Clinical trial results:
A randomized, double-blind, placebo-controlled study to investigate the efficacy and safety of mepolizumab in the treatment of adolescent and adult subjects with severe hypereosinophilic syndrome

Summary

EudraCT number	2014-001232-11
Trial protocol	GB ES DE FR BE PL IT
Global end of trial date	08 August 2019

Results information

Result version number	v1 (current)
This version publication date	23 February 2020
First version publication date	23 February 2020

Trial information

Trial identification

Sponsor protocol code	200622

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, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com

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	13 November 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of mepolizumab compared with placebo based on maintenance of control of hypereosinophilic syndrome (HES) symptoms during the treatment period.

Protection of trial subjects:

As this was a double-blind trial the participants' eosinophil (EOS) levels were monitored by an unblinded Medical Monitor. According to a pre-defined process, if a EOS level was met then oral corticosteroids were issued and administered to the participant. This was managed by the unblinded team to ensure the blind was maintained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	108
EEA total number of subjects	70

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)	4
Adults (18-64 years)	90
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This 32-week, randomized, double-blind, placebo-controlled study assessed the efficacy and safety of mepolizumab 300 milligrams (mg) subcutaneous (SC) every 4 weeks compared with placebo in adolescent and adult participants with severe hypereosinophilic syndrome (HES) receiving standard of care (SoC) therapy.

Pre-assignment

Screening details:

A total of 108 participants were enrolled in the study and randomized. The study was conducted in 13 countries.

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 were randomized to receive matching placebo SC every 4 weeks during the 32-Week treatment period while continuing their HES therapy. The final dose was administered at Week 28 with the completion of study treatment period achieved in the next 4-weekly visit.

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

Dosage and administration details:

Participants received matching placebo as 0.9 percent (%) sodium chloride solution every 4 weeks. Participants were dosed with three separate placebo SC injections every 4 weeks.

Arm title	Mepolizumab 300 mg SC

Arm description:

Participants were randomized to receive 300 mg mepolizumab SC every 4 weeks during the 32-Week treatment period while continuing their HES therapy. The final dose was administered at Week 28 with the completion of study treatment period achieved in the next 4-weekly visit.

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

Dosage and administration details:

Participants received 300 milligrams (mg) mepolizumab lyophilized powder for injection reconstituted with sterile water subcutaneously (SC) every 4 weeks. Participants were dosed with three separate 100 mg SC injections every 4 weeks.

Number of subjects in period 1	Placebo	Mepolizumab 300 mg SC
Started	54	54
Completed	52	52
Not completed	2	2
Adverse event, non-fatal	2	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants were randomized to receive matching placebo SC every 4 weeks during the 32-Week treatment period while continuing their HES therapy. The final dose was administered at Week 28 with the completion of study treatment period achieved in the next 4-weekly visit.	
Reporting group title	Mepolizumab 300 mg SC
Reporting group description:	
Participants were randomized to receive 300 mg mepolizumab SC every 4 weeks during the 32-Week treatment period while continuing their HES therapy. The final dose was administered at Week 28 with the completion of study treatment period achieved in the next 4-weekly visit.	

Reporting group values	Placebo	Mepolizumab 300 mg SC	Total
Number of subjects	54	54	108
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	3	1	4
Adults (18-64 years)	41	49	90
From 65-84 years	10	4	14
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	45.4	46.6	
standard deviation	± 18.25	± 12.99	-
Sex: Female, Male Units: Participants			
Female	27	30	57
Male	27	24	51
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	2	1	3
Asian-Central/South Asian Heritage	0	1	1
Asian-East Asian Heritage	1	0	1
Asian-South East Asian Heritage	1	0	1
Black or African American	2	0	2
White-Arabic/North African Heritage	1	0	1
White-White/Caucasian/European Heritage	47	52	99

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants were randomized to receive matching placebo SC every 4 weeks during the 32-Week treatment period while continuing their HES therapy. The final dose was administered at Week 28 with the completion of study treatment period achieved in the next 4-weekly visit.	
Reporting group title	Mepolizumab 300 mg SC
Reporting group description:	
Participants were randomized to receive 300 mg mepolizumab SC every 4 weeks during the 32-Week treatment period while continuing their HES therapy. The final dose was administered at Week 28 with the completion of study treatment period achieved in the next 4-weekly visit.	

Primary: Percentage of participants who experienced an HES flare or who withdrew from the study during the 32-Week study treatment period

End point title	Percentage of participants who experienced an HES flare or who withdrew from the study during the 32-Week study treatment period
End point description:	
Percentage of participants who experienced >=1 HES flare during the 32-Week treatment period or who withdrew from the study has been presented. A HES flare is defined as a HES related clinical manifestation based on a physician-documented change in clinical signs or symptoms which resulted in need for an increase in the maintenance Oral Corticosteroid (OCS) dose by at least 10 mg per day for 5 days or an increase in or addition of any cytotoxic or immunosuppressive HES therapy. HES flare is also defined as receipt of two or more courses of blinded active OCS during the treatment period. Intent-to-treat (ITT) Population comprises of all randomized participants. This population was based on the treatment to which the participants were randomized. Any participant who received a treatment randomization number were considered to be randomized.	
End point type	Primary
End point timeframe:	
Up to Week 32	

End point values	Placebo	Mepolizumab 300 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[1]	54[2]		
Units: Percentage of participants	56	28		

Notes:

[1] - ITT Population.

[2] - ITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Mepolizumab 300 mg SC
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [3]

Method	Cochran-Mantel-Haenszel

Notes:

[3] - Cochran-Mantel-Haenszel test stratified by Baseline oral corticosteroid (OCS) (0-<=20 mg per day and >20mg perday prednisone or equivalent) and region

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Mepolizumab 300 mg SC
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.003 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.64

Notes:

[4] - Treatment comparison between placebo and mepolizumab 300 mg using odds ratio and 95% confidence interval (CI) has been presented. Odds ratio <1 indicated lower odds of HES flare with Mepolizumab compared with placebo.

[5] - Logistic regression analysis adjusted for Baseline OCS dose and region.

Secondary: Percentage of participants who experienced a HES Flare or who withdrew from the study during Week 20 Through Week 32

End point title	Percentage of participants who experienced a HES Flare or who withdrew from the study during Week 20 Through Week 32

End point description:

HES flare during Week 20 through Week 32 was defined as a HES flare starting or ongoing on or after the date of the Week 20 visit up to and including the date of the Week 32 visit. Percentage of participants who experienced >=1 HES flare during Week 20 through Week 32 or who withdrew from the study has been presented.

End point type	Secondary

End point timeframe:

Week 20 to Week 32

End point values	Placebo	Mepolizumab 300 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[6]	54[7]		
Units: Percentage of participants	35	17		

Notes:

[6] - ITT Population.

[7] - ITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Mepolizumab 300 mg SC
Number of subjects included in analysis	108

Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02 [8]
Method	Cochran-Mantel-Haenszel

Notes:

[8] - Cochran-Mantel-Haenszel test stratified by Baseline OCS (0-<=20 mg per day and >20mg perday prednisone or equivalent) and region.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Mepolizumab 300 mg SC
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.022 [10]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.85

Notes:

[9] - Treatment comparison between placebo and mepolizumab 300 mg using odds ratio and 95% CI has been presented. Odds ratio <1 indicated lower odds of HES flare with Mepolizumab compared with placebo.
[10] - Logistic regression analysis adjusted for Baseline OCS dose and region

Secondary: Time to first HES flare

End point title	Time to first HES flare

End point description:

The time to first HES flare was calculated as (onset date of first HES flare minus date of first dose of study treatment) plus 1. Probability of first flare (by week 4, 8, 12, 16, 20, 24, 28, and 32) and corresponding 95% CI have been presented, calculated using the Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 16, 20, 24, 28 and 32

End point values	Placebo	Mepolizumab 300 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[11]	54[12]		
Units: Probability expressed as percentage				
number (confidence interval 95%)				
Flares by Week 4	7.4 (2.8 to 18.5)	5.6 (1.8 to 16.2)		
Flares by Week 8	14.9 (7.7 to 27.5)	7.4 (2.8 to 18.5)		
Flares by Week 12	26.2 (16.4 to 40.2)	9.3 (4.0 to 20.8)		

Flares by Week 16	33.8 (22.8 to 48.1)	13.0 (6.4 to 25.3)		
Flares by Week 20	41.3 (29.5 to 55.7)	13.0 (6.4 to 25.3)		
Flares by Week 24	48.9 (36.5 to 63.0)	14.8 (7.7 to 27.4)		
Flares by Week 28	50.8 (38.3 to 64.8)	20.5 (11.9 to 34.0)		
Flares by Week 32	52.7 (40.1 to 66.5)	26.3 (16.5 to 40.3)		

Notes:

[11] - ITT Population.

[12] - ITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Mepolizumab 300 mg SC
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.002 [14]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	0.67

Notes:

[13] - Treatment comparison between placebo and mepolizumab 300 mg using hazards ratio and its corresponding 95% CI has been presented. Hazard ratio <1 indicated a lower risk of HES flare with Mepolizumab compared with Placebo.

[14] - Cox proportional hazards regression analysis adjusted for Baseline OCS dose and region.

Secondary: Number of HES flares per participant per year

End point title	Number of HES flares per participant per year

End point description:

The rate of HES flares for each participant was calculated as the number of observed HES flares divided by the time (expressed in years) between randomization and either the week 32 visit date if available, or the study withdrawal date. Negative binomial generalized linear model including Baseline OCS dose, region, treatment and observed time (offset variable). Wilcoxon test stratified by Baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region. Adjusted mean and 95% CI rate/year has been presented.

End point type	Secondary

End point timeframe:

Up to Week 32

End point values	Placebo	Mepolizumab 300 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[15]	54[16]		
Units: Flares per participant per year				
arithmetic mean (confidence interval 95%)	1.46 (1.05 to 2.02)	0.50 (0.30 to 0.84)		

Notes:

[15] - ITT Population.

[16] - ITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Mepolizumab 300 mg SC
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.002 [18]
Method	Wilcoxon Rank Sum Test
Parameter estimate	Rate Ratio
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.63

Notes:

[17] - Treatment comparison between placebo and mepolizumab 300 mg using rate ratio and 95% CI has been presented. Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.
[18] - Wilcoxon test stratified by Baseline OCS (0-<=20 mg/day, >20 mg/day prednisone or equivalent) and region.

Secondary: Number of participants with change from Baseline in fatigue severity based on Brief Fatigue Inventory (BFI) in item 3 (worst level of fatigue during past 24 hours) at Week 32 by category

End point title	Number of participants with change from Baseline in fatigue severity based on Brief Fatigue Inventory (BFI) in item 3 (worst level of fatigue during past 24 hours) at Week 32 by category

End point description:

The change from Baseline in fatigue severity (worst level of fatigue during past 24 hours) at Week 32 was calculated using the mean of the 7 daily assessments of BFI item 3 up to and including the date of the Week 32 visit as the Week 32 assessment, and the mean of the 7 daily assessments of BFI item 3 up to but not including the date of first dose of study treatment as the Baseline assessment. Wilcoxon Rank Sum test stratified by Baseline fatigue severity ("severe" defined as BFI item 3>=7 and "not severe" defined as BFI item 3<7), Baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region. Participants with missing change from Baseline at Week 32 were included in the worst category (>=4 point increase).

End point type	Secondary

End point timeframe:

Baseline (Week 0) and at Week 32

End point values	Placebo	Mepolizumab 300 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54[19]	54[20]		
Units: Participants				
>=4 point increase (>=3.5)	7	5		
3 point increase (>=2.5 to <3.5)	4	0		
2 point increase (>=1.5 to <2.5)	4	5		
1 point increase (>=0.5 to <1.5)	9	6		
No change (>-0.5 to <0.5)	14	9		
1 point reduction (>-1.5 to <=-0.5)	5	11		
2 point reduction (>-2.5 to <=-1.5)	3	7		
3 point reduction (>-3.5 to <=-2.5)	5	2		
>=4 point reduction (<=-3.5)	3	9		

Notes:

[19] - ITT Population.

[20] - ITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Mepolizumab 300 mg SC
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 [21]
Method	Wilcoxon Rank Sum Test

Notes:

[21] - P-value was calculated using Wilcoxon Rank Sum Test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events (non-SAEs) from start of study treatment until 28 days after last dose (Up to 32 weeks) are reported. SAEs were collected from the day of randomization (Week 0) up to end of study (Up to Week 40).

Adverse event reporting additional description:

Non-SAEs and SAEs were collected for Safety Population. The Safety Population comprises of all participants who were randomized and who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Mepolizumab 300 mg SC

Reporting group description:

Participants were randomized to receive 300 mg mepolizumab SC every 4 weeks during the 32-Week treatment period while continuing their HES therapy. The final dose was administered at Week 28 with the completion of study treatment period achieved in the next 4-weekly visit.

Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive matching placebo SC every 4 weeks during the 32-Week treatment period while continuing their HES therapy. The final dose was administered at Week 28 with the completion of study treatment period achieved in the next 4-weekly visit.

Serious adverse events	Mepolizumab 300 mg SC	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 54 (18.52%)	9 / 54 (16.67%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restrictive cardiomyopathy			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-cell lymphoma			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
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			
Respiratory failure			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Hypereosinophilic syndrome			
subjects affected / exposed	1 / 54 (1.85%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 54 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Costochondritis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (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	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tooth infection			
subjects affected / exposed	1 / 54 (1.85%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Mepolizumab 300 mg SC	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 54 (75.93%)	43 / 54 (79.63%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 54 (1.85%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 54 (5.56%)	5 / 54 (9.26%)	
occurrences (all)	3	9	
Pyrexia			
subjects affected / exposed	4 / 54 (7.41%)	2 / 54 (3.70%)	
occurrences (all)	5	2	
Asthenia			
subjects affected / exposed	0 / 54 (0.00%)	5 / 54 (9.26%)	
occurrences (all)	0	6	
Influenza like illness			
subjects affected / exposed	3 / 54 (5.56%)	2 / 54 (3.70%)	
occurrences (all)	3	2	

Injection site reaction			
subjects affected / exposed	3 / 54 (5.56%)	2 / 54 (3.70%)	
occurrences (all)	5	10	
Peripheral swelling			
subjects affected / exposed	1 / 54 (1.85%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Malaise			
subjects affected / exposed	2 / 54 (3.70%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Vaginal haemorrhage			
subjects affected / exposed	2 / 54 (3.70%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 54 (5.56%)	1 / 54 (1.85%)	
occurrences (all)	3	2	
Skin abrasion			
subjects affected / exposed	2 / 54 (3.70%)	0 / 54 (0.00%)	
occurrences (all)	3	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 54 (3.70%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 54 (3.70%)	5 / 54 (9.26%)	
occurrences (all)	2	7	
Dyspnoea			
subjects affected / exposed	3 / 54 (5.56%)	2 / 54 (3.70%)	
occurrences (all)	5	3	
Nasal obstruction			
subjects affected / exposed	3 / 54 (5.56%)	2 / 54 (3.70%)	

occurrences (all)	3	2	
Rhinorrhoea			
subjects affected / exposed	1 / 54 (1.85%)	4 / 54 (7.41%)	
occurrences (all)	1	4	
Cough			
subjects affected / exposed	0 / 54 (0.00%)	4 / 54 (7.41%)	
occurrences (all)	0	4	
Epistaxis			
subjects affected / exposed	1 / 54 (1.85%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Oropharyngeal pain			
subjects affected / exposed	1 / 54 (1.85%)	2 / 54 (3.70%)	
occurrences (all)	2	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 54 (7.41%)	3 / 54 (5.56%)	
occurrences (all)	4	3	
Headache			
subjects affected / exposed	7 / 54 (12.96%)	7 / 54 (12.96%)	
occurrences (all)	11	15	
Hypoaesthesia			
subjects affected / exposed	3 / 54 (5.56%)	1 / 54 (1.85%)	
occurrences (all)	3	1	
Paraesthesia			
subjects affected / exposed	3 / 54 (5.56%)	0 / 54 (0.00%)	
occurrences (all)	3	0	
Presyncope			
subjects affected / exposed	0 / 54 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Somnolence			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	2 / 54 (3.70%)	0 / 54 (0.00%)	
occurrences (all)	2	0	

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 54 (9.26%)	7 / 54 (12.96%)	
occurrences (all)	7	7	
Vomiting			
subjects affected / exposed	3 / 54 (5.56%)	3 / 54 (5.56%)	
occurrences (all)	3	3	
Nausea			
subjects affected / exposed	3 / 54 (5.56%)	2 / 54 (3.70%)	
occurrences (all)	4	3	
Constipation			
subjects affected / exposed	3 / 54 (5.56%)	1 / 54 (1.85%)	
occurrences (all)	6	2	
Abdominal pain			
subjects affected / exposed	1 / 54 (1.85%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Abdominal pain upper			
subjects affected / exposed	1 / 54 (1.85%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Stomatitis			
subjects affected / exposed	2 / 54 (3.70%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Toothache			
subjects affected / exposed	2 / 54 (3.70%)	1 / 54 (1.85%)	
occurrences (all)	3	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	4 / 54 (7.41%)	7 / 54 (12.96%)	
occurrences (all)	4	8	
Urticaria			
subjects affected / exposed	0 / 54 (0.00%)	5 / 54 (9.26%)	
occurrences (all)	0	7	
Alopecia			
subjects affected / exposed	4 / 54 (7.41%)	0 / 54 (0.00%)	

occurrences (all)	4	0	
Rash			
subjects affected / exposed	2 / 54 (3.70%)	2 / 54 (3.70%)	
occurrences (all)	2	2	
Eczema			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Erythema			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Hyperhidrosis			
subjects affected / exposed	2 / 54 (3.70%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 54 (7.41%)	4 / 54 (7.41%)	
occurrences (all)	10	4	
Pain in extremity			
subjects affected / exposed	6 / 54 (11.11%)	2 / 54 (3.70%)	
occurrences (all)	7	2	
Myalgia			
subjects affected / exposed	4 / 54 (7.41%)	3 / 54 (5.56%)	
occurrences (all)	7	3	
Back pain			
subjects affected / exposed	3 / 54 (5.56%)	3 / 54 (5.56%)	
occurrences (all)	4	4	
Musculoskeletal chest pain			
subjects affected / exposed	3 / 54 (5.56%)	0 / 54 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 54 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	

Infections and infestations			
Bronchitis			
subjects affected / exposed	7 / 54 (12.96%)	10 / 54 (18.52%)	
occurrences (all)	7	12	
Nasopharyngitis			
subjects affected / exposed	7 / 54 (12.96%)	7 / 54 (12.96%)	
occurrences (all)	7	9	
Rhinitis			
subjects affected / exposed	5 / 54 (9.26%)	6 / 54 (11.11%)	
occurrences (all)	6	6	
Upper respiratory tract infection			
subjects affected / exposed	8 / 54 (14.81%)	2 / 54 (3.70%)	
occurrences (all)	10	2	
Sinusitis			
subjects affected / exposed	2 / 54 (3.70%)	4 / 54 (7.41%)	
occurrences (all)	2	5	
Urinary tract infection			
subjects affected / exposed	5 / 54 (9.26%)	0 / 54 (0.00%)	
occurrences (all)	6	0	
Influenza			
subjects affected / exposed	3 / 54 (5.56%)	1 / 54 (1.85%)	
occurrences (all)	3	1	
Oral herpes			
subjects affected / exposed	2 / 54 (3.70%)	2 / 54 (3.70%)	
occurrences (all)	3	2	
Cystitis			
subjects affected / exposed	1 / 54 (1.85%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Gastroenteritis			
subjects affected / exposed	1 / 54 (1.85%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Arthritis infective			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	

Gastroenteritis viral			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	3	
Onychomycosis			
subjects affected / exposed	0 / 54 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Respiratory tract infection			
subjects affected / exposed	2 / 54 (3.70%)	0 / 54 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported