race Units: Subjects			
African American/African Heritage	14	14	
American Indian or Alaskan Native	2	2	
Asian - Central/South Asian Heritage	3	3	
Asian - East Asian Heritage	44	44	
Asian - Japanese Heritage	45	45	
Asian - South East Asian Heritage	7	7	
Native Hawaiian or Other Pacific Islander	1	1	
White - Arabic/North African Heritage	13	13	
White - White/Caucasian/European Heritage	517	517	
Mixed Race	5	5	

End points

End points reporting groups

Reporting group title	Mepolizumab 100 mg SC

Reporting group description:

Participants received mepolizumab 100 milligrams (mg) administered via subcutaneous (SC) injection into the upper arm or thigh approximately every 4 weeks for 12 months. Participants remained on standard of care asthma therapy which could be adjusted during the study at the discretion of the physician.

Primary: Number of participants with adverse events (AEs) including both systemic (i.e. allergic/immunoglobulin (Ig)E-mediated and non-allergic) and local site reactions

End point title	Number of participants with adverse events (AEs) including both systemic (i.e. allergic/immunoglobulin (Ig)E-mediated and non-allergic) and local site reactions[1]

End point description:

AEs were collected from the Baseline visit until the follow-up visit (approx. 12 weeks post-last dose). Participants were monitored to evaluate the AEs of systemic and local site reaction. AE is defined as any untoward medical occurrence in a patient or clinical investigation subject, 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.

End point type	Primary

End point timeframe:

From Baseline visit until the follow-up visit (approximately [approx.] 12 weeks post-last dose)

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	651[2]			
Units: Participants				
number (not applicable)				
Any AEs	558			
AEs related to study treatment	119			
Any SAEs	94			
SAEs related to study treatment	1			
Fatal SAEs	0			

Notes:

[2] - As Treated (AT) Population: all participants who received at least 1 dose of open label mepolizumab.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with positive anti-mepolizumab binding antibodies and neutralizing antibodies (NAb) at the indicated time points

End point title	Number of participants with positive anti-mepolizumab binding

	antibodies and neutralizing antibodies (NAb) at the indicated time points

End point description:

Blood samples were collected for the determination of anti-mepolizumab antibodies (ADA) just prior to administration of mepolizumab at indicated time points. Samples that tested positive for anti-mepolizumab antibodies were further tested for the presence of NAb. Participants who switched from the 250 mg vial to the 100 mg vial required one immunogenicity sample prior to the first dose from the 100 mg vial and one sample prior to the second dose from the 100 mg vial at the next visit. 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.

End point type	Secondary

End point timeframe:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651			
Units: Participants				
number (not applicable)				
Highest value post-baseline, ADA, positive, n=646	31			
Highest value post-baseline, ADA, negative, n=646	615			
Highest value post-baseline, NAb, positive, n=31	0			
Highest value post-baseline, NAb, negative, n=31	31			

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized rate of exacerbations per year

End point title	Annualized rate of exacerbations per year

End point description:

Exacerbations are defined as the worsening of asthma which requires use of systemic corticosteroids (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. Analysis of the number of exacerbations was performed using a negative binomial model with covariates of region, exacerbations in the year prior to the start of MEA115588 or MEA115575 (as an ordinal variable) and baseline percent (%) predicted forced expiratory volume in 1 second (FEV1), and with logarithm of time on treatment as an offset variable.

End point type	Secondary

End point timeframe:

Baseline up to Exit Visit (approx. 52 weeks) or if Early Withdrawal 4 weeks post last dose

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651[3]			
Units: Exacerbations per year				
arithmetic mean (confidence interval 95%)	0.93 (0.83 to 1.04)			

Notes:

[3] - 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 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). The change from Baseline is defined as the difference between the value of the endpoint at the time point of interest and Baseline value.

End point type	Secondary

End point timeframe:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651			
Units: Score on scale				
arithmetic mean (standard deviation)				
Week 4, n=603	-0.09 (± 0.812)			
Week 16, n=592	-0.11 (± 0.92)			
Week 28, n=577	-0.05 (± 1.021)			
Week 40, n=564	-0.1 (± 0.944)			
Week 52, n=556	-0.09 (± 0.99)			
Follow-up visit, n=338	0.2 (± 1.132)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in clinic pre-bronchodilator FEV1 over the 52-week treatment period

End point title	Mean change from Baseline in clinic pre-bronchodilator FEV1 over the 52-week treatment period

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, Week 16, Week 28 and Week 52. Spirometry was performed within ± 1 hour of the Baseline assessment. The change from Baseline is defined as the difference between the value of the end point at the time point of interest and Baseline value. AT Population, 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:

From Baseline and up to Week 52

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651			
Units: Milliliters (mL)				
arithmetic mean (standard deviation)				
Week 16, n=632	67 (± 362.7)			
Week 28, n=615	50 (± 409.8)			
Week 52, n=602	29 (± 406.2)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

AE is defined as any untoward medical occurrence in a patient or clinical investigation subject, 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. For marketed medicinal products, this also includes failure to produce expected benefits (i.e., lack of efficacy), abuse or misuse.

End point type	Secondary

End point timeframe:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651[4]			
Units: Participants				
number (not applicable)				
Withdrawals due to lack of efficacy	19			
Withdrawals due to adverse events	11			

Notes:

[4] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants hospitalized due to exacerbations and adverse events

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

End point description:

AE is defined as any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Exacerbation is defined as worsening of asthma which requires use of systemic corticosteroids (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.

End point type	Secondary

End point timeframe:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651[5]			
Units: Participants				
number (not applicable)				
No hospitalisation due to exacerbations	612			
One time hospitalisation due to exacerbations	29			
Two times hospitalisation due to exacerbations	4			
Three times hospitalisation due to exacerbations	4			
Four times hospitalisation due to exacerbations	0			
Five times hospitalisation due to exacerbations	0			
Six times hospitalisation due to exacerbations	1			
Seven times hospitalisation due to exacerbations	0			
Eight times hospitalisation due to exacerbations	0			

Nine times hospitalisation due to exacerbations	0			
Ten times hospitalisation due to exacerbations	1			
No hospitalisation due to AEs	560			
One time hospitalisation due to AEs	61			
Two times hospitalisation due to AEs	13			
Three times hospitalisation due to AEs	11			
Four times hospitalisation due to AEs	4			
Five times hospitalisation due to AEs	0			
Six times hospitalisation due to AEs	1			
Seven times hospitalisation due to AEs	0			
Eight times hospitalisation due to AEs	0			
Nine times hospitalisation due to AEs	0			
Ten times hospitalisation due to AEs	0			
Eleven times hospitalisation due to AEs	0			
Twelve times hospitalisation due to AEs	0			
Thirteen times hospitalisation due to AEs	0			
Fourteen times hospitalisation due to AEs	0			
Fifteen times hospitalisation due to AEs	0			
Sixteen times hospitalisation due to AEs	1			

Notes:

[5] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Systemic (i.e., Allergic/IgE-mediated and Non-allergic) and Local Site Reactions

End point title	Number of Participants With Systemic (i.e., Allergic/IgE-mediated and Non-allergic) and Local Site Reactions

End point description:

Participants were monitored to evaluate the AEs of systemic and local site reaction. AE is defined as any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Hypersensitivity reactions (i.e., allergic or IgEmediated reactions) were monitored using the diagnostic criteria for anaphylaxis as outlined by the 2006 Joint NIAID/FAAN Second Symposium on Anaphylaxis. Information was also collected to assess localized site reactions as determined by the investigator. On treatment AEs were defined as events occurring from the first dose until 28 days after the last dose of mepolizumab.

End point type	Secondary

End point timeframe:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651[6]			
Units: Participants				
number (not applicable)				
Any systemic infusion/injection site reaction	13			
Injection related reaction	7			
Hypersensitvity	4			
Type IV hypersensitivity reaction	3			
Any local infusion/injection site reaction	29			

Notes:

[6] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with electrocardiogram (ECG) findings at any time post Baseline

End point title	Number of participants with electrocardiogram (ECG) findings at any time post Baseline

End point description:

12-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. ECG was performed at Baseline, Week 28, Week 52 and at the end of follow-up period (approx. 12 weeks post-last dose). ECG findings were summarised at any time post Baseline for participants as normal, abnormal-not clinically significant (A-NCS) and abnormal-clinically significant (A-CS).

End point type	Secondary

End point timeframe:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	638[7]			
Units: Participants				
number (not applicable)				
Normal	262			
A-NCS	295			
A-CS	81			

Notes:

[7] - AT Population, only participants with ECG results post-baseline were analyzed

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 ECG

Assessed at Baseline, Week 28, Week 52 and at Follow-up Visit (Approx. 12 Weeks Post-last Dose)

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 ECG Assessed at Baseline, Week 28, Week 52 and at Follow-up Visit (Approx. 12 Weeks Post-last Dose)

End point description:

12-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. ECG was performed at Baseline, Week 28, Week 52 and at the end of follow-up period (approx. 12 weeks post-last dose). The change from Baseline is defined as the difference between the value of the end point at the time point of interest and Baseline value.

End point type	Secondary

End point timeframe:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651			
Units: Milliseconds (msec)				
arithmetic mean (standard deviation)				
QTcB, Week 28, n=592	-5.5 (± 19.1)			
QTcB, Week 52, n=573	-3.2 (± 18.9)			
QTcB, Follow-up, n=299	-3.4 (± 19.67)			
QTcF, Week 28, n=592	-7.1 (± 16.15)			
QTcF, Week 52, n=573	-3.5 (± 15.68)			
QTcF, Follow-up, n=299	-5.5 (± 17.01)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

12-lead ECG measurements were recorded after the participant has rested in the supine position for 5 minutes. ECG was performed at Baseline, Week 28, Week 52 and at the end of follow-up period (approx. 12 weeks post-last dose). Participants with maximum change (MC) 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. The change from Baseline is defined as the difference between the value of the end point at the time point of interest and Baseline value. QTc intervals shown at any time post Baseline are the maximum seen in each participant over the course of the trial. 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:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	614[8]			
Units: Participants				
number (not applicable)				
MC <-60, n=614	2			
MC >=-60 to <-30, n=614	11			
MC >=-30 to <0, n=614	252			
MC >=0 to <30, n=614	328			
MC >=30 to <60, n=614	20			
MC >=60, n=614	1			

Notes:

[8] - AT Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

12-lead ECG measurements were recorded after the participant has rested in the supine position for 5 minutes. ECG was performed at Baseline, Week 28, Week 52 and at the end of follow-up period (approx. 12 weeks post-last dose). Participants with maximum change (MC) from Baseline were summarized at any time post Baseline for the following categories <-60, >=-60 to <-30, >=-30 to <0, >=0 to <30, >=30 to <60 and >=60. The change from Baseline is defined as the difference between the value of the end point at the time point of interest and Baseline value. QTc intervals shown at any time post Baseline are the maximum seen in each participant over the course of the trial. 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:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	614[9]			
Units: participants				
number (not applicable)				
MC <-60, n=614	3			
MC >=-60 to <-30, n=614	16			
MC >=-30 to <0, n=614	222			
MC >=0 to <30, n=614	330			
MC >=30 to <60, n=614	41			
MC >=60, n=614	2			

Notes:

[9] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in systolic blood pressure and diastolic blood pressure assessed at Week 52

End point title	Change from Baseline in systolic blood pressure and diastolic blood pressure assessed at Week 52

End point description:

Vital sign measurements including systolic blood pressure (SBP) and diastolic blood pressure (DBP) were performed at Baseline, at Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 and follow-up visit (approx. 12 weeks post-last dose). Vital measurements 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. 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 and Week 52

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	581[10]			
Units: Millimeter of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP, Week 52, n=581	0.3 (± 12.9)			
DBP, Week 52, n=581	-0.4 (± 9.47)			

Notes:

[10] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in pulse rate assessed at Week 52

End point title	Change from Baseline in pulse rate assessed at Week 52

End point description:

Vital sign measurements including sitting pulse was performed at Baseline, at Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 and follow-up visit (approx. 12 weeks post-last dose). Vital measurements 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.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	581[11]			
Units: Beats per minute (BPM)				
arithmetic mean (standard deviation)	0.2 (± 10.52)			

Notes:

[11] - AT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinical Chemistry Parameters outside the Normal Range at Any Time Post-baseline

End point title	Number of Participants With Clinical Chemistry Parameters outside the Normal Range at Any Time Post-baseline

End point description:

Clinical chemistry laboratory parameters: alanine aminotransferase, albumin, alkaline phosphatase, aspartate aminotransferase, bilirubin, calcium, chloride, cholesterol, creatine kinase, creatinine, direct bilirubin, gamma glutamyl transferase, high density lipoprotein (HDL) cholesterol, indirect bilirubin, low density lipoprotein (LDL) cholesterol, lactate dehydrogenase, phosphate, plasma/serum protein, potassium, serum glucose, sodium, triglycerides, urea, and very low density lipoprotein (VLDL) cholesterol assessed at the indicated time points. Laboratory abnormalities outside the normal range at any time post baseline were presented. Any time post Baseline = all visits (including scheduled and unscheduled). If participant had given both high and low value at least once then participant is counted under both high and low category for this visit. 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:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651[12]			
Units: Participants				
number (not applicable)				
Alanine aminotransferase, High, n=649	70			
Albumin, Low, n=649	1			
Albumin, High, n=649	23			
Alkaline phosphatase, High, n=649	37			
Aspartate aminotransferase, High, n=649	53			
Bilirubin, High, n=649	38			
Calcium, Low, n=649	19			

Calcium, High, n=649	49			
Chloride, Low, n=649	9			
Chloride, High, n=649	126			
Cholesterol, High, n=649	492			
Creatine kinase, High, n=649	178			
Creatinine, Low, n=649	170			
Creatinine, High, n=649	18			
Direct bilirubin, High, n=649	10			
Gamma glutamyl transferase, High, n=649	146			
HDL cholesterol, Low, n=616	22			
Indirect bilirubin, High, n=649	12			
LDL cholesterol, High, n=604	207			
Lactate dehydrogenase, High, n=649	36			
Phosphate, Low, n=649	149			
Phosphate, High, n=649	84			
Plasma/serum protein, Low, n=649	29			
Potassium, Low, n=649	24			
Potassium, High, n=649	22			
Serum glucose, Low, n=649	62			
Serum glucose, High, n=649	239			
Sodium, Low, n=649	25			
Sodium, High, n=649	9			
Triglycerides, High, n=617	102			
Urea, Low, n=649	17			
Urea, High, n=649	53			
VLDL cholesterol, Low, n=605	13			
VLDL cholesterol, High, n=605	99			

Notes:

[12] - AT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Haematology Laboratory Parameters Outside the Normal Range at Any Time Post baseline

End point title	Number of Participants With Haematology Laboratory Parameters Outside the Normal Range at Any Time Post baseline

End point description:

Haematology laboratory parameters included basophils, basophils/leukocytes, blood erythrocytes, blood leukocytes, eosinophils, eosinophils/leukocytes, mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), erythrocytes distribution width (EDW), hematocrit, hemoglobin, lymphocytes, lymphocytes/leukocytes, monocytes, monocytes/leukocytes, neutrophils segmented (NS), neutrophils/ leukocytes, platelets, reticulocytes assessed at Baseline, Week 4, Week 16, Week 28, Week 52 and follow-up visit (approx. 12 weeks post-last dose). Hematology abnormalities outside the normal range (high and low values) at any time post baseline were presented. Any time post Baseline is equal to all visits (including scheduled and unscheduled) post Baseline were considered for this visit derivation. If participant had given both high and low value at least once then participant is counted under both high and low category for this visit. AT Population.

End point type	Secondary

End point timeframe:

From Baseline visit until the follow-up visit (approx. week 60 [12 weeks post-last dose])

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	651[13]			
Units: Participants				
number (not applicable)				
Basophils, High, n=649	2			
Basophils/Leukocytes, High, n=649	3			
Blood Erythrocytes, Low, n=649	52			
Blood Erythrocytes, High, n=649	36			
Blood Leukocytes, Low, n=649	25			
Blood Leukocytes, High, n=649	146			
Eosinophils, Low, n=649	429			
Eosinophils, High, n=649	51			
Eosinophils/Leukocytes, High, n=649	60			
MCHC, Low, n=649	276			
MCH, Low, n=649	58			
MCH, High, n=649	26			
MCV, Low, n=649	32			
MCV, High, n=649	32			
EDW, High, n=649	322			
Hematocrit, Low, n=649	57			
Hematocrit, High, n=649	94			
Hemoglobin, Low, n=649	116			
Hemoglobin, High, n=649	14			
Lymphocytes, Low, n=649	48			
Lymphocytes, High, n=649	25			
Lymphocytes/Leukocytes, Low, n=649	168			
Lymphocytes/Leukocytes, High, n=649	68			
Monocytes, Low, n=649	156			
Monocytes, High, n=649	15			
Monocytes/Leukocytes, High, n=649	45			
NS, Low, n=649	31			
NS, High, n=649	151			
Neutrophils/Leukocytes, Low, n=649	39			
Neutrophils/Leukocytes, High, n=649	226			
Platelets, Low, n=649	8			
Platelets, High, n=649	58			
Reticulocytes, Low, n=649	77			
Reticulocytes, High, n=649	294			

Notes:

[13] - Only those available at the specified time points were analyzed (n=X in the category titles).

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) and Serious adverse events (SAEs) were collected from the first dose of study treatment until 28 days after the last dose of mepolizumab, up to the follow-up visit (approx. week 60 [12 weeks post-last dose]).

Adverse event reporting additional description:

Serious adverse events (SAEs) and Non-serious AEs were collected in members of As-Treated (AT) Population, comprised of all participants who received at least one dose of open label mepolizumab medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Mepolizumab 100 mg SC

Reporting group description:

Participants received mepolizumab 100 milligrams (mg) administered via subcutaneous (SC) injection into the upper arm or thigh approximately every 4 weeks for 12 months. 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	94 / 651 (14.44%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign salivary gland neoplasm			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder cancer			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			

subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endometrial cancer			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric cancer			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 651 (0.15%)		
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 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anaphylactic shock			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Type IV hypersensitivity reaction				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Ovarian cyst				
subjects affected / exposed	1 / 651 (0.15%)			
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	38 / 651 (5.84%)			
occurrences causally related to treatment / all	0 / 67			
deaths causally related to treatment / all	0 / 0			
Atelectasis				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nasal polyps				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				

subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sleep apnoea syndrome				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Depression				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Panic attack				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Ejection fraction decreased				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Acetabulum fracture				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Brain contusion				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Fibula fracture			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laceration			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skull fracture			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thermal burn			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	3 / 651 (0.46%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive heart disease			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mitral valve incompetence			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Restless legs syndrome			

subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VIIth nerve paralysis			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyskinesia oesophageal			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspepsia			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Haemorrhoids			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus paralytic			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gallbladder disorder			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jaundice cholestatic			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Nephrocalcinosis			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract pain			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spondylolisthesis			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Vertebral foraminal stenosis			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			

subjects affected / exposed	4 / 651 (0.61%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	2 / 651 (0.31%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	2 / 651 (0.31%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	2 / 651 (0.31%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	2 / 651 (0.31%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Aspergillus infection				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic sinusitis				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis infectious				

subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
H1N1 influenza				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Labyrinthitis				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngeal abscess				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 651 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinusitis				

subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection staphylococcal			
subjects affected / exposed	1 / 651 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
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	461 / 651 (70.81%)		
Nervous system disorders			
Headache			
subjects affected / exposed	87 / 651 (13.36%)		
occurrences (all)	212		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	29 / 651 (4.45%)		
occurrences (all)	65		
Fatigue			
subjects affected / exposed	24 / 651 (3.69%)		
occurrences (all)	28		
Gastrointestinal disorders			

Nausea			
alternative dictionary used: MedDRA MedDRA			
subjects affected / exposed	27 / 651 (4.15%)		
occurrences (all)	30		
Diarrhoea			
alternative dictionary used: MedDRA MedDRA			
subjects affected / exposed	21 / 651 (3.23%)		
occurrences (all)	25		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	61 / 651 (9.37%)		
occurrences (all)	89		
Oropharyngeal pain			
subjects affected / exposed	34 / 651 (5.22%)		
occurrences (all)	38		
Cough			
subjects affected / exposed	26 / 651 (3.99%)		
occurrences (all)	32		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	46 / 651 (7.07%)		
occurrences (all)	49		
Arthralgia			
subjects affected / exposed	44 / 651 (6.76%)		
occurrences (all)	52		
Pain in extremity			
subjects affected / exposed	21 / 651 (3.23%)		
occurrences (all)	23		
Musculoskeletal pain			
subjects affected / exposed	21 / 651 (3.23%)		
occurrences (all)	22		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	196 / 651 (30.11%)		
occurrences (all)	320		
Bronchitis			

subjects affected / exposed	78 / 651 (11.98%)		
occurrences (all)	106		
Upper respiratory tract infection			
subjects affected / exposed	99 / 651 (15.21%)		
occurrences (all)	143		
Sinusitis			
subjects affected / exposed	66 / 651 (10.14%)		
occurrences (all)	100		
Influenza			
subjects affected / exposed	28 / 651 (4.30%)		
occurrences (all)	31		
Lower respiratory tract infection			
subjects affected / exposed	26 / 651 (3.99%)		
occurrences (all)	30		
Rhinitis			
subjects affected / exposed	23 / 651 (3.53%)		
occurrences (all)	28		
Urinary tract infection			
subjects affected / exposed	21 / 651 (3.23%)		
occurrences (all)	28		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2013	The primary purpose of Amendment 01 was to remove the entry criterion requiring a positive neutralizing antibody status based upon any sample obtained during the MEA115588 or the MEA115575 study. The amendment also included a number of additional corrections and edits (Appendix 7).
21 June 2013	The primary purpose of Amendment 02 is to permit use of the 100mg vial presentation as soon as it is available at the site versus the original switch point of Visit 8. This amendment also includes additional corrections/clarifications noted since Amendment 01 (Appendix 8).
28 June 2013	The primary purpose of Amendment 03 is to remove the dose given at Visit 14. This amendment also includes additional corrections/clarifications noted since Amendment 02 (Appendix 9).
19 February 2014	The primary purpose of Amendment 04 is to allow subjects in MEA115661 who have life-threatening or severely debilitating asthma to continue to receive treatment after the end of the treatment period (Appendix 10).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported