Clinical trial results:
A randomised, double-blind, parallel group PhIII study to assess the clinical efficacy and safety of 100 mg SC Mepolizumab as an add on to maintenance treatment in adults with severe bilateral nasal polyps

Summary

EudraCT number	2016-004255-70
Trial protocol	DE GB SE NL
Global end of trial date	11 December 2019

Results information

Result version number	v1 (current)
This version publication date	06 December 2020
First version publication date	06 December 2020

Trial information

Trial identification

Sponsor protocol code	205687

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 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	02 April 2020

Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	11 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of 100 mg mepolizumab compared to placebo

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 May 2017
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	Germany: 71
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Romania: 58
Country: Number of subjects enrolled	Sweden: 26
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	United States: 56
Country: Number of subjects enrolled	Argentina: 55
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	Korea, Republic of: 11
Country: Number of subjects enrolled	Russian Federation: 64
Worldwide total number of subjects	414
EEA total number of subjects	174

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	355
From 65 to 84 years	59

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants (par.) were enrolled across 11 countries (Germany, Netherlands, Romania, Sweden, United Kingdom, United States, Argentina, Australia, Canada, Republic of Korea and Russian Federation).

Pre-assignment

Screening details:

A total of 414 participants were enrolled and randomized in the study, of which only 407 participants received study treatment and were included in the Intent-to-Treat Population (defined as all randomized participants who took at least 1 dose of study treatment). Seven participants did not receive study treatment as they were randomized in error.

Period 1

Period 1 title	Treatment Period (TP) (52 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants were randomized to receive up to 13 subcutaneous (SC) doses of mepolizumab matching placebo every 4 weeks to Week 52 (Wk 52) on top of standard of care (SoC) for nasal polyps (NP) which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received subcutaneous (SC) doses of mepolizumab matching placebo every 4 weeks until 52 Weeks.

Investigational medicinal product name	Mometasone furorate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Mometasone furorate nasal spray as a Standard of care (SoC) for nasal polyps (NP).

Arm title	Mepolizumab 100 mg SC

Arm description:

Participants were randomized to receive up to 13 SC doses of mepolizumab 100 milligrams per milliliter (mg/mL) every 4 weeks to Week 52 on top of SoC for nasal polyps which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.

Arm type	Experimental

Investigational medicinal product name	Mepolizumab 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 100 mg SC doses of Mepolizumab every 4 weeks until 52 Weeks.

Investigational medicinal product name	Mometasone furorate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Mometasone furorate nasal spray as a Standard of care (SoC) for nasal polyps (NP).

Number of subjects in period 1[1]	Placebo	Mepolizumab 100 mg SC
Started	201	206
Completed Investigational Product (IP)	167 [2]	183 [3]
Not Completed IP	34 [4]	23 [5]
Withdrew IP Due to: Adverse Event	4 [6]	4 [7]
Withdrew IP Due to: Lack of Efficacy	11 [8]	5 [9]
Withdrew IP Due to: Protocol Deviation	1 [10]	0 [11]
Withdrew IP Due to: Stopping Criteria	1 [12]	1 [13]
Withdrew IP Due to: Physician Decision	2 [14]	1 [15]
Withdrew IP Due to: Withdrawal by par.	15 [16]	12 [17]
Completed	184	189
Not completed	17	17
Consent withdrawn by subject	16	17
Lost to follow-up	1	-

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 414 participants were enrolled and randomized in the study, of which only 407 participants received study treatment and were included in the Intent-to-Treat Population (defined as all randomized participants who took at least 1 dose of study treatment). Seven participants did not receive study treatment as they were randomized in error.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This number indicates the number of participants with withdrawal from investigational product only.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This number indicates the number of participants with withdrawal from investigational product only.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[12] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[13] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[14] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[15] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[16] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This number indicates the number of participants with withdrawal from investigational product only.
[17] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that

completed, minus those who left.

Justification: This number indicates the number of participants with withdrawal from investigational product only.

Period 2

Period 2 title	No-treatment Follow-up Period (6 months)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants were randomized to receive up to 13 subcutaneous (SC) doses of mepolizumab matching placebo every 4 weeks to Week 52 (Wk 52) on top of standard of care (SoC) for nasal polyps (NP) which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received subcutaneous (SC) doses of mepolizumab matching placebo every 4 weeks until 52 Weeks.

Investigational medicinal product name	Mometasone furorate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Mometasone furorate nasal spray as a Standard of care (SoC) for nasal polyps (NP).

Arm title	Mepolizumab 100 mg SC

Arm description:

Participants were randomized to receive up to 13 SC doses of mepolizumab 100 milligrams per milliliter (mg/mL) every 4 weeks to Week 52 on top of SoC for nasal polyps which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.

Arm type	Experimental
Investigational medicinal product name	Mepolizumab 100 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 100 mg SC doses of Mepolizumab every 4 weeks until 52 Weeks.

Investigational medicinal product name	Mometasone furorate
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Nasal spray
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Mometasone furorate nasal spray as a Standard of care (SoC) for nasal polyps (NP).

Number of subjects in period 2[18]	Placebo	Mepolizumab 100 mg SC
Started	65	69
Completed	65	68
Not completed	0	1
Consent withdrawn by subject	-	1

Notes:

[18] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only 134 participants (65 + 69) continued in No-treatment Follow-up period to check maintenance of response after stopping treatment per protocol.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo

Reporting group description:

Participants were randomized to receive up to 13 subcutaneous (SC) doses of mepolizumab matching placebo every 4 weeks to Week 52 (Wk 52) on top of standard of care (SoC) for nasal polyps (NP) which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.

Reporting group title	Mepolizumab 100 mg SC

Reporting group description:

Participants were randomized to receive up to 13 SC doses of mepolizumab 100 milligrams per milliliter (mg/mL) every 4 weeks to Week 52 on top of SoC for nasal polyps which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.

Reporting group values	Placebo	Mepolizumab 100 mg SC	Total
Number of subjects	201	206	407
Age categorical Units: Subjects			
All participants	201	206	407
Age Continuous Units: Years			
arithmetic mean	48.9	48.6	
standard deviation	± 12.46	± 13.55	-
Sex: Female, Male Units: Participants			
Female	76	67	143
Male	125	139	264
Race/Ethnicity, Customized Units: Subjects			
Asian-Central/South Asian Heritage (H.)	1	2	3
Asian-Japanese H./East Asian H. /SouthEast Asian H.	8	7	15
Black or African American (AA)	4	5	9
White	187	192	379
AA/African H. and American Indian or Alaska Native	1	0	1

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants were randomized to receive up to 13 subcutaneous (SC) doses of mepolizumab matching placebo every 4 weeks to Week 52 (Wk 52) on top of standard of care (SoC) for nasal polyps (NP) which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.	
Reporting group title	Mepolizumab 100 mg SC
Reporting group description:	
Participants were randomized to receive up to 13 SC doses of mepolizumab 100 milligrams per milliliter (mg/mL) every 4 weeks to Week 52 on top of SoC for nasal polyps which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.	
Reporting group title	Placebo
Reporting group description:	
Participants were randomized to receive up to 13 subcutaneous (SC) doses of mepolizumab matching placebo every 4 weeks to Week 52 (Wk 52) on top of standard of care (SoC) for nasal polyps (NP) which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.	
Reporting group title	Mepolizumab 100 mg SC
Reporting group description:	
Participants were randomized to receive up to 13 SC doses of mepolizumab 100 milligrams per milliliter (mg/mL) every 4 weeks to Week 52 on top of SoC for nasal polyps which included daily mometasone furorate nasal spray. By design, some randomized participants were eligible to enter a further 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment.	

Primary: Change from Baseline in total endoscopic nasal polyps score at Week 52

End point title	Change from Baseline in total endoscopic nasal polyps score at Week 52
End point description:	
Independent reviewers, blinded to treatment, reviewed image recordings of nasal endoscopies to determine total endoscopic NP score based on NP size. The right and left nostrils were scored from 0 to 4 (0 = No polyps; 1 = Small polyps in the middle meatus not reaching below the inferior border of the middle concha; 2 = Polyps reaching below the lower border of the middle turbinate; 3 = Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle concha; and 4 = Large polyps causing complete obstruction/congestion of the inferior meatus). The total score is the sum of the right and left nostril scores and ranges from 0 to 8, higher scores indicate greater disease severity. Data up to Week 52, including from participants who remained in the study after early discontinuation from IP, were included in analysis. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value.	
End point type	Primary
End point timeframe:	
Baseline (Day 1) and Week 52	

End point values	Placebo	Mepolizumab 100 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201[1]	206[2]		
Units: Scores on a scale				
median (full range (min-max))	0.0 (-5 to 3)	-1.0 (-6 to 3)		

Notes:

[1] - ITT Population included all randomized participants who took at least 1 dose of study treatment.

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Quantile regression with covariates: treatment,region,Baseline score,Baseline eosinophilcount(BEC). Par. with nasal surgery prior to Wk52/withdrew early with no nasal surgery assigned their worst observed score prior to nasal surgery/study withdrawal

Comparison groups	Placebo v Mepolizumab 100 mg SC
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	Wilcoxon rank-sum test
Parameter estimate	Difference in Medians
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.11
upper limit	-0.34

Notes:

[3] - p-Value was based on Wilcoxon rank-sum test.

Primary: Change from Baseline in nasal obstruction visual analog scale (VAS) score during the 4 weeks prior to Week 52

End point title	Change from Baseline in nasal obstruction visual analog scale (VAS) score during the 4 weeks prior to Week 52

End point description:

Participants rated individual (nasal obstruction, nasal discharge, mucus in the throat, loss of smell, facial pain) and overall symptoms on a visual analog scale (VAS) using an electronic diary (eDiary). Captured scores ranged between 0 (none) and 100 (as bad as you can imagine), final scores derived from the electronically captured scores by dividing by 10. The final nasal obstruction VAS score ranged between 0 and 10, with higher scores indicating greater disease severity. Data up to Week 52, including from participants who remained in the study after early discontinuation from IP, were included in analysis. The average of daily scores in 4-weekly intervals were calculated and data is presented for Weeks 49-52. Baseline was defined as the average score from the 7 days of eDiary data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and Weeks 49 to 52

End point values	Placebo	Mepolizumab 100 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201[4]	206[5]		
Units: Scores on a scale				
median (full range (min-max))	-0.82 (-9.23 to 2.58)	-4.41 (-9.90 to 1.54)		

Notes:

[4] - ITT Population

[5] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Quantile regression with covariates: treatment, region, Baseline score, Baseline BEC. Par. with nasal surgery prior to Wks 49-52/withdrew early with no nasal surgery assigned their worst observed 4-wk mean prior to nasal surgery/study withdrawal.

Comparison groups	Placebo v Mepolizumab 100 mg SC
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [6]
Method	Wilcoxon rank-sum test
Parameter estimate	Difference in Medians
Point estimate	-3.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.09
upper limit	-2.18

Notes:

[6] - p-Value was based on Wilcoxon rank-sum test.

Secondary: Percentage of participants with nasal surgery over time

End point title	Percentage of participants with nasal surgery over time

End point description:

The percentage of participants with nasal surgery over time (by Weeks 8, 16, 24, 32, 40, 48 and 52) was derived from Kaplan-Meier time-to-event analyses for the event ‘first nasal surgery’. Nasal surgery was defined as any procedure involving instruments resulting in incision and removal of tissue (polypectomy) in the nasal cavity. Time to first nasal surgery was defined as (Date of first nasal surgery – Date of first dose of study treatment) + 1. Percentage of participants with nasal surgery over time (by Weeks 8, 16, 24, 32, 40, 48 and 52) and corresponding 95% CI have been presented, calculated using the Kaplan-Meier method. Analysis included surgeries occurring up to Week 52, reported on-treatment and those reported after early discontinuation from IP by participants who remained in the study.

End point type	Secondary

End point timeframe:

Weeks 8, 16, 24, 32, 40, 48 and 52

End point values	Placebo	Mepolizumab 100 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201[7]	206[8]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 8	1.0 (0.3 to 3.9)	0.5 (0.1 to 3.4)		
Week 16	3.5 (1.7 to 7.2)	1.0 (0.2 to 3.8)		
Week 24	9.1 (5.8 to 14.0)	4.0 (2.0 to 7.8)		
Week 32	14.2 (10.0 to 19.9)	6.0 (3.5 to 10.4)		
Week 40	18.9 (14.0 to 25.1)	7.6 (4.6 to 12.3)		
Week 48	22.0 (16.8 to 28.5)	9.2 (5.9 to 14.2)		
Week 52	23.6 (18.3 to 30.3)	9.2 (5.9 to 14.2)		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis using a Cox Proportional Hazards Model with covariates of treatment, geographic region, Baseline total endoscopic score (centrally read), Baseline nasal obstruction VAS, Baseline BEC, number of previous surgeries (1, 2, >2 as ordinal).

Comparison groups	Placebo v Mepolizumab 100 mg SC
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [9]
Method	Cox Proportional Hazards Model
Parameter estimate	Hazard Ratio (Mepolizumab/Placebo)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.76

Notes:

[9] - p-Value was based on Cox Proportional Hazards Model.

Secondary: Change from Baseline in overall VAS score during the 4 weeks prior to Week 52

End point title	Change from Baseline in overall VAS score during the 4 weeks prior to Week 52

End point description:

Participants rated individual (nasal obstruction, nasal discharge, mucus in the throat, loss of smell, facial pain) and overall symptoms on a visual analog scale using an eDiary. Captured scores ranged between 0 (none) and 100 (as bad as you can imagine), final scores derived from the electronically captured scores by dividing by 10. The final overall VAS score ranged between 0 and 10, with higher scores indicating greater disease severity. Data up to Week 52, including from participants who remained in the study after early discontinuation from IP, were included in analysis. The average of daily scores in 4-weekly

intervals were calculated and data is presented for Weeks 49-52. Baseline was defined as the average score from the 7 days of eDiary data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value.

End point type	Secondary

End point timeframe:

Baseline and Weeks 49 to 52

End point values	Placebo	Mepolizumab 100 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201[10]	206[11]		
Units: Scores on a scale				
median (full range (min-max))	-0.90 (-9.11 to 1.19)	-4.48 (-10.00 to 1.62)		

Notes:

[10] - ITT Population

[11] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Quantile regression with covariates: treatment, region, Baseline score, Baseline BEC. Par. with nasal surgery prior to Wks 49-52/withdrew early with no nasal surgery assigned their worst observed 4-wk mean prior to nasal surgery/study withdrawal.

Comparison groups	Placebo v Mepolizumab 100 mg SC
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003 [12]
Method	Wilcoxon rank-sum test
Parameter estimate	Difference in Medians
Point estimate	-3.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	-2.26

Notes:

[12] - p-Value was based on Wilcoxon rank-sum test and is adjusted for multiplicity.

Secondary: Change from Baseline in sino-nasal outcome test (SNOT)-22 total score at Week 52

End point title	Change from Baseline in sino-nasal outcome test (SNOT)-22 total score at Week 52

End point description:

The SNOT-22 is a 22-item self-reported questionnaire developed to measure symptoms and impacts related to chronic rhinosinusitis. The 22 questions are self-completed by participants based on their recall of their symptoms over the previous 2 weeks using a 6-point rating scale (0 = Not present/no problem; 1 = Very mild problem; 2 = Mild or slight problem; 3 = Moderate problem; 4 = Severe problem; 5 = Problem as “bad as it can be”). Scores for each question are summed to derive the total score. The SNOT-22 total score ranges from 0 to 110, with higher scores representing worse quality of life. Data up to Week 52, including from participants who remained in the study after early

discontinuation from IP, were included in analysis. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. Only those participants with data available at the specified data point were analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 52

End point values	Placebo	Mepolizumab 100 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198[13]	205[14]		
Units: Scores on a scale				
median (full range (min-max))	-14.0 (-86 to 38)	-30.0 (-93 to 42)		

Notes:

[13] - ITT Population

[14] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Quantile regression with covariates: treatment, region, Baseline score, Baseline BEC. Par. with nasal surgery prior to Wk 52/withdrew early with no nasal surgery assigned their worst observed score prior to nasal surgery/study withdrawal.

Comparison groups	Placebo v Mepolizumab 100 mg SC
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003 [15]
Method	Wilcoxon rank-sum test
Parameter estimate	Difference in Medians
Point estimate	-16.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.57
upper limit	-9.42

Notes:

[15] - p-Value was based on Wilcoxon rank-sum test and is adjusted for multiplicity.

Secondary: Percentage of participants requiring at least one course of systemic steroids for nasal polyps up to Week 52

End point title	Percentage of participants requiring at least one course of systemic steroids for nasal polyps up to Week 52

End point description:

The number of courses of systemic steroids received by participants were recorded. For the purpose of this study, a course of systemic corticosteroid separated by less than 7 days was considered as a continuation of the same course. Percentage of participants requiring at least one course of systemic steroids for nasal polyps up to Week 52 is presented. Data up to Week 52, including from participants who remained in the study after early discontinuation from IP, were included in analysis.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Mepolizumab 100 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201[16]	206[17]		
Units: Percentage of participants	37	25		

Notes:

[16] - ITT Population

[17] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Covariates: treatment group, geographic region, number of oral corticosteroids courses for NP in last 12 months(0,1,>1 as ordinal), Baseline total endoscopic score(centrally read),Baseline nasal obstruction VAS score,log(e) Baseline eosinophil count.

Comparison groups	Placebo v Mepolizumab 100 mg SC
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.02 [18]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.92

Notes:

[18] - p-Value was based on logistic regression model and is adjusted for multiplicity.

Secondary: Change from Baseline in the composite VAS score (combining VAS scores for nasal obstruction, nasal discharge, mucus in the throat and loss of smell) during the 4 weeks prior to Week 52

End point title	Change from Baseline in the composite VAS score (combining VAS scores for nasal obstruction, nasal discharge, mucus in the throat and loss of smell) during the 4 weeks prior to Week 52

End point description:

Participants rated individual (nasal obstruction, nasal discharge, mucus in the throat, loss of smell, facial pain) and overall symptoms on a visual analog scale using an eDiary. Captured scores ranged between 0 (none) and 100 (as bad as you can imagine), final scores derived from electronically captured scores by dividing by 10. The composite VAS score was calculated as average of individual scores of nasal obstruction, nasal discharge, mucus in the throat and loss of smell and ranged between 0 and 10, with higher scores indicating greater disease severity. Data up to Week 52, including from participants who remained in the study after early discontinuation from IP, were included in analysis. The average of daily scores in 4-weekly intervals were calculated and data is presented for Weeks 49-52. Baseline was defined as the average score from the 7 days of eDiary data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value.

End point type	Secondary

End point timeframe:

Baseline and Weeks 49 to 52

End point values	Placebo	Mepolizumab 100 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201[19]	206[20]		
Units: Scores on a scale				
median (full range (min-max))	-0.89 (-9.29 to 2.90)	-3.96 (-9.93 to 1.37)		

Notes:

[19] - ITT Population

[20] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Quantile regression with covariates: treatment, region, Baseline score, Baseline BEC. Par. with nasal surgery prior to Wks 49-52/withdrew early with no nasal surgery assigned their worst observed 4-wk mean prior to nasal surgery/study withdrawal.

Comparison groups	Placebo v Mepolizumab 100 mg SC
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.02 [21]
Method	Wilcoxon rank-sum test
Parameter estimate	Difference in Medians
Point estimate	-2.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.44
upper limit	-1.91

Notes:

[21] - p-Value was based on Wilcoxon rank-sum test and is adjusted for multiplicity.

Secondary: Change from Baseline in individual VAS symptom score: loss of smell during the 4 weeks prior to Week 52

End point title	Change from Baseline in individual VAS symptom score: loss of smell during the 4 weeks prior to Week 52

End point description:

Participants rated individual (nasal obstruction, nasal discharge, mucus in the throat, loss of smell, facial pain) and overall symptoms on a visual analog scale using an eDiary. Captured scores ranged between 0 (none) and 100 (as bad as you can imagine), final scores derived from the electronically captured scores by dividing by 10. The final loss of smell VAS score ranged between 0 and 10, with higher scores indicating greater disease severity. Data up to Week 52, including from participants who remained in the study after early discontinuation from IP, were included in analysis. The average of daily scores in 4-weekly intervals were calculated and data is presented for Weeks 49-52. Baseline was defined as the average score from the 7 days of eDiary data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value.

End point type	Secondary

End point timeframe:

End point values	Placebo	Mepolizumab 100 mg SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201[22]	206[23]		
Units: Scores on a scale				
median (full range (min-max))	0.00 (-9.97 to 1.94)	-0.53 (-10.00 to 1.27)		

Notes:

[22] - ITT Population

[23] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Quantile regression with covariates: treatment, region, Baseline score, Baseline BEC. Par. with nasal surgery prior to Wks 49-52/withdrew early with no nasal surgery assigned their worst observed 4-wk mean prior to nasal surgery/study withdrawal.

Comparison groups	Placebo v Mepolizumab 100 mg SC
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.02 [24]
Method	Wilcoxon rank-sum test
Parameter estimate	Difference in Medians
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	-0.08

Notes:

[24] - p-Value was based on Wilcoxon rank-sum test and is adjusted for multiplicity.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events (AEs) and serious AEs were collected from start of study treatment (Day 1) up to Week 52 for treatment period and up to 6 months during no-treatment follow-up period after Week 52 visit

Adverse event reporting additional description:

Non-serious AEs and serious AEs were collected for Safety Population which consisted of all randomized participants who took at least one dose of study treatment. Adverse events are presented treatment-wise and period-wise.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Placebo (Treatment period)

Reporting group description:

Participants were randomized to receive up to 13 SC doses of mepolizumab matching placebo every 4 weeks to Week 52 on top of SoC for nasal polyps which included daily mometasone furorate nasal spray.

Reporting group title	Mepolizumab 100 mg SC (Treatment period)

Reporting group description:

Participants were randomized to receive up to 13 SC doses of mepolizumab 100 mg/mL every 4 weeks to Week 52 on top of SoC for nasal polyps which included daily mometasone furorate nasal spray.

Reporting group title	Placebo (Follow-up)

Reporting group description:

Participants entered in a 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment. Participants received mepolizumab matching placebo during treatment period.

Reporting group title	Mepolizumab 100 mg SC (Follow-up)

Reporting group description:

Participants entered in a 6-month no-treatment follow-up period to assess maintenance of response after cessation of treatment. Participants received mepolizumab 100 mg/mL during treatment period.

Serious adverse events	Placebo (Treatment period)	Mepolizumab 100 mg SC (Treatment period)	Placebo (Follow-up)
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 201 (6.97%)	12 / 206 (5.83%)	4 / 65 (6.15%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			

subjects affected / exposed	0 / 201 (0.00%)	0 / 206 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign vulval neoplasm			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenoma			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 201 (0.00%)	2 / 206 (0.97%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural complication			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)

occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocardial ischaemia			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to	0 / 0	0 / 1	0 / 0

treatment / all			
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 201 (0.00%)	2 / 206 (0.97%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 201 (0.00%)	0 / 206 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine with aura			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal polyp			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 201 (0.00%)	0 / 206 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Focal segmental glomerulosclerosis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 201 (0.00%)	0 / 206 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Back pain			
subjects affected / exposed	0 / 201 (0.00%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 201 (0.00%)	2 / 206 (0.97%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 201 (0.50%)	1 / 206 (0.49%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Mepolizumab 100 mg SC (Follow-up)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 69 (2.90%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events			
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign vulval neoplasm			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal adenoma			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine polyp			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural			

complications				
Contusion				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Procedural complication				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mitral valve incompetence				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Myocardial infarction			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial ischaemia			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		

deaths causally related to treatment / all	0 / 0			
Migraine with aura				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Anal polyp				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis erosive				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hiatus hernia				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			

deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Focal segmental glomerulosclerosis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrotic syndrome			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc disorder			

subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Type 2 diabetes mellitus				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	1 / 69 (1.45%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute sinusitis				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 69 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periorbital cellulitis				

subjects affected / exposed	0 / 69 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo (Treatment period)	Mepolizumab 100 mg SC (Treatment period)	Placebo (Follow-up)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	141 / 201 (70.15%)	139 / 206 (67.48%)	13 / 65 (20.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 201 (4.48%)	8 / 206 (3.88%)	0 / 65 (0.00%)
occurrences (all)	11	11	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 201 (0.00%)	0 / 206 (0.00%)	2 / 65 (3.08%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	18 / 201 (8.96%)	17 / 206 (8.25%)	0 / 65 (0.00%)
occurrences (all)	20	24	0
Oropharyngeal pain			
subjects affected / exposed	10 / 201 (4.98%)	16 / 206 (7.77%)	0 / 65 (0.00%)
occurrences (all)	11	19	0
Nasal polyps			
subjects affected / exposed	16 / 201 (7.96%)	8 / 206 (3.88%)	1 / 65 (1.54%)
occurrences (all)	28	11	1
Asthma			
subjects affected / exposed	17 / 201 (8.46%)	4 / 206 (1.94%)	0 / 65 (0.00%)
occurrences (all)	20	31	0
Cough			
subjects affected / exposed	13 / 201 (6.47%)	7 / 206 (3.40%)	2 / 65 (3.08%)
occurrences (all)	15	9	3
Nasal congestion			
subjects affected / exposed	6 / 201 (2.99%)	7 / 206 (3.40%)	0 / 65 (0.00%)

occurrences (all)	9	12	0
Rhinorrhoea			
subjects affected / exposed	0 / 201 (0.00%)	0 / 206 (0.00%)	2 / 65 (3.08%)
occurrences (all)	0	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	44 / 201 (21.89%)	37 / 206 (17.96%)	5 / 65 (7.69%)
occurrences (all)	141	114	14
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	8 / 201 (3.98%)	4 / 206 (1.94%)	2 / 65 (3.08%)
occurrences (all)	14	5	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	5 / 201 (2.49%)	7 / 206 (3.40%)	0 / 65 (0.00%)
occurrences (all)	5	11	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	14 / 201 (6.97%)	15 / 206 (7.28%)	0 / 65 (0.00%)
occurrences (all)	16	24	0
Arthralgia			
subjects affected / exposed	5 / 201 (2.49%)	13 / 206 (6.31%)	0 / 65 (0.00%)
occurrences (all)	6	14	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	46 / 201 (22.89%)	52 / 206 (25.24%)	4 / 65 (6.15%)
occurrences (all)	64	83	6
Sinusitis			
subjects affected / exposed	22 / 201 (10.95%)	10 / 206 (4.85%)	0 / 65 (0.00%)
occurrences (all)	29	12	0
Acute sinusitis			
subjects affected / exposed	13 / 201 (6.47%)	13 / 206 (6.31%)	0 / 65 (0.00%)
occurrences (all)	18	17	0
Upper respiratory tract infection			
subjects affected / exposed	14 / 201 (6.97%)	12 / 206 (5.83%)	0 / 65 (0.00%)
occurrences (all)	18	20	0
Bronchitis			

subjects affected / exposed	13 / 201 (6.47%)	10 / 206 (4.85%)	0 / 65 (0.00%)
occurrences (all)	16	10	0
Influenza			
subjects affected / exposed	8 / 201 (3.98%)	7 / 206 (3.40%)	0 / 65 (0.00%)
occurrences (all)	10	7	0
Otitis media			
subjects affected / exposed	10 / 201 (4.98%)	5 / 206 (2.43%)	0 / 65 (0.00%)
occurrences (all)	12	5	0
Rhinitis			
subjects affected / exposed	8 / 201 (3.98%)	5 / 206 (2.43%)	0 / 65 (0.00%)
occurrences (all)	10	5	0

Non-serious adverse events	Mepolizumab 100 mg SC (Follow-up)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 69 (20.29%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Nasal polyps			
subjects affected / exposed	3 / 69 (4.35%)		
occurrences (all)	3		
Asthma			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		

Cough			
subjects affected / exposed	2 / 69 (2.90%)		
occurrences (all)	2		
Nasal congestion			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	2 / 69 (2.90%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 69 (7.25%)		
occurrences (all)	8		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 69 (8.70%)		
occurrences (all)	8		
Sinusitis			
subjects affected / exposed	3 / 69 (4.35%)		
occurrences (all)	3		
Acute sinusitis			
subjects affected / exposed	0 / 69 (0.00%)		

occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Otitis media			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 69 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2017	Amendment 1: The amendment was made to support country-specific requirements and amendments for South Korea. The changes included the Investigational Product (IP) label, provided additional clarification about the inclusion criteria age as per local regulations and provided details of oral corticosteroids (OCS) supplied for South Korea.
14 July 2017	Amendment 2: The main purpose of this amendment was to reflect comments from investigators to clarify points in the protocol that might be confusing or inconsistent. In addition, it also reflected the removal of computerized tomography (CT) scans and exit interviews as well as simplifying some of the endpoints such as reduction of endoscopic NP endpoints.
20 February 2018	Amendment 3: The purpose of this amendment was to clarify that screen failures could also be re-screened (not just run-in failures) and that the electrocardiogram (ECG) machine did not need to be automated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported