Clinical trial results:
A randomized, double-blind, placebo-controlled, parallel-group, multi-center 24-week study to evaluate the efficacy and safety of mepolizumab adjunctive therapy in subjects with severe eosinophilic asthma on markers of asthma control.

Summary

EudraCT number	2014-002513-27
Trial protocol	IT SK BE DE CZ GR EE ES NL
Global end of trial date	10 June 2016

Results information

Result version number	v1 (current)
This version publication date	21 December 2016
First version publication date	21 December 2016

Trial information

Trial identification

Sponsor protocol code	200862

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 October 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of mepolizumab 100 mg subcutaneous (SC) every 4 weeks versus placebo on health-related quality of life (HR-QoL) in adult and adolescent participants with severe eosinophilic asthma.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 December 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 67
Country: Number of subjects enrolled	Belgium: 46
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Canada: 17
Country: Number of subjects enrolled	Czech Republic: 17
Country: Number of subjects enrolled	Estonia: 15
Country: Number of subjects enrolled	France: 53
Country: Number of subjects enrolled	Germany: 56
Country: Number of subjects enrolled	Greece: 40
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Netherlands: 41
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Peru: 20
Country: Number of subjects enrolled	Russian Federation: 40
Country: Number of subjects enrolled	Slovakia: 9
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	Ukraine: 79
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	United States: 66
Worldwide total number of subjects	641
EEA total number of subjects	352

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)	10
Adults (18-64 years)	531
From 65 to 84 years	100
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 830 participants were screened (Visit 1) and entered into the run-in period, of which 556 participants were randomized and 551 participants received either mepolizumab 100 milligrams (mg) or placebo in addition to standard of care asthma treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo subcutaneously in upper arm or thigh following randomization at Visit 2 (Week 0) and every 4 weeks thereafter (last dose at Week 20) along with their standard of care asthma treatment up to 24 weeks.

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

Dosage and administration details:

Participants received 0.9% Sodium Chloride subcutaneously into the upper arm or thigh

Arm title	Mepolizumab 100 mg

Arm description:

Participants received mepolizumab 100 mg subcutaneously in upper arm or thigh following randomization at Visit 2 (Week 0) and every 4 weeks thereafter (last dose at Week 20) along with their standard of care asthma treatment up to 24 weeks.

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

Dosage and administration details:

Participants received Mepolizumab 100 mg subcutaneously into the upper arm or thigh

Number of subjects in period 1[1]	Placebo	Mepolizumab 100 mg
Started	277	274
Completed	263	269
Not completed	14	5
Consent withdrawn by subject	6	2
Physician decision	2	-
Adverse event, non-fatal	2	2
Lost to follow-up	2	1
Lack of efficacy	2	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 830 participants were screened (Visit 1) and entered into the run-in period, of which 556 participants were randomized and 551 participants received either mepolizumab 100 milligrams (mg) or placebo in addition to standard of care asthma treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneously in upper arm or thigh following randomization at Visit 2 (Week 0) and every 4 weeks thereafter (last dose at Week 20) along with their standard of care asthma treatment up to 24 weeks.	
Reporting group title	Mepolizumab 100 mg
Reporting group description:	
Participants received mepolizumab 100 mg subcutaneously in upper arm or thigh following randomization at Visit 2 (Week 0) and every 4 weeks thereafter (last dose at Week 20) along with their standard of care asthma treatment up to 24 weeks.	

Reporting group values	Placebo	Mepolizumab 100 mg	Total
Number of subjects	277	274	551
Age categorical Units: Subjects			
Age continuous			
Age continuous description			
Units: years			
arithmetic mean	52.1	49.8	
standard deviation	± 12.94	± 14.01	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	176	149	325
Male	101	125	226
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	10	9	19
Asian-Central/South Asian Heritage	0	1	1
Asian-East Asian Heritage	0	2	2
Asian-South East Asian Heritage	0	1	1
Black or African American	7	8	15
Native Hawaiian or Other Pacific Islander	1	1	2
White-Arabic/North African Heritage	8	1	9
White-White/Caucasian/European Heritage	251	251	502

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo subcutaneously in upper arm or thigh following randomization at Visit 2 (Week 0) and every 4 weeks thereafter (last dose at Week 20) along with their standard of care asthma treatment up to 24 weeks.	
Reporting group title	Mepolizumab 100 mg
Reporting group description:	
Participants received mepolizumab 100 mg subcutaneously in upper arm or thigh following randomization at Visit 2 (Week 0) and every 4 weeks thereafter (last dose at Week 20) along with their standard of care asthma treatment up to 24 weeks.	

Primary: Mean change from Baseline in St. George's Respiratory Questionnaire (SGRQ) score at Week 24

End point title	Mean change from Baseline in St. George's Respiratory Questionnaire (SGRQ) score at Week 24
End point description:	
SGRQ is an instrument, comprised of 50 questions (scored from 0-100) designed to measure Quality of Life in participants (par.) with diseases of airway obstruction, measuring symptoms, impact, and activity. The questions were designed to be self-completed by the par. with a recall over the past 4 weeks. The change from Baseline (BL) in SGRQ was calculated as value at Week 24 minus the value at BL for each par. and was analyzed using mixed model repeated measures allowing for covariates of BL value, region, BL maintenance oral corticosteroid (OCS) therapy, exacerbations in the year prior to the study (as an ordinal variable), BL % predicted FEV1 and visit, plus interaction terms for visit by BL and visit by treatment group. The Modified Intent-to-Treat (mITT) Population consisted of all randomized par. who received at least one dose of trial medication. Those with a missing BL covariate value or with no observed change from BL at any time point were excluded from the analysis model.	
End point type	Primary
End point timeframe:	
Baseline and Week 24	

End point values	Placebo	Mepolizumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	260[1]	265[2]		
Units: Scores on a scale				
least squares mean (standard error)	-7.9 (± 1.01)	-15.6 (± 1)		

Notes:

[1] - mITT Population.

[2] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Mepolizumab 100 mg v Placebo

Number of subjects included in analysis	525
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed model repeated measures analysis
Parameter estimate	Mean difference (final values)
Point estimate	-7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.5
upper limit	-4.9

Secondary: Mean change from Baseline in clinic pre-bronchodilator Forced Expiratory Volume in one second (FEV1) at Week 24

End point title	Mean change from Baseline in clinic pre-bronchodilator Forced Expiratory Volume in one second (FEV1) at Week 24

End point description:

FEV1 is the volume of air that can be forced out in one second after taking a deep breath. The change from Baseline in pre-bronchodilator FEV1 was calculated as the value at Week 24 minus the value at Baseline for each subject and was analyzed using a mixed model repeated measures adjusting for Baseline absolute pre-bronchodilator FEV1, region, Baseline maintenance OCS therapy, exacerbations in the year prior to the study and visit, plus interaction terms for visit by Baseline and visit by treatment group. Participants with a missing Baseline covariate value or with no observed change from Baseline at any time point were excluded from the analysis model.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Mepolizumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	259[3]	264[4]		
Units: Milliliters (mL)				
least squares mean (standard error)	56 (± 26.2)	176 (± 26.1)		

Notes:

[3] - mITT Population.

[4] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Mepolizumab 100 mg v Placebo

Number of subjects included in analysis	523
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Mixed model repeated measures analysis
Parameter estimate	Mean difference (final values)
Point estimate	120
Confidence interval	
level	95 %
sides	2-sided
lower limit	47
upper limit	192

Secondary: Percentage of participants achieving a 4 point or greater reduction from Baseline in SGRQ score at Week 24

End point title	Percentage of participants achieving a 4 point or greater reduction from Baseline in SGRQ score at Week 24

End point description:

The percentage of participants achieving a 4 point or greater reduction from Baseline in SGRQ at Week 24 was compared between treatment groups using a logistic regression model with covariates of Baseline value, region, Baseline maintenance OCS therapy, exacerbations in the year prior to the study (as an ordinal variable) and Baseline % predicted FEV1. Participants with a missing Baseline covariate value were excluded from the analysis model.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Mepolizumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275[5]	273[6]		
Units: Percentage of participants	55	73		

Notes:

[5] - mITT Population.

[6] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Mepolizumab 100 mg v Placebo
Number of subjects included in analysis	548
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.23

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.55
upper limit	3.22

Secondary: Mean change from Baseline in Asthma Control Questionnaire (ACQ-5) score at Week 24

End point title	Mean change from Baseline in Asthma Control Questionnaire (ACQ-5) score at Week 24

End point description:

The ACQ-5 is a five-item questionnaire, designed to be self-completed by the participants. The five questions inquired about the frequency and/or severity of symptoms over the previous week. The response options for all these questions consisted of a zero (no impairment/limitation) to six (total impairment/limitation) scale. The mean change from Baseline was calculated as the value at Week 24 minus the Baseline value for each participant and analyzed using a mixed model repeated measures allowing for covariates of Baseline value, region, Baseline maintenance OCS therapy, exacerbations in the year prior to the study (as an ordinal variable), Baseline % predicted FEV1 and visit, plus interaction terms for visit by Baseline and visit by treatment group. Participants with a missing Baseline covariate value or with no observed change from Baseline at any time point were excluded from the analysis model.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Placebo	Mepolizumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[7]	266[8]		
Units: Scores on a scale				
least squares mean (standard error)	-0.4 (± 0.064)	-0.8 (± 0.064)		

Notes:

[7] - mITT Population.

[8] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Mepolizumab 100 mg v Placebo
Number of subjects included in analysis	527
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed model repeated measures analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	-0.22

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All serious adverse events (SAEs) and on-treatment non-serious adverse events (AEs) were collected from the start of investigational product and until 28 days after the IP stop date (on-treatment) and to the end of the study for SAEs (Week 24).

Adverse event reporting additional description:

The Safety Population consisted of all randomized participants who received at least one dose of trial medication. Subjects were analysed according to treatment actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Mepolizumab 100 mg SC

Reporting group description:

Participants received mepolizumab 100 mg subcutaneously in upper arm or thigh following randomization at Visit 2 (Week 0) and every 4 weeks thereafter (last dose at Week 20) along with their standard of care asthma treatment up to 24 weeks.

Reporting group title	Placebo

Reporting group description:

Participants received placebo subcutaneously in upper arm or thigh following randomization at Visit 2 (Week 0) and every 4 weeks thereafter (last dose at Week 20) along with their standard of care asthma treatment up to 24 weeks.

Serious adverse events	Mepolizumab 100 mg SC	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 273 (5.49%)	23 / 278 (8.27%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			

subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic granulomatous angiitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 273 (1.10%)	9 / 278 (3.24%)	
occurrences causally related to treatment / all	0 / 3	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			

subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal polyps			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Post procedural complication			
subjects affected / exposed	0 / 273 (0.00%)	2 / 278 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Myocardial ischemia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis atopic			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urethral stenosis			

subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rheumatic disorder			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hemophilus infection			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localized infection			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteremia			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 273 (0.37%)	0 / 278 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 273 (0.00%)	1 / 278 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Mepolizumab 100 mg SC	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	124 / 273 (45.42%)	140 / 278 (50.36%)	
Nervous system disorders			
Headache			
subjects affected / exposed	45 / 273 (16.48%)	59 / 278 (21.22%)	
occurrences (all)	105	123	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 273 (2.56%)	11 / 278 (3.96%)	
occurrences (all)	9	15	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	10 / 273 (3.66%)	7 / 278 (2.52%)	
occurrences (all)	11	8	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	4 / 273 (1.47%)	14 / 278 (5.04%)	
occurrences (all)	5	15	
Oropharyngeal pain			
subjects affected / exposed	11 / 273 (4.03%)	8 / 278 (2.88%)	
occurrences (all)	13	9	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	13 / 273 (4.76%)	18 / 278 (6.47%)	
occurrences (all)	17	19	
Arthralgia			
subjects affected / exposed	9 / 273 (3.30%)	18 / 278 (6.47%)	
occurrences (all)	10	21	
Muscle spasms			
subjects affected / exposed	3 / 273 (1.10%)	10 / 278 (3.60%)	
occurrences (all)	3	12	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	31 / 273 (11.36%)	46 / 278 (16.55%)	
occurrences (all)	41	54	
Upper respiratory tract infection			
subjects affected / exposed	17 / 273 (6.23%)	14 / 278 (5.04%)	
occurrences (all)	17	16	
Sinusitis			
subjects affected / exposed	11 / 273 (4.03%)	12 / 278 (4.32%)	
occurrences (all)	12	15	
Bronchitis			
subjects affected / exposed	6 / 273 (2.20%)	11 / 278 (3.96%)	
occurrences (all)	6	14	
Rhinitis			
subjects affected / exposed	10 / 273 (3.66%)	7 / 278 (2.52%)	
occurrences (all)	12	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2014	Amendment No. 1 • Text added to Section 7.2.2.1.4 Asthma Symptom Utility Index (ASUI) and Section 7.2.2.1.5 Sino-nasal Outcomes Test-22 (SNOT-22) to indicate that these questionnaires should only be administered to participants for whom an appropriate translation is available. • Time and Events Table (Table 7) updated
17 March 2015	Amendment No. 2 • The study acronym (MUSCA) has been included in the title. • The contact details of the Secondary Medical Monitor/SAE Contact have been updated to reflect a change in study personnel. • Details added on the Pre-Screening Visit, including the information to be captured in the eCRF for pre-screening failures. Several sections of the protocol have been amended accordingly. • As a result of now being able to test for immunogenicity after only 4 weeks postlast-dose, the overall safety profile of mepolizumab and pragmatic considerations to reduce participant burden and enable greater flexibility in their asthma management, the post-last-dose follow-up period has been reduced from 12 weeks to 4 weeks; therefore, Visit 9 has been removed from the study design. Several sections of the protocol have been amended accordingly. • The referenced mepolizumab Investigator's Brochure (CM2003/00010/08) and associated supplement (2014N200212_00) have been replaced by a new version of the Investigator's Brochure (CM2003/00010/09) throughout the protocol. • An endpoint related to the SNOT-22 questionnaire has been included in Table 1. • In Section 6.9.1, information has been added regarding the asthma exacerbation medication to be captured in the eCRF in the 12 months prior to Visit 1. • The Time and Events Schedule (Table 7) has been updated. • In Section 7.2.2.1.2, the areas covered by the 5 questions asked in the Asthma Control Questionnaire have been clarified. • In Section 7.2.2.4, the need to use eDiary data to verify the occurrence of a clinically significant asthma exacerbation has been removed. • In Section 7.3.5, it has been clarified that only a single twelve-lead ECG is needed at each time-point specified in the Time and Events Schedule (Table 7) unless a prolonged QT interval is observed in which case 2 further ECGs need to be collected (as defined in Section 5.5.4.). • Typographical errors have been corrected throughout the document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported